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

THESIS SUBMITTED TO
COCHIN UNIVERSITY OF SCIENCE AND TECHNOLOGY
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FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN CHEMISTRY UNDER THE FACULTY OF SCIENCE

BY

TESMOL G. GEORGE

UNDER THE SUPERVISION OF

Dr. G. VIJAY NAIR

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

MARCH, 2000

DEDICATED

TO

MY PARENTS AND TEACHERS

DECLARATION

I hereby declare that the matter embodied in the thesis entitled "*CARBON-HETEROATOM BOND FORMING REACTIONS MEDIATED BY CERIUM(IV) AMMONIUM NITRATE AND RELATED CHEMISTRY*" is the result of investigations carried out by me at the Organic Chemistry Division of Regional Research Laboratory [CSIR], Trivandrum under the supervision of **Dr. G. Vijay Nair** and the same has not been submitted elsewhere for a degree.

Tesmol

27 March 2000 **Tesmol G. George**

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क्षेत्रीय अनुसंधान प्रयोगशाला, तिरुवनन्तपुरम - 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, F . A . Sc
Director

27 March 2000

CERTIFICATE

This is to certify that the work contained in the thesis entitled "*CARBON-HETEROATOM BOND FORMING REACTIONS MEDIATED BY CERIUM(IV) AMMONIUM NITRATE AND RELATED CHEMISTRY*" has been carried out by **Ms. Tesmol G. George** under my supervision at the Organic Chemistry Division of Regional Research Laboratory [CSIR], Trivandrum and the same has not been submitted elsewhere for any other degree.

G. Vijay Nair

G. Vijay Nair
Thesis Supervisor

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Thiruvananthapuram
March 2000

Tesmol G. George

CONTENTS

PREFACE

Ever since the discovery of radicals by Gomberg in 1900, a large amount of work has been done in this field by a number of eminent scientists. In spite of this, a prevailing erroneous notion that radical reactions lack selectivity and are uncontrollable precluded their serious use in organic synthesis. The situation, however, changed recently and radical methodology is now finding acceptance in organic synthesis. This renewed interest in radical methodology and its use in organic synthesis can be attributed in large measure to the conceptualization and demonstration by Stork that the controlled formation as well as the addition of vinyl radicals to alkenes offers a unique and powerful method for complex carbocyclic constructions. It is worthy of note that radical reactions offer the advantages of high chemoselectivity and regioselectivity over their ionic counterparts. A variety of procedures involving chemical, electrochemical and photochemical methods have been developed for the generation of radicals, and those mediated by transition metal salts have received much attention recently. Among the one-electron oxidants cerium(IV) ammonium nitrate (CAN) is slowly emerging as the reagent of choice due to its stability and solubility in organic solvents. The use of CAN in carbon-carbon bond formation has been studied in detail recently. We have carried out some investigations to explore the synthetic utility of CAN in carbon-heteroatom bond forming reactions and the results are embodied in the thesis entitled **"Carbon-Heteroatom Bond Forming Reactions Mediated by Cerium(IV) Ammonium Nitrate and Related Chemistry"**. The thesis is

divided into four chapters. Relevant references are given at the end of each chapter.

The first chapter contains selective literature coverage of CAN mediated reactions with special emphasis on CAN mediated carbon-heteroatom bond forming reactions. A definition of the research problem is also given in this chapter.

The second chapter deals with the azidation of α,β-unsaturated carbonyl compounds mediated by CAN and the chemical transformations of the azidonitrates obtained.

An experimentally simple, facile and efficient CAN mediated thiocyanation of arenes and dienes is described in chapter 3.

Chapter 4 deals with a one-pot synthesis of iodoazides and iodothiocyanates mediated by CAN.

It may be noted that each chapter of the thesis is presented as a separate unit and therefore figures, schemes and structures are numbered accordingly. All the compounds are named according to IUPAC nomenclature in the experimental section. However, for the sake of convenience, occasionally trivial names are used in the text.

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

ABBREVIATIONS

Ac	: Acetyl
BAIB	: Bis(acetoxy) iodobenzene
brs	: broad singlet
CAN	: Cerium(IV) ammonium nitrate
d	: doublet
dd	: double doublet
DEPT	: Distortionless Enhancement by Polarization Transfer
Et	: Ethyl
GC-MS	: Gas Chromatography-Mass Spectrum
h	: hour(s)
HFP	: 1,1,1,3,3,3-Hexafluoropropanol
HRMS	: High Resolution Mass Spectrum
IR	: Infrared
J	: Coupling constant
m	: multiplet
m	: *meta*
Me	: Methyl
min	: minutes
NMR	: Nuclear magnetic resonance
o	: *ortho*
p	: *para*
PIFA	: Phenyliodine(III) bis(trifluoroacetate)
RT	: Room temperature
s	: singlet
t	: triplet
THF	: Tetrahydrofuran
TLC	: Thin layer chromatography
TMS	: Tetramethylsilane
$TMSN_3$	: Trimethylsilyl azide
TMSNCS	: Trimethylsilyl isothiocyanate

CHAPTER 1

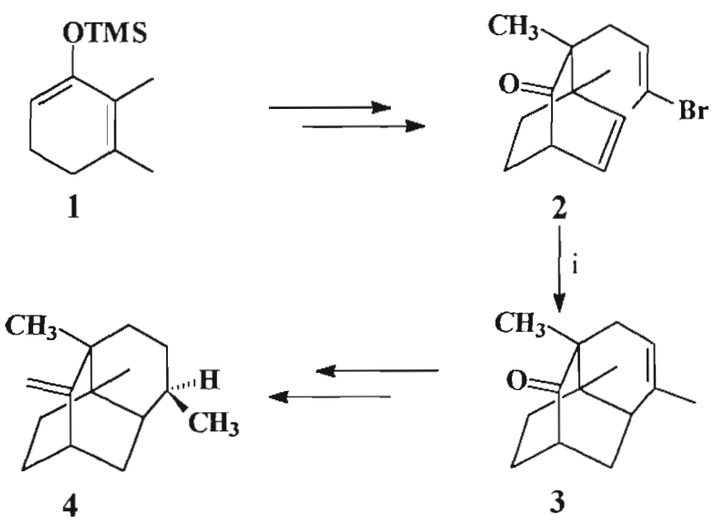
CERIUM(IV) AMMONIUM NITRATE MEDIATED CARBON-HETEROATOM BOND FORMING REACTIONS: AN OVERVIEW

1.1 A General Introduction to Radical Reactions

Radical chemistry dates back to 1900 with the investigations of Gomberg[1] leading to the formation and reactions of triphenyl methyl radical. Organic synthesis with radicals began in 1937 by the work of Hey and Waters,[2] describing the phenylation of aromatic compounds using benzoyl peroxide and Kharasch[3] who recognized that anti-Markovnikov addition of HBr to alkenes is proceeding *via* a radical chain process.

The past two decades have witnessed a dramatic resurgence of interest in the use of radical methodology.[4a-f] Apart from the novel chemistry involved in the radical mediated C-C bond forming reactions, attention may also be drawn to their application in the synthesis of structurally fascinating and biologically important natural products.[4f,5] The renewed interest in radical methodology and its widespread application in organic synthesis can be attributed in large measure to the conceptualization and demonstration by

Stork that the controlled formation as well as the addition of vinyl radicals to alkenes offers a unique and powerful method for complex carbocyclic construction.[5] An illustrative example for the use of vinyl radical cyclization in organic synthesis is described by the synthesis of Saychellene **4** (Scheme 1).[5b]



i. Bu_3SnH, benzene, reflux

Scheme 1

The insightful investigations of Julia,[6] Beckwith[7] and Ingold[8] have contributed to a clear understanding of the structure and reactivity of carbon centered radicals. Today there is widespread appreciation of the potential offered by radical process in organic synthesis.

Radical reactions offer a number of advantages over their ionic counterparts. These include high chemoselectivity[9] and regioselectivity.[7] In particular, cyclic radicals display very high stereoselectivity.[10] Since radical reactions are very fast, side reactions like radical rearrangements, β-elimination and racemization at chiral centers do not pose serious problems. Moreover, most radical reactions are carried out in the absence of strong acids and bases, so that competing ionic reactions such as

racemization does not occur. Also, radical reactions are ideally suited for the construction of quaternary and neopentyl centers. Another advantage of radical reactions over the alternative ionic processes is the avoidance of protecting groups for alcohols, amines and related functional groups.

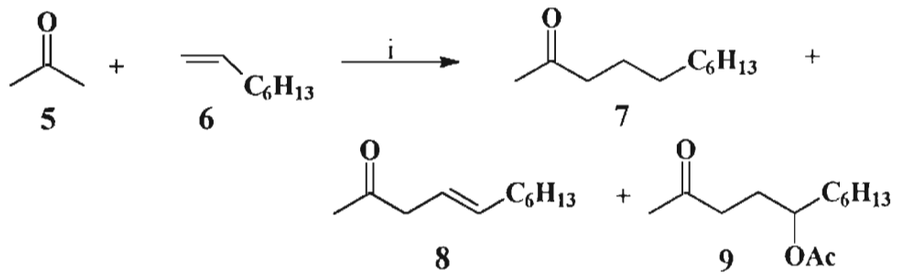
A number of procedures involving chemical,[4] electrochemical[11] and photochemical methods[4d,12] have been developed for the generation of radicals. Principal chemical methods include metal hydride mediated reactions,[4,13] fragmentation reactions[4a,14] and atom transfer reactions.[4,15] Transition metal salts promoted generation of carbon centered radical by an electron transfer process can be achieved efficiently and this process has found numerous applications in the synthesis of a wide variety of organic molecules.[16] Among the various one electron oxidants such as Mn(III), Ce(IV), Cu(II), Ag(I), Co(II), V(V), Fe(III) etc., the first two have received much attention recently. Despite the fact that $Mn(OAc)_3$ occupies a unique position among the one-electron oxidants and has served as a key reagent in the synthesis of a number of important natural products,[17] the procedural problems associated with the use of this reagent often limit its application. On the other hand, Ce(IV) salts do not pose such problems and have been shown to be superior to $Mn(OAc)_3$ in many aspects.[18] Among the Ce(IV) reagents, Cerium(IV) ammonium nitrate (CAN) is the acceptable reagent in terms of its stability and solubility in organic solvents. The experimental simplicity, ease of handling and non-toxicity combined with its solubility in a number of organic solvents like MeOH, CH_3CN and THF make this reagent attractive in organic synthesis.

The literature on CAN mediated reactions is extensive and a comprehensive coverage of this field is unnecessary, as it does not fall within the scope of this thesis. To put the subject matter of the thesis in perspective, a brief introduction to the carbon-carbon bond forming

reactions mediated by CAN followed by a complete review of carbon-heteroatom bond forming reactions is presented here.

1.2 Carbon-Carbon Bond Forming Reactions Mediated by CAN: A Brief Outline

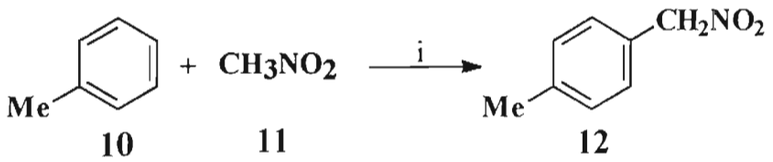
The use of Ce(IV) salts in carbon-carbon bond formation was started by the pioneering work of Heiba and Dessau in 1971.[19] Acetone was shown to react with 1-octene in the presence of cerium(IV) acetate to give saturated ketone **7**, unsaturated ketone **8** and ketoacetate **9** (Scheme 2).



i. $Ce(OAc)_4$, AcOH

Scheme 2

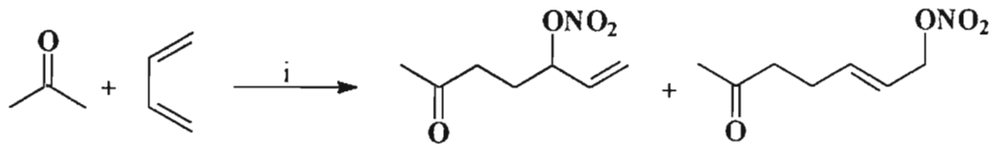
Free radical nitromethylation,[20] acetonylation[21] and malonylation[22] of arenes using CAN are known in the literature. Illustrative example for nitromethylation of arene is given in Scheme 3.



i. CAN, AcOH, reflux, 24 h, 100%

Scheme 3

Baciocchi and Ruzziconi have carried out CAN mediated 1,2- and 1,4- additions of carbonyl compounds such as acetone, ethyl acetoacetate etc. to 1,3-butadiene (Scheme 4).[23]

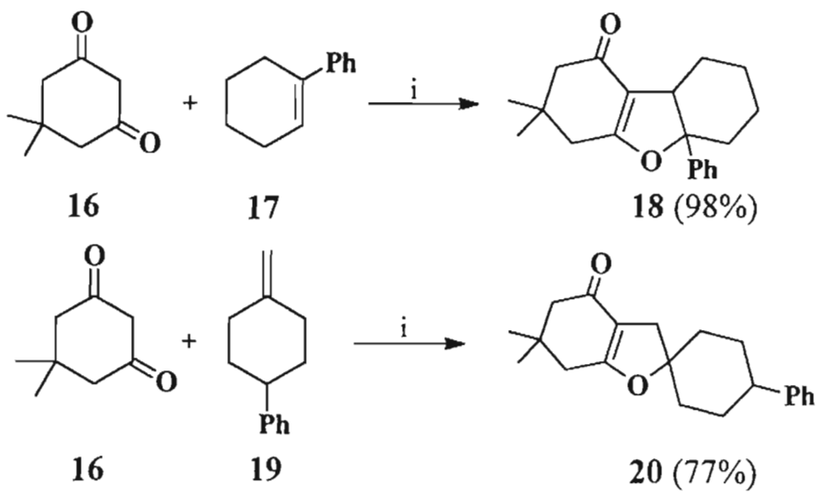


5 **13** **14** **15**

i. CAN, CH_3CN

Scheme 4

Studies in our laboratory have shown that CAN mediated oxidative addition of 1,3-dicarbonyl compounds to alkenes and dienes afforded dihydrofuran derivatives, whereas exocyclic alkenes yielded spirodihydrofurans.[24] Illustrative examples are given in Scheme 5.



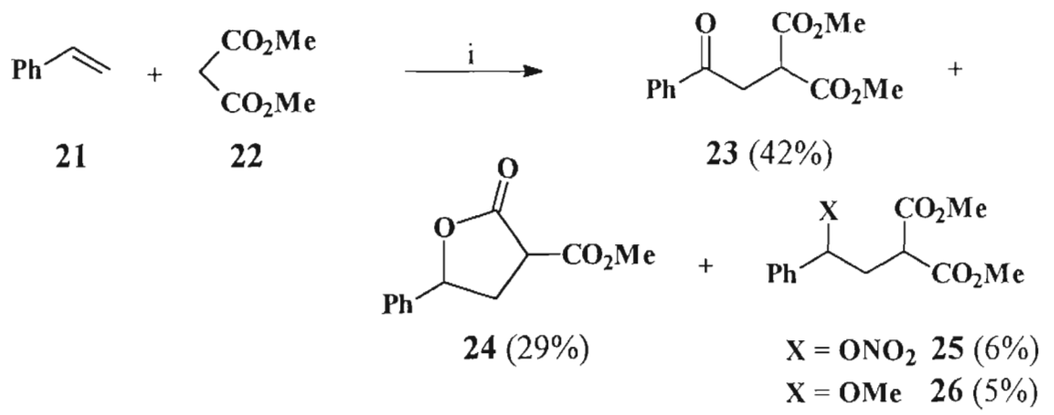
16 **17** **18** (98%)

16 **19** **20** (77%)

i. CAN, MeOH, 5 °C, 15 min

Scheme 5

An interesting and mechanistically fascinating reaction was observed in the CAN mediated oxidative addition of dimethyl malonate to styrenes (Scheme 6).[25]



21 **22** **23** (42%)

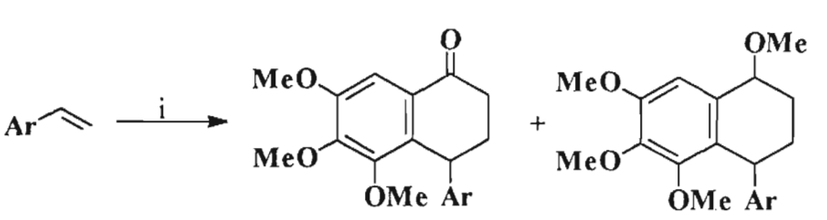
24 (29%)

X = ONO$_2$ **25** (6%)
X = OMe **26** (5%)

i. CAN, MeOH, 20 °C

Scheme 6

CAN mediated single electron transfer reactions of methoxy styrenes afforded dimerization products *via* a cation radical mechanism (Scheme 7).[26]



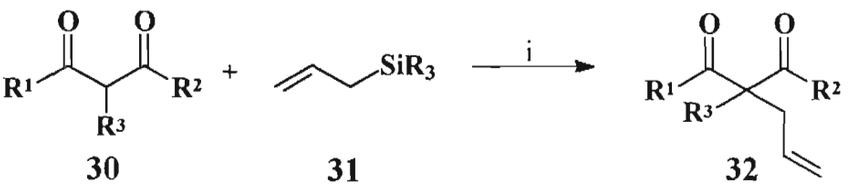
Ar = 3,4,5-trimethoxyphenyl

27 **28** (60%) **29** (12%)

i. CAN, MeOH, 0 °C, 30 min, O_2

Scheme 7

Monoallylation of 1,3-dicarbonyl compounds mediated by CAN has been reported by Hwu *et al.* (Scheme 8).[27]

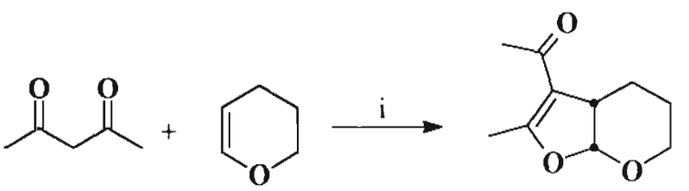


30 **31** **32**

i. CAN, MeOH, 25 °C

Scheme 8

CAN mediated oxidative addition of 1,3-dicarbonyl compounds to enol ethers afforded fused acetals in good yields (Scheme 9).[28]

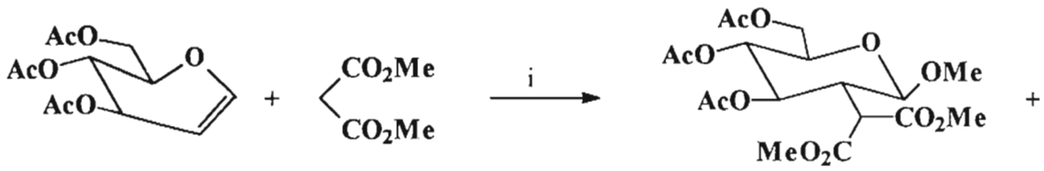


33 **34** **35**

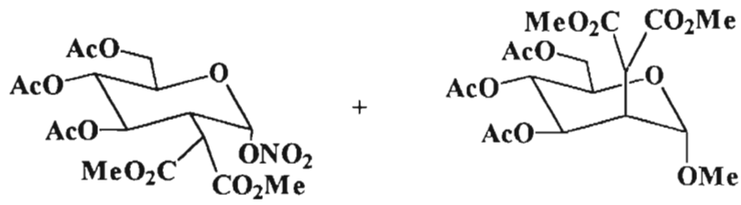
i. CAN, $NaHCO_3$, CH_3CN, 0 °C, 68%

Scheme 9

The CAN mediated addition of malonate to glycals has been developed by Linker as an easy route to C-2 branched sugars (Scheme 10).[18b,29]



36 **22** **37** (62%)

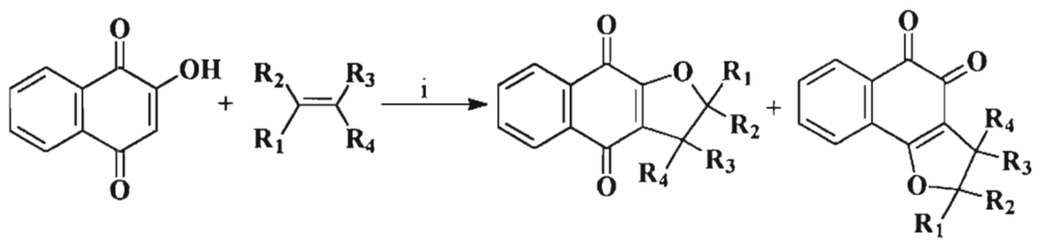


38 (16%) **39** (14%)

i. CAN, MeOH, 0 °C

Scheme 10

[3+2] Cycloaddition of 2-hydroxy-1,4-naphthoquinones and 2-hydroxy-1,4-benzoquinones with alkenes resulted in the formation of furo-*p*-quinones along with the corresponding *o*-quinone derivatives (Scheme 11).[30]



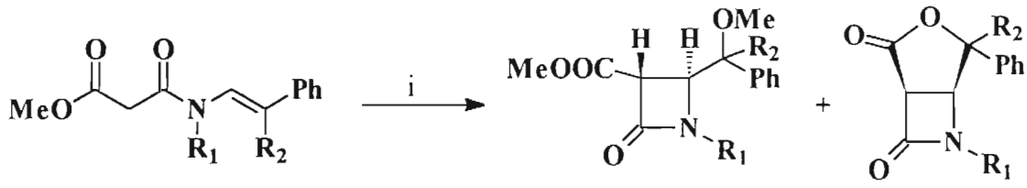
40 **41** **42** **43**

i. CAN, CH_3CN, 0 °C

Scheme 11

There are only a few reports available on the intramolecular cyclization mediated by CAN. CAN mediated Pictet-Spengler cyclization[31] and cyclization of enamides leading to variously functionalized β-lactams

have been reported recently.[32] An illustrative example for the latter is given in Scheme 12.



44 **45** **46**

i. CAN, MeOH, RT, 30 min

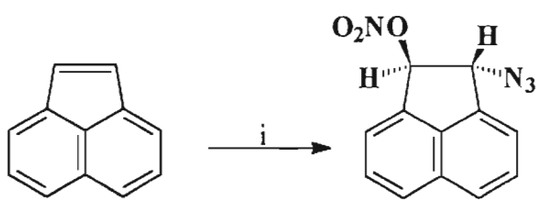
Scheme 12

1.3 Carbon-Heteroatom Bond Forming Reactions Mediated by CAN

Although to a lesser extent, the use of CAN in carbon-heteroatom bond formation has also received attention. A complete overview of CAN mediated carbon-nitrogen, carbon-oxygen, carbon-sulfur, carbon-selenium and carbon-halogen bond formation is presented here.

1.3.1 Carbon-nitrogen bond formation

CAN mediated addition of azide to alkenes resulting in 1-azido-2-nitrates by Trahanovsky in 1971 is the first report in this area (Scheme 13).[33]

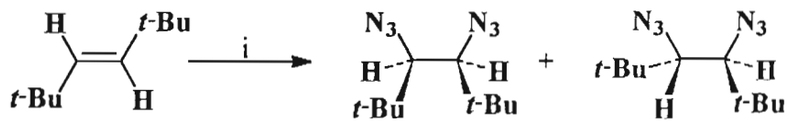


47 **48**

i. NaN_3, CAN, CH_3CN, RT

Scheme 13

However sterically hindered alkenes afforded 1,2-diazides as the only isolable products (Scheme 14).[34]

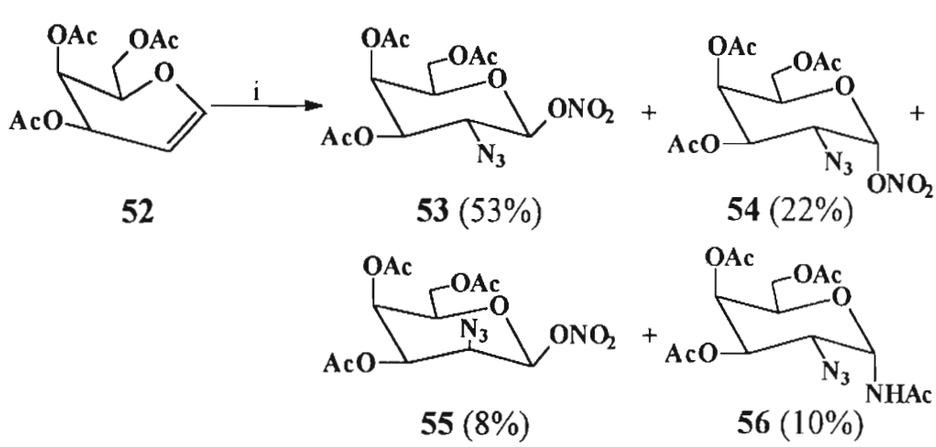


49 **50** **51**

i. NaN_3, CAN, CH_3CN: H_2O (9:1), 0 °C

Scheme 14

Subsequently, Lemieux has applied this reaction to glycals. Reaction of 3,4,6-tri-O-acetyl-D-galactal with excess of CAN and NaN_3 afforded 2-azido-1-nitrato addition products and N-acetyl-3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-galactopyranosylamine (Scheme 15).[35] The azidonitrates thus obtained have found application in the synthesis of aminosugars.



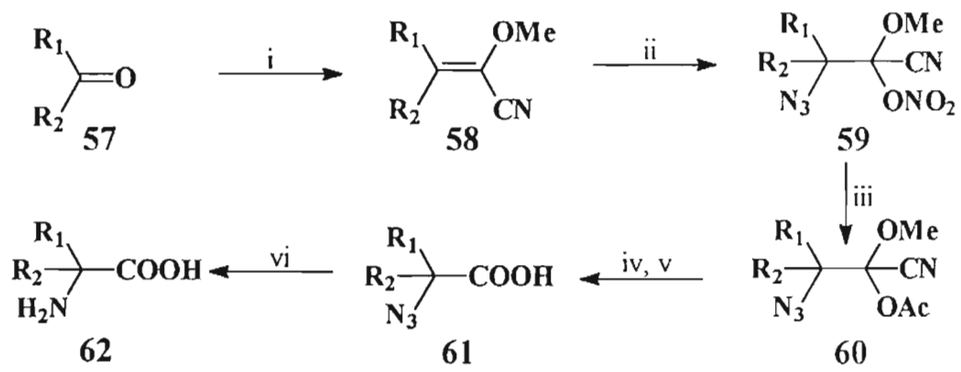
52 **53** (53%) **54** (22%)

55 (8%) **56** (10%)

i. NaN_3, CAN, CH_3CN, -15 °C

Scheme 15

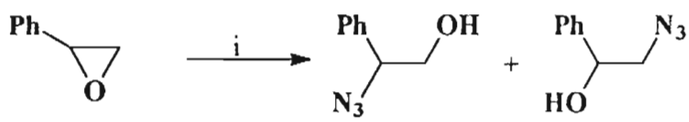
Azidonitrates obtained by the reaction of acrylonitriles with NaN_3 in presence of CAN followed by other transformations afforded α-aminoacids (Scheme 16).[36]



i. PPh_3=C(OMe)CN; ii. NaN_3, CAN; iii. AcOH, AcONa;
iv. K_2CO_3, MeOH, H_2O; v. HCl; vi. H_2, Pd-C

Scheme 16

Regioselective conversion of epoxides to 1,2-azidoalcohols was achieved by using NaN_3 in *t*-butanol in the presence of catalytic amounts of CAN (Scheme 17).[37]

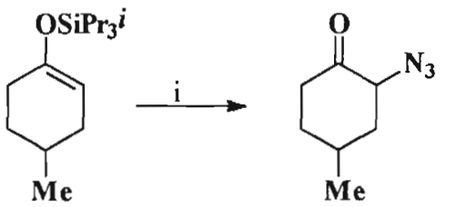


63 **64** **65**

i. CAN (0.2 M), NaN_3, *t*-butanol, RT, 8 h, 96% (95:5)

Scheme 17

Oxidative addition of azide to triisopropylsilyl enol ethers with CAN in acetonitrile afforded α-azidoketones in average to good yields (Scheme 18).[38]

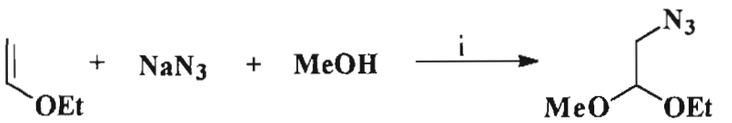


66 **67**

i. NaN_3, CAN, CH_3CN, argon, -20 °C, 30 min, 81%

Scheme 18

CAN mediated azidoalkoxylation of alkenes has been reported very recently.[39] This constitutes a practical route for the synthesis of aminoacetals. An illustrative example is given in Scheme 19.



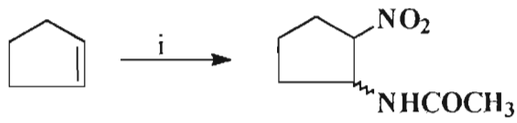
68 **69**

i. CAN, CH_3CN, argon, 0 °C-RT, overnight, 60%

Scheme 19

Recent work in our own laboratory has shown that CAN mediates a direct synthesis of phenacyl azide by the reaction of styrene with NaN_3 in methanol under oxygen atmosphere.[40] Details of this work will be given in chapter 2.

Nitroacetamidation of olefins using CAN/$NaNO_2$ reagent combination in acetonitrile has been reported (Scheme 20).[41]

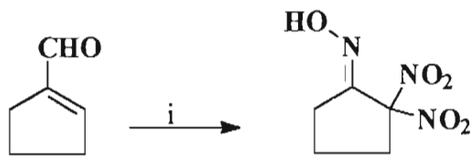


70 **71**

i. $NaNO_2$, CAN, CH_3CN, 64%

Scheme 20

The conversion of cyclopentene carboxaldehyde to dinitrooxime on reaction with $NaNO_2$ and CAN in acetonitrile was reported recently (Scheme 21).[42]

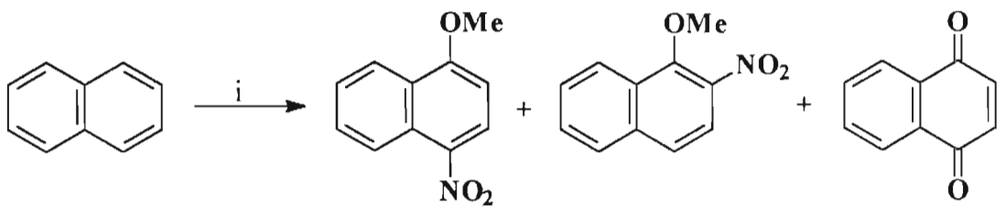


72 **73**

i. $NaNO_2$, CAN, CH_3CN, H_2O, 24 h, 21%

Scheme 21

Nitration of naphthalene using CAN (suspended on silica gel or in homogeneous solution in alcohol), tetrabutylammoniumnitrite and acid affording alkoxy nitronaphthalene has been reported (Scheme 22).[43]



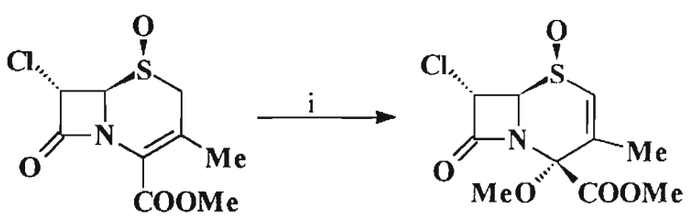
74 **75** (70%) **76** (15%) 77 (10%)

i. Bu_4NNO_2, CAN, H_2SO_4, MeOH

Scheme 22

1.3.2 Carbon-oxygen bond formation

CAN mediated methoxylation of cephem sulfoxides has been reported by Alpegiani *et al.* (Scheme 23).[44]

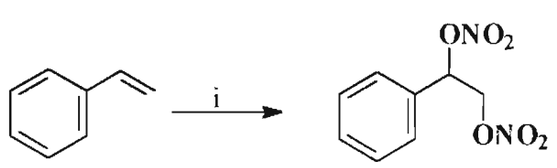


78 **79**

i. CAN, MeOH, RT, 5 h

Scheme 23

Baciocchi has reported the formation of dinitrato compound by the reaction of styrene with CAN in acetonitrile (Scheme 24).[45]

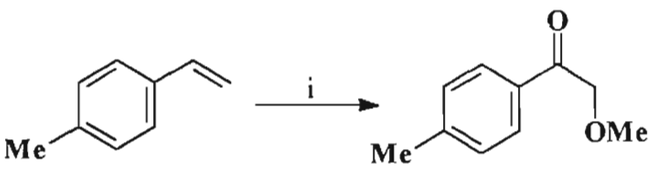


21 **80**

i. CAN, CH_3CN, RT

Scheme 24

When this reaction was carried out in methanol, α-methoxyacetophenone was obtained as the sole product (Scheme 25).[46]

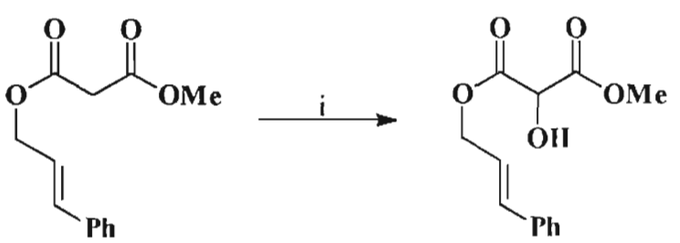


81 **82**

i. CAN, MeOH, RT, 2 h, 50%

Scheme 25

Recently, a facile synthesis of tartronic acid derivatives by CAN mediated oxygenation of alkyl malonates has been reported from our group (Scheme 26).[47]



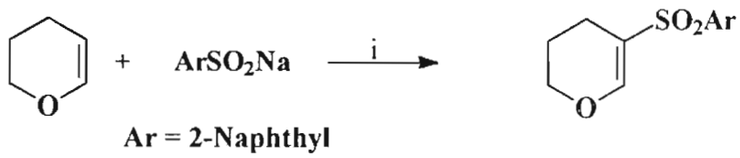
83 **84**

i. CAN, MeOH, 0 °C-RT, O_2, 6 h, 62%

Scheme 26

1.3.3 Carbon-sulfur bond formation

In comparison to the carbon-nitrogen bond forming reactions mediated by CAN, there are only a few reports available on carbon-sulfur bond forming reactions. Narasaka *et al.* have reported sulfonylation of electron rich olefins with cerium(IV) tetrabutyl ammonium nitrate (TBACN) in presence of K_2CO_3 (Scheme 27).[48]

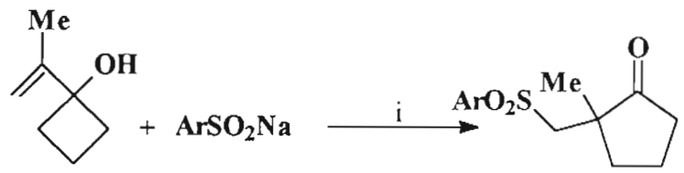


34 **85** **86**

i. TBACN, K_2CO_3, CH_2Cl_2, 0 °C, overnight, 86%

Scheme 27

The same authors have also reported sulfonylation of 1-vinyl cyclic alcohols using CAN, which proceeded with ring enlargement (Scheme 28).[49]



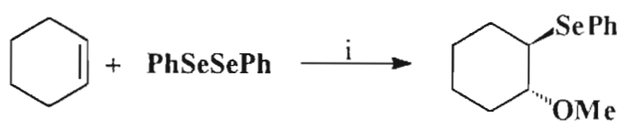
87 **85** **88**

i. CAN, CH_3CN, 0 °C, 2 h, 72%

Scheme 28

1.3.4 Carbon-selenium bond formation

There is only one report on carbon-selenium bond formation using CAN. This involves the selenomethoxylation of alkenes using CAN in methanol reported by Bosman *et al.* (Scheme 29).[50]



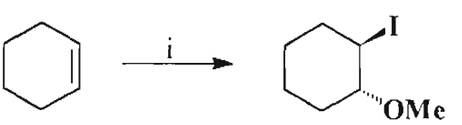
89 **90** **91**

i. CAN, MeOH, RT, argon, 30 min, 93%

Scheme 29

1.3.5 Carbon-halogen bond formation

Cycloalkenes on reaction with I_2-CAN reagent combination in alcohol furnished the corresponding vicinal alkoxyiodocycloalkanes in good yields (Scheme 30).[51]



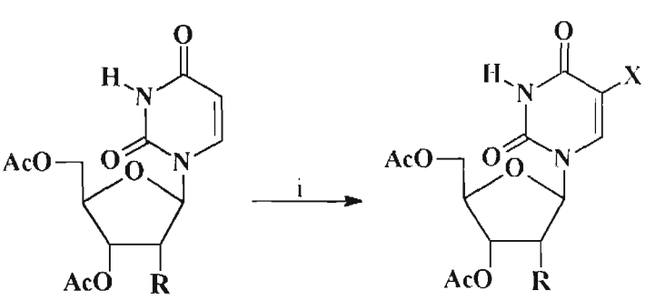
89 **92**

i. I_2-CAN, MeOH, 50 °C, 6 h, 92%

Scheme 30

The same group has also reported the alkoxyiodination of dienes[52] and nitroiodination of α,β-unsaturated ketones and esters.[53]

CAN mediated halogenation at C-5 of uracil derivatives has also been reported (Scheme 31).[54]



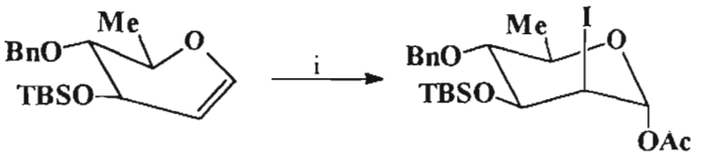
R = H, OAc; X = I, Br, Cl

93 **94**

i. LiX, CAN, CH_3CN, 80 °C

Scheme 31

Very recently, Roush has reported a highly stereoselective synthesis of 2-deoxy-2-iodo-α-mannopyranosyl acetate **96** by CAN mediated reaction of glycal with NaI and acetic acid (Scheme 32).[55]



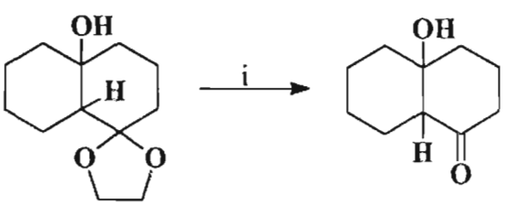
95 **96**

i. NaI, CAN, AcOH, CH_3CN, -25 °C to -5 °C, 76%

Scheme 32

1.4 Miscellaneous reactions mediated by CAN

In addition to the reactions described above, CAN has also been used effectively in a large number of other oxidative transformations. CAN mediated deprotection of TBDMS and THP ethers,[56] *t*-butoxycarbonyl group[57] and acetals[58,59] have been reported. Representative example of the deprotection of acetals is given in Scheme 33.

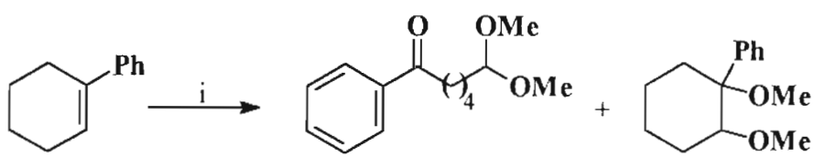


97 **98**

i. CAN, CH_3CN, H_2O, 70 °C, 80%

Scheme 33

A very interesting CAN mediated oxidative fragmentation of phenylcycloalkenes leading to the monoacetal of 1,n-dicarbonyl compounds, along with the dimethoxy compound was observed in our laboratory (Scheme 34).[60]

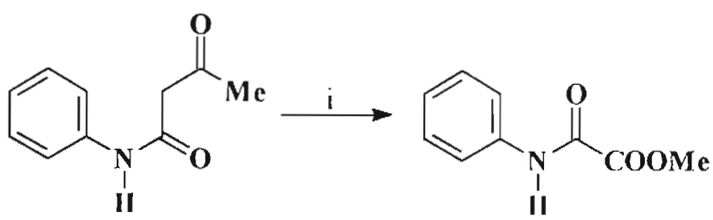


17 **99** (68%) **100** (18%)

i. CAN, MeOH, 0 °C-RT, 30 min

Scheme 34

Recently, a facile CAN mediated transformation of acetoacetamides to oxamates was also observed (Scheme 35).[61]



101 **102**

i. CAN, MeOH, O_2, RT, 15 min, 70%

Scheme 35

Further investigations of the above reactions (Scheme 34 and 35) are in progress in our laboratory.

1.5 Definition of the Problem

It is clear from the above discussion that CAN is a powerful one-electron oxidant and can be used for various synthetic transformations. Even though CAN mediated addition of azide to alkenes, enol ethers etc. has been reported, its reactions with electron deficient alkenes like α,β-unsaturated carbonyl compounds are hither to unknown. Moreover, the earlier attempts at such reactions have failed.[33,39] Against this background, it was decided to study the CAN mediated addition of azide to α,β-unsaturated carbonyl compounds like cinnamic esters and acids with the assumption that these would lead to precursors of biologically important α-amino-β-hydroxy acids.

Organic thiocyanates are valuable precursors of sulfur containing heterocycles and other sulfur functional groups. A complete study of the literature has shown that there has been no report on the thiocyanation reaction using CAN, except the thiocyanation of aryl alkenes reported from our own group. As a logical extension of this work, it was decided to study the thiocyanation of arenes and dienes using NH_4SCN-CAN reagent combination.

In the final phase of the present work, it was decided to explore the azidoiodination and iodothiocyanation of alkenes.

The above investigations have yielded much fascinating results and the details are presented in the subsequent chapters of this thesis.

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CHAPTER 2

CERIUM(IV) AMMONIUM NITRATE MEDIATED ADDITION OF AZIDE TO α,β-UNSATURATED CARBONYL COMPOUNDS AND RELATED CHEMISTRY

2.1 Introduction

The chemistry of azides and nitrenes has attracted the attention of organic chemists since the discovery of phenyl azide by Griess over 100 years ago.[1] Of topical interest, azido nucleosides such as AZT (3'-azido-3'-deoxythymidine) have received international attention for their therapeutic use against AIDS and ARC (AIDS-related complex).[2] α-Azido acids are precursors of α-amino acids,[3] which play a central role in chemistry and biology, for example as enzyme inhibitors, antibacterial agents, neuroactive compounds, pharmaceutical starting materials, herbicides and fungicides. β-Hydroxylated α-amino acids are of considerable biological importance. They are components of various peptides possessing a wide range of biological activities such as antibiotic and immunosuppressive properties. Marine alkaloids like Isonaamine A **1**, Dorimidazole A **2** and Preclathridine A **3** (Figure 1) are synthesized from α-azido esters *via* an iminophosphorane mediated preparation of 2-amino-1,4 -disubstituted imidazoles.[4]

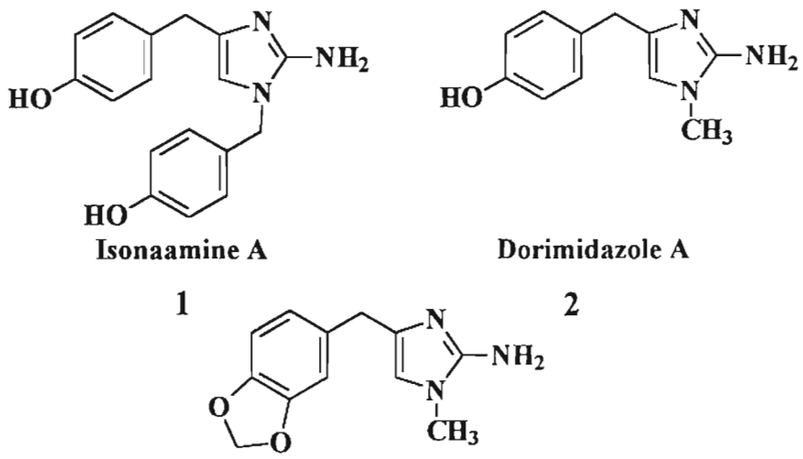
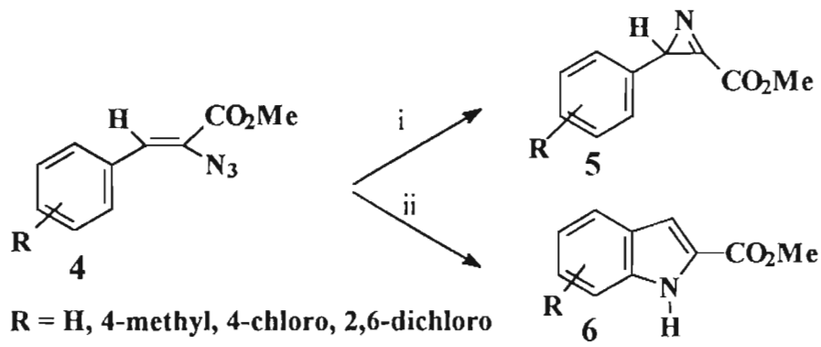


Figure 1

An important method for the construction of five, six and seven membered fused nitrogen heterocycles based on the cyclization of azido acrylate has been developed into a powerful synthetic method by Moody and Rees.[5] Hemetsberger and co-workers[6] found that azidocinnamates undergo ring closure to indoles. Knittel[7] obtained indoles in virtually quantitative yields at 140 °C and azirines at 80 °C starting from azidocinnamates (Scheme 1).

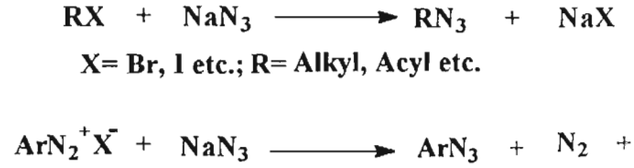


i. 80 °C, C_6H_{12}; ii. 140 °C, *p*-xylene

Scheme 1

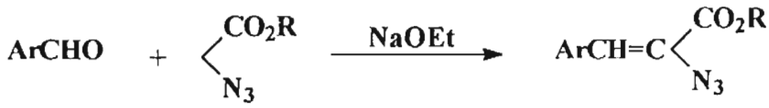
2.1.1 General methods for the preparation of azides

The general methods for the preparation of azides and their use in organic synthesis have been reviewed by Scriven and Turnbull.[8a] The most common method for preparing alkyl and acyl azides consists of the displacement of other functional groups by azide ion.[8b] Another procedure for the preparation of azides involves the reaction of diazonium salt with sodium azide (Scheme 2).[8b]



Scheme 2

Azido carboxylates undergo base induced condensation with aryl or heteroaryl aldehydes to form vinyl azides (Scheme 3).[5,9,10]



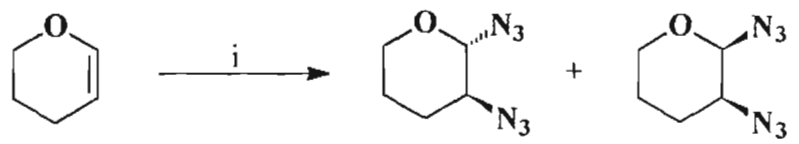
7

Scheme 3

2.1.2 Azidation by one-electron oxidants

Other than ionic reactions, there are a few reports of azidation reactions mediated by different one-electron oxidants. A one step conversion of alkenes into α-azidoketones using trimethylsilyl azide ($TMSN_3$)-chromium trioxide reagent combination in dichloromethane has been reported.[11]

Snider *et al.* have reported that alkenes and glycals react with $Mn(OAc)_3.2H_2O$ and NaN_3 in 9:1 acetonitrile-trifluoroacetic acid to give 1,2-diazides in good yields.[12] An illustrative example is given in Scheme 4.

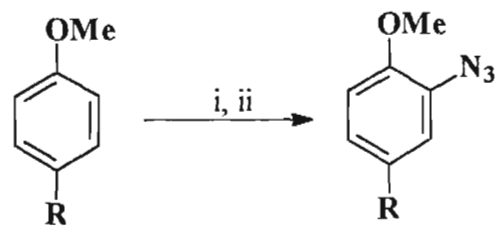


8 **9** (81%) **10** (16%)

i. $Mn(OAc)_3.2H_2O$, NaN_3, CH_3CN /TFA (9:1), -20 °C

Scheme 4

Combination of hypervalent iodine reagent and $TMSN_3$ has been known to generate azidoiodine(III) species and the latter has found use in the transformation of alkenes to α-azidoketones[13] and vicinal diazides,[14,15] β-dicarbonyl compounds into α-azido-β-dicarbonyl compounds,[16] and 2-trimethylsilyloxyfuran into 5-azido-2(5H)-furanone.[17] Kita and co-workers have developed a facile method for the azidation of aromatic compounds, which involves the sequential reaction of hypervalent iodine reagent, phenyl iodine(III) bis(trifluoroacetate) (PIFA) in 1,1,1,3,3,3-hexafluoro-2-propanol and trimethylsilyl azide (Scheme 5). [18,19]



R = OMe, Me, $CH(CH_3)_2$, Br, Cl

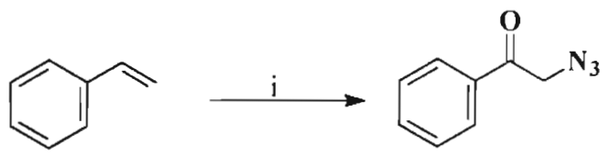
11 **12**

i. PIFA, $(CF_3)_2CHOH$; ii. $TMSN_3$

Scheme 5

As early as 1971 Trahanovsky has reported the CAN mediated addition of azide to styrenes.[20] Subsequent reports have involved the addition of azido radical to glycals[21] and other enol ethers.[22] Details of these reactions are discussed in chapter 1.

Recent work in our own laboratory has shown that CAN mediated addition of azide to styrenes in presence of oxygen leads to a novel and facile synthesis of phenacyl azide.[23] A representative example is given in Scheme 6.



13 **14**

i. NaN_3, CAN, CH_3CN, 0 °C, O_2, 30 min, 74%

Scheme 6

A complete survey of the literature revealed that the CAN mediated oxidative addition of azide to α,β-unsaturated carbonyl compounds like cinnamic esters and acids is hitherto unknown; inexplicably attempts at such reactions have failed.[20,22] With the premise that the reaction can give rise to α-azido-β-nitrato compounds that can serve as precursors to biologically important α-amino-β-hydroxy acids, it was considered worthwhile to undertake a detailed investigation in this area. Therefore a systematic study involving cinnamic acids, cinnamic esters, chalcones and cinnamamide was carried out to assess the synthetic potential of the reaction.

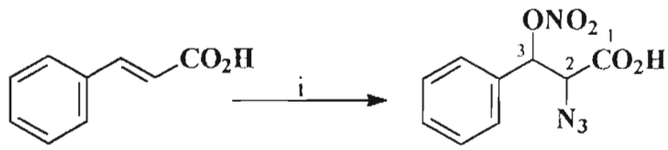
2.2 Results and Discussion

This section is divided into two parts. The first part deals with the CAN mediated oxidative addition of azide to α,β-unsaturated carbonyl compounds. In the second part, the chemical transformations of azidonitrates are described.

2.2.1 CAN mediated addition of azide to α,β-unsaturated carbonyl compounds

2.2.1.1 CAN mediated oxidative addition of azide to cinnamic acids

Our initial work involved the reaction of cinnamic acid with sodium azide. A deoxygenated solution of cinnamic acid and sodium azide in dry acetonitrile, on treatment with a deoxygenated solution of CAN in the same solvent, afforded the product **16** in 70% yield as a 1:1 mixture of *syn* and *anti* isomers (Scheme 7). The ratio was determined from the ^{1}H NMR spectrum of the crude product.



15 **16**

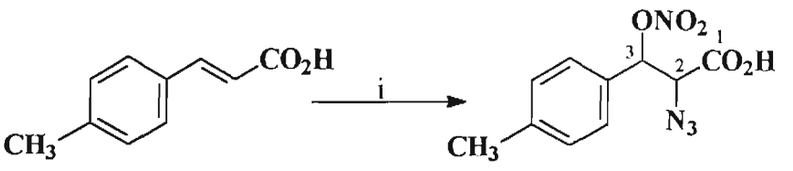
i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, overnight, 70%

Scheme 7

The product **16** was purified by silica gel column chromatography and characterized by the usual spectroscopic methods. The IR spectrum of the

isomeric mixture showed the characteristic absorption of azide at 2119 cm^{-1}. The -OH presented a broad band in the region 3300-2500 cm^{-1}. The absorption due to $-ONO_2$ was visible at 1647 cm^{-1}. The carbonyl absorption was observed at 1735 cm^{-1}. In the ^1H NMR spectrum, the C-3 protons of the isomers were visible as doublets at δ 6.26 (J = 5.1 Hz) and 6.16 (J = 6.6 Hz). The C-2 protons also appeared as doublets at δ 4.45 (J = 6.6 Hz) and 4.28 (J = 5.1 Hz) for the two isomers. The $-CO_2\underline{H}$ proton resonated as a broad singlet at δ 7.15 (exchangeable with D_2O). In the ^{13}C NMR spectrum, the carbonyl carbons were discernible at δ 170.75 and 170.46. The C-3 carbons of the isomers resonated at δ 82.55 and 82.02 and the C-2 carbons were visible at δ 64.77 and 63.70. All other signals were in agreement with the assigned structure.

4-Methylcinnamic acid also gave the α-azido-β-nitrato acid **18** as a 1:1 mixture of isomers, under similar reaction conditions (Scheme 8). The structure of the product **18** was established on the basis of spectral data.

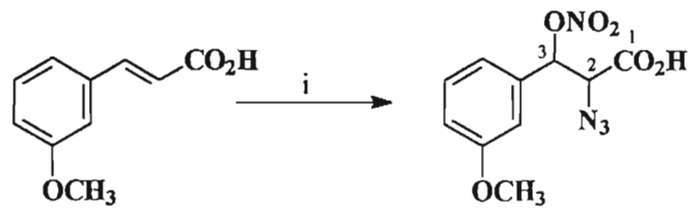


17 **18**

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, overnight, 64%

Scheme 8

A similar reaction occurred with 3-methoxycinnamic acid (Scheme 9).



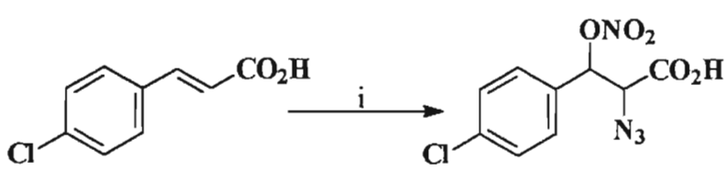
19 **20**

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, overnight, 70% (*syn:anti* = 1:1)

Scheme 9

The product **20** was characterized by the usual spectroscopic methods. The IR spectrum showed the absorption due to $-N_3$ and $-ONO_2$ groups at 2119 and 1651 cm^{-1} respectively. In the ^1H NMR spectrum, C-3 protons of the two isomers were discernible as doublets at δ 6.24 (J = 4.9 Hz) and 6.13 (J = 6.5 Hz). The C-2 protons of the isomers appeared as doublets at δ 4.44 (J = 6.5 Hz) and 4.29 (J = 4.9 Hz). The -OMe protons resonated as a singlet at δ 3.81. In the ^{13}C NMR spectrum, carbonyl peaks were observed at δ 170.93 and 170.89. All other NMR signals were in agreement with the assigned structure.

Similar reactivity was displayed by 4-chlorocinnamic acid also (Scheme 10). The spectral data of **22** were found to be in agreement with the proposed structure.

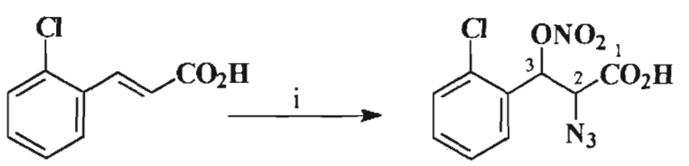


21 **22**

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, overnight, 56% (*syn:anti* = 1:1)

Scheme 10

In the case of 2-chlorocinnamic acid, the resulting α-azido-β-nitrato acid **24** was isolated as a 2:1 mixture of *syn* and *anti* isomers (Scheme 11).



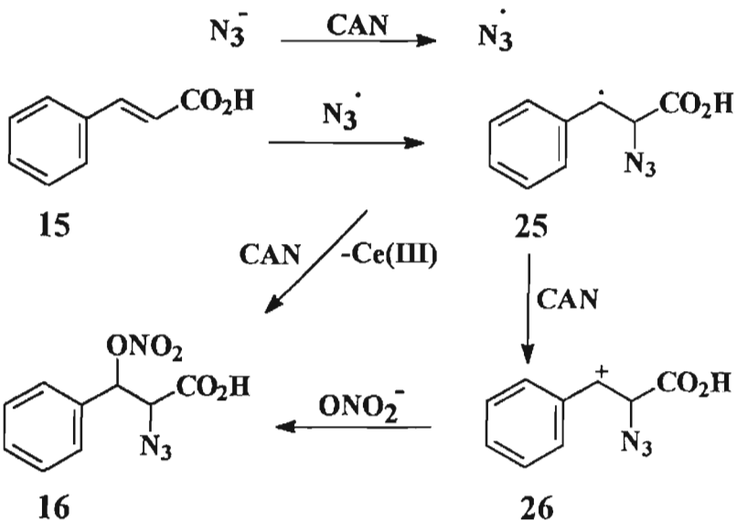
23 **24**

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, overnight, 54%

Scheme 11

The IR spectrum of **24** showed the carbonyl absorption at 1738 cm^{-1}. The -OH absorption was visible as a broad band in the region 3400-2500 cm^{-1}. The $-N_3$ and $-ONO_2$ absorptions were visible at 2119 and 1657 cm^{-1} respectively. In the ^1H NMR spectrum, the $-CO_2\underline{H}$ proton resonated as a broad singlet at δ 8.94 (exchangeable with D_2O). The C-3 protons of the isomers were discernible as doublets at δ 6.81 (J = 3.1 Hz) and 6.64 (J = 6.4 Hz) and the C-2 protons resonated as doublets at δ 4.51 (J = 3.1 Hz) and 4.49 (J = 6.4 Hz). In the ^{13}C NMR spectrum, the carbonyl carbons resonated at δ 171.71 and 171.46.

Mechanistically, this reaction can be rationalized along the following lines (Scheme 12). Oxidation of azide anion by CAN would lead to the azido radical. This radical adds to the cinnamic acid leading to benzylic radical **25**. The latter can be oxidized to benzylic cation **26** by a second equivalent of CAN and the cation is then quenched by $-ONO_2$ to yield the product **16**. Alternatively a ligand transfer from CAN to benzylic radical can also lead to the formation of the azidonitrate.



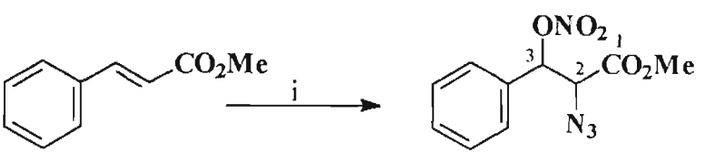
Scheme 12

2.2.1.2 CAN mediated oxidative addition of azide to cinnamic esters

It was of interest to see if the CAN mediated addition of azide to cinnamic esters would follow the same pattern observed in the case of cinnamic acids. Results of the investigations carried out with this objective are presented in this section.

Our initial experiment involved the reaction of methyl cinnamate and sodium azide. A deoxygenated solution of methyl cinnamate and sodium azide in dry acetonitrile, when treated with a solution of CAN in acetonitrile, afforded the α-azido-β-nitrato ester **28** in 75% yield as a 1:1 mixture of *syn* and *anti* isomers (Scheme 13). Pure samples of *syn* and *anti* isomers were obtained by very careful and repetitive column chromatography. Tentative stereochemical assignment was made on the basis of coupling constants for $C\underline{H}ONO_2$ and $C\underline{H}N_3$ protons, which as expected was slightly greater for the *anti* isomer. The assignment was

further supported by the difference in the rate of elimination of HNO_3, which was faster for the *syn* isomer (Section 2.2.2.2).



27 **28**

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, 2 h, 75%

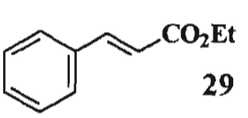
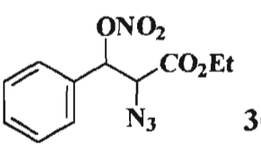
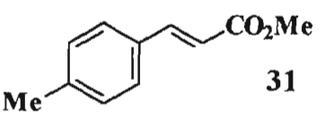
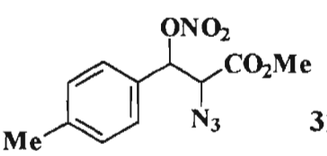
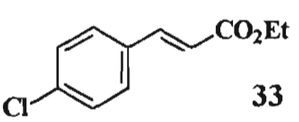
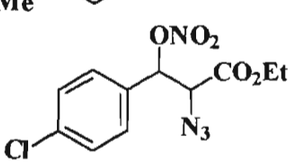
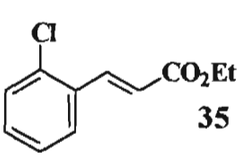
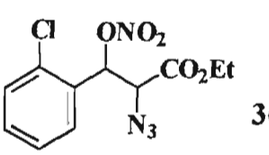
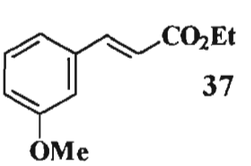
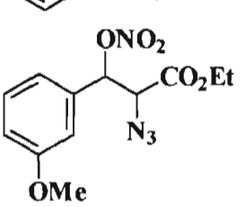
Scheme 13

The IR spectrum of the *syn* isomer showed the characteristic absorptions for $-N_3$, -C=O and $-ONO_2$ groups at 2133, 1755, 1647 cm^{-1} respectively. In the ^1H NMR spectrum, the aromatic protons resonated as a singlet at δ 7.41. The C-3 proton resonated as a doublet at δ 6.19 (J = 6.2 Hz) and C-2 proton resonated at δ 4.21 (d, J = 6.2 Hz). A singlet observed at δ 3.72 was attributed to -OMe protons. In the ^{13}C NMR spectrum, the carbonyl carbon was discernible at δ 166.95. The C-3 carbon was observed at δ 82.65 and C-2 carbon at 64.75. The GC-MS spectrum displayed the $[M^+-HNO_3-N_2]$ peak at *m/z* 175.

The *anti* isomer also yielded similar spectral data. The $-N_3$, -C=O and $-ONO_2$ absorptions were observed at 2123, 1758 and 1650 cm^{-1} respectively in the IR spectrum. In the ^1H NMR spectrum, the benzylic proton appeared as a doublet at δ 6.14 (J = 6.9 Hz). The C-2 proton also resonated as a doublet at δ 4.36 (J = 6.9 Hz). The -OMe protons resonated as a singlet at δ 3.82. In the ^{13}C NMR spectrum, the carbonyl carbon was visible at δ 167.04. The C-3 and C-2 carbons were observed at δ 81.93 and 63.54 respectively. Satisfactory analytical data was also obtained for the product.

Ethyl cinnamate **29**, methyl 4-methylcinnamate **31**, ethyl 4-chloro-cinnamate **33**, ethyl 2-chlorocinnamate **35** and ethyl 3-methoxy cinnamate **37** also afforded the corresponding α-azido-β-nitratocinnamates under similar reaction conditions (Table 1).

Table 1: Azidonitration of cinnamic esters

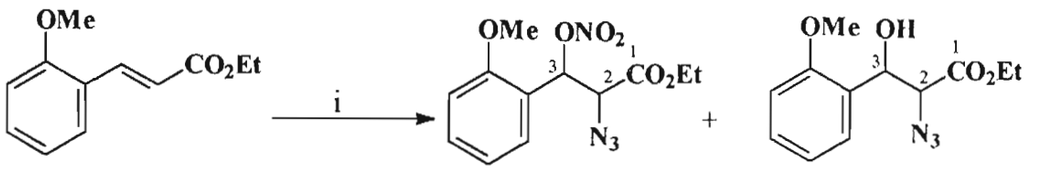
Entry	Substrate	Product	Yield (%)*
1	 **29**	 **30**	73
2	 **31**	 **32**	86
3	 **33**	 **34**	69
4	 **35**	 **36**	62
5	 **37**	 **38**	74

Reaction conditions: CAN (2.5 equiv.), NaN_3 (1.5 equiv.), dry acetonitrile, argon, 0 °C-RT, 1-3 h; * Isolated yield.

The structures of products **30, 32, 34, 36** and **38** were confirmed by the usual spectroscopic methods. In all cases, with the exception of

2-chlorocinnamate, the azidonitrates were obtained as a 1:1 mixture of *syn* and *anti* isomers. In the case of **35**, the isomers were obtained in a 2:1 ratio.

Both ethyl 2-methoxycinnamate **39** and ethyl 4-methoxycinnamate **42** exhibited slightly different reactivity pattern. Under the usual reaction conditions **39** afforded two products, *viz.* α-azido-β-nitrato ester **40** and α-azido-β-hydroxy ester **41** (Scheme 14). Both the products were found to be mixture of isomers.



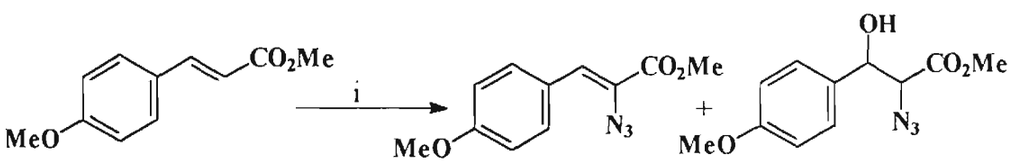
39 **40** (50%) **41** (13%)

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, 2 h

Scheme 14

The products **40** and **41** were separated by column chromatography and characterized by the usual spectroscopic methods. From the ^1H NMR spectrum, product **40** was found to be a mixture of *syn* and *anti* isomers in the ratio 3:2. Product **41** was also isolated as a mixture of isomers in the ratio 3:1. In the IR spectrum of product **41**, the -OH group was visible at 3505 cm^{-1}. The $-N_3$ and carbonyl group absorptions were observed at 2113 and 1738 cm^{-1} respectively. In the ^1H NMR spectrum, the -OH protons resonated as broad singlets at δ 3.51 and 3.07 (exchangeable with D_2O). The benzylic protons of the isomers resonated as multiplets at δ 5.42 and 5.15. The signal for $C\underline{H}N_3$ overlapped with that of $-OC\underline{H}_2-$ in the region δ 4.27-4.15 resulting in a multiplet. In the ^{13}C NMR spectrum, the two carbonyl carbons resonated at δ 168.89 and 168.81. The C-3 carbons of the isomers resonated at δ 71.75 and 71.21 and C-2 carbons at 65.49 and 65.01 respectively.

Methyl 4-methoxycinnamate under similar reaction conditions afforded α-azidocinnamate **43** and α-azido-β-hydroxy ester **44** (Scheme 15).



42 **43** (20%) **44** (48%)

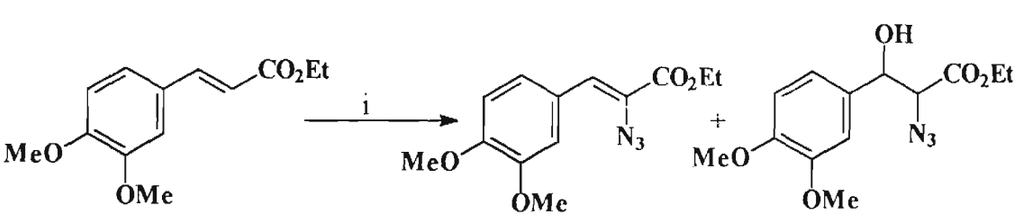
i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, 2 h

Scheme 15

The IR spectrum of product **43** displayed -N_3 and carbonyl group absorptions at 2125 and 1707 cm^{-1} respectively. The olefinic proton resonated as a singlet at δ 6.86 in the ^1H NMR spectrum. In the ^{13}C NMR spectrum, the carbonyl carbon resonated at δ 164.19. The GC-MS showed a peak at *m/z* 205 corresponding to $[M^+-N_2]$.

The α-azido-β-hydroxy ester **44** was isolated as a mixture of isomers in the ratio 3:2. In this case, the isomers were separated by crystallization. As usual, the structures of the products were established on the basis of spectral data.

3,4-Dimethoxycinnamate also underwent a similar reaction affording the α-azidocinnamate **46** and α-azido-β-hydroxy ester **47** (Scheme 16).



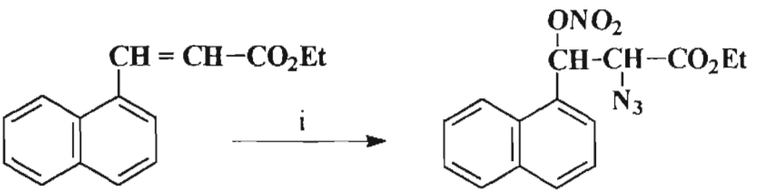
45 **46** (32%) **47** (23%)

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, 1.5 h

Scheme 16

Product **47** was found to be a mixture of isomers in the ratio 2:1. Both the products **46** and **47** were characterized by the spectral data. All the NMR signals were in agreement with the assigned structures. The GC-MS of **47** displayed [M^+-N_2-2] peak at *m/z* 265.

Ethyl 3-(1'-naphthyl)prop-2-enoate **48** also on reaction with sodium azide and CAN in dry acetonitrile afforded α-azido-β-nitrato ester **49** as a 2.5:1 mixture of *syn* and *anti* isomers (Scheme 17).



48 **49**

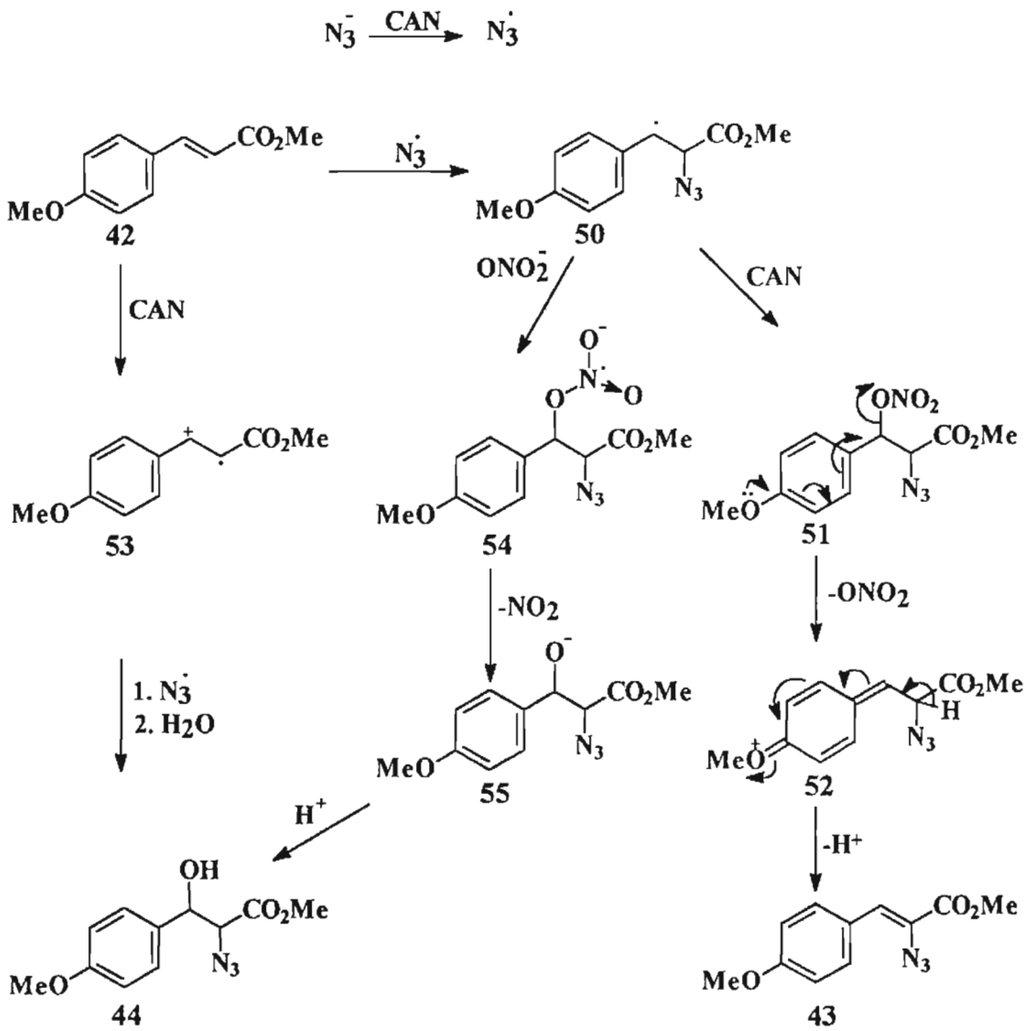
i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, 2 h, 67%

Scheme 17

The IR spectrum of the product **49** showed the absorptions due to -N_3, -CO and -ONO_2 groups at 2119, 1744 and 1645 cm^{-1} respectively. All the ^1H and ^{13}C NMR signals were in agreement with the assigned structure. GC-MS displayed a peak at *m/z* 239 corresponding to [M^+-HNO_3-N_2].

A mechanistic rationalization for the formation of α-azidocinnamates and α-azido-β-hydroxy esters can be given as follows (Scheme 18). In the first step the azide anion is oxidized to azido radical. The latter adds to the cinnamic ester to form the benzylic radical **50**, which is then converted to α-azido-β-nitrato ester **51** as depicted in Scheme 12. This can undergo spontaneous elimination of nitric acid to form the α-azidocinnamate **43**. It is also possible that CAN would oxidize the ester to a cation radical **53** which

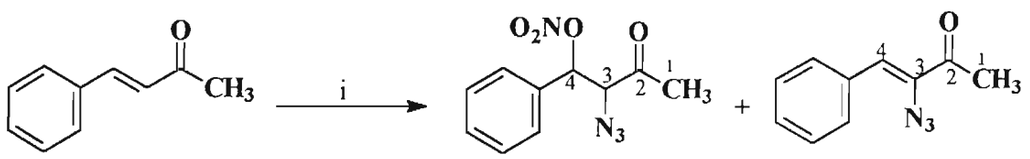
is then quenched by azido radical and H_2O to form the α-azido-β-hydroxylated product **44**. An alternative mechanism for the formation of **44** is as follows.[24] The radical **50** gets trapped by $-ONO_2$ to form the unstable radical anion **54**. The direct fragmentation of **54** followed by protonation of the resulting alkoxide **55** would give the carbinol **44**.



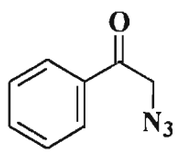
Scheme 18

2.2.1.3 CAN mediated oxidative addition of azide to benzylidene acetone

In view of the interesting results obtained in the oxidative addition of azide to cinnamic esters and acids, it was decided to extend the studies to α,β-unsaturated ketones. Benzylidene acetone **56** was selected as an example. Oxidative addition of sodium azide to **56** under deoxygenated atmosphere afforded the α-azido-β-nitrato ketone **57** and α-azido-α,β-unsaturated ketone **58** along with phenacyl azide **14** as a minor product (Scheme 19).



56 **57** (45%) **58** (32%)



14 (6%)

i. NaN_3, CAN, dry CH_3CN, argon, 0 °C-RT, 2 h

Scheme 19

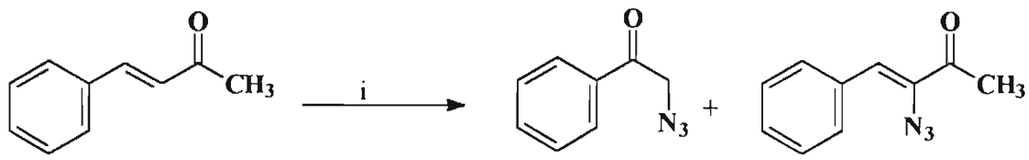
All the three products were characterized by the usual spectroscopic methods. The IR spectrum of **57** displayed -N_3, -CO and -ONO_2 absorptions at 2110, 1725 and 1646 cm^{-1} respectively. In the ^1H NMR spectrum, the C<u>H</u>ONO_2 and C<u>H</u>N_3 protons were visible as doublets at δ 6.16 (J = 6.3 Hz) and 4.32 (J = 6.3 Hz) respectively. The aromatic protons resonated as a singlet at δ 7.40. A singlet observed at δ 2.15 was attributed to methyl group

protons. In the ^{13}C NMR spectrum, the carbonyl carbon resonated at δ 201.76 and C-3 at δ 70.55.

The azide and carbonyl absorptions of product **58** were observed at 2119 and 1676 cm^{-1} respectively in the IR spectrum. In the ^{1}H NMR spectrum, a singlet observed at δ 6.57 was attributed to the olefinic proton. The aromatic protons resonated as a doublet at δ 7.73 (2H, J = 6.7 Hz) and a multiplet (3H) centered at δ 7.29. The methyl group protons resonated as a singlet at δ 2.39. In the ^{13}C NMR spectrum, the carbonyl carbon was discernible at δ 193.99. The GC-MS showed a peak at *m/z* 159 corresponding to $[M^{+}-N_2]$. Satisfactory analytical data was also obtained for the product.

The IR spectrum of **14** showed $-N_3$ absorption at 2106 cm^{-1} and the carbonyl absorption at 1694 cm^{-1}. In the ^{1}H NMR spectrum, $-C\underline{H}_2N_3$ protons resonated as a sharp singlet at δ 4.56. The carbonyl carbon and the carbon bearing the azide group appeared at δ 193.22 and 54.91 respectively in the ^{13}C NMR spectrum. The identity of phenacyl azide **14** was confirmed by comparing the spectral data with that reported in the literature.[11]

When this reaction was carried out under oxygen atmosphere, phenacyl azide was obtained as the major product (Scheme 20).



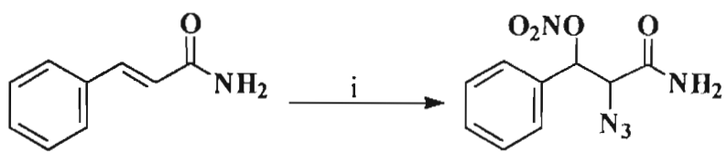
56 **14** (42%) **58** (16%)

i. NaN_3, CAN, dry CH_3CN, O_2, 0 °C-RT, 2 h

Scheme 20

2.2.1.4 CAN mediated oxidative addition of azide to cinnamamide

Successful reactions with cinnamic acids, cinnamic esters and benzylidine acetone prompted us to extend our investigations to cinnamamide also. Reaction of cinnamamide with sodium azide and CAN afforded the α-azido-β-nitrato amide **60** in 91% yield as a 1:1 mixture of *syn* and *anti* isomers (Scheme 21).



59 **60** (91%)

i. NaN_3, CAN, CH_3CN, argon, 0 °C-RT, overnight

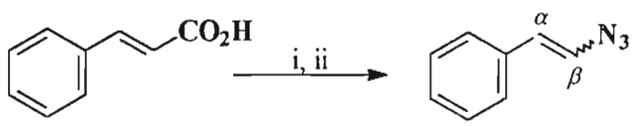
Scheme 21

The IR spectrum of the isomeric mixture showed the NH_2 absorptions at 3467 and 3318 cm^{-1}. The $-N_3$ and carbonyl absorptions of the isomers were visible at 2119 and 1688 cm^{-1} respectively. The $-ONO_2$ absorption was visible at 1645 cm^{-1}. In the ^1H NMR spectrum, the benzylic protons resonated as a multiplet centered at δ 6.39. The C<u>H</u>N_3 protons of the isomers resonated as doublets at δ 4.60 (J = 4.1 Hz) and 4.28 (J = 3.9 Hz). The NH_2 protons appeared as broad singlets at δ 6.73, 6.60, 6.50 and 6.26 (exchangeable with D_2O). In the ^{13}C NMR spectrum, the carbonyl carbons of the isomers resonated at δ 168.39 and 168.00. All other signals were in agreement with the assigned structure.

2.2.2 Chemical transformations of α-azido-β-nitrates

2.2.2.1 Transformation of cinnamic acids to β-azidostyrenes

As described earlier (Section 2.2.1.1) CAN mediates a facile addition of azide to cinnamic acid leading to the formation of α-azido-β-nitrato acid **16** (Scheme 7). In an attempt to isolate the acid, the product was treated with sodium carbonate followed by acidification with hydrochloric acid. However, the α-azido-β-nitrato acid was not obtained; instead the product isolated was found to be the β-azidostyrene **61**. In subsequent efforts to optimize the reaction conditions we found that, the α-azido-β-nitrato acid on treatment with anhydrous sodium acetate in dry acetone under reflux conditions afforded the product in better yield. The β-azidostyrene was isolated as a 1:1 mixture of *E* and *Z* isomers (Scheme 22).[25] The ratio was determined from the ^{1}H NMR spectrum.



15 **61** (61%)

i. NaN_3, CAN, CH_3CN, 0 °C-RT, argon, overnight

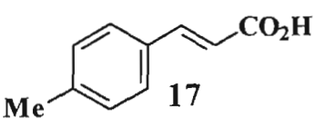
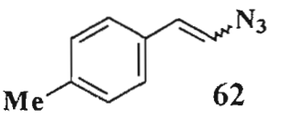
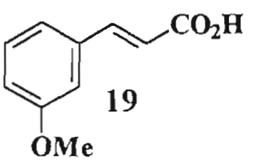
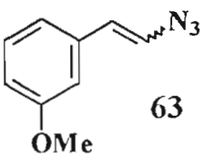
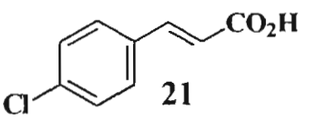
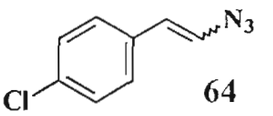
ii. CH_3COONa, dry acetone, reflux, 2 h

Scheme 22

The IR spectrum of **61** showed the azide absorption at 2106 cm^{-1}. The α protons of the *E* and *Z* isomers resonated as doublets at δ 6.58 (J = 13.7 Hz) and 6.33 (J = 8.4 Hz) respectively. The β protons resonated as doublets at δ 6.25 (J = 13.7) and 5.67 (J = 8.4 Hz). The [M^+-N_2] peak observed at *m/z* 117 in GC-MS further supported the assigned structure.

4-Methyl, 3-methoxy and 4-chlorocinnamic acids also afforded the corresponding β-azidostyrenes **62**, **63** and **64** respectively under similar reaction conditions. The results are summarized in Table 2.

Table 2: Synthesis of β-azidostyrenes

Entry	Substrate	Product	Yield (%)[a,b]
1	 **17**	 **62**	65
2	 **19**	 **63**	64
3	 **21**	 **64**	39

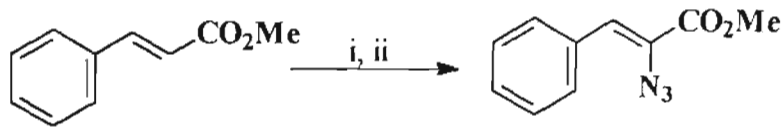
Reaction conditions: i. NaN_3, CAN, dry CH_3CN, argon, 0 °C-RT, overnight;
ii. Sodium acetate, dry acetone, reflux, 2-3 h; (a) Isolated yield; (b) *E*:*Z* = 1:1.

Diagnostic spectral data were obtained for the products **62**, **63** and **64**. The IR spectrum of these compounds showed -N_3 absorption around 2100 cm^{-1}. The ^1H and ^{13}C NMR signals of the compounds were also in agreement with the assigned structures.

2.2.2.2 Transformation of cinnamic esters to α-azidocinnamates

Encouraged by the transformation of α-azido-β-nitrato acids to β-azidostyrenes by treatment with sodium acetate, it was decided to investigate the applicability of this reaction to α-azido-β-nitrato esters also.

Our initial experiment involved the reaction of methyl cinnamate. Reaction of the latter with sodium azide and CAN in dry acetonitrile afforded the corresponding α-azido-β-nitrate **28** (Scheme 13). This crude product was treated with sodium acetate in dry acetone to afford the α-azidocinnamate **65** in 70% yield (Scheme 23).[25]



27 **65** (70%)

i. NaN_3, CAN, dry CH_3CN, 0 °C-RT, argon, 2 h

ii. CH_3COONa, dry acetone, RT, overnight

Scheme 23

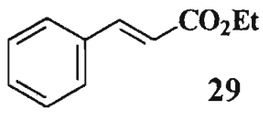
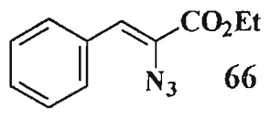
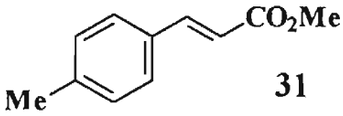
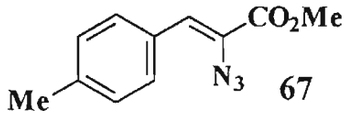
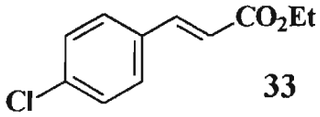
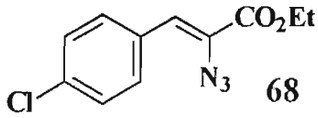
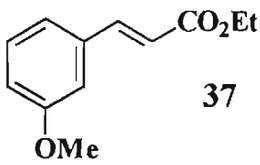
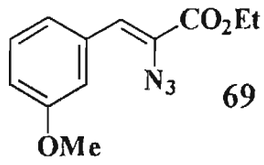
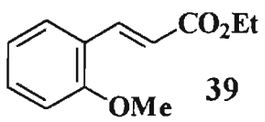
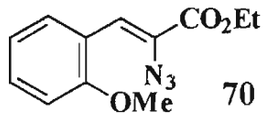
The IR spectrum of the α-azidocinnamate **65** exhibited -N_3 and carbonyl absorptions at 2123 and 1717 cm^{-1} respectively. In the ^1H NMR spectrum, the olefinic proton resonated as a singlet at δ 6.85. The aromatic protons resonated as two multiplets centered at δ 7.75 (2H) and δ 7.30 (3H). This downfield shift of the *ortho* protons suggests that azide and phenyl groups are in a *cis* configuration. This is consistent with the literature report also.[6c] The -OC$\underline{H}_3$ protons resonated as a singlet at δ 3.85. In the ^{13}C NMR spectrum, the carbonyl carbon was discernible at δ 163.73. The GC-MS displayed [M^+-N_2] peak at *m/z* 175.

Interestingly, when the reaction mixture was worked up after one hour, it was found that the *syn* isomer has completely reacted leaving behind the unreacted *anti* isomer. On overnight stirring, the *anti* isomer also underwent complete elimination of nitrate. This rate difference observed in

the case of *syn* and *anti* isomers further supported their structure assignment based on ^1H coupling constants.

Ethyl cinnamate, methyl 4-methylcinnamate, ethyl 4-chlorocinnamate, ethyl 3-methoxycinnamate and ethyl 2-methoxycinnamate also afforded the corresponding α-azidocinnamates under similar reaction conditions (Table 3).

Table 3: Synthesis of α-azidocinnamates

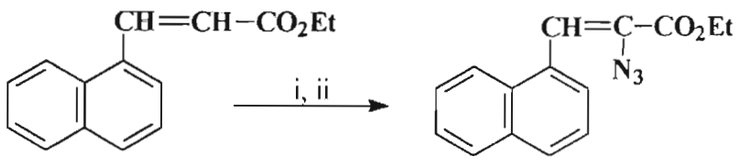
Entry	Substrate	Product	Yield (%)[a,b]
1	 **29**	 **66**	68
2	 **31**	 **67**	74
3	 **33**	 **68**	67
4	 **37**	 **69**	64
5	 **39**	 **70**	60

Reaction conditions: 1. NaN_3, CAN, dry CH_3CN, argon, 0 °C-RT, 2-3 h;

2. Sodium acetate, dry acetone, RT, overnight; (a) Isolated yield; (b) In the case of 2-methoxycinnamic ester **39**, 12% of α-azido-β-hydroxy ester **41** was also isolated.

The structures of the products **66-70** were assigned by comparing their spectral data with those of the authentic samples reported in the literature.[6,7]

Ethyl 3-naphthylprop-2-enoate **48** also afforded the α-azido-α,β-unsaturated ester **71** under similar reaction conditions (Scheme 24).



48 **71** (64%)

i. NaN_3, CAN, dry CH_3CN, argon, 0 °C-RT, 2 h

ii. CH_3COONa, dry acetone, RT, overnight

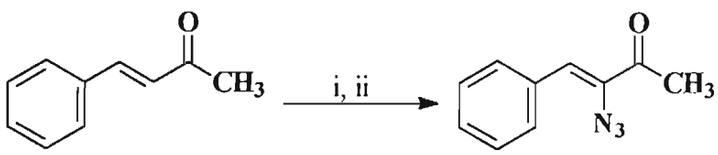
Scheme 24

In the IR spectrum, the azide absorption was visible at 2119 cm^{-1} and the carbonyl absorption at 1707 cm^{-1}. In the ^1H NMR spectrum, the olefinic proton resonated as singlet at δ 7.64. The methylene protons resonated as a quartet at δ 4.41 (J = 7.1 Hz) and methyl group protons appeared at δ 1.44 as a triplet (J = 7.1 Hz). In the ^{13}C NMR spectrum, the carbonyl carbon was discernible at δ 166.19. The GC-MS showed a peak at m/z 239 corresponding to $[M^+-N_2]$.

α-Azidocinnamates being the precursors of indoles, azirines and isoquinolines, the present method of synthesis offers a novel and facile route to these heterocyclic compounds.[5,6]

2.2.2.3 Transformation of α,β-unsaturated ketones to α-azido-α,β-unsaturated ketones

In order to probe the generality of the above reaction we have extended our studies to α,β-unsaturated ketones including chalcones. Our initial experiment was with benzylidene acetone **56** which on reaction with sodium azide and CAN afforded a mixture of α-azido-β-nitrato ketone **57** and α-azido-α,β-unsaturated ketone **58** (Scheme 19). When the crude product was dissolved in dry acetone and treated with sodium acetate, **58** was obtained as the only isolable product (Scheme 25).[25]



56 **58** (65%)

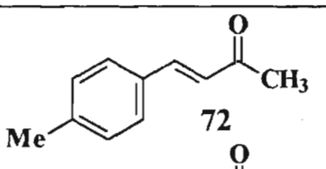
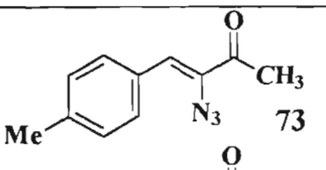
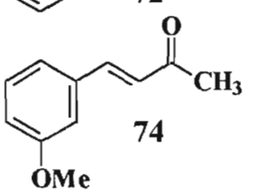
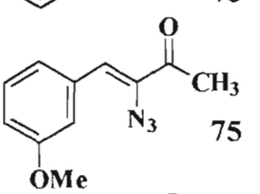
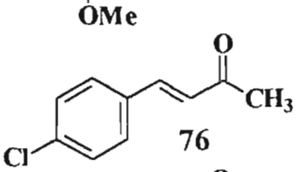
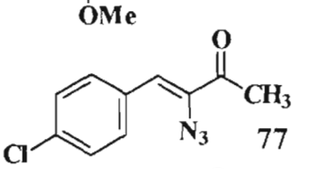
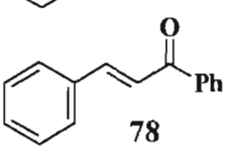
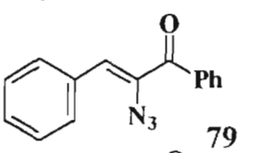
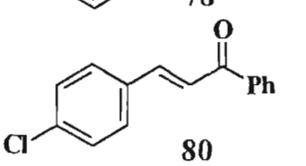
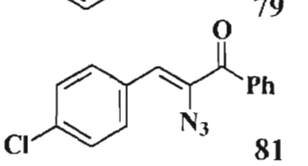
i. NaN_3, CAN, CH_3CN, argon, 0 °C-RT, 2 h

ii. CH_3COONa, dry acetone, RT, 1 h

Scheme 25

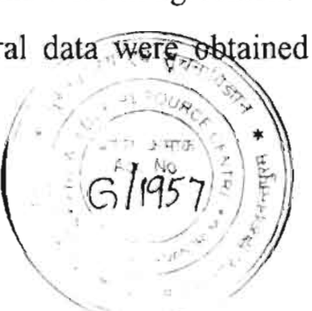
Other phenyl substituted benzylidene acetones and chalcones also afforded the corresponding α-azido-α,β-unsaturated ketones under the above reaction conditions (Table 4).

Table 4: Synthesis of α-azido-α,β-unsaturated ketones

Entry	Substrate	Product	Yield (%)*
1	 **72**	 **73**	66
2	 **74**	 **75**	76
3	 **76**	 **77**	60
4	 **78**	 **79**	72
5	 **80**	 **81**	67

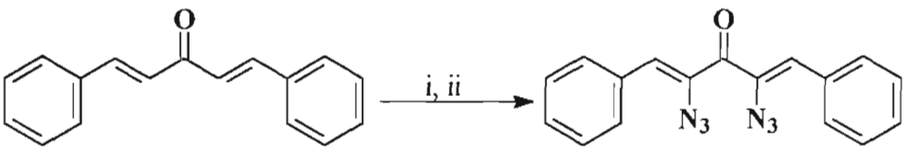
Reaction conditions: 1. NaN_3, CAN, dry CH_3CN, argon, 0 °C-RT, 1-2 h;
2. Sodium acetate, dry acetone, RT, 1 h; * Isolated yield.

Structure of the product **73** was established on the basis of spectral data. The IR spectrum showed -N_3 absorption at 2113 cm^{-1} and carbonyl absorption at 1660 cm^{-1}. In the ^1H NMR spectrum, the olefinic proton resonated as a singlet at δ 6.64. In the ^{13}C NMR spectrum, the carbonyl carbon was discernible at δ 193.90. All other signals were in agreement with the proposed structure. Similar diagnostic spectral data were obtained for products **75** and **77** also.



The IR spectrum of **79** and **81** showed the azide peak at 2112 and 2119 cm^{-1} respectively. The carbonyl absorption was visible at 1654 and 1661 cm^{-1} respectively. The olefinic protons of **79** and **81** resonated as singlets at δ 6.43 and 6.36 cm^{-1} respectively. In the ^{13}C NMR spectrum, the carbonyl carbons were discernible at δ 192.10 and 191.63 respectively. All other signals were in agreement with the assigned structures.

Sequential treatment of dibenzylidene acetone with NaN_3 and CAN followed by sodium acetate afforded the product **83** in 30% yield (Scheme 26).



82 **83** (30%)

i. NaN_3, CAN, CH_3CN, argon, 0 °C-RT, 2 h

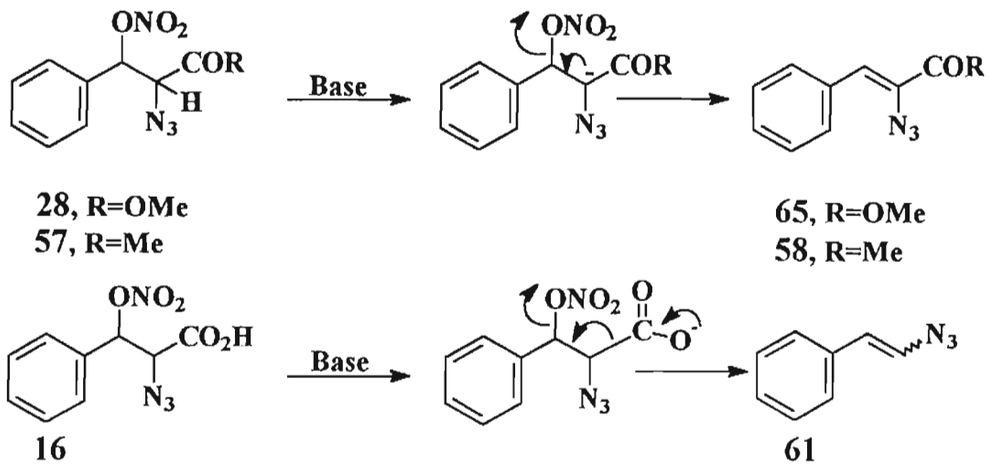
ii. Sodium acetate, dry acetone, RT, 1 h

Scheme 26

The IR spectrum of **83** showed azide absorption at 2113 cm^{-1} and that of carbonyl group at 1626 cm^{-1}. In the ^1H NMR spectrum, the singlet at δ 6.62 was attributed to the olefinic protons. Aromatic protons resonated as two multiplets centered at δ 7.83 and 7.38 respectively. In the ^{13}C NMR spectrum, the carbonyl carbon was discernible at δ 186.44.

A mechanistic rationalization for the results obtained may be presented as follows. The oxidation of azide by CAN would give the azido radical and the latter on addition to the cinnamic ester, cinnamic acid or α,β-unsaturated ketone would give rise to a benzylic radical. This is then

transformed to the α-azido-β-nitrato product as illustrated in Scheme 12. The α-azido-β-nitrates derived from cinnamic esters and α,β-unsaturated ketones, even under mildly basic conditions undergo HNO_3 elimination. The α-azido-β-nitrato acid undergoes concomitant elimination of CO_2 and HNO_3 to form β-azidostyrene (Scheme 27).



Scheme 27

In conclusion, we have encountered a facile route to the synthesis of α-azido-β-nitrato acids and esters that are precursors of biologically important α-amino acids. The present work constitutes a novel and expeditious process for the synthesis of α-azidocinnamates, α-azido-α,β-unsaturated ketones and β-azidostyrenes. In view of the experimental simplicity, this process is likely to emerge as the method of choice for the synthesis of these compounds of proven versatility in heterocyclic synthesis.

2.3 Experimental

2.3.1 General

Melting points were recorded on a Toshniwal and Büchi melting point apparatus and are uncorrected. The infrared (IR) spectra were recorded on Perkin-Elmer-882 and Nicolet Impact 400D FT-IR spectrophotometers. The NMR spectra were recorded at 300 (^{1}H) and 75 (^{13}C) MHz with $CDCl_3$ as the solvent using Bruker-300 MHz spectrometer. Chemical shifts (δ) are reported relative to TMS (^{1}H) and $CDCl_3$ (^{13}C) as the internal standards. Mass spectra were recorded on Fisons MD 800 and Hewlett Packard 5890 mass spectrometers. The relative intensities of *m/z* values (in percentage) are given in parenthesis. Elemental analyses were done using a Perkin-Elmer 2400 CHN analyzer.

Purification by gravity column chromatography was done using 100-200 mesh silica gel and appropriate mixture of hexane and ethyl acetate for elution. Commercial grade solvents were distilled prior to use. Analytical thin layer chromatography was performed on glass plates coated with silica gel GF_{254} containing 13% calcium sulfate as binder. All the 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 and cinnamamide were purchased from Aldrich Co. and cinnamic acid and sodium azide were purchased from local sources. Substituted cinnamic acids were prepared from the corresponding aldehydes and malonic acid *via* Knoevenagel condensation. Cinnamic esters were prepared either from the corresponding cinnamic acids by acid catalyzed esterification reaction in methanol or from the corresponding

aldehydes *via* Wittig reaction using (carbethoxymethylene)-triphenylphosphorane. Benzylidine acetones and chalcones were prepared by the base catalysed condensation of aldehydes and acetone or acetophenones. All the solid products were recrystallized from dichloromethane-hexane mixture. The ratio of the isomers was determined from the ^{1}H NMR of the crude product.

2.3.2 CAN mediated addition of azide to cinnamic acids

2-Azido-3-nitrato-3-phenylpropionic acid (16)

A mixture of cinnamic acid (148 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) was taken in dry acetonitrile (5 mL) in a two necked round-bottomed flask fitted with a pressure equalizing funnel containing CAN (1.370 g, 2.5 mmol) dissolved in dry acetonitrile (10 mL). Both the solutions were simultaneously bubbled with argon, which was deoxygenated by passing through Fieser's solution,[26] for 15 minutes. Then CAN solution was added dropwise at 0 °C and the reaction mixture was stirred vigorously under argon atmosphere for 1 hour. The argon bubbling was then stopped but the stirring was continued overnight at room temperature. When the reaction was completed, acetonitrile was evaporated off, the reaction mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25mL). The combined organic extract was washed with water, then with saturated brine and dried over anhydrous sodium sulfate. It was filtered and the solvent was removed in *vacuo* to obtain the crude residue. Column chromatography on silica gel using hexane-ethyl acetate (80:20) afforded **16** (176 mg, 70%, 1:1 mixture of *syn* and *anti* isomers) as a pale yellow viscous liquid.

IR (neat) ν_{max} : 3300-2500, 2119, 1735, 1647, 1290, 852, 724 cm^{-1}.

^{1}H NMR : δ 7.42 (s, 10H, ArH), 7.15 (brs, 2H, CO_2H), 6.26 (d, J = 5.1 Hz, 1H, $CHONO_2$), 6.16 (d, J = 6.6 Hz, 1H, $CHONO_2$), 4.45 (d, J = 6.6 Hz, 1H, CHN_3), 4.28 (d, J = 5.1 Hz, 1H, CHN_3).

^{13}C NMR : δ 170.75, 170.46, 133.60, 132.81, 130.09, 129.90, 129.08, 128.99, 127.67, 127.00, 82.55, 82.02, 64.77, 63.70.

2-Azido-3-(4'-methylphenyl)-3-nitratopropionic acid (18)

A deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise to a deoxygenated solution of 4-methylcinnamic acid (162 mg, 1 mmol) and NaN_3 (98 mg, 1.5 mmol) in dry acetonitrile (5 mL) at 0 °C and stirred overnight. On completion of the reaction, the reaction mixture was worked up and purified as described previously to afford **18** (171 mg, 64%, 1:1 mixture of *syn* and *anti* isomers) as a yellow viscous liquid.

IR (neat) ν_{max} : 3300-2500, 2119, 1730, 1647, 1276, 852 cm^{-1}.

^{1}H NMR : δ 7.37 (brs, 2H, CO_2H, exchangeable with D_2O), 7.32 (d, J = 7.6 Hz, 4H, ArH), 7.22 (d, J = 7.6 Hz, 4H, ArH), 6.22 (d, J = 5.3 Hz, 1H, $CHONO_2$), 6.13 (d, J = 6.6 Hz, 1H, $CHONO_2$), 4.43 (d, J = 6.6 Hz, 1H, CHN_3), 4.26 (d, J = 5.3 Hz, 1H, CHN_3), 2.37 (s, 6H, CH_3).

^{13}C NMR : δ 171.67, 171.53, 140.33, 140.18, 130.33, 129.87, 129.80, 129.65, 127.68, 127.09, 82.43, 81.91, 64.74, 63.67, 21.39.

GC-MS (*m/z*) : 145 [M^+-HNO_2-N_2-CO_2-2] (3), 136 (60), 131 (2), 119 (60), 116 (3), 91 (100), 77 (7), 65 (20), 63 (15), 51 (7).

2-Azido-3-(3'-methoxyphenyl)-3-nitratopropionic acid (20)

A deoxygenated solution of CAN (2.741 g, 5 mmol) in dry acetonitrile (20 mL) was added dropwise to a deoxygenated solution of 3-methoxycinnamic acid (356 mg, 2 mmol) and NaN_3 (195 mg, 3 mmol) in dry acetonitrile (10 mL) at 0 °C and stirred overnight. On completion of the reaction, the mixture was worked up and purified as described earlier to afford **20** (394 mg, 70%, 1:1 mixture of *syn* and *anti* isomers) as a yellow viscous liquid.

IR (neat) ν_{max} : 3400-2500, 2119, 1732, 1651, 1276, 846 cm^{-1}.

^1H NMR : δ 8.42 (brs, 2H, $CO_2\underline{H}$, exchangeable with D_2O), 7.34-7.29 (m, 2H, Ar$\underline{H}$), 7.01-6.91 (m, 6H, Ar$\underline{H}$), 6.24 (d, J = 4.9 Hz, 1H, C$\underline{H}ONO_2$), 6.13 (d, J = 6.5 Hz, 1H, C$\underline{H}ONO_2$), 4.44 (d, J = 6.5 Hz, 1H, C$\underline{H}N_3$), 4.29 (d, J = 4.9 Hz, 1H, C$\underline{H}N_3$), 3.81 (s, 6H, O$\underline{Me}$).

^{13}C NMR : δ 170.93, 170.89, 159.88, 159.77, 134.80, 134.03, 130.18, 130.07, 119.69, 118.95, 115.44, 115.23, 113.15, 112.47, 82.16, 81.67, 64.57, 63.48, 55.25.

2-Azido-3-(4'-chlorophenyl)-3-nitratopropionic acid (22)

To a deoxygenated solution of 4-chlorocinnamic acid (365 mg, 2 mmol) and NaN_3 (195 mg, 3 mmol) in dry acetonitrile (10 mL), a deoxygenated solution of CAN (2.741 g, 5 mmol) in dry acetonitrile (20 mL) was added dropwise at 0 °C and stirred overnight. The reaction mixture on completion of the reaction, was worked up and purified as described previously to afford **22** (321 mg, 56%, 1:1 mixture of *syn* and *anti* isomers) as a pale yellow oil.

IR (neat) ν_{max} : 3300-2500, 2124, 1734, 1649, 1493, 1276, 1088, 841 cm^{-1}.

^1H NMR : δ 8.31 (brs, 2H, $CO_2\underline{H}$, exchangeable with D_2O), 7.39 (brs, 8H, Ar$\underline{H}$), 6.23 (d, J = 4.9 Hz, 1H, C$\underline{H}ONO_2$), 6.13 (d, J = 6.3 Hz, 1H, C$\underline{H}ONO_2$), 4.48 (d, J = 6.3 Hz, 1H, C$\underline{H}N_3$), 4.27 (d, J = 4.9 Hz, 1H, C$\underline{H}N_3$).

^{13}C NMR : δ 171.30, 136.37, 136.19, 131.78, 130.96, 129.41, 129.29, 129.07, 128.40, 81.51, 80.93, 64.41, 63.44.

2-Azido-3-(2'-chlorophenyl)-3-nitratopropionic acid (24)

To a deoxygenated solution of 2-chlorocinnamic acid (365 mg, 2 mmol) and NaN_3 (195 mg, 3 mmol) in dry acetonitrile (10 mL), a deoxygenated solution of CAN (2.741 g, 5 mmol) in dry acetonitrile (20 mL) was added dropwise at 0 °C and stirred overnight. On completion of the reaction, the reaction mixture was worked up as usual and the residue was subjected to column chromatography to afford **24** (310 mg, 54%, 2:1 mixture of *syn* and *anti* isomers) as a colorless oil.

IR (neat) ν_{max} : 3400-2500, 2119, 1738, 1657, 1283, 839 cm^{-1}.

^1H NMR : δ 8.94 (brs, $CO_2\underline{H}$, exchangeable with D_2O), 7.56-7.34 (m, Ar$\underline{H}$), 6.81 (d, J = 3.1 Hz, C$\underline{H}ONO_2$), 6.64 (d, J = 6.4 Hz, C$\underline{H}ONO_2$), 4.51 (d, J = 3.1 Hz, C$\underline{H}N_3$), 4.49 (d, J = 6.4 Hz, C$\underline{H}N_3$).

^{13}C NMR : δ 171.71, 171.46, 133.56, 131.74, 131.51, 130.99, 130.71, 130.06, 129.90, 128.36, 127.86, 127.55, 127.48, 78.90, 78.60, 62.65, 62.37.

2.3.3 CAN mediated addition of azide to cinnamic esters

Methyl 2-azido-3-nitrato-3-phenylpropionate (28)

To a deoxygenated solution of methyl cinnamate (500 mg, 3.08 mmol) and sodium azide (300 mg, 4.62 mmol) in dry acetonitrile (10 mL), a deoxygenated solution of CAN (4.221 g, 7.7 mmol) in dry acetonitrile (20 mL) was added dropwise at ice temperature and stirred well. After 1 hour, the argon bubbling was stopped and the stirring continued at room temperature until the TLC showed the absence of starting material (2 h). On completion of the reaction, the acetonitrile was evaporated off, then the mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The combined organic extract was washed with water and saturated brine respectively. Finally, the extract was dried using anhydrous sodium sulfate and concentrated in *vacuo*. The residue obtained was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (95:5) afforded **28** (614 mg, 75 %) as a 1:1 mixture of *syn* and *anti* isomers. This mixture, on careful and repetitive column chromatography, afforded pure samples of both the isomers along with their mixture.

***Syn* isomer**

Pale yellow oil.

IR (neat) ν_{max} : 2969, 2847, 2133, 1755, 1647, 1283, 852 cm^{-1}.

^1H NMR : δ 7.41 (s, 5H, Ar<u>H</u>), 6.19 (d, J = 6.2 Hz, 1H, C<u>H</u>ONO_2), 4.21 (d, J = 6.2 Hz, 1H, C<u>H</u>N_3), 3.72 (s, 3H, O<u>Me</u>).

^{13}C NMR : δ 166.95, 133.47, 130.11, 129.10, 127.12, 82.65, 64.75, 53.20.

GC-MS (*m/z*) : 175 [M^+-HNO_3-N_2] (4), 143 (4), 116 (3), 106 (100), 77 (75), 61 (5), 51 (18).

***Anti* isomer**

Pale yellow oil.

IR (neat) ν_{max} : 2962, 2123, 1758, 1650, 1282, 988, 851, 697 cm^{-1}.

^1H NMR : δ 7.41 (s, 5H, ArH), 6.14 (d, *J* = 6.9 Hz, 1H, CHONO$_2$), 4.36 (d, *J* = 6.9 Hz, 1H, CHN$_3$), 3.82 (s, 3H, OMe).

^{13}C NMR : δ 167.04, 132.89, 129.99, 128.92, 127.49, 81.93, 63.54, 53.11.

Anal. Calcd for $C_{10}H_{10}N_4O_5$: C, 45.11; H, 3.78; N, 21.04.

Found : C, 44.28; H, 3.77; N, 20.38.

Ethyl 2-azido-3-nitrato-3-phenylpropionate (30)

To a deoxygenated solution of ethyl cinnamate **29** (300 mg, 1.7 mmol) and sodium azide (166 mg, 2.55 mmol) in dry acetonitrile (8 mL), a deoxygenated solution of CAN (2.329 g, 4.25 mmol) in dry acetonitrile (17 mL) was added dropwise at 0 °C and stirred well. The mixture, on completion of the reaction was worked up and purified as described earlier to afford **30** (348 mg, 73%, 1:1 mixture of *syn* and *anti* isomers) as a pale yellow oil.

IR (neat) ν_{max} : 2993, 2119, 1745, 1651, 1276, 1202, 852 cm^{-1}.

^1H NMR : δ 7.40 (brs, 10H, ArH), 6.19 (d, *J* = 6.4 Hz, 1H, CHONO$_2$), 6.14 (d, *J* = 6.9 Hz, 1H, CHONO$_2$), 4.34-4.14 (m, 6H, OCH$_2$CH$_3$ & CHN$_3$), 1.32 (t, *J* = 7.1 Hz, 3H, CH$_3$), 1.16 (t, *J* = 7.1 Hz, 3H, CH$_3$).

^{13}C NMR : δ 166.51, 166.30, 133.33, 132.92, 129.94, 129.83, 128.91, 128.86, 127.52, 127.12, 82.65, 81.95, 64.57, 63.53, 62.61, 62.49, 13.99, 13.81.

GC-MS (*m/z*) : 189 [M^+-HNO_3-N_2] (58), 143 (100), 115 (30), 105 (35), 89 (15), 77 (12).

Methyl 2-azido-3-(4'-methylphenyl)-3-nitratopropionate (32)

To a deoxygenated solution of cinnamic ester **31** (88 mg, 0.5 mmol) and sodium azide (49 mg, 0.75 mmol) in dry acetonitrile (2 mL), a deoxygenated solution of CAN (685 mg, 1.25 mmol) in dry acetonitrile (6 mL) was added dropwise at 0 °C and stirred well. On completion of the reaction, the reaction mixture was worked up and purified as described previously to afford **32** (120 mg, 86%, 1:1 mixture of *syn* and *anti* isomers) as a pale yellow oil.

IR (neat) ν_{max} : 2956, 2119, 1751, 1645, 1276, 846 cm^{-1}.

^{1}H NMR : δ 7.30-7.19 (m, 8H, ArH), 6.15 (d, J = 6.4 Hz, 1H, CHONO$_2$), 6.11 (d, J = 7.0 Hz, 1H, CHONO$_2$), 4.34 (d, J = 7.0 Hz, 1H, CHN$_3$), 4.19 (d, J = 6.4 Hz, 1H, CHN$_3$), 3.82 (s, 3H, OMe), 3.72 (s, 3H, OMe), 2.36 (s, 6H, Me).

^{13}C NMR : δ 167.10, 166.82, 140.01, 139.89, 130.59, 130.28, 129.81, 129.62, 127.45, 126.99, 82.54, 81.91, 64.63, 63.50, 53.06, 53.01, 21.23.

HRMS : 219.0882 [M^+-ONO_2+1].

Ethyl 2-azido-3-(4'-chlorophenyl)-3-nitratopropionate (34)

To a deoxygenated solution of cinnamic ester **33** (210 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a

deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise and stirred well. On completion of the reaction, the mixture was worked up as usual. Column chromatography on silica gel using hexane-ethyl acetate (98:2) afforded 60 mg (19%) of *anti* isomer, 120 mg (38.2%) of mixture of isomers followed by 36 mg (11.4 %) of *syn* isomer. The ratio of the isomers was found to be 1:1 from the ^{1}H NMR of the crude residue.

Syn isomer

Pale yellow oil.

IR (neat) ν_{max} : 2987, 2119, 1744, 1645, 1276, 846 cm^{-1}.

^{1}H NMR : δ 7.42-7.35 (m, 4H, Ar<u>H</u>), 6.18 (d, *J* = 6.1 Hz, 1H, C<u>H</u>ONO$_2$), 4.30-4.18 (m, 3H, C<u>H</u>N$_3$ & OC<u>H</u>$_2$CH$_3$), 1.23 (t, *J* = 7.1 Hz, 3H, OCH$_2$C<u>H</u>$_3$).

^{13}C NMR : δ 166.07, 136.04, 131.90, 129.91, 128.53, 81.74, 64.40, 62.65, 14.08.

Anti isomer

Pale yellow oil.

IR (neat) ν_{max} : 2974, 2119, 1744, 1645, 1270, 839 cm^{-1}.

^{1}H NMR : δ 7.41-7.32 (m, 4H, Ar<u>H</u>), 6.12 (d, *J* = 6.7 Hz, 1H, C<u>H</u>ONO$_2$), 4.37 (d, *J* = 6.7 Hz, 1H, C<u>H</u>N$_3$), 4.26 (q, *J* = 7.1 Hz, 2H, OC<u>H</u>$_2$CH$_3$), 1.31 (t, *J* = 7.1 Hz, 3H, OCH$_2$C<u>H</u>$_3$).

^{13}C NMR : δ 166.30, 136.12, 131.69, 129.11, 128.54, 81.06, 63.39, 62.75, 14.02.

Ethyl 2-azido-3-(2'-chlorophenyl)-3-nitratopropionate (36)

To an ice cooled deoxygenated solution of ethyl 2-chlorocinnamate (300 mg, 1.42 mmol) and sodium azide (138 mg, 2.13 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.946 g, 3.55 mmol) in dry acetonitrile (17 mL) was added dropwise while the reaction mixture was continuously being purged with argon. On completion of the reaction, the mixture was worked up and purified as described earlier to afford **36** (276 mg, 62%, 2:1 mixture of *syn* and *anti* isomers) as a colorless oil.

IR (neat) ν_{max} : 2987, 2119, 1751, 1651, 1476, 1283, 1201, 1026, 839, 752 cm^{-1}.

^1H NMR : δ 7.51-7.32 (m, Ar<u>H</u>), 6.77 (d, *J* = 3.8 Hz, C<u>H</u>ONO_2), 6.62 (d, *J* = 6.5 Hz, C<u>H</u>ONO_2), 4.42-4.17 (m, C<u>H</u>N_3 & O$C\underline{H}_2CH_3$), 1.32-1.24 (m, $OCH_2C\underline{H}_3$).

^{13}C NMR : δ 166.26, 166.15, 133.60, 131.91, 131.70, 130.86, 130.63, 129.98, 129.84, 128.43, 128.13, 127.47, 127.38, 79.13, 78.75, 62.86, 62.64, 62.61, 13.95.

Ethyl 2-azido-3-(3'-methoxyphenyl)-3-nitratopropionate (38)

A deoxygenated solution of 3-methoxycinnamic ester **37** (309 mg, 1.5 mmol) and sodium azide (145 mg, 2.25 mmol) in dry acetonitrile (5 mL) was treated with a deoxygenated solution of CAN (2.055 g, 3.75 mmol) in dry acetonitrile (17 mL) at 0 °C. On completion of the reaction, the mixture was worked up and purified as described previously to afford **38** (342 mg, 74%, 1:1 mixture of *syn* and *anti* isomers) as a yellow oil.

IR (neat) ν_{max} : 2987, 2837, 2119, 1744, 1645, 1601, 1489, 1457, 1276, 852 cm^{-1}.

^{1}H NMR : δ 7.33-7.26 (m, 2H, ArH), 6.98-6.92 (m, 6H, ArH), 6.17 (d, J = 6.3 Hz, 1H, CHONO$_2$), 6.11 (d, J = 7.0 Hz, 1H, CHONO$_2$), 4.34-4.14 (m, 6H, OCH$_2$CH$_3$ & CHN$_3$), 3.81 (s, 6H, OMe), 1.37 (t, 3H, J = 7.1 Hz, CH$_3$), 1.19 (t, 3H, J = 7.1 Hz, CH$_3$).

^{13}C NMR : δ 166.50, 166.29, 159.94, 159.88, 134.80, 134.37, 130.01, 129.94, 119.57, 119.10, 115.34, 115.23, 113.42, 113.09, 82.49, 81.83, 64.58, 63.49, 62.60, 62.51, 55.16, 13.99, 13.84.

GC-MS (*m/z*) : 219 [M^+-HNO_3-N_2] (5), 205 (3), 188 (8), 160 (7), 134 (100), 107 (15), 92 (16), 77 (20), 63 (14), 51 (5).

Ethyl 2-azido-3-(2'-methoxyphenyl)-3-nitratopropionate (40) and Ethyl 2-azido-3-hydroxy-3-(2'-methoxyphenyl)propionate (41)

To a deoxygenated solution of 2-methoxycinnamic ester **39** (412 mg, 2 mmol) and sodium azide (195 mg, 3 mmol) in dry acetonitrile (10 mL), a deoxygenated solution of CAN (2.742 g, 5 mmol) in dry acetonitrile (20 mL) was added dropwise at 0 °C and stirred well. On completion of the reaction, the mixture was worked up as usual. Column chromatography on silica gel using hexane-ethyl acetate (97:3) afforded **40** (312 mg, 51%) as a colorless oil. Further elution using hexane-ethyl acetate (90:10) afforded **41** (68 mg, 13%) as a pale yellow viscous liquid.

Product 40

3:2 Mixture of *syn* and *anti* isomers.

IR (neat) ν_{max} : 2980, 2837, 2113, 1744, 1645, 1189, 1020, 839 cm^{-1}.

^{1}H NMR : δ 7.39-7.34 (m, ArH), 7.03-6.91 (m, ArH), 6.71 (d, J = 4.4 Hz, CHONO$_2$), 6.58 (d, J = 6.8 Hz, CHONO$_2$), 4.43 (d, J = 4.4 Hz, CHN$_3$), 4.32-4.20 (m, CHN$_3$ & OCH$_2$CH$_3$), 3.89 (s, OMe), 1.26 (m, OCH$_2$CH$_3$).

^{13}C NMR : δ 166.89, 166.77, 156.99, 155.96, 130.96, 130.62, 127.93, 127.33, 121.94, 121.62, 121.00, 120.64, 110.87, 110.68, 78.34, 77.94, 62.92, 62.46, 62.30, 55.57, 13.94.

GC-MS (*m/z*) : 219 [M$^+$-HNO$_3$-N$_2$] (50), 173 (100), 158 (11), 144 (9), 130 (7), 119 (7), 102 (5), 89 (3), 76 (4).

Product 41

3:1 Mixture of *syn* and *anti* isomers.

IR (neat) ν_{max} : 3505, 2987, 2837, 2113, 1738, 1601, 1495, 1245, 1020, 752 cm^{-1}.

^{1}H NMR : δ 7.43-7.26 (m, ArH), 7.02-6.85 (m, ArH), 5.42 (m, CHOH), 5.15 (m, CHOH), 4.27-4.15 (m, CHN$_3$ & OCH$_2$CH$_3$), 3.51 (brs, OH, exchangeable with D$_2$O), 3.07 (brs, OH, exchangeable with D$_2$O), 1.29-1.19 (m, CH$_3$).

^{13}C NMR : δ 168.89, 168.81, 156.35, 155.85, 129.44, 129.19, 128.02, 127.54, 127.24, 126.85, 120.83, 110.43, 110.17, 71.75, 71.21, 65.49, 65.01, 61.79, 61.58, 55.25, 14.03.

Methyl 2-azido-3-(4'-methoxyphenyl)prop-2-enoate (43) and Methyl 2-azido-3-hydroxy-3-(4'-methoxyphenyl)propionate (44)

To a deoxygenated solution of 4-methoxycinnamic ester **42** (350 mg, 1.82 mmol) and sodium azide (177 mg, 2.73 mmol) in dry acetonitrile (10 mL), a deoxygenated solution of CAN (2.49 g, 4.5 mmol) in dry acetonitrile

(20 mL) was added dropwise at 0 °C and stirred well. The reaction mixture on completion was worked up as usual. Column chromatography was done on silica gel using hexane-ethyl acetate (95:5) as eluent to afford **43** (83 mg, 20%) as a yellow viscous liquid. Further elution using hexane-ethyl acetate (80:20) afforded **44** (239 mg, 48%, 3:2 mixture of *syn* and *anti* isomers) as a colorless solid.

Product 43[7]

IR (neat) ν_{max} : 2962, 2843, 2125, 1707, 1607, 1520, 1257 cm^{-1}.

^1H NMR : δ 7.77 (d, *J* = 8.8 Hz, 2H, ArH), 6.88 (d, *J* = 8.8 Hz, 2H, ArH), 6.86 (s, 1H, olefinic), 3.88 (s, 3H, OMe), 3.83 (s, 3H, OMe).

^{13}C NMR : δ 164.19, 160.63, 132.50, 126.12, 125.73, 123.23, 114.02, 55.29, 52.72.

GC-MS (*m/z*) : 205 [M^+-N_2] (83), 173 (100), 145 (42).

Product 44

Syn and *anti* isomers were separated by crystallization.

***Syn* isomer**

Colorless crystals (mp 92-94 °C).

IR (KBr) ν_{max} : 3451, 2106, 1720, 1614, 1521, 1240, 1023 cm^{-1}.

^1H NMR : δ 7.28 (d, *J* = 8.6 Hz, 2H, ArH), 6.87 (d, *J* = 8.6 Hz, 2H, ArH), 5.10 (m, 1H, CHOH), 3.96 (d, *J* = 4.6 Hz, 1H, CHN_3), 3.79 (s, 3H, OMe), 3.75 (s, 3H, OMe), 2.71 (brs, 1H, OH, exchangeable with D_2O).

^{13}C NMR : δ 169.06, 159.83, 131.34, 127.58, 114.19, 74.23, 67.89, 55.28, 52.77.

GC-MS (*m/z*) : 221 [M^+-N_2-2] (1), 164 (4), 135 (100), 121 (1), 107 (7), 92 (12), 77 (18), 64 (5), 51 (2).

***Anti* isomer**

Colorless crystals (mp 114-116 °C).

IR (KBr) ν_{max} : 3424, 2112, 1718, 1610, 1513, 1239, 1028 cm^{-1}.

^1H NMR : δ 7.29 (d, *J* = 8.6 Hz, 2H, ArH), 6.89 (d, *J* = 8.6 Hz, 2H, ArH), 4.94 (m, 1H, CHOH), 4.05 (d, *J* = 7.2 Hz, 1H, CHN_3), 3.80 (s, 3H, OMe), 3.79 (s, 3H, OMe), 2.73 (brs, 1H, OH, exchangeable with D_2O).

^{13}C NMR : δ 169.28, 159.87, 131.02, 127.79, 113.97, 73.63, 66.82, 55.06, 52.52.

Ethyl 2-azido-3-(3',4'-dimethoxyphenyl)prop-2-enoate (46) and Ethyl 2-azido-3-hydroxy-(3',4'-dimethoxyphenyl)propionate (47)

To a deoxygenated solution of 3,4-dimethoxycinnamic ester (247 mg, 1.04 mmol) and sodium azide (102 mg, 1.56 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.425 g, 2.6 mmol) in the same solvent (17 mL) was added dropwise at 0 °C and stirred well. On completion of the reaction, the mixture was worked up as usual. Column chromatography on silica gel using hexane-ethyl acetate (90:10) afforded **46** (92 mg, 32%) as yellow crystals. Further elution using hexane-ethyl acetate (80:20) afforded **47** (70 mg, 23%, 2:1 mixture of *syn* and *anti* isomers) as a yellow viscous liquid.

Product 46[6c]

Recrystallized from dichloromethane-hexane mixture (mp 95-97 °C).

IR (KBr) ν_{max} : 2937, 2843, 2119, 1707, 1600, 1513, 1245, 1145 cm^{-1}.

^1H NMR : δ 7.48 (s, 1H, ArH), 7.33-7.29 (m, 1H, ArH), 6.82 (m, 2H, ArH & olefinic), 4.35 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 3.90 (s, 3H, OMe), 3.89 (s, 3H, OMe), 1.39 (t, J = 7.1 Hz, 3H, OCH_2CH_3).

^{13}C NMR : δ 163.65, 150.34, 148.75, 126.42, 125.59, 124.94, 123.56, 113.22, 110.86, 62.06, 55.94, 55.88, 14.39.

Product 47

IR (neat) ν_{max} : 3488, 2940, 2840, 2112, 1738, 1514, 1259, 1023 cm^{-1}.

^1H NMR : δ 6.91-6.80 (m, ArH), 5.08 (d, J = 4.7 Hz, CHOH), 4.92 (d, J = 7.2 Hz, CHOH), 4.25-4.17 (m, OCH_2CH_3), 4.01 (d, J = 7.2 Hz, CHN_3), 3.93 (d, J = 4.7 Hz, CHN_3), 3.86 (s, OMe), 3.85 (s, OMe), 3.02 (brs, OH, exchangeable with D_2O), 1.31-1.21 (m, OCH_2CH_3).

^{13}C NMR : δ 168.94, 168.49, 149.22, 149.03, 131.81, 131.66, 119.15, 118.57, 110.93, 109.55, 109.41, 74.20, 73.76, 67.73, 66.78, 61.95, 55.78, 14.01.

GC-MS (*m/z*) : 265 [M^+-N_2-2] (10), 165 (100), 77 (15).

Ethyl 2-azido-3-naphthyl-3-nitratopropionate (49)

To a deoxygenated solution of **48** (226 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise at 0 °C and stirred well. After completion of the reaction, the mixture was

subjected to usual work-up and purification to afford **49** (220 mg, 67%, 2.5:1 mixture of *syn* and *anti* isomers) as a yellow viscous liquid.

IR (neat) ν_{max} : 2987, 2119, 1744, 1645, 1276 cm^{-1}.

^1H NMR : δ 8.06-7.48 (m, Ar<u>H</u>), 7.07 (d, *J* = 5.4 Hz, C<u>H</u>ONO$_2$), 6.87 (d, *J* = 7.6 Hz, C<u>H</u>ONO$_2$), 4.48 (d, *J* = 7.6 Hz, C<u>H</u>N$_3$), 4.42 (d, *J* = 5.4 Hz, C<u>H</u>N$_3$), 4.28 (q, *J* = 7.1 Hz, OC<u>H</u>$_2$CH$_3$), 4.13 (q, *J* = 7.1 Hz, OC<u>H</u>$_2$CH$_3$), 1.25 (t, *J* = 7.1 Hz, OCH$_2$C<u>H</u>$_3$), 1.10 (t, *J* = 7.1 Hz, OCH$_2$C<u>H</u>$_3$).

^{13}C NMR : δ 166.80, 166.69, 133.89, 130.78, 130.42, 129.92, 129.47, 129.36, 129.29, 128.80, 128.64, 127.44, 127.33, 126.66, 126.36, 126.20, 125.41, 125.25, 125.06, 124.51, 122.54, 121.86, 79.57, 79.33, 64.17, 63.75, 62.80, 14.10, 13.92.

GC-MS (*m/z*) : 239 [M^+-HNO_3-N_2] (70), 193 (100), 165 (70), 139 (56), 113 (5), 83 (8), 69 (12), 63 (7).

2.3.4 CAN mediated addition of azide to benzylidene acetone

2.3.4.1 CAN mediated azidation under deoxygenated atmosphere

A deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise to a deoxygenated solution of benzylidene acetone **56** (146 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL) at 0 °C and stirred well. On completion of the reaction, the mixture was worked up as usual and purified by silica gel column chromatography. Successive elution using hexane-ethyl acetate (98:2) afforded **57** (113 mg, 45%), **58** (60 mg, 32%) and **14** (11 mg, 6%).

3-Azido-4-nitrato-4-phenyl-2-butanone (57)

Yellow oil.

IR (neat) ν_{max} : 3058, 2912, 2110, 1725, 1646, 1275, 844, 698 cm^{-1}.

^1H NMR : δ 7.40 (s, 5H, ArH), 6.16 (d, J = 6.3 Hz, 1H, CHONO$_2$), 4.32 (d, J = 6.3 Hz, 1H, CHN$_3$), 2.15 (s, 3H, CH$_3$).

^{13}C NMR : δ 201.76, 133.96, 130.30, 129.60, 127.25, 82.94, 70.55, 30.08.

3-Azido-4-phenyl-3-buten-2-one (58)

Yellow solid; it was recrystallized from dichloromethane-hexane mixture (mp 76-78 °C).

IR (KBr) ν_{max} : 3063, 2928, 2119, 1676, 1613, 1452, 1364, 1209, 757, 697 cm^{-1}.

^1H NMR : δ 7.43 (d, J = 6.7 Hz, 2H, ArH), 7.31-7.24 (m, 3H, ArH), 6.57 (s, 1H, olefinic), 2.39 (s, 3H, CH$_3$).

^{13}C NMR : δ 193.99, 133.96, 133.22, 130.72, 129.75, 128.57, 126.55, 25.73.

GC-MS (*m/z*) : 159 [M^+-N_2] (7), 117 (100), 103 (2), 90 (15), 77 (3), 63 (5), 51 (2).

Anal. Calcd for $C_{10}H_9N_3O$: C, 64.16; H, 4.85; N, 22.45.

Found : C, 64.12; H, 4.87; N, 22.60.

Phenacyl azide (14)[11]

Yellow viscous liquid.

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

^1H NMR : δ 7.90 (m, 2H, ArH), 7.58-7.49 (m, 3H, ArH), 4.56 (s, 2H, CH$_2$N$_3$).

^{13}C NMR : δ 193.22, 134.46, 129.00, 128.85, 127.95, 54.91.

2.3.4.2 CAN mediated azidation under oxygen atmosphere

To an oxygenated solution of benzylidine acetone (146 mg, 1 mmol) and NaN_3 (98 mg, 1.5 mmol) in acetonitrile (5 mL), an oxygenated solution of CAN (1.370 g, 2.5 mmol) in the same solvent (10 mL) was added dropwise at 0 °C and stirred for 2 h. On completion of the reaction, usual work-up followed by chromatographic purification afforded **58** (30 mg, 16%) and **14** (68 mg, 42%).

2.3.5 CAN mediated addition of azide to cinnamamide

To a deoxygenated solution of cinnamamide (294 mg, 2 mmol) and sodium azide (195 mg, 3 mmol) in dry acetonitrile (10 mL), a deoxygenated solution of CAN (2.741 g, 5 mmol) in dry acetonitrile (20 mL) was added dropwise at 0 °C. After 1 h stirring, the argon bubbling was stopped and the stirring continued overnight at room temperature. On completion of the reaction, the mixture was worked up as usual and the crude product was subjected to column chromatography on silica gel using hexane-ethyl acetate (70:30) to afford **60** (460 mg, 91%, 1:1 mixture of *syn* and *anti* isomers) as a colorless viscous liquid.

IR (KBr) ν_{max} : 3467, 3318, 2119, 1688, 1645, 1276, 839 cm^{-1}.

^{1}H NMR : δ 7.44-7.37 (m, 10H, Ar<u>H</u>), 6.73, 6.60, 6.50, 6.26 (4 brs, 4H, N<u>H</u>, exchangeable with D_2O), 6.39 (m, 2H, C<u>H</u>ONO$_2$), 4.60 (d, J = 4.1 Hz, 1H, C<u>H</u>N$_3$), 4.28 (d, J = 3.9 Hz, 1H, C<u>H</u>N$_3$).

^{13}C NMR : δ 168.39, 168.00, 133.81, 132.27, 129.67, 129.19, 128.64, 127.52, 127.38, 126.30, 83.56, 82.32, 66.93, 65.36.

2.3.6 Synthesis of *β*-azidostyrenes from cinnamic acids

1-Azido-2-phenylethene (61)

To a deoxygenated solution of cinnamic acid (148 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile, a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in the same solvent (10 mL) was added dropwise at 0 °C. After 1 h, the reaction mixture was allowed to attain room temperature and the stirring continued overnight. After completion of the reaction, acetonitrile was evaporated off, diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The organic layer was washed successively with water, saturated brine and dried and concentrated. The crude product was treated with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) and refluxed for 2-3 h. The mixture was worked up as usual and the product purified by silica gel column chromatography using hexane as eluent to afford **61** (89 mg, 61%, 1:1 mixture of *E* and *Z* isomers) as a yellow oil.

IR (neat) ν_{max} : 3088, 3025, 2106, 1633, 1444, 1399, 1256, 925, 685 cm^{-1}.

^{1}H NMR : δ 7.56-7.15 (m, 10H, ArH), 6.58 (d, *J* = 13.7 Hz, 1H, Ph-CH, *E* isomer), 6.33 (d, *J* = 8.4 Hz, 1H, Ph-CH, *Z* isomer), 6.25 (d, *J* = 13.7 Hz, 1H, CHN$_3$, *E* isomer), 5.67 (d, 1H, *J* = 8.4 Hz, CHN$_3$, *Z* isomer).

^{13}C NMR : δ 134.94, 134.45, 128.91, 128.66, 128.18, 127.29, 127.20, 126.59, 127.73, 125.01, 119.77, 117.90.

GC-MS (*m/z*) : 117 [M^+-N_2] (100), 116 (10), 91 (3), 90 (34), 63 (6), 58 (5).

1-Azido-2-(4'-methylphenyl)ethene (62)

To a deoxygenated solution of 4-methylcinnamic acid (162 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in 10 mL dry acetonitrile was added dropwise at 0 °C and stirred overnight. The crude product obtained after usual work-up was refluxed with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone. On completion of the reaction (monitored by TLC), the mixture was worked up and purified as described earlier to afford **62** (103 mg, 65%, 1:1 mixture of *E* and *Z* isomers) as a yellow oil.

IR (neat) ν_{max} : 3056, 2935, 2112, 1634, 1418, 1270, 831 cm^{-1}.

^{1}H NMR : δ 7.45 (d, *J* = 8.0 Hz, 2H, ArH), 7.1 (m, 6H, ArH), 6.52 (d, *J* = 13.7 Hz, 1H, Ph-CH, *E* isomer), 6.26 (d, *J* = 8.4 Hz, 1H, PhCH, *Z* isomer), 6.21 (d, *J* = 13.7 Hz, 1H, CHN$_3$, *E* isomer), 5.63 (d, *J* = 8.4 Hz, 1H, CHN$_3$, *Z* isomer), 2.33 (s, 3H, CH$_3$), 2.32 (s, 3H, CH$_3$).

^{13}C NMR : δ 137.26, 137.17, 132.33, 131.89, 129.56, 129.08, 129.06, 125.81, 124.32, 119.94, 118.10, 21.43, 21.33.

GC-MS (*m/z*) : 131 [M^+-N_2] (68), 119 (30), 116 (55), 104 (35), 91 (100), 77 (18), 65 (20), 51 (16).

1-Azido-2-(3'-methoxyphenyl)ethene (63)

The residue obtained by the reaction of 3-methoxycinnamic acid (178 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) with CAN (1.370 g, 2.5 mmol) in dry acetonitrile (15 mL), as described previously, was refluxed with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL). After completion of the reaction, the mixture was worked up and purified as described earlier to afford **63** (113 mg, 64%, 1:1 mixture of *E* and *Z* isomers) as a yellow oil.

IR (neat) ν_{max} : 3037, 2937, 2837, 2106, 1632, 1595, 1426, 1251, 1151, 1039, 920 cm^{-1}.

^1H NMR : δ 7.23-6.73 (m, 8H, ArH) 6.57 (d, J = 13.7 Hz, 1H, PhCH, *E* isomer), 6.31 (d, J = 8.4 Hz, 1H, PhCH, *Z* isomer), 6.22 (d, J = 13.7 Hz, 1H, CHN_3, *E* isomer), 5.63 (d, J = 8.4 Hz, 1H, CHN_3, *Z* isomer), 3.80 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3).

^{13}C NMR : δ 159.81, 159.37, 136.31, 135.68, 129.62, 129.08, 126.89, 125.26, 121.65, 119.67, 118.32, 117.79, 114.10, 113.07, 112.82, 111.27, 55.01.

GC-MS (*m/z*) : 147 [M^+-N_2] (100), 132 (30), 121 (2), 116 (15), 104 (20), 103 (3), 90 (8), 88 (2), 77 (20), 63 (5), 51 (4).

1-Azido-2-(4'-chlorophenyl)ethene (64)

The residue obtained by the reaction of 4-chlorocinnamic acid (182 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) with CAN (1.370 g, 2.5 mmol) in dry acetonitrile, as described earlier, was refluxed with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL). On completion of

the reaction, the mixture was worked up and purified as described previously to afford **64** (70 mg, 39%, 1:1 mixture of *E* and *Z* isomers) as a yellow oil.

IR (neat) ν_{max} : 3037, 2106, 1632, 1489, 1407, 1270, 1089, 833 cm^{-1}.

^1H NMR : 7.51-7.14 (m, 8H, ArH), 6.58 (d, J = 13.7 Hz, 1H, PhCH, *E* isomer), 6.33 (d, J = 8.4 Hz, 1H, PhCH, Z isomer), 6.18 (d, J = 13.8 Hz, 1H, CHN_3, *E* isomer), 5.59 (d, J = 8.4 Hz, 1H, CHN_3, *Z* isomer).

^{13}C NMR : δ 133.52, 132.99, 132.83, 130.19, 128.90, 128.40, 127.29, 126.90, 125.69, 118.53, 116.58, 113.89.

2.3.7 Synthesis of α-azidocinnamates from cinnamic esters

Methyl 2-azido-3-phenylprop-2-enoate (65)[7]

Methyl cinnamate (162 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) were taken in dry acetonitrile (5 mL) at 0 °C and deoxygenated using argon. After 10 minutes, a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise and the reaction mixture was stirred for 2 h. After completion of the reaction (monitored by TLC), acetonitrile was evaporated off, the mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The combined organic extract was washed sequentially with water and saturated brine. It was then dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude product was treated with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) at room temperature and stirred overnight. After completion of the reaction (monitored by TLC), the mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The organic layer was washed successively with water and saturated brine. It was

then dried over anhydrous sodium sulfate and concentrated. The product was purified by silica gel column chromatography using hexane-ethyl acetate (98:2) as eluent to afford **65** (143 mg, 70%) as a yellow viscous liquid.

IR (neat) ν_{max} : 2956, 2123, 1717, 1617, 1437, 1378, 1262, 770 cm^{-1}.

^1H NMR : δ 7.75 (m, 2H, ArH), 7.35-7.27 (m, 3H, ArH), 6.85 (s, 1H, olefinic), 3.85 (s, 3H, OMe).

^{13}C NMR : δ 163.73, 133.12, 130.55, 129.32, 128.37, 125.42, 125.26, 52.68.

GC-MS (*m/z*) : 175 [M^+-N_2] (75), 143 (95), 131 (15), 116 (100), 89 (40), 59 (15).

Ethyl 2-azido-3-phenylprop-2-enoate (66)[6c]

To a deoxygenated solution of ethyl cinnamate **29** (176 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise at 0 °C and stirred well. The crude product obtained after usual work-up was treated with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) at room temperature. Usual work-up followed by purification afforded **66** (148 mg, 68%) as a pale yellow viscous liquid.

IR (neat) ν_{max} : 2987, 2119, 1707, 1613, 1376, 1251, 1083 cm^{-1}.

^1H NMR : δ 7.79 (m, 2H, ArH), 7.38-7.27 (m, 3H, ArH), 6.88 (s, 1H, olefinic), 4.35 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 1.39 (t, J = 7.1 Hz, 3H, OCH_2CH_3).

^{13}C NMR : δ 163.31, 133.16, 130.51, 129.25, 128.35, 125.51, 125.16, 62.09, 14.18.

Methyl 2-azido-3-(4'-methylphenyl)prop-2-enoate (67)[6c]

A deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise to a deoxygenated solution of methyl 4-methylcinnamate **31** (176 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL) at 0 °C and stirred well. The crude product on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone, followed by usual work-up and chromatographic purification afforded **67** (161 mg, 74%) as a pale yellow solid and it was recrystallized from dichloromethane-hexane mixture (mp 56-58 °C).

IR (KBr) ν_{max} : 2956, 2125, 1713, 1601, 1436, 1322, 1251, 1078, 820 cm^{-1}.

^1H NMR : δ 7.67 (d, J = 8.0 Hz, 2H, Ar<u>H</u>), 7.15 (d, J = 8.0 Hz, 2H, Ar<u>H</u>), 6.85 (s, 1H, olefinic), 3.86 (s, 3H, O<u>Me</u>), 2.35 (s, 3H, <u>Me</u>).

^{13}C NMR : δ 163.96, 139.72, 130.66, 130.45, 129.21, 125.73, 124.38, 52.70, 21.51.

Ethyl 2-azido-3-(4'-chlorophenyl)prop-2-enoate (68)[6c]

A deoxygenated solution of ethyl 4-chlorocinnamate **33** (215 mg, 1.02 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile was treated with a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in the same solvent at 0 °C. The crude product on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone followed by usual work-up and chromatographic purification afforded **68** (171 mg, 67%) as a pale yellow viscous liquid.

IR (neat) ν_{max} : 2987, 2119, 1713, 1613, 1376, 1251, 1083, 1008, 821 cm^{-1}.

^{1}H NMR : δ 7.72 (d, J = 8.4 Hz, 2H, ArH), 7.31 (d, J = 8.4 Hz, 2H, ArH), 6.79 (s, 1H, olefinic), 4.34 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 1.39 (t, J = 7.1 Hz, 3H, OCH_2CH_3).

^{13}C NMR : δ 163.07, 134.97, 131.64, 128.56, 127.26, 125.91, 123.44, 62.22, 14.13.

Ethyl 2-azido-3-(3'-methoxyphenyl)prop-2-enoate (69)[6c]

A deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (5 mL) was added dropwise to a deoxygenated solution of ethyl 3-methoxycinnamate **37** (206 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL) at 0 °C and stirred well. The crude product was treated with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone as described earlier to afford **69** (158 mg, 64%) as a pale yellow solid; it was recrystallised from dichloromethane-hexane mixture (mp 44-46 °C).

IR (KBr) ν_{max} : 2987, 2106, 1710, 1619, 1385, 1300, 1232, 1083, 879, 778 cm^{-1}.

^{1}H NMR : δ 7.40 (s, 1H, ArH), 7.33-7.23 (m, 2H, ArH), 6.86 (m, 1H, ArH), 6.84 (s, 1H, olefinic), 4.35 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 1.39 (t, J = 7.1 Hz, 3H, OCH_2CH_3)

^{13}C NMR : δ 163.40, 159.51, 134.47, 129.37, 125.78, 125.15, 123.46, 115.50, 115.37, 62.25, 55.22, 14.32.

Ethyl 2-azido-3-(2'-methoxyphenyl)prop-2-enoate (70)[6c]

To a deoxygenated solution of ethyl 2-methoxycinnamate **39** (206 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in the same solvent

was added dropwise (10 mL) at 0 °C and stirred well. The crude product was treated with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) at room temperature. On completion of the reaction, the mixture was worked up as usual and purified by silica gel column chromatography using hexane-ethyl acetate (98:2) as eluent to afford **70** (148, 60%) as a yellow semi solid. Further elution using hexane-ethyl acetate (90:10) afforded **41** (33 mg, 12%) as a pale yellow viscous liquid.

Product 70[6c]

IR (CH_2Cl_2) ν_{max} : 2987, 2837, 2119, 1707, 1595, 1457, 1258, 1076, 1020, 752 cm^{-1}.

^1H NMR : δ 8.16 (d, J = 7.6 Hz, 1H, ArH), 7.35 (s, 1H, olefinic), 7.30-7.25 (m, 1H, ArH), 6.96 (m, 1H, ArH), 6.84 (d, J = 8.2 Hz, 1H, ArH), 4.35 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 3.85 (s, 3H, OMe), 1.39 (t, J = 7.1 Hz, 3H, OCH_2CH_3).

^{13}C NMR : δ 163.70, 157.62, 130.75, 125.38, 122.25, 120.44, 119.47, 110.40, 62.09, 55.57, 14.38.

GC-MS (*m/z*) : 219 [M^+-N_2] (40), 204 (2), 173 (100), 158 (12), 144 (10), 130 (7), 119 (7), 116 (5), 102 (5), 89 (3), 76 (4), 63 (5).

Ethyl 2-azido-3-(1'-naphthyl)prop-2-enoate (71)

A deoxygenated solution of ester **48** (226 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile was treated with a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in the same solvent (10 mL) at 0 °C. On completion of the reaction, the mixture was worked up and concentrated.

The crude product on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) followed by usual work-up and purification afforded **71** (171 mg, 64%) as a yellow viscous liquid.

IR (neat) ν_{max} : 3055, 2987, 2119, 1707, 1607, 1507, 1239, 1070, 771 cm^{-1}.

^1H NMR : δ 8.08 (d, J = 7.3 Hz, 1H, ArH), 8.01 (d, 1H, J = 7.7 Hz, ArH), 7.83-7.79 (m, 2H, ArH), 7.64 (s, 1H, olefinic), 7.57-7.45 (m, 3H, ArH), 4.41 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 1.44 (t, J = 7.1 Hz, 3H, OCH_2CH_3).

^{13}C NMR : δ 166.19, 133.49, 131.61, 129.59, 128.34, 128.15, 126.53, 126.03, 125.09, 123.40, 123.23, 120.98, 113.17, 62.21, 14.22.

GC-MS (*m/z*) : 239 [M^+-N_2] (95), 224 (1), 211 (3), 193 (100), 165 (85), 153 (2), 139 (80), 113 (5), 97 (2), 89 (4), 69 (5), 51 (2).

2.3.8 Synthesis of α-azido-α,β-unsaturated ketones from α,β-unsaturated ketones

3-Azido-4-phenyl-3-buten-2-one (58)

To a deoxygenated solution of benzylidene acetone **56** (146 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in the same solvent (10 mL) was added dropwise at 0 °C and stirred for 1-2 h. On completion of the reaction, acetonitrile was evaporated off, the mixture diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The combined organic extract was sequentially washed with water and saturated brine,

dried over anhydrous sodium sulfate and concentrated. The crude product was dissolved in dry acetone (5 mL) and stirred with anhydrous sodium acetate (123 mg, 1.5 mmol) at room temperature for 1 h. After completion of the reaction, the mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The organic layer was washed with water, then with saturated brine, dried over anhydrous sodium sulfate and evaporated. The crude product was purified by silica gel column chromatography using a mixture of hexane-ethyl acetate (95:5) as eluent to afford **58** (123 mg, 65%) as yellow crystals. It was recrystallized from dichloromethane-hexane mixture (mp 76-78 °C).

3-Azido-4-*(*4'-methylphenyl*)*-3-buten-2-one (73)

To a deoxygenated solution of 4'-methylbenzylidene acetone **72** (160 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise at 0 °C and stirred well. The crude product on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) followed by usual work-up and purification afforded **73** (132 mg, 66 %) as a yellow solid. It was recrystallised from dichloromethane-hexane mixture (mp 57-59 °C).

IR (KBr) ν_{max} : 3055, 2918, 2113, 1660, 1320, 1239, 1176, 802, 683 cm^{-1}.

^1H NMR : δ 7.72 (d, *J* = 8.1 Hz, 2H, Ar<u>H</u>), 7.17 (d, *J* = 8.0 Hz, 2H, Ar<u>H</u>), 6.64 (s, 1H, olefinic), 2.46 (s, 3H, $COC\underline{H}_3$), 2.34 (s, 3H, $ArC\underline{H}_3$).

^{13}C NMR : δ 193.90, 140.09, 133.10, 130.69, 130.40, 129.26, 126.80, 25.62, 21.49.

3-Azido-4-(3'-methoxyphenyl)-3-buten-2-one (75)

The residue obtained by the reaction of 3'-methoxybenzylidene acetone **74** (176 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) with CAN (1.370 g, 2.5 mmol) in dry acetonitrile, as described earlier, was treated with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) and stirred for 2 h. After completion of the reaction, the mixture was worked up and purified as described previously to afford **75** (164 mg, 76%) as a yellow viscous liquid.

IR (neat) ν_{max} : 2937, 2837, 2119, 1682, 1610, 1574, 1435, 1384, 1348, 1300, 1223, 1041, 685 cm^{-1}.

^1H NMR : δ 7.43 (s, 1H, Ar<u>H</u>), 7.34-7.24 (m, 2H, Ar<u>H</u>), 6.87 (m, 1H, Ar<u>H</u>), 6.62 (s, 1H, olefinic), 3.82 (s, 3H, OC<u>H</u>$_3$), 2.48 (s, 3H, COC<u>H</u>$_3$).

^{13}C NMR : δ 193.77, 159.41, 134.27, 133.97, 129.29, 126.23, 123.37, 115.52, 115.44, 55.04, 25.60.

GC-MS (*m/z*) : 189 [M^+-N_2] (18), 174 (2), 147 (100), 146 (10), 132 (6), 116 (5), 107 (2), 103 (6), 89 (6), 76 (6), 62 (2), 51 (2).

3-Azido-4-(4'-chlorophenyl)-3-buten-2-one (77)

A deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise to a deoxygenated solution of 4'-chlorobenzylidene acetone **76** (180 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL) at 0 °C and stirred well. The reaction mixture on completion of the reaction was worked up and concentrated. The crude product on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone (5 mL) followed by usual work-

up and purification afforded **77** (133 mg, 60%) as a yellow solid. It was recrystallized from dichloromethane-hexane mixture (mp 106-108 °C).

IR (KBr) ν_{max} : 3068, 3006, 2110, 1668, 1606, 1585, 1484, 1318, 1088, 869, 685 cm^{-1}.

^1H NMR : δ 7.77 (d, J = 8.4 Hz, 2H, Ar<u>H</u>), 7.34 (d, J = 8.4 Hz, 2H, Ar<u>H</u>), 6.61 (s, 1H, olefinic), 2.49 (s, 3H, $COC\underline{H}_3$).

^{13}C NMR : δ 193.70, 135.44, 134.28, 131.74, 131.59, 128.71, 124.72, 25.61.

2-Azido-1,3-diphenyl-2-propen-1-one (79)

To a deoxygenated solution of chalcone **78** (208 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL), a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in dry acetonitrile (10 mL) was added dropwise at 0 °C and stirred well. The crude product on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone followed by the usual work-up afforded **79** (178 mg, 72%) as a yellow viscous liquid.

IR (neat) ν_{max} : 3070, 2112, 1654, 1607, 1445, 1384, 1263, 690 cm^{-1}.

^1H NMR : δ 7.79-7.24 (m, 10H, Ar<u>H</u>), 6.43 (s, 1H, olefinic).

^{13}C NMR : δ 192.10, 136.95, 133.82, 133.32, 132.72, 130.78, 129.79, 129.74, 128.64, 128.59.

GC-MS (*m/z*) : 221 [M^+-N_2] (6), 190 (2), 177 (1), 165 (3), 143 (2), 139 (1), 105 (100), 103 (1), 89 (4), 77 (30), 63 (2), 51 (6).

2-Azido-3-(4'-chlorophenyl)-1-phenyl-2-propen-1-one (81)

A deoxygenated solution of chalcone **80** (242 mg, 1 mmol) and sodium azide (98 mg, 1.5 mmol) in dry acetonitrile (5 mL) was treated with a deoxygenated solution of CAN (1.370 g, 2.5 mmol) in 10 mL dry

acetonitrile at 0 °C. The crude product on treatment with anhydrous sodium acetate (123 mg, 1.5 mmol) in dry acetone followed by the usual work-up afforded **81** (189 mg, 67%) as a yellow viscous liquid.

IR (neat) ν_{max} : 3070, 2119, 1661, 1600, 1371, 1270, 1115, 710 cm^{-1}.

^1H NMR : δ 7.83-7.25 (m, 9H, ArH), 6.36 (s, 1H, olefinic).

^{13}C NMR : δ 191.63, 136.56, 135.39, 134.07, 132.64, 131.71, 131.60, 129.52, 128.70, 128.45, 127.68.

2,4-Diazido-1,5-diphenyl-1,4-pentadien-3-one (83)

A deoxygenated solution of dibenzylidene acetone **82** (234 mg, 1 mmol) and sodium azide (195 mg, 3 mmol) in dry acetonitrile (5 mL) was treated with a deoxygenated solution of CAN (2.741 g, 5 mmol) in dry acetonitrile (20 mL) at 0 °C. The crude product on treatment with anhydrous sodium acetate (246 mg, 3 mmol) in dry acetone (5 mL) followed by the usual work-up and purification afforded **83** (94 mg, 30%) as a yellow viscous liquid.

IR (neat) ν_{max} : 3055, 2113, 1626, 1603, 1370, 1262, 1157, 920, 760 cm^{-1}.

^1H NMR : δ 7.83 (m, 4H, ArH), 7.38 (m, 6H, ArH), 6.62 (s, 2H, olefinic).

^{13}C NMR : δ 186.44, 132.76, 130.77, 129.91, 128.99, 128.58, 128.32.

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CHAPTER 3

CERIUM(IV) AMMONIUM NITRATE MEDIATED THIOCYANATION OF ARENES AND DIENES

3.1 Introduction

In view of the potential transformations of the thiocyanato group into various sulfur functional groups[1] and the applications of thiocyanates in the synthesis of sulfur containing heterocycles,[2-5] the direct thiocyanation of organic compounds has attracted the attention of synthetic organic chemists. The thiocyanato group undergoes a variety of reactions due to its ability to react either as a pseudohalide group or as a sulfenyl cyanide group. Among the thiocyanates, α-thiocyanato ketones and aldehydes are recognized as favorite precursors of thiazoles,[6] some of which have recently drawn attention as herbicides or other important biologically active compounds.[7]

3.2 General Methods for the Preparation of Thiocyanates

The various methods for the preparation of thiocyanates include the use of thiocyanic acid or its salts, reaction with thiocyanogen, cyanation of organo-sulfur compounds and the reactions that involve the use of different one-electron oxidants. These methods are briefly discussed in this section.

3.2.1 Preparation of thiocyanates by the reaction of isothiocyanic acid or its salts with organic compounds

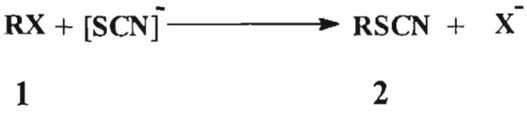
The thiocyanate anion is an ambident nucleophile due to the following resonance (Figure 1).

$$\bar{S}-C\equiv N \longleftrightarrow S=C=\bar{N}$$

Figure 1

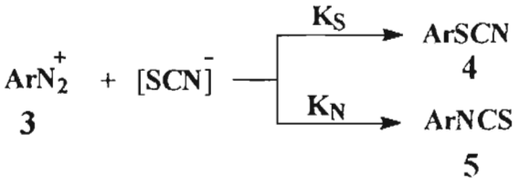
Consequently, kinetically controlled reaction of the thiocyanate anion with organic compounds may lead to thiocyanate *via* nucleophilic attack by the sulfur atom, isothiocyanates *via* nucleophilic attack by the nitrogen atom, or mixtures of both.

The archetypal method of preparing alkyl or arylalkyl thiocyanates and the one on which most mechanistic studies have been made, is the reaction of the corresponding halide with metal thiocyanate in suitable solvents (Scheme 1).[8-10] The only by-product of this reaction is the corresponding isothiocyanate.



Scheme 1

Reaction of metal thiocyanates with diazotized primary aromatic amines[10,11] is the traditional method of preparing aryl and heteroaromatic thiocyanates; the corresponding isothiocyanate may also be formed in a competing kinetically controlled reaction (Scheme 2). Catalysts like cuprous thiocyanate increase the K_s/K_N ratio due to the formation of *N*-bonded complexes like $K_3Cu(NCS)_4$ which would react preferentially *via* sterically favorable sulfur atom to give the thiocyanate.



Scheme 2

Thiocyanate anion readily attacks epoxides, opening the ring in an S_N2 reaction and giving vicinal thiocyanato alkoxides (Scheme 3).[12]

Scheme 3

3.2.2 Preparation of thiocyanates by the reaction of thiocyanogen or related reagents with organic compounds

Thiocyanogen, $(SCN)_2$ and the thiocyanogen halides (XSCN; X= Cl, Br and I respectively) are pseudohalogen analogues of the halogens and interhalogens respectively. Thiocyanogen reacts with aromatic compounds that are highly susceptible to electrophilic substitution with the formation of aryl thiocyanates. Anthracene,[13] azulene,[14] pyrrole[15] and indole[16] afforded thiocyanates **8-11** respectively on reaction with thiocyanogen (Figure 2).

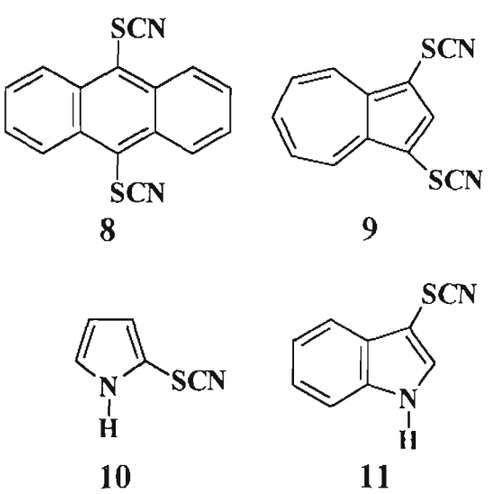
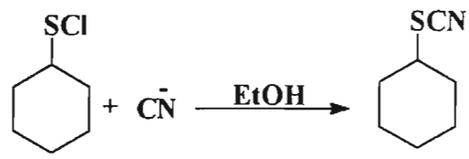


Figure 2

Under heterolytic conditions, thiocyanogen chloride is a stronger electrophilic reagent than thiocyanogen. It reacts readily with aryl ethers, naphthalene and alkyl benzenes containing two or more alkyl groups[17,18] which are unreactive towards thiocyanogen to afford the corresponding thiocyanated products.

3.2.3 Preparation of thiocyanates by cyanation of organosulfur compounds

The most common cyanating agents are cyanide ion and cyanogen halides. Cyanide ion reacts with organo-sulfur compounds containing stable leaving groups leading to the formation of thiocyanates by nucleophilic displacement on sulfur as illustrated in the case of sulfenyl chloride (Scheme 4).[19]

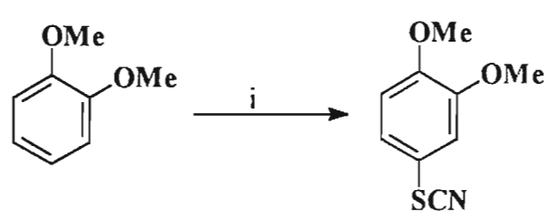


12 **13**

Scheme 4

3.2.4 Preparation of thiocyanates by miscellaneous methods

Kita *et al.* have reported a direct thiocyanation of phenol ethers and related compounds using phenyliodine(III) bis(trifluoroacetate) (PIFA).[20] The reaction proceeds smoothly in 1,1,1,3,3,3-hexafluoro-2-propanol (HFP), a poorly nucleophilic and polar solvent. An illustrative example is given in Scheme 5.

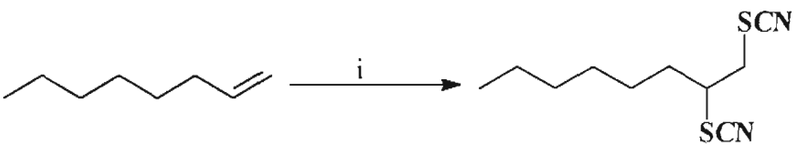


14 **15**

i. TMSNCS, PIFA, HFP, RT, 95%

Scheme 5

Recently, dithiocyanation of alkenes using a reagent combination of bis(acetoxy)iodobenzene (BAIB)/trimethylsilyl isothiocyanate (TMSNCS) in dichloromethane has been reported (Scheme 6).[21]

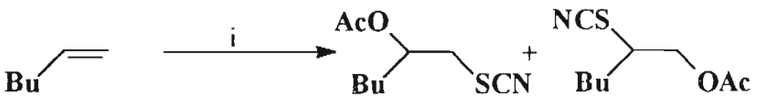


16 **17**

i. BAIB, TMSNCS, CH_2Cl_2, RT, 80%

Scheme 6

Acetoxy thiocyanation of alkenes mediated by BAIB in $(CF_3)_2CHOH$ has been reported by the same group (Scheme 7).[22]

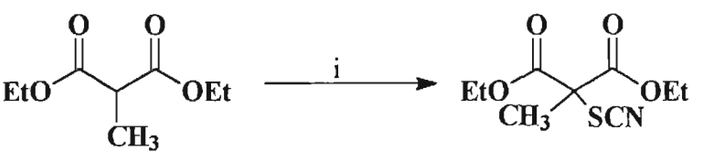


18 **19** **20**

i. BAIB, KSCN, HFP, RT, 90% (83:17)

Scheme 7

α-Thiocyanation of 1,3-dicarbonyl compounds was achieved in a one-pot reaction using $CuBr_2/Al_2O_3$-KSCN/SiO_2 supported reagent system as illustrated in Scheme 8.[23]

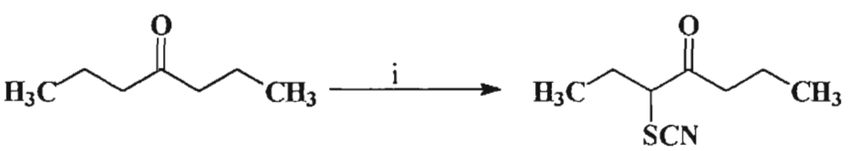


21 **22**

i. $CuBr_2/Al_2O_3$-KSCN/SiO_2, 50 °C, 18 h, benzene, 83%

Scheme 8

Tanabe *et al.* reported the formation of α-thiocyanato ketones and aldehydes using TMSNCS and sufuryl chloride (Scheme 9).[24]

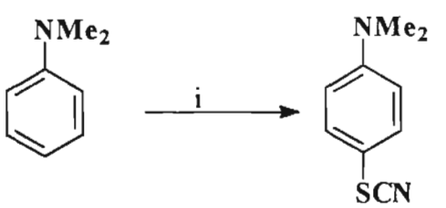


23 **24**

i. TMSNCS, SO_2Cl_2, CH_3CN, RT, 80%

Scheme 9

Still has reported the thiocyanation of aromatic compounds using *N*-thiocyanatosuccinimide (NTS), the latter being generated *in situ* from NBS and NaSCN.[25] An example is provided by the reaction of *N,N*-dimethylaniline with NTS in dry methanol leading to the formation of *N,N*-dimethyl-4-thiocyanatoaniline **26** in 99% yield (Scheme 10).



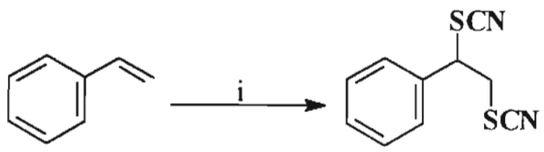
25 **26**

i. NBS, NaSCN, MeOH, 99%

Scheme 10

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

Recently, investigations in our own laboratory have shown that Cerium(IV) ammonium nitrate mediates a facile addition of thiocyanate to styrenes resulting in dithiocyanates (Scheme 11).[26]

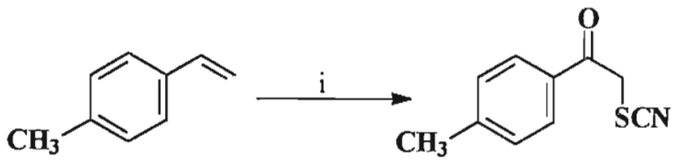


27 **28**

i. NH_4SCN, CAN, CH_3CN, RT, 15 min, 95%

Scheme 11

When the above reaction was carried out in oxygen atmosphere in methanol, the phenacyl thiocyanate was the major product isolated (Scheme 12).[27]



29 **30**

i. NH_4SCN, CAN, MeOH, 0 °C, O_2, 30 min, 70%

Scheme 12

As a logical extension of this work and in view of the versatility of thiocyanato group in heterocyclic constructions, it was of interest to probe the thiocyanation of arenes and dienes. A detailed and systematic study was carried out and the results are presented in the following section.

3.3 Results and Discussion

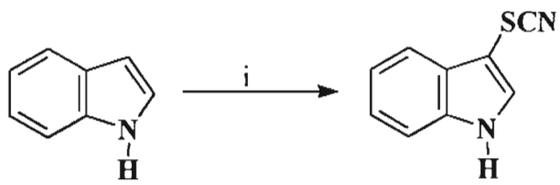
This section is divided mainly into two parts. First part deals with the thiocyanation of arenes and the second part describes the thiocyanation of dienes.

3.3.1 CAN mediated thiocyanation of arenes

It was evident from the literature survey that no work on thiocyanation of arenes using CAN has been reported. We have therefore undertaken a detailed investigation in this area with a view to determine the scope and limitations of the method using NH_4SCN/CAN reagent combination in methanol. The types of aromatic compounds selected for our study are indole, pyrrole, thiophene, aniline and alkoxy benzene.

3.3.1.1 Thiocyanation of indoles mediated by CAN

Our initial work involved the reaction of indole with NH_4SCN and CAN in methanol at room temperature, which led to the formation of 3-thiocyanatoindole **11** in quantitative yield as colorless crystals (Scheme 13).[28]



31 **11**

i. NH_4SCN, CAN, MeOH, RT, 15 min, 100%

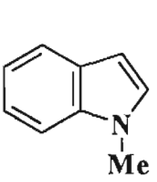
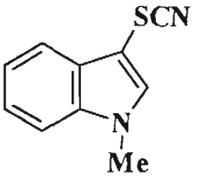
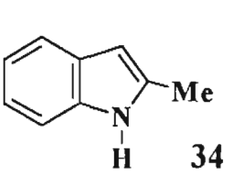
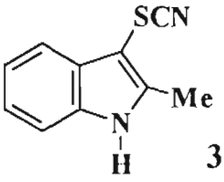
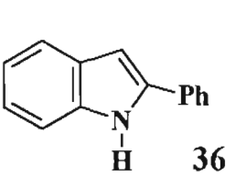
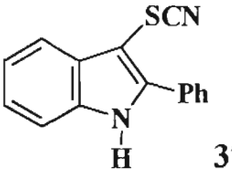
Scheme 13

The structure of the product **11** was assigned on the basis of spectral data. The IR spectrum of **11** showed strong absorptions at 2160 cm^{-1} and 3339 cm^{-1} indicating the presence of -SCN and -NH moieties respectively. In the ^1H NMR spectrum a broad singlet observed at δ 8.65 was attributed to -NH proton. This was further confirmed by exchange with D_2O. The aromatic protons resonated as two separate multiplets in the region

δ 7.82-7.79 and 7.52-7.30. In the ^{13}C NMR spectrum, the -SCN carbon was visible at δ 112.47 and the carbon bearing thiocyanato group at δ 91.27. All other signals were in good agreement with the assigned structure. The identity of the compound was further confirmed by comparing its melting point with that reported in the literature.[16]

The reaction of 1-methylindole, 2-methylindole and 2-phenylindole proceeded in a similar fashion affording 3-thiocyanated products **33**, **35** and **37** respectively in excellent yields (Table 1).

Table 1: Thiocyanation of indoles

Entry	Substrate	Product	Yield (%)*
1	 **32**	 **33**	99
2	 **34**	 **35**	84
3	 **36**	 **37**	86

Reaction conditions: NH_4SCN, CAN, MeOH, RT, 15 min.

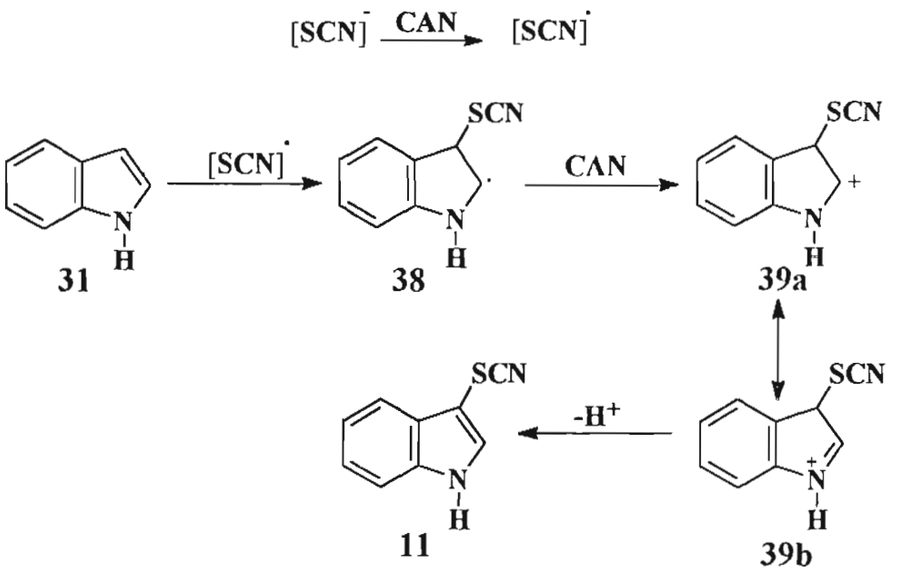
* Isolated yield

The structure of the product **33** was ascertained from the spectral data. The IR spectrum of **33** showed a sharp peak at 2150 cm^{-1}, which is characteristic of -SCN absorption. In the ^1H NMR spectrum, the aromatic

protons resonated as two multiplets in the region δ 7.78-7.76 and δ 7.34-7.29. The methyl protons appeared as a singlet at δ 3.75. In the ^{13}C NMR spectrum, the -SCN carbon was discernible at δ 111.88. The mass spectrum displayed a molecular ion peak at *m/z* 188. All other signals were in agreement with the assigned structure.

The products **35** and **37** were also characterized on the basis of spectral data, which confirmed the assigned structures.

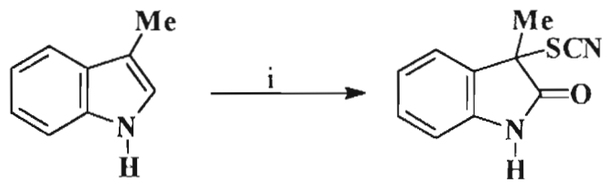
Mechanistically this reaction can be rationalized along the following lines (Scheme 14). Oxidation of thiocyanate anion by CAN would conceivably lead to the thiocyanate radical. This can add to indole forming the radical **38**, which then undergoes further oxidation to form the resonance stabilized cation **39**. The latter can easily lose a proton to form the 3-thiocyanatoindole **11**.



Scheme 14

In all the cases mentioned above, as expected, thiocyanation occurred at 3-position. In order to see the effect of a 3-substitution, we studied the

reaction of 3-methyl indole **40**. However, **40** reacted very sluggishly to afford 2-oxo-3-thiocyanatoindole **41** as the only isolable product in very low yield along with some unreacted starting material (Scheme 15).



40 **41**

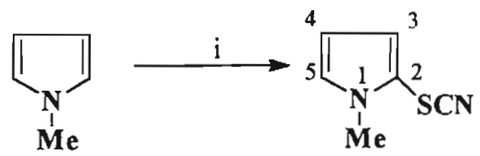
i. NH_4SCN, CAN, MeOH, RT, overnight, 22%

Scheme 15

The structure of the product **41** was assigned on the basis of spectral data. The IR spectrum showed absorptions due to -NH, -SCN and carbonyl groups at 3258, 2166 and 1728 cm^{-1} respectively. In the ^1H NMR spectrum, the -NH proton resonated as a broad singlet at δ 9.95 (exchangeable with D_2O) and the aromatic protons resonated as a multiplet at δ 7.40-6.94. The ^{13}C NMR spectrum showed the carbonyl and -SCN carbons at δ 176.48 and 110.05 respectively.

3.3.1.2 Thiocyanation of pyrroles mediated by CAN

Encouraged by the facile reaction observed in the case of indoles, we turned our attention to pyrroles also. The reaction of *N*-methylpyrrole with NH_4SCN and CAN in methanol afforded the thiocyanated product **43** in very good yield (Scheme 16).



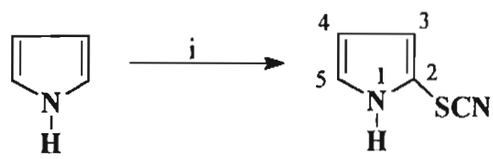
42 **43**

i. NH_4SCN, CAN, MeOH, RT, 15 min, 84%

Scheme 16

The structure of the product **43** was assigned on the basis of spectral data. The IR spectrum showed -SCN absorption at 2156 cm^{-1}. The C-2 position of -SCN was discernible from the coupling constants of the aromatic protons.[29] The C-5 proton resonated as a multiplet centered at δ 6.92. The C-3 and C-4 protons resonated as double doublets at δ 6.63 (J = 3.8, 1.7 Hz) and 6.19 (J = 3.8, 2.9 Hz) respectively. In the ^{13}C NMR spectrum, the -SCN carbon resonated at δ 109.75. All other signals were in agreement with the assigned structure. The molecular ion peak at *m/z* 138 also supported this structure.

Pyrrole also underwent a similar reaction affording 2-thiocyanatopyrole **10** (Scheme 17). In this case a trace amount of 2,5-dithiocyanated product was also observed.



44 **10**

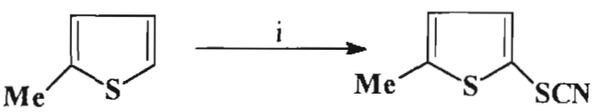
i. NH_4SCN, CAN, MeOH, RT, 15 min, 88%

Scheme 17

The structure of **10** was assigned by comparing its spectral data with those of the authentic sample reported in the literature.[15] The IR spectrum showed two strong bands at 3339 cm^{-1} and 2153 cm^{-1} corresponding to -NH and -SCN absorptions respectively. The mass spectrum displayed molecular ion peak at *m/z* 124.

3.3.1.3 Thiocyanation of thiophenes mediated by CAN

In view of the very good results obtained with pyrrole, it was of interest to study the reaction of another heteroarene *viz.* thiophene. However, the reaction of 2-methylthiophene under similar experimental conditions afforded the thiocyanated product **46** in very low yield (Scheme 18).



45 **46**

i. NH_4SCN, CAN, MeOH, RT, 20 min, 15%

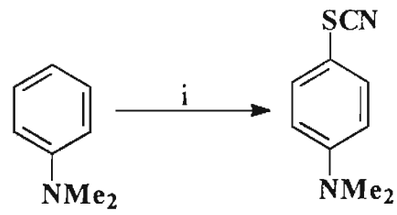
Scheme 18

The structure of **46** was assigned on the basis of spectral data. The IR spectrum showed the -SCN absorption at 2160 cm^{-1}. In the ^1H NMR spectrum, the aromatic protons resonated as separate doublets at δ 7.22 (J = 3.5 Hz) and 6.73 (J = 3.5 Hz). The methyl protons resonated as a singlet at δ 2.52. In the ^{13}C NMR spectrum, the -SCN carbon resonated at δ 110.18. All other signals were also in agreement with the assigned structure.

Thiophene also afforded 2-thiocyanated product in extremely low yield. The poor results obtained in these two cases precluded further investigation in the thiophene series.

3.3.1.4 Thiocyanation of aromatic amines mediated by CAN

Prompted by the facility with which indoles and pyrroles underwent thiocyanation reaction, it was decided to probe the thiocyanation of anilines under similar reaction conditions. Our initial experiment was with *N,N*-dimethylaniline which on treatment with NH_4SCN and CAN in methanol afforded the *p*-thiocyanated product **26** in 75% yield (Scheme 19).



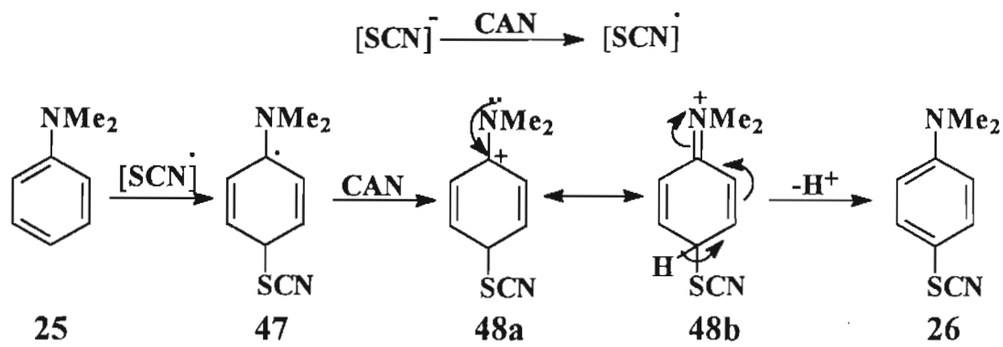
25 **26**

i. NH_4SCN, CAN, MeOH, RT, 30 min, 75%

Scheme 19

As usual, the structure of the product **26**[25] was established by the spectral data. In the IR spectrum of **26**, the -SCN absorption was observed at 2146 cm^{-1}. In the ^1H NMR spectrum, the two doublets at δ 7.42 (J = 8.8 Hz) and 6.68 (J = 8.8 Hz) were attributed to the aromatic protons. The protons of the two methyl groups resonated as a singlet at δ 2.99 integrating for 6 protons. In the ^{13}C NMR spectrum, the -SCN carbon resonated at δ 112.57. All other signals were in agreement with the assigned structure. The mass spectrum displayed the molecular ion peak at *m/z* 178.

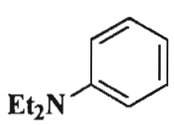
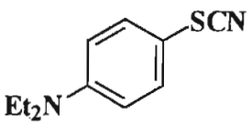
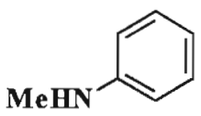
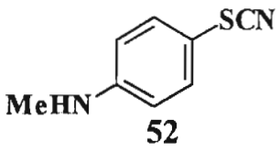
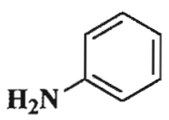
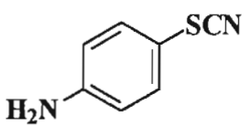
The mechanistic rationalization for the formation of **26** from *N,N*-dimethylaniline may be given as in Scheme 20.



Scheme 20

N,N-Diethylaniline, *N*-methylaniline and aniline also afforded *p*-thiocyanated products **50**, **52** and **54** respectively under similar reaction conditions (Table 2).

Table 2: Thiocyanation of anilines

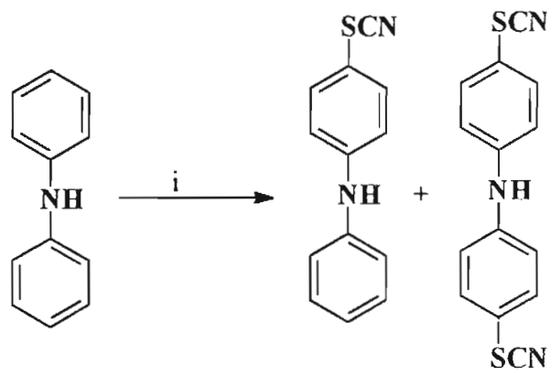
Entry	Substrate	Product	Yield (%)*
1	 **49**	 **50**	68
2	 **51**	 **52**	44
3	 **53**	 **54**	38

Reaction conditions: NH_4SCN, CAN, MeOH, RT, 30 min.

* Isolated yield

The structures of the products **50**,[30] **52**[30] and **54**[31] were assigned on the basis of spectral data.

Diphenylamine on reaction with NH_4SCN and CAN afforded the monothiocyanated product **56** in 32% yield along with 6% of dithiocyanated product **57**[32] (Scheme 21).



55 **56** (32%) **57** (6%)

i. NH_4SCN, CAN, MeOH, RT, 30 min

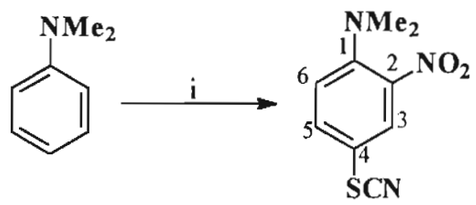
Scheme 21

IR spectrum of **56** showed the -SCN absorption at 2166 cm^{-1} and the absorption due to -NH at 3366 cm^{-1}. In the ^1H NMR spectrum, aromatic protons resonated as a multiplet between δ 7.35-6.93 integrating for nine protons. A broad singlet observed at δ 5.95 (exchangeable with D_2O) was attributed to -NH proton. In the ^{13}C NMR spectrum, the -SCN carbon was discernible at δ 111.83. The mass spectrum displayed the molecular ion peak at *m/z* 226. All other signals were in agreement with the assigned structure.

The IR spectrum of **57** showed -SCN and -NH absorptions at 2150 cm^{-1} and 3370 cm^{-1} respectively. In the ^1H NMR spectrum, the aromatic protons resonated as two doublets at δ 7.48 (J = 8.6 Hz, 4H) and 7.11 (J = 8.6 Hz, 4H). The -NH proton appeared as a broad singlet at δ 6.15 (exchangeable with D_2O). In the ^{13}C NMR spectrum, the -SCN carbon was

discernible at δ 110.92. All other signals were in agreement with the assigned structure.

In order to assess the effect of solvent on the thiocyanation reaction, we studied the reaction of **25** in acetonitrile. Interestingly this reaction afforded the 2-nitro-4-thiocyanato-*N,N*-dimethylaniline **58** as the only isolable product in moderate yield (Scheme 22).



25 **58**

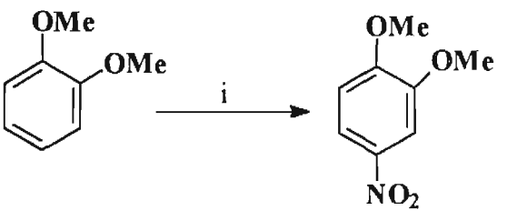
i. NH_4SCN, CAN, CH_3CN, RT, 30 min, 43%

Scheme 22

The IR spectrum of **58** showed the absorption due to -SCN moiety at 2153 cm^{-1}. Two bands in the region 1526 and 1351 cm^{-1} were diagnostic for the presence of NO_2 group. In the ^1H NMR spectrum, a doublet observed at δ 8.02 (J = 2.2 Hz) was attributed to C-3 proton. The proton attached to C-5 resonated as a double doublet at δ 7.58 (J = 9.0, 2.2 Hz). The C-6 proton was observed as a doublet at δ 7.05 (J = 9.0 Hz). The methyl protons resonated as a singlet at δ 2.96. In the ^{13}C NMR spectrum, the -SCN carbon was discernible at δ 110.32. GC-MS displayed the molecular ion peak at *m/z* 223.

After having studied the thiocyanation reaction of anilines, we turned our attention to alkoxybenzenes. However in these cases, we could not isolate any thiocyanated product. For example, when 1,2-dimethoxybenzene was treated with NH_4SCN and CAN in methanol, the only product isolated

was the corresponding 4-nitro compound **59** in low yield (Scheme 23) along with some unreacted starting material.



14 **59**

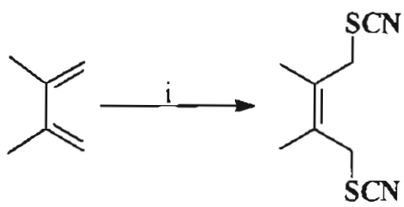
i. NH_4SCN, CAN, MeOH, RT, overnight, 15%

Scheme 23

The structure of **59** was established on the basis of spectral data. The IR spectrum of **59** showed two strong bands at 1507 and 1345 cm^{-1} which are attributed to the $-NO_2$ absorption. The mass spectrum displayed the molecular ion peak at *m/z* 183. All other signals were in agreement with the assigned structure.

3.3.2 CAN mediated thiocyanation of dienes

Subsequent to the investigations on the thiocyanation of arenes, a study of the reaction of various 1,3-dienes with ammonium thiocyanate and CAN was undertaken; the initial experiment was conducted with 2,3-dimethylbutadiene which afforded the 1,4-dithiocyanate **61** as the only isolable product (Scheme 24).



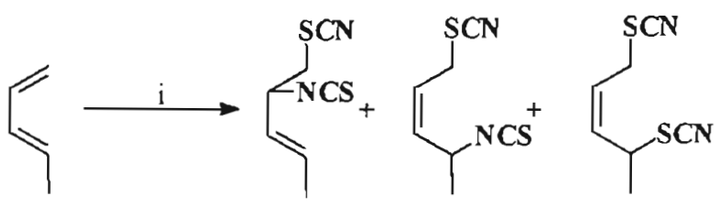
60 **61**

i. NH_4SCN, CAN, CH_3CN, 0 °C, 30 min, 44%

Scheme 24

The product **61** was characterized by the usual spectroscopic methods. The IR spectrum of the product showed a sharp peak at 2160 cm^{-1}, which is attributed to the presence of -SCN group. In the ^1H NMR spectrum, methylene protons and methyl protons resonated as separate singlets at δ 3.72 and 1.98 respectively. In the ^{13}C NMR spectrum, the -SCN carbon was discernible at δ 111.29. HRMS with molecular ion peak at 198.0281 is also in accordance with the proposed structure.

1,3-Pentadiene under similar reaction conditions afforded three products **63-65** (Scheme 25).



62 **63** (14%) **64** (15%) **65** (35%)

i. NH_4SCN, CAN, CH_3CN, 0 °C, 30 min.

Scheme 25

The products were characterized by the usual spectroscopic methods. The IR spectrum of **63** showed a sharp peak at 2160 cm^{-1}, which is characteristic of the thiocyanate group. The absorption due to -NCS was

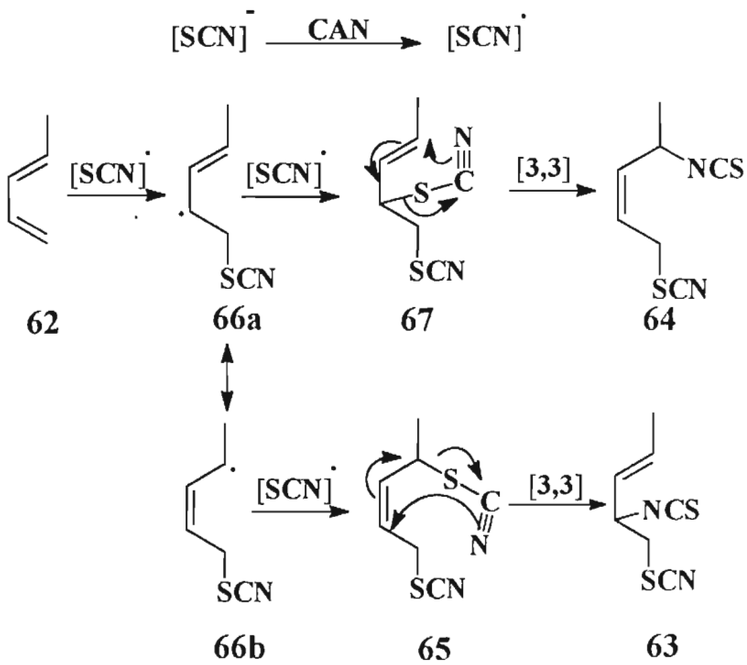
visible as a broad band in the region 2058 cm^{-1}. In the ^{1}H NMR spectrum, -C<u>H</u>NCS proton resonated as a multiplet centered at δ 4.45, whereas the -C<u>H_2</u>SCN protons appeared as a multiplet in the region δ 3.15-2.99. The C<u>H_3</u> protons resonated as a doublet at δ 1.73 (J = 6.3 Hz). In the ^{13}C NMR spectrum, the -NCS carbon was discernible at δ 132.15 and the -SCN carbon at δ 110.65.

The IR spectrum of **64** showed -SCN absorption at 2160 cm^{-1} and -NCS absorption at 2052 cm^{-1}. The olefinic protons resonated as a multiplet in the region δ 5.94-5.77. The -C<u>H_2</u>SCN protons appeared as a doublet at δ 3.56 (J = 5.8 Hz) and the proton geminal to -NCS at δ 4.45-4.42 as a multiplet. The methyl protons resonated as a doublet at δ 1.52 (J = 6.8 Hz). In the ^{13}C NMR spectrum, -NCS and -SCN carbons resonated at δ 133.37 and 110.68 respectively. All other signals were in agreement with the assigned structure. As expected the mass spectrum displayed the molecular ion peak at *m/z* 184.

In the case of **65**, the SCN absorption was observed as a sharp peak at 2166 cm^{-1} in the IR spectrum. The -C<u>H</u>SCN and C<u>H_2</u>SCN protons were visible as two multiplets centered at δ 3.94 and 3.54 respectively. The CH_3 protons resonated as a doublet at δ 1.55 (J = 6.8 Hz). In the ^{13}C NMR spectrum, the -SCN carbons were discernible at δ 110.34 and 110.09.

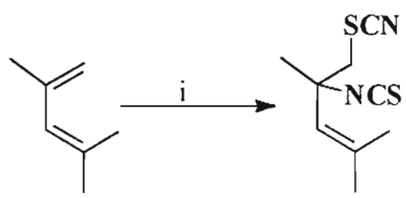
A mechanistic rationalization for the results obtained is given in Scheme 26. In the first step, the thiocyanate anion undergoes oxidation by CAN to thiocyanate radical and the latter on addition to diene gives rise to radical **66a**. This is then quenched by another thiocyanate radical to form 1,2-dithiocyanate **67** and the latter can conceivably undergo a [3,3] sigmatropic rearrangement to form the thermodynamically stable

isothiocyanato-thiocyanate **64**. The radical **66a** which is in resonance with **66b** can undergo an alternative mode of reaction with SCN radical to form 1,4-dithiocyanate **65** which in turn undergoes [3,3] sigmatropic rearrangement to form **63**.



Scheme 26

In a similar reaction, 2,4-dimethylpentadiene on treatment with NH_4SCN and CAN afforded **69** as the only isolable product (Scheme 27).



68 **69**

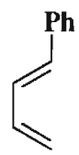
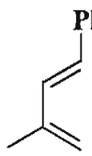
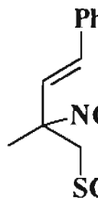
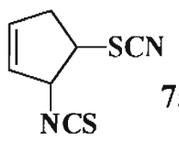
i. NH_4SCN, CAN, CH_3CN, 0 °C, 30 min, 50%

Scheme 27

As usual the product **69** was characterized on the basis of spectral data. All the signals were in agreement with the assigned structure.

1-Phenyl-1,3-butadiene, 3-methyl-1-phenyl-1,3-butadiene and cyclopentadiene also afforded the rearranged products **71**, **73** and **75** respectively under similar reaction conditions (Table 3).

Table 3: Thiocyanation of dienes

Entry	Substrate	Product	Yield (%)*
1	 **70**	 **71**	45
2	 **72**	 **73**	65
3	 **74**	 **75**	37

Reaction conditions: NH_4SCN, CAN, CH_3CN, 0 °C, 30 min.

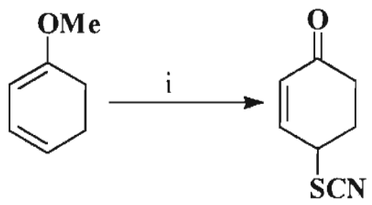
* Isolated yield.

The IR spectrum of the product **71** showed -SCN absorption at 2156 cm^{-1} and that due to -NCS at 2057 cm^{-1}. In the ^1H NMR spectrum, the olefinic protons resonated as a doublet at δ 6.77 (J = 15.6 Hz) and a double doublet at δ 6.09 (J = 15.6, 6.6 Hz). In the ^{13}C NMR spectrum, the -NCS and SCN carbons were discernible at δ 134.73 and 110.63 respectively. All other

signals were in agreement with the assigned structure. HRMS with molecular ion peak at 246.0283 is also in accordance with the proposed structure. Similar diagnostic spectral data were observed for **73** also.

The IR spectrum of the product **75** showed the -SCN and -NCS absorptions at 2166 and 2058 cm^{-1} respectively. In the ^1H NMR spectrum, the olefinic protons resonated as separate multiplets centered at δ 6.05 and 5.85. The protons geminal to -NCS and -SCN appeared as multiplets centered at δ 4.88 and 3.71 respectively. The -NCS and -SCN carbons resonated at δ 134.56 and 109.39 respectively in the ^{13}C NMR spectrum. All other signals were in agreement with the assigned structure.

In an attempt to extend this reaction to electron rich dienes, 1-methoxycyclohexadiene was treated with NH_4SCN and CAN in acetonitrile; the reaction afforded the γ-thiocyanatocyclohexenone **77** in 64% yield (Scheme 28).



76 **77**

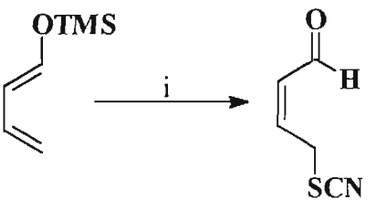
i. NH_4SCN, CAN, CH_3CN, 0 °C, 30 min, 64%

Scheme 28

The structure of the product **77** was ascertained from the spectral data. The IR spectrum showed a strong absorption at 2153 cm^{-1} diagnostic for -SCN moiety. The carbonyl absorption was visible at 1688 cm^{-1}. In the ^1H NMR spectrum, the olefinic protons resonated as separate double doublets at δ 6.89 (J = 10.0, 3.9 Hz) and 6.18 (J = 10.0, 1.2 Hz). The -CHSCN proton

appeared as a multiplet centered at δ 4.26. In the ^{13}C NMR spectrum, the carbonyl carbon resonated at δ 195.60 and -SCN carbon at δ 109.89. The carbon bearing -SCN was visible at δ 43.79. All other signals were in agreement with the assigned structure. The molecular ion peak at *m/z* 153 also agreed with the proposed structure.

1-Trimethylsilyloxy-1,3-butadiene also underwent a similar reaction affording the product **79** in low yield (Scheme 29).



78 **79**

i. NH_4SCN, CAN, CH_3CN, 0 °C, 30 min, 22%

Scheme 29

The structure of **79** was established on the basis of spectral data. The IR spectrum showed the -SCN absorption at 2160 cm^{-1} and carbonyl group absorption at 1694 cm^{-1}. In the ^1H NMR spectrum, the aldehyde proton resonated as a doublet at δ 9.63 (J = 7.3 Hz). The $C\underline{H_2}SCN$ protons appeared as a doublet at δ 3.78 (J = 7.2 Hz). In ^{13}C NMR spectrum, the carbonyl carbon and thiocyanate carbon appeared at δ 191.58 and 109.97 respectively. All other signals were in agreement with the assigned structure.

In conclusion, we have uncovered a novel and efficient procedure for the thiocyanation of electron rich heteroarenes and arenes. The products are important intermediates in heterocyclic synthesis. The present procedure is attractive for its experimental simplicity and generally high yields of products. In addition to being mechanistically interesting, the thiocyanation

of dienes may also prove to be synthetically useful with further optimization studies.

3.4 Experimental

General information about the experiments is given in chapter 2 (Section 2.3.1). CAN, indoles, pyrroles, 2,3-dimethylbutadiene, 1,3-pentadiene, 1-methoxycyclohexadiene and 1-trimethylsilyloxybutadiene were procured from Aldrich. 1-Phenyl-1,3-butadiene and 3-methyl-1-phenyl-1,3-butadiene were prepared from cinnamaldehyde and benzylidine acetone respectively *via* Wittig reaction. *N,N*-Dimethylaniline, *N,N*-diethylaniline, *N*-methylaniline, aniline and diphenylamine were purchased from the local sources.

3.4.1 Synthesis of arylthiocyanates

3-Thiocyanatoindole (11)[16]

A solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) was added dropwise to a solution of indole (117 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL) at room temperature and stirred well for 15 minutes. On completion of the reaction (monitored by TLC), the mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The combined organic extract was washed with water, then with saturated brine and finally dried over anhydrous sodium sulfate. The solvent was evaporated off under reduced pressure and the residue was subjected to column chromatography on silca gel (100-200 mesh) using a mixture of hexane-ethyl acetate (80:20) as eluent to afford **11**

(173 mg, 100%) as a colorless solid. It was recrystallized from dichloromethane-hexane mixture (mp 76 °C; lit.,[16] mp 75-76 °C).

IR (KBr) ν_{max} : 3339, 2160, 1418, 1317, 1236, 1094, 737 cm^{-1}.

^1H NMR : δ 8.65 (brs, 1H, NH, exchangeable with D_2O), 7.82-7.79 (m, 1H, ArH), 7.52-7.30 (m, 4H, ArH).

^{13}C NMR : δ 136.02, 131.23, 127.54, 123.68, 121.74, 118.43, 112.47, 112.24, 91.27.

1-Methyl-3-thiocyanatoindole (33)

A solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) was added dropwise to a solution of 1-methylindole (131 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL) at room temperature and stirred well for 15 minutes. On completion of the reaction, the mixture was worked up as described previously. Column chromatography on silica gel using hexane-ethyl acetate (90:10) afforded **33** (186 mg, 99%) as a colorless solid; it was recrystallized from dichloromethane-hexane (mp 87-88 °C).

IR (KBr) ν_{max} : 2150, 1512, 1242, 1154, 763 cm^{-1}.

^1H NMR : δ 7.78-7.76 (m, 1H, ArH), 7.34-7.29 (m, 4H, ArH), 3.75 (s, 3H, CH_3).

^{13}C NMR : δ 137.13, 135.05, 128.42, 123.39, 121.55, 118.86, 111.88, 110.20, 89.74, 33.35.

GC-MS (*m/z*) : 188 (M^+, 100), 187 (20), 173 (30), 155 (40), 146 (25), 121 (15), 120 (20), 102 (5), 94 (4), 77 (5).

2-Methyl-3-thiocyanatoindole (35)

To a solution of 2-methylindole (131 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL), a solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) was added dropwise at room temperature and stirred well. After completion of the reaction, usual work-up followed by chromatographic purification of the residue using hexane-ethyl acetate (80:20) afforded **35** (158 mg, 84%) as a colorless solid. It was recrystallized from dichloromethane-hexane mixture (mp 102 °C).

IR (KBr) ν_{max} : 3326, 2160, 1593, 1553, 1458, 1411, 1310, 1243, 764 cm^{-1}.

^1H NMR : δ 8.53 (brs, 1H, NH, exchangeable with D_2O), 7.67-7.65 (m, 1H, ArH), 7.30-7.21 (m, 3H, ArH), 2.50 (s, 3H, CH_3).

^{13}C NMR : δ 142.19, 135.16, 128.69, 122.95, 121.54, 118.00, 112.34, 111.33, 88.60, 12.00.

GC-MS (*m/z*) : 188 (M^+, 100), 187 (45), 161 (15), 155 (25), 146 (10), 130 (15), 117 (15), 102 (10), 94 (10), 77 (12).

2-Phenyl-3-thiocyanatoindole (37)

To a solution of 2-phenylindole (193 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL), a solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) was added dropwise at room temperature and stirred well. On completion of the reaction, the mixture was worked up and purified as described earlier to afford **37** (215 mg, 86%) as a colorless solid; it was recrystallized from dichloromethane-hexane (mp 171-172 °C).

IR (KBr) ν_{max} : 3339, 2152, 1632, 1442, 737 cm^{-1}.

^{1}H NMR : δ 8.71 (brs, 1H, NH, exchangeable with D_2O), 7.83-7.29 (m, 9H, ArH).

^{13}C NMR : δ 135.35, 130.75, 130.20, 130.03, 129.69, 129.49, 129.04, 128.54, 124.05, 122.11, 119.10, 111.44.

3-Methyl-2-oxo-3-thiocyanatoindole (41)

To a solution of 3-methylindole (262 mg, 2 mmol) and ammonium thiocyanate (182 mg, 2.4 mmol) in methanol (10 mL), a solution of CAN (2.521 g, 4.6 mmol) in methanol (30 mL) was added dropwise at room temperature and stirred well. After overnight stirring, the mixture was worked up as usual and the residue was purified by column chromatography using hexane-ethyl acetate (80:20) as eluent to afford **41** (90 mg, 22%) as a yellow viscous liquid. [126 mg (48%) of the starting material was recovered unchanged].

IR (neat) ν_{max} : 3258, 2166, 1728, 1620, 1479, 1337, 1202, 757 cm^{-1}.

^{1}H NMR : δ 9.95 (brs, 1H, NH, exchangeable with D_2O), 7.40-6.94 (m, 4H, ArH), 1.93 (s, 3H, CH_3).

^{13}C NMR : δ 176.48, 140.37, 130.86, 127.87, 124.00, 123.58, 111.34, 110.05, 53.68, 22.23.

1-Methyl-2-thiocyanatopyrrole (43)

To a solution of 1-methylpyrrole (162 mg, 2 mmol) and ammonium thiocyanate (182 mg, 2.4 mmol) in methanol (10 mL), a solution of CAN (2.521 g, 4.6 mmol) in methanol (30 mL) was added dropwise at room temperature and stirred well for 15 minutes. On completion of the reaction, usual work-up followed by silica gel column chromatography using hexane-ethyl acetate (98:2) as eluent furnished **43** (232 mg, 84%) as a colorless oil.

IR (neat) ν_{max} : 2956, 2156, 1463, 1289, 727 cm^{-1}.

^1H NMR : δ 6.92 (m, 1H, ArH), 6.63 (dd, *J* = 3.8, 1.7 Hz, 1H, ArH), 6.19 (dd, *J* = 3.8, 2.9 Hz, 1H, ArH), 3.75 (s, 3H, CH_3).

^{13}C NMR : δ 128.24, 120.65, 109.75, 109.50, 105.13, 34.34.

GC-MS (*m/z*) : 138 (M^+, 100), 123 (28), 112 (29), 105 (15), 96 (11), 85 (7), 78 (18), 71 (20), 68 (15), 58 (15), 52 (7).

2-Thiocyanatopyrrole (10)[15]

A solution of CAN (2.521 g, 4.6 mmol) in methanol (30 mL) was added dropwise to a solution of pyrrole (134 mg, 2 mmol) and ammonium thiocyanate (182 mg, 2.4 mmol) in methanol (10 mL) at room temperature and stirred well. On completion of the reaction, usual work-up followed by chromatographic purification afforded **10** (219 mg, 88%) as a colorless oil.

IR (neat) ν_{max} : 3339, 2153, 1539, 1438, 1128, 1088, 1034, 744 cm^{-1}.

^1H NMR : δ 8.76 (brs, 1H, NH, exchangeable with D_2O), 7.00-6.97 (m, 1H, ArH), 6.65-6.63 (m, 1H, ArH), 6.29-6.26 (m, 1H, ArH).

^{13}C NMR : δ 124.31, 119.99, 111.11, 110.78, 102.73.

GC-MS (*m/z*) : 124 (M^+, 100), 98 (60), 96 (10), 84 (2), 79 (2), 70 (30), 58 (5), 54 (15).

2-Methyl-5-thiocyanatothiophene (46)

A solution of CAN (3.782 g, 6.9 mmol) in methanol (35 mL) was added dropwise to a solution of 2-methylthiophene (294 mg, 3 mmol) and ammonium thiocyanate (274 mg, 3.6 mmol) in methanol (10 mL) at room temperature and stirred well. Usual work-up followed by column

chromatography using hexane-ethyl acetate (96:4) as eluent afforded **46** (70 mg, 15%) as a colorless oil.

IR (neat) ν_{max} : 2921, 2160, 1438, 1222, 811, 683, 542, 461 cm^{-1}.

^1H NMR : δ 7.22 (d, J = 3.5 Hz, 1H, Ar<u>H</u>), 6.73 (d, J = 3.5 Hz, 1H, Ar<u>H</u>), 2.52 (s, 3H, C<u>H</u>$_3$).

^{13}C NMR : δ 148.94, 138.02, 126.64, 114.88, 110.18, 15.75.

***N,N*-Dimethyl-4-thiocyanatoaniline (26)**[25]

To a solution of *N,N*-dimethylaniline (121 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL), a solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) was added dropwise at room temperature and stirred well for 30 minutes. On completion of the reaction, the mixture was worked up and the residue on column chromatography using hexane-ethyl acetate (98:2) as eluent afforded **26** (133 mg, 75%) as a colorless solid; it was recrystallized from dichloromethane-hexane (mp 71-72 °C ; lit.,[25] mp 72-73 °C).

IR (KBr) ν_{max} : 2908, 2146, 1593, 1512, 1371, 1196, 811, 528 cm^{-1}.

^1H NMR : δ 7.42 (d, J = 8.8 Hz, 2H, Ar<u>H</u>), 6.68 (d, J = 8.8 Hz, 2H, Ar<u>H</u>), 2.99 (s, 6H, N<u>Me$_2$</u>).

^{13}C NMR : δ 151.68, 134.44, 113.13, 112.57, 106.50, 40.11.

GC-MS (*m/z*) : 179 [M^++1] (15), 178 (M^+, 100), 161 (15), 145 (65), 136 (20), 118 (20), 104 (10), 91 (10), 88 (12), 69 (15), 63 (15), 51 (10).

***N,N*-Diethyl-4-thiocyanatoaniline (50)**[30]

A solution of *N,N*-diethylaniline (149 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL) was treated with a

solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) at room temperature and stirred well. On completion of the reaction, the reaction mixture was worked up and purified as described earlier to afford **50** (141 mg, 68%) as a pale yellow viscous liquid.

IR (neat) ν_{max} : 2974, 2150, 1588, 1501, 1401, 1351, 1270, 1195, 1089, 808 cm^{-1}.

^1H NMR : δ 7.36 (d, J = 9.0 Hz, 2H, ArH), 6.61 (d, J = 9.0 Hz, 2H, ArH), 3.35 (q, J = 7.0 Hz, 4H, CH_2), 1.16 (t, J = 7.0 Hz, 6 H, CH_3).

^{13}C NMR : δ 149.24, 134.89, 112.61, 112.39, 105.21, 44.49, 12.41.

_N_-Methyl-4-thiocyanatoaniline (52)[30]

A solution of *N*-methylaniline (107 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL) was treated with a solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) at room temperature and stirred well. After completion of the reaction, usual work-up followed by silica gel column chromatography using hexane-ethyl acetate (85:15) afforded **52** (73 mg, 44%) as a brown viscous liquid.

IR (neat) ν_{max} : 3427, 2935, 2894, 2813, 2153, 1600, 1512, 1337, 1196, 831 cm^{-1}.

^1H NMR : δ 7.37 (d, J = 8.6 Hz, 2H, ArH), 6.57 (d, J = 8.6 Hz, 2H, ArH), 4.08 (brs, 1H, NH, exchangeable with D_2O), 2.84 (s, 3H, NMe).

^{13}C NMR : δ 151.15, 134.68, 113.36, 112.71, 107.27, 30.18.

4-Thiocyanatoaniline (54)[31]

To a solution of aniline (93 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in methanol (5 mL), a solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) was added dropwise at room temperature and stirred well. On completion of the reaction, the reaction mixture was worked up as described earlier. Column chromatography on silica gel using hexane-ethyl acetate (70:30) afforded **54** (57 mg, 38%) as a yellow viscous liquid.

IR (neat) ν_{max} : 3474, 3380, 2153, 1634, 1600, 1506, 1324, 1189, 838, 535 cm^{-1}.

^1H NMR : δ 7.36 (d, *J* = 8.4 Hz, 2H, ArH), 6.67 (d, *J* = 8.4 Hz, 2H, ArH), 3.95 (brs, 2H, NH_2, exchangeable with D_2O).

^{13}C NMR : 148.68, 134.35, 115.84, 111.98, 109.53.

GC-MS (*m/z*) : 150 (M^+, 100), 124 (24), 118 (41), 106 (14), 99 (10), 96 (12), 80 (27), 69 (13), 65 (20).

***N*-Phenyl-4-thiocyanatoaniline (56) and Di-(4-thiocyanatophenyl)amine (57)**

A solution of diphenylamine (253 mg, 1.5 mmol) and ammonium thiocyanate (137 mg, 1.8 mmol) in methanol (10 mL) was treated with a solution of CAN (1.891 g, 3.45 mmol) in methanol (25 mL) at room temperature and stirred well. On completion of the reaction, the mixture was worked up as usual and the residue on column chromatography using hexane-ethyl acetate (90:10) as eluent afforded **56** (109 mg, 32%) as a pale yellow viscous liquid. Further elution using hexane-ethyl acetate (80:20) afforded **57** (23 mg, 6%) as yellow solid; it was recrystallized from dichloromethane-hexane (mp 115-117 °C).

Product 56

IR (neat) ν_{max} : 3366, 3063, 2166, 1593, 1512, 1317, 825, 764 cm^{-1}.

^1H NMR : δ 7.35-6.93 (m, 9H, ArH), 5.95 (brs, 1H, NH, exchangeable with D_2O).

^{13}C NMR : δ 146.13, 140.89, 133.88, 129.44, 122.95, 120.03, 117.01, 111.83, 111.14.

GC-MS (*m/z*) : 226 (M^+, 100), 225 (37), 211 (15), 193 (20), 167 (25), 83 (14), 77 (10).

Product 57[32]

IR (KBr) ν_{max} : 3370, 2150, 1586, 1520, 1487, 1334, 1175, 811 cm^{-1}.

^1H NMR : δ 7.48 (d, *J* = 8.6 Hz, 4H, ArH), 7.11 (d, *J* = 8.6 Hz, 4H, ArH), 6.15 (s, 1H, NH, exchangeable with D_2O).

^{13}C NMR : δ 143.68, 133.36, 119.16, 114.75, 110.92.

***N,N*-Dimethyl-2-nitro-4-thiocyanatoaniline (58)**

A solution of CAN (1.260 g, 2.3 mmol) in acetonitrile (25 mL) was added dropwise to a solution of *N,N*-dimethylaniline (121 mg, 1 mmol) and ammonium thiocyanate (91 mg, 1.2 mmol) in acetonitrile (5 mL) at room temperature and stirred well. On completion of the reaction, the mixture was worked up as usual. The residue on column chromatography using hexane-ethyl acetate (94:6) as eluent afforded **58** (97 mg, 43%) as a reddish yellow viscous liquid.

IR (neat) ν_{max} : 2928, 2153, 1607, 1526, 1351, 1276, 1162 cm^{-1}.

^1H NMR : δ 8.02 (d, *J* = 2.2 Hz, 1H, ArH), 7.58 (dd, *J* = 9.0, 2.2 Hz, 1H, ArH), 7.05 (d, *J* = 9.0 Hz, 1H, ArH), 2.96 (s, 6H, NMe_2).

^{13}C NMR : δ 146.95, 136.60, 131.39, 127.84, 119.22, 110.32, 109.14, 42.13.

GC-MS (*m/z*) : 223 (M^+, 53), 206 (52), 195 (7), 178 (35), 161 (40), 148 (100), 136 (30), 119 (40), 91 (14), 77 (10), 63 (15).

1,2-Dimethoxy-4-nitrobenzene (59)

To a solution of 1,2-dimethoxybenzene (138 mg, 1 mmol) and ammonium thiocyanate (92 mg, 1.2 mmol) in methanol (5 mL), a solution of CAN (1.260 g, 2.3 mmol) in methanol (25 mL) was added dropwise at room temperature and stirred overnight. Usual work-up followed by column chromatography afforded **59** (27 mg, 15%) as a yellow solid; it was recrystallized from dichloromethane hexane (mp 94-95 °C). [96 mg (70%) of the starting material was recovered unchanged].

IR (KBr) ν_{max} : 2943, 2837, 1588, 1507, 1345, 1270, 1233, 1183, 1083, 846, 796 cm^{-1}.

^{1}H NMR : δ 7.93 (dd, *J* = 8.8, 2.2 Hz, 1H, ArH), 7.75 (d, *J* = 2.2 Hz, 1H, ArH), 6.92 (d, *J* = 8.8 Hz, ArH), 3.98 (s, 3H, OMe), 3.97 (s, 3H, OMe).

^{13}C NMR : δ 154.54, 148.92, 141.56, 117.82, 109.88, 106.52, 56.46, 56.34.

GC-MS (*m/z*) : 183 (M^+, 10), 182 (100), 167 (5), 152 (10), 136 (10), 125 (8), 107 (9), 94 (6), 92 (8), 79 (18).

3.4.2 Thiocyanation of dienes

2,3-Dimethyl-1,4-dithiocyanato-2-butene (61)

A solution of CAN (2.521 g, 4.6 mmol) in acetonitrile (20 mL) was added dropwise to a solution of diene **60** (164 mg, 2 mmol) and ammonium thiocyanate (334 mg, 4.4 mmol) in acetonitrile (10 mL) at 0 °C and stirred well for 30-45 minutes, until the solution became colorless. After completion of the reaction, acetonitrile was evaporated off and the residue was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The combined organic extract was washed successively with water, saturated brine and dried (anhydrous Na_2SO_4) and concentrated. Purification was done by column chromatography (silca gel 100-200 mesh) using hexane-ethyl acetate (80:20) as eluent to afford **61** (174 mg, 44%) as a colorless solid. It was recrystallized from dichloromethane-hexane mixture (mp 125-127 °C).

IR (KBr) ν_{max} : 3009, 2915, 2160, 1445, 1249, 663 cm^{-1}.

^1H NMR ($CDCl_3$+DMSO) : δ 3.72 (s, 4H, $C\underline{H_2}SCN$), 1.98 (s, 6H, $C\underline{H_3}$).

^{13}C NMR ($CDCl_3$+DMSO) : δ 130.23, 111.29, 37.76, 17.74.

HRMS calcd for $C_8H_{10}S_2N_2$: 198.0285; found: 198.0281.

4-Isothiocyanato-5-thiocyanato-2-pentene (63), 4-Isothiocyanato-1-thiocyanato-2-pentene (64) and 1,4-Dithiocyanato-2-pentene (65)

To a solution of diene **62** (68 mg, 1 mmol) and ammonium thiocyanate (167 mg, 2.2 mmol) in acetonitrile (5 mL), a solution of CAN (1.260 g, 2.3 mmol) in acetonitrile (10 mL) was added dropwise at 0 °C and stirred well until the solution became colorless. On completion of the reaction, the mixture was worked up and purified as described earlier.

Successive elution using hexane-ethyl acetate (98:2) afforded **63** (26 mg, 14%), **64** (27 mg, 15%) and **65** (64 mg, 35%).

Product 63

Yellow viscous liquid.

IR (neat) ν_{max} : 2935, 2160, 2058, 1654, 1445, 1344, 1283, 980 cm^{-1}.

^1H NMR : δ 5.92-5.80 (m, 1H, olefinic), 5.43-5.35 (m, 1H, olefinic), 4.48-4.42 (m, 1H, C<u>H</u>NCS), 3.15-2.99 (m, 2H, C<u>H</u>$_2$SCN), 1.73 (d, J = 6.3 Hz, 3H, C<u>H</u>$_3$).

^{13}C NMR : δ 135.49, 132.15, 125.34, 110.65, 58.99, 39.24, 17.54.

Product 64

Pale yellow oil.

IR (neat) ν_{max} : 2989, 2942, 2160, 2052, 1627, 1351, 1276, 973, 865 cm^{-1}.

^1H NMR : δ 5.94-5.77 (m, 2H, olefinic), 4.45-4.42 (m, 1H, C<u>H</u>NCS), 3.56 (d, J = 5.8 Hz, 2H, C<u>H</u>$_2$SCN), 1.52 (d, J = 6.8 Hz, 3H, C<u>H</u>$_3$).

^{13}C NMR : δ 135.54, 133.37, 123.54, 110.68, 53.79, 34.72, 22.54.

GC-MS (*m/z*) : 184 (M^+, 4), 183 (10), 51 (10), 126 (10), 98 (23), 86 (100), 84 (53), 67 (11), 51 (30), 49 (84).

Product 65

Yellow viscous liquid.

IR (neat) ν_{max} : 2989, 2166, 1634, 1465, 973 cm^{-1}.

^1H NMR : δ 5.82-5.80 (m, 2H, olefinic), 3.96-3.92 (m, 1H, C<u>H</u>SCN), 3.58-3.51 (m, 2H, C<u>H</u>$_2$SCN), 1.55 (d, J = 6.8 Hz, 3H, C<u>H</u>$_3$).

^{13}C NMR : δ 135.10, 125.87, 110.34, 110.09, 45.09, 34.43, 20.01.

2,4-Dimethyl-4-isothiocyanato-5-thiocyanato-2-pentene (69)

A solution of CAN (1.890 g, 3.45 mmol) in acetonitrile (15 mL) was added dropwise to a solution of diene **68** (144 mg, 1.5 mmol) and ammonium thiocyanate (251 mg, 3.3 mmol) in acetonitrile (5 mL) at 0 °C and stirred well until the solution became colorless. On completion of the reaction, the mixture was processed as described earlier. Column chromatography on silica gel using hexane-ethyl acetate (95:5) afforded **69** (160 mg, 50%) as a pale yellow liquid.

IR (neat) ν_{max} : 2989, 2935, 2166, 2079, 1667, 1452, 1378, 1236, 1169, 1000, 521 cm^{-1}.

^{1}H NMR : δ 5.52 (s, 1H, olefinic), 3.45 (s, 2H, C$\underline{H_2}$SCN), 2.03 (s, 3H, C$\underline{H_3}$), 1.60 (s, 6H, C$\underline{H_3}$).

^{13}C NMR : δ 134.66, 133.92, 131.87, 110.72, 59.20, 43.98, 31.00, 15.15.

GC-MS (*m/z*) : 212 (M^+, 1), 154 (3), 112 (5), 100 (100), 79 (3), 72 (12), 55 (3), 53 (7).

3-Isothiocyanato-1-phenyl-4-thiocyanato-1-butene (71)

A solution of CAN (2.521 g, 4.6 mmol) in acetonitrile (20 mL) was added dropwise to a solution of diene **70** (260 mg, 2 mmol) and ammonium thiocyanate (335 mg, 4.4 mmol) in acetonitrile (10 mL) at 0 °C and stirred well until the solution became colorless. On completion of the reaction, the mixture was processed as described previously. Column chromatography on silica gel using hexane-ethyl acetate (95:5) afforded **71** (223 mg, 45%) as a yellow viscous liquid.

IR (neat) ν_{max} : 3025, 2156, 2057, 1646, 1487, 1447, 1321, 963 cm^{-1}.

^1H NMR : δ 7.40-7.31 (m, 5H, ArH), 6.77 (d, *J* = 15.6 Hz, 1H, olefinic), 6.09 (dd, *J* = 15.6, 6.6 Hz, 1H, olefinic), 4.73 (m, 2H, CHNCS), 3.26 (dd, *J* = 13.5, 4.8 Hz, 1H, CH_2SCN), 3.15 (dd, *J* = 13.5, 7.6 Hz, 1H, CH_2SCN).

^{13}C NMR : δ 135.09, 134.73, 128.95, 128.80, 126.93, 126.45, 122.72, 110.63, 59.28, 39.40.

GC-MS (*m/z*) : 187 [M^+-SCN-1] (26), 160 (10), 147 (82), 129 (100), 115 (45), 102 (10), 91 (18), 77 (30), 59 (26), 51 (20).

HRMS calcd for $C_{12}H_{10}N_2S_2$: 246.0285; found: 246.0283.

3-Isothiocyanato-3-methyl-1-phenyl-4-thiocyanato-1-butene (73)

To a solution of diene **72** (100 mg, 0.694 mmol) and ammonium thiocyanate (110 mg, 1.52 mmol) in acetonitrile (2 mL), a solution of CAN (875 mg, 1.6 mmol) in acetonitrile (10 mL) was added dropwise at 0 °C and stirred well for 30 minutes. On completion of the reaction, the reaction mixture was processed as described earlier to afford **73** (117 mg, 65%) as a yellow viscous liquid.

IR (neat) ν_{max} : 3070, 2989, 2160, 2045, 1661, 1499, 1458, 1283, 973 cm^{-1}.

^1H NMR : δ 7.39-7.26 (m, 5H, ArH), 6.77 (d, *J* = 15.6 Hz, 1H, Ph-CH=CH-), 6.04 (d, *J* = 15.6 Hz, 1H, Ph-CH=CH-), 3.27 (s, 2H, CH_2SCN), 1.75 (s, 3H, CH_3).

^{13}C NMR : δ 138.38, 134.84, 132.17, 128.98, 128.69, 127.71, 126.88, 111.37, 64.72, 45.84, 27.50.

GC-MS (*m/z*) : 202 [M^+-SCN] (4), 201 [M^+-SCN-1] (25), 174 (9), 160 (5), 143 (56), 128 (100), 115 (30), 77 (14).

HRMS calcd for $C_{13}H_{12}N_2S_2$: 260.0441; found: 260.0437.

3-Isothiocyanato-4-thiocyanatocyclopentene (75)

A solution of diene **74** (99 mg, 1.5 mmol) and ammonium thiocyanate (281 mg, 3.7 mmol) in acetonitrile (5 mL) was treated with a solution of CAN (1.890 g, 3.45 mmol) in acetonitrile (17 mL) at 0 °C. On completion of the reaction, usual work-up followed by chromatographic purification afforded **75** (101 mg, 37%) as a pale yellow viscous liquid.

IR (neat) ν_{max} : 3070, 2166, 2058, 1620, 1445, 1357, 1310, 791 cm^{-1}.

^1H NMR : δ 6.06-6.04 (m, 1H, olefinic), 5.87-5.84 (m, 1H, olefinic), 4.89-4.87 (m, 1H, C<u>H</u>NCS), 3.73-3.69 (m, 1H, C<u>H</u>SCN), 3.17-3.08 (m, 1H, C<u>H</u>$_2$), 2.64-2.56 (m, 1H, C<u>H</u>$_2$).

^{13}C NMR : δ 134.56, 133.57, 129.04, 109.39, 68.19, 50.73, 38.71.

GC-MS (*m/z*) : 184 [M^++2] (3), 183 [M^++1] (3), 182 (M^+, 24), 124 (100), 118 (7), 97 (12), 80 (14), 66 (50), 58 (5).

4-Thiocyanato-2-cyclohexenone (77)

To a solution of diene **76** (110 mg, 1mmol) and ammonium thiocyanate (167 mg, 2.2 mmol) in acetonitrile (5 mL) a solution of CAN (1.260 g, 2.3 mmol) in acetonitrile (10 mL) was added dropwise at 0 °C and stirred well for 30 minutes. Completion of the reaction followed by usual work-up and chromatographic purification using hexane-ethyl acetate (80:20) afforded **77** (98 mg, 64%) as a yellow oil.

IR (neat) ν_{max} : 2962, 2153, 1688, 1620, 1391, 1222, 973, 831 cm^{-1}.

^{1}H NMR : δ 6.89 (dd, *J* = 10.0, 3.9 Hz, 1H, olefinic), 6.18 (dd, *J* = 10.0, 1.2 Hz, 1H, olefinic), 4.27-4.25 (m, 1H, C<u>H</u>SCN), 2.80-2.35 (m, 4H, C<u>H</u>$_2$).

^{13}C NMR : δ 195.60, 143.68, 132.61, 109.89, 43.79, 34.71, 29.56.

GC-MS (*m/z*) : 155 [M^++2] (5), 154 [M^++1] (10), 153 (M^+, 100), 125 (12), 124 (8), 111 (15), 97 (27), 84 (12), 70 (12).

4-Thiocyanato-2-butenal (79)

A solution of diene **78** (142 mg, 1mmol) and ammonium thiocyanate (167 mg, 2.2 mmol) in acetonitrile (5 mL) was treated with a solution of CAN (1.260 g, 2.3 mmol) in acetonitrile (10 mL) at 0 °C. On completion of the reaction, the reaction mixture was processed as described earlier. Column chromatography on silica gel using hexane-ethyl acetate (70:30) afforded **79** (28 mg, 22%) as a yellow oil.

IR (neat) ν_{max} : 2942, 2840, 2160, 1694, 1640, 1425, 1175, 1115, 987, 899, 569 cm^{-1}.

^{1}H NMR : δ 9.63 (d, *J* = 7.3 Hz, 1H, C<u>H</u>O), 6.87-6.77 (m, 1H, CHO-CH=C<u>H</u>-), 6.32 (dd, *J* = 15.3, 7.3 Hz, 1H, CHO-C<u>H</u>=CH-), 3.78 (d, *J* = 7.2 Hz, 2H, C<u>H</u>$_2$SCN).

^{13}C NMR : δ 191.58, 145.37, 135.80, 109.97, 34.25.

3.5 References

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CHAPTER 4

AZIDOIODINATION AND IODOTHIOCYANATION OF ALKENES MEDIATED BY CERIUM(IV) AMMONIUM NITRATE

This chapter is divided into two sections. The first section describes the azidoiodination of alkenes mediated by cerium(IV) ammonium nitrate and the second section deals with the corresponding iodothiocyanation reactions.

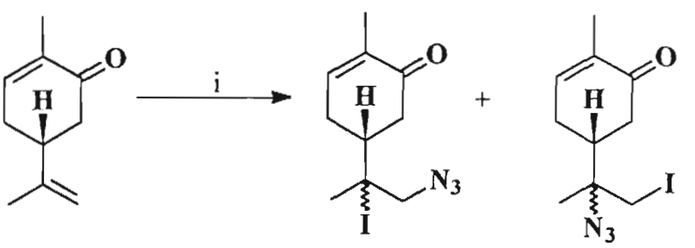
4.1 CAN Mediated Azidoiodination of Alkenes

4.1.1 Introduction

Cohalogenation of alkenes constitutes an important class of reaction used to form a carbon-heteroatom bond in a regio-, chemo- and stereoselective manner.[1] Since the pioneering work of Hassner,[2] considerable attention has been given to the haloazidation of alkenes using iodine azide reagent.[3] This is a very useful method for introducing a nitrogen functionality into a carbon skeleton leading to vinyl azides,[4] amines[5] and heterocycles,[6] particularly aziridines.[7]

Iodine azide has been generated *in situ* from sodium azide and iodine chloride in polar solvents;[8] however, its use has often been hampered as a result of its explosive character.

Very recently, Kirsching *et al.* have reported a novel procedure for the synthesis of iodoazides using $Et_4NI(N_3)_2$ (Scheme 1).[9]

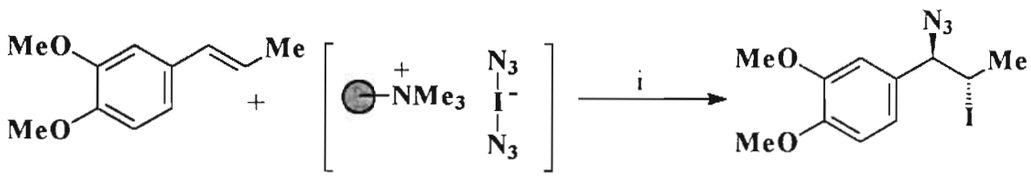


1 **2** (1:1) **3** (1:1)

i. $Et_4NI(N_3)_2$, CH_2Cl_2, -20 °C, 75% (7.5:1)

Scheme 1

The same authors have reported a new polymer bound iodine azide reagent **5** also.[10] Reaction of alkenes with this new reagent afforded *anti* addition products and the regiochemistry of the 1,2-addition is governed by the more stable intermediate carbonium ion formed after the electrophilic attack. An illustrative example is given in Scheme 2.



4 **5** **6**

i. CH_2Cl_2, 12 h, RT, 78%

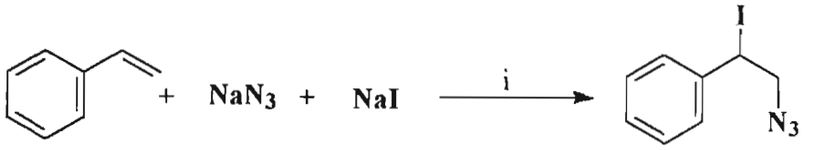
Scheme 2

Though both of these reagents are not explosive, their preparation involves tedious procedures.

Intrigued by the significance of iodoazides in organic synthesis[4-7] and as a part of our current interest in the CAN mediated oxidative addition of azide to alkenes, we studied the azidoiodination reaction using NaN_3/NaI/ CAN reagent combination in methanol. Details of these investigations are discussed in the following section.

4.1.2 Results and Discussion

The starting point of our investigations was the one-pot reaction of styrene with NaN_3, NaI and CAN in methanol affording the iodoazide **8** in 71% yield (Scheme 3).



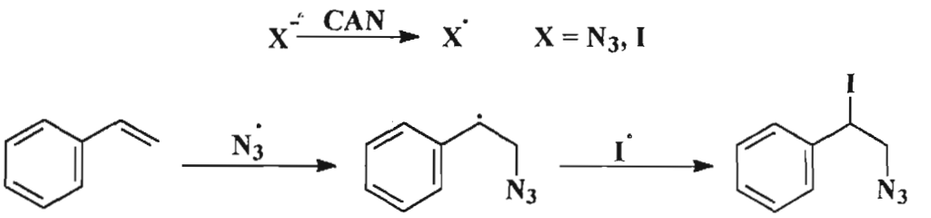
7 8

i. CAN, MeOH, 0 °C, 30 min, 71%

Scheme 3

The structure of the product **8** was established by spectral analysis. The IR spectrum showed the characteristic absorption due to azide group at 2100 cm^{-1}. In the ^1H NMR spectrum, the aromatic protons resonated as a multiplet in the region δ 7.39-7.23. The C<u>H</u>I proton resonated as a triplet at δ 5.10 (J = 7.7 Hz) and C<u>H</u>$_2$N$_3$ protons appeared at δ 3.88 (J = 7.7 Hz) as a doublet. The ^{13}C NMR spectrum showed the carbon bearing iodine, at δ 27.76 and the one bearing the azide group at δ 58.58. The regiochemistry of 1,2-addition was ascertained on the basis of ^{13}C NMR spectrum[10] and finally by DEPT-135 spectrum, which showed the presence of a methylene moiety at δ 58.58. The GC-MS displayed a peak at *m/z* 146 corresponding to [M^+-I]. All other signals were in agreement with the proposed structure.

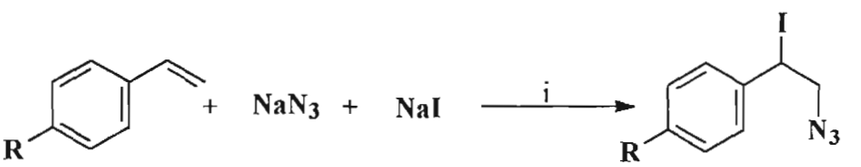
Mechanistically the formation of iodoazide can be rationalized along the following lines (Scheme 4). Azido radical formed in the first step adds to the alkene regioselectively to form the stable radical **9**, which is then quenched by the iodine radical to afford the iodoazide.



7 9 8

Scheme 4

Analogous results were obtained with 4-methyl and 4-chlorostyrenes also (Scheme 5).



10 (R=Me) **11** (70%)

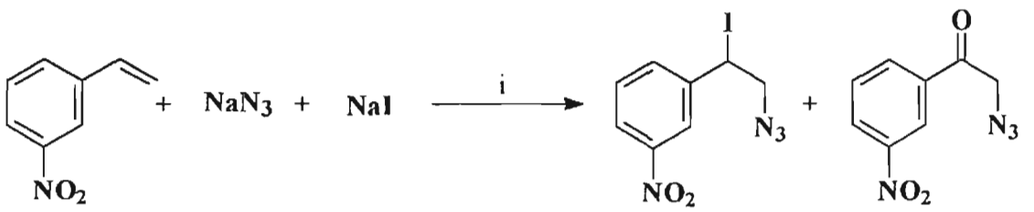
12 (R=Cl) **13** (78%)

i. CAN, MeOH, 0 °C, 30 min.

Scheme 5

The structures of **11** and **13** were established on the basis of spectral data. All the signals were in agreement with the assigned structures.

3-Nitrostyrene under the above reaction conditions afforded the corresponding iodoazide **15** in 66% yield along with a small amount of phenacyl azide **16** (Scheme 6).



14 **15** (66%) **16** (7%)

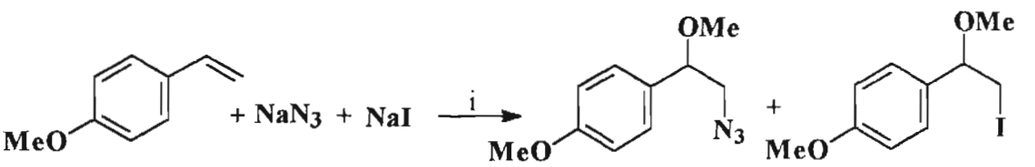
i. CAN, MeOH, 0 °C, 30 min.

Scheme 6

As usual, the structures of the products were ascertained by spectral data. The IR spectrum of **15** showed the absorption due to $-N_3$ group at 2106 cm^{-1} and that of $-NO_2$ at 1527 and 1346 cm^{-1}. In the ^1H NMR spectrum, C<u>H</u>I proton resonated as a double doublet at δ 5.19 (J = 8.4, 6.8 Hz) and C<u>H</u>$_2N_3$ protons resonated as a multiplet centered at δ 4.01. In the ^{13}C NMR spectrum, the carbon bonded to $-N_3$ appeared at δ 58.52 and the one bearing iodine at δ 24.50. The GC-MS displayed a peak at *m/z* 149, which corresponds to the fragment resulting from the loss of iodine and N_3.

In the IR spectrum of **16** the azide absorption occurred at 2100 $cm^{-1}$and the carbonyl absorption at 1701 cm^{-1}. A singlet observed at δ 4.61 in the ^1H NMR spectrum was due to the C<u>H</u>$_2N_3$ protons. In the ^{13}C NMR spectrum, the carbonyl carbon resonated at δ 191.08 and <u>C</u>H$_2N_3$ carbon at δ 54.95.

Reaction of 4-methoxystyrene under the above reaction conditions afforded an inseparable mixture of *β*-methoxy azide **18** and *β*-methoxy iodide **19** (Scheme 7). In this case, iodoazide formation was not observed.



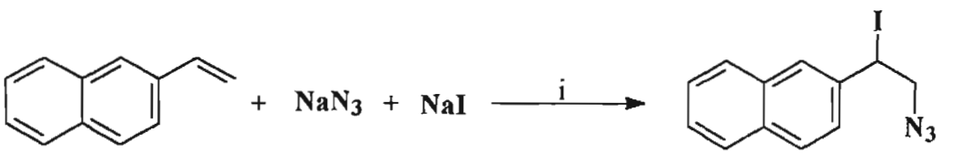
17 **18** **19**

i. CAN, MeOH, 0 °C, 30 min, 85%

Scheme 7

The ^{1}H NMR spectrum was diagnostic for a 1:1 mixture of **18** and **19**. The inseparable mixture showed the azide absorption at 2100 cm^{-1} in the IR spectrum. In the ^{1}H NMR spectrum, the C<u>H</u>OMe protons resonated as a multiplet in the region δ 4.30-4.20. The O<u>Me</u> protons appeared as two singlets at δ 3.79 and 3.26. In the ^{13}C NMR spectrum, the benzylic carbon signals were discernible at δ 83.08 and 82.63. The carbon bonded to -N_3 was discernible at δ 56.90 and the <u>C</u>H$_2$I carbon resonated at δ 10.53.

Similar experiment with 2-vinylnaphthalene afforded the iodoazide **21** in 55% yield (Scheme 8).



20 **21**

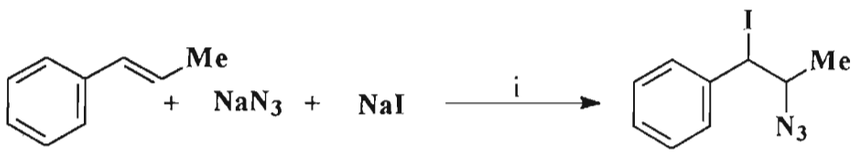
i. CAN, MeOH, 0 °C, 30 min, 55%

Scheme 8

The IR spectrum of the product **21** exhibited the azide absorption at 2100 cm^{-1}. In the ^{1}H NMR spectrum, the C<u>H</u>I proton resonated as a triplet at δ 5.26 (J = 7.7 Hz) and C<u>H</u>$_2$N$_3$ protons appeared at δ 3.95 as a doublet

(J = 7.7 Hz). In the ^{13}C NMR spectrum, the carbon bearing -N_3 resonated at δ 58.26 and the CHI carbon resonated at δ 28.42.

Subsequent to the above investigations we extended our studies to β-substituted styrenes. β-Methylstyrene, under the usual reaction conditions afforded the iodoazide **23** in 46% yield (Scheme 9). In this case the *syn* and *anti* isomers were isolated as an inseparable mixture in the ratio 1:1, as evident from the ^1H NMR spectrum.



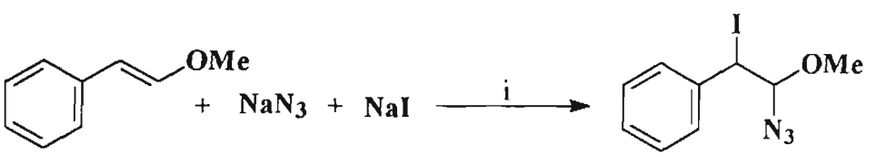
22 **23**

i. CAN, MeOH, 0 °C, 30 min, 46% (1:1)

Scheme 9

The IR spectrum of **23** showed a strong absorption at 2100 cm^{-1} due to the azide group. The CHI proton appeared as doublets at δ 4.96 (J = 8.0 Hz) and 4.90 (J = 7.7 Hz) indicating that the product is a mixture of isomers. The CHN_3 protons appeared as a multiplet between δ 3.97-3.76. The methyl protons resonated as separate doublets at δ 1.52 (J = 6.4 Hz) and 1.23 (J = 6.4 Hz). In the ^{13}C NMR spectrum, the azide bearing carbons were discernible at δ 63.73 and 63.21. The signals due to CHI carbon atoms appeared at δ 37.18 and 36.27. The GC-MS displayed a peak at *m/z* 217, corresponding to the fragment resulting from the loss of CHN_3Me.

β-Methoxystyrene also underwent a similar reaction to yield the iodoazide **25** as a 1:1 mixture of isomers (Scheme 10).



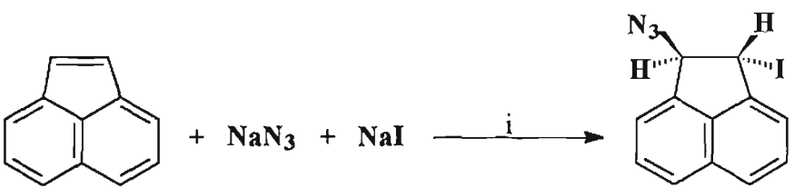
24 **25**

i. CAN, MeOH, 0 °C, 30 min, 57% (1:1)

Scheme 10

The structure of the product **25** was ascertained from its spectral data. All the signals were in agreement with the proposed structure.

The reaction of acenaphthylene with NaN_3, NaI and CAN in methanol afforded the *trans*-iodoazide **27** as the only isolable product in moderate yield (Scheme 11).



26 **27**

i. CAN, MeOH, 0 °C, 30 min, 28%

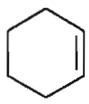
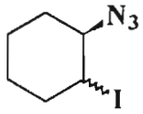
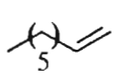
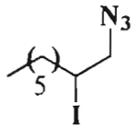
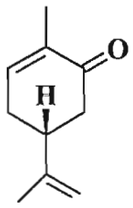
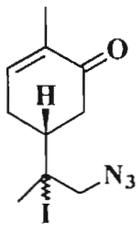
Scheme 11

In the IR spectrum of **27**, the azide absorption was visible at 2093 cm^{-1}. In the ^1H NMR spectrum, the C<u>H</u>I and C<u>H</u>N_3 protons appeared as singlets at δ 5.77 and 5.64. The coupling constants for C<u>H</u>N_3 and C<u>H</u>I protons is less than 2 Hz. This is in keeping with Dewar's demonstration that in *trans* 1,2-disubstituted acenaphthene the *J* value is less than 2 Hz, while in *cis* isomer it is greater than 6 Hz.[11] Thus *trans* stereochemistry is assigned for the product. In the ^{13}C NMR spectrum, the <u>C</u>HN_3 carbon resonated at

δ 75.15 and CHI carbon was discernible at δ 25.62. All other signals were in agreement with the proposed structure.

After having studied the reactivity profile of aryl alkenes, we turned our attention to cyclic and acyclic alkenes such as cyclohexene, 1-octene and carvone. The results are summarized in Table 1.

Table 1: Azidoiodination of alkenes

Entry	Substrate		Product		Yield (%)[a]
1		**28**		**29**	60[b]
2		**30**		**31**	37
3		**1**		**2**	64[c]

Reaction conditions: NaN_3, NaI, CAN, MeOH, 0 °C, 30 min.

(a) Isolated yield; (b) 2:3 mixture of *cis* and *trans* isomers.

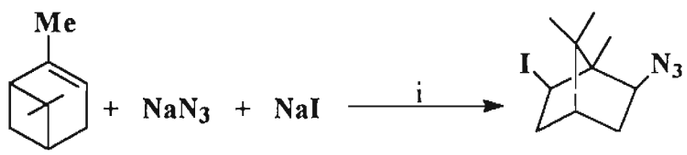
(c) 1:1 Mixture of diastereomers.

From the ^1H NMR spectrum, the product **29** was found to be a 2:3 mixture of *cis* and *trans* isomers. The IR spectrum showed the characteristic absorption of azide group at 2093 cm^{-1}. The structure of the product was confirmed by comparing its spectral data with those reported in the literature for authentic sample.[9] In GC-MS the molecular ion peak was observed at *m/z* 251.

The azide absorption for **31** was observed at 2100 cm^{-1} in the IR spectrum. The C<u>H</u>I proton resonated as a multiplet centered at δ 4.08. The C<u>H</u>$_2$N$_3$ protons appeared as two double doublets at δ 3.75 (J = 12.7, 5.9 Hz) and 3.61 (J = 12.7, 7.1 Hz). In the ^{13}C NMR spectrum the carbon bonded to -N_3 was visible at δ 59.00 and the one bonded to iodine at δ 14.08. The regiochemistry of the product was confirmed by the DEPT-135 spectrum, which showed the presence of a methylene moiety at δ 59.00 and methine carbon at δ 14.08. GC-MS displayed the molecular ion peak at *m/z* 281. All other signals were in agreement with the assigned structure.

The structure of the product **2** was established by comparing its spectral data with those reported for an authentic sample.[9] From the ^{1}H NMR spectrum it was found to be a 1:1 mixture of *syn* and *anti* isomers.

Interestingly, α-pinene under the same reaction conditions afforded the rearranged product **33** albeit in low yield (Scheme 12).



32 **33**

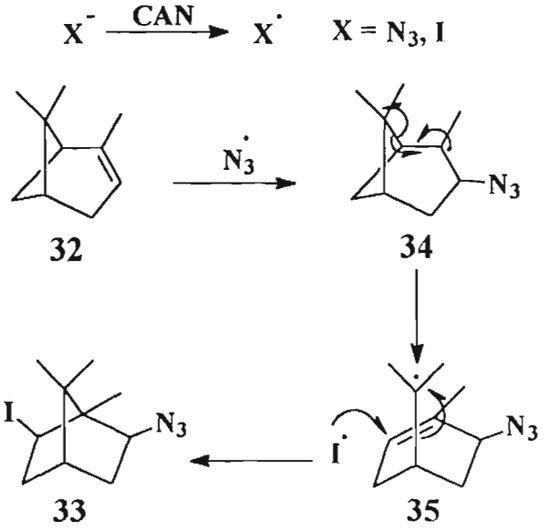
i. CAN, MeOH, 0 °C, 30 min, 30%

Scheme 12

The IR spectrum of product **33** displayed the azide absorption at 2087 cm^{-1}. In the ^{1}H NMR spectrum, C<u>H</u>I proton resonated as a multiplet centered at δ 4.27. The C<u>H</u>N$_3$ proton also appeared as a multiplet in the region δ 4.04-3.99. The <u>C</u>HN$_3$ and <u>C</u>HI carbons were discernible at δ 66.39 and 26.47 respectively in the ^{13}C NMR spectrum. The regiochemistry was assigned on the basis of DEPT-135, which showed the presence of <u>C</u>HI carbon at

δ 26.47. The structure was further supported by the GC-MS, which exhibited the molecular ion peak at *m/z* 305.

A mechanistic rationalization for the formation of **33** is given in Scheme 13. The azido radical adds to the α-pinene to form a radical **34**, which then undergoes fragmentation to yield an alkenyl radical **35**. The addition of iodine radical to this alkene followed by ring closure affords the product **33**.



Scheme 13

In all these cases we have observed the products formed by the initial attack of azido radical resulting in a stable carbon centered radical. The possibility of the addition of iodine as iodide ion can be excluded on the basis of the fact that the reaction failed in the case of *p*-methoxystyrene, which is known to generate a radical cation in presence of CAN.[12]

In conclusion, we have uncovered a novel regioselective and chemoselective route to iodoazides, which are important intermediates in

organic synthesis. The present one-pot reaction is especially attractive due to its experimental simplicity.

4.1.3 Experimental

General information about the experimental procedure is given in Chapter 2 (Section 2.3.1). Styrene, 4-methylstyrene, β-methoxystyrene, acenaphthylene, carvone and α-pinene were purchased from Aldrich. Other styrenes and 2-vinyl naphthalene were prepared from the corresponding aldehydes *via* Wittig olefination reaction. Cyclohexene was purchased from a local source. Distilled methanol was used in all these experiments.

2-Azido-1-iodo-1-phenylethane (8)

A solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) was added dropwise to a mixture of styrene (104 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL) at 0 °C. On completion of the reaction, the reaction mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The combined organic extract was washed with water, followed by saturated brine, finally dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was subjected to column chromatography (silica gel 60-120 mesh) using hexane as eluent to afford **8** (195 mg, 71%) as a pale yellow oil.

IR (neat) ν_{max} : 3033, 2100, 1452, 1253, 693 cm^{-1}.

^1H NMR : δ 7.39-7.23 (m, 5H, Ar<u>H</u>), 5.10 (t, J = 7.7 Hz, 1H, C<u>H</u>I), 3.88 (d, J = 7.7 Hz, 2H, C<u>H</u>$_2$N$_3$).

^{13}C NMR : δ 140.14, 128.87, 128.65, 127.49, 58.58, 27.76.

GC-MS (*m/z*) : 146 [M^+-I] (10), 117 (30), 104 (48), 91 (100).

2-Azido-1-iodo-1-(4'-methylphenyl)ethane (11)

To a mixture of 4-methylstyrene (118 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL), a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) was added dropwise at 0 °C. After completion of the reaction, the mixture was worked up as described above and the product purified by column chromatography using hexane as eluent to afford **11** (200 mg, 70%) as a pale yellow oil.

IR (neat) ν_{max} : 3027, 2921, 2100, 1508, 1446, 1259, 811, 718 cm^{-1}.

^1H NMR : δ 7.27 (d, J = 7.8 Hz, 2H, Ar<u>H</u>), 7.09 (d, J = 7.8 Hz, 2H, Ar<u>H</u>), 5.09 (t, J = 7.7 Hz, 1H, C<u>H</u>I), 3.87 (d, J = 7.7 Hz, 2H, C<u>H</u>$_2$N$_3$), 2.3 (s, 3H, C<u>H</u>$_3$).

^{13}C NMR : δ 138.54, 137.24, 129.57, 127.36, 58.61, 28.17, 21.20.

2-Azido-1-(4'-chlorophenyl)-1-iodoethane (13)

The reaction of 4-chlorostyrene (138 mg, 1 mmol) with sodium azide (65 mg, 1 mmol), sodium iodide (149 mg, 1 mmol) and CAN (1.151 g, 2.1 mmol) in methanol as described earlier afforded **13** (239 mg, 78%) as a pale yellow oil.

IR (neat) ν_{max} : 2927, 2100, 1589, 1489, 1253, 1085, 823 cm^{-1}.

^1H NMR : δ 7.36-7.28 (m, 4H, Ar<u>H</u>), 5.08 (dd, J = 8.3, 6.9 Hz, 1H, C<u>H</u>I), 3.93-3.88 (m, 2H, C<u>H</u>$_2$N$_3$).

^{13}C NMR : δ 138.75, 134.42, 129.12, 128.80, 58.50, 26.01.

GC-MS (*m/z*) : 138 [M^+-I-N_3] (100), 127 (30), 103 (85), 77 (60).

2-Azido-1-iodo-1-(3'-nitrophenyl)ethane (15) and

2-Azido-3'-nitroacetophenone (16)

A mixture of 3-nitrostyrene (149 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature for 30 minutes. The reaction mixture was worked up as usual and the residue on column chromatography using hexane-ethyl acetate (95:5) as eluent afforded **15** (209 mg, 66%) as a yellow oil. Further elution using hexane-ethyl acetate (90:10) afforded **16** (15 mg, 7%) as a yellow semi solid.

Product 15

IR (neat) ν_{max} : 3089, 2106, 1527, 1346, 687 cm^{-1}.

^1H NMR : δ 8.28 (s, 1H, Ar<u>H</u>), 8.16 (dd, *J* = 8.1, 1.0 Hz, 1H, Ar<u>H</u>), 7.76 (d, *J* = 7.5 Hz, 1H, Ar<u>H</u>), 7.57-7.52 (m, 1H, Ar<u>H</u>), 5.19 (dd, *J* = 8.4, 6.8 Hz, 1H, C<u>H</u>I), 4.06-3.93 (m, 2H, C<u>H</u>$_2$N$_3$).

^{13}C NMR : δ 148.69, 142.84, 133.89, 130.30, 123.74, 122.83, 58.52, 24.50.

GC-MS (*m/z*) : 149 [M^+-I-N_3] (100), 127 (3), 103 (55), 77 (50).

Product 16

IR (CH_2Cl_2) ν_{max} : 3089, 2921, 2100, 1701, 1614, 1527, 1340, 1209 cm^{-1}.

^1H NMR : δ 8.72 (s, 1H, Ar<u>H</u>), 8.50 (d, *J* = 7.8 Hz, 1H, Ar<u>H</u>), 8.27 (d, *J* = 7.5 Hz, 1H, Ar<u>H</u>), 7.77-7.72 (m, 1H, Ar<u>H</u>), 4.61 (s, 2H, C<u>H</u>$_2$N$_3$).

^{13}C NMR : δ 191.08, 135.52, 133.35, 130.20, 128.17, 123.11, 122.81, 54.95.

2-Azido-1-methoxy-1-(4'-methoxyphenyl)ethane (18) and 2-Iodo-1-methoxy-1-(4'-methoxyphenyl)ethane (19)

A solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) was added dropwise to a mixture of 4-methoxystyrene (134 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL) at 0 °C. After completion of the reaction, the mixture was worked up as usual and the residue chromatographed to afford an inseparable mixture of **18** and **19** (205 mg, 85%) as a pale yellow oil.

IR (neat) ν_{max} : 2934, 2834, 2100, 1608, 1508, 1240, 1097 cm^{-1}.

^{1}H NMR : δ 7.22-7.19 (m, 4H, ArH), 6.89-6.85 (m, 4H, ArH), 4.30-4.20 (m, 2H, CHOMe), 3.79 (s, 6H, OMe), 3.44 (dd, J = 12.8, 8.5 Hz, 1H), 3.35-3.25 (m, 8H), 3.13 (dd, J = 12.8, 3.5 Hz, 1H).

^{13}C NMR : δ 159.58, 159.55, 131.64, 130.42, 127.76, 127.61, 113.97, 113.94, 83.08, 82.63, 56.90, 56.47, 55.03, 10.53.

2-Azido-1-iodo-1-(2'-naphthyl)ethane (21)

A solution of CAN (1.220 g, 2.2 mmol) in methanol (10 mL) was added dropwise to a mixture of 2-vinylnaphthalene (164 mg, 1.06 mmol), sodium azide (70 mg, 1.08 mmol) and sodium iodide (161 mg, 1.08 mmol) in methanol (2 mL) at 0 °C and stirred for 30 minutes. The reaction mixture was worked up as usual and the crude residue was chromatographed to afford **21** (179 mg, 55%) as a yellow oil.

IR (neat) ν_{max} : 3052, 2100, 1589, 1259, 1122, 805, 742 cm^{-1}.

^{1}H NMR : δ 7.78-7.76 (m, 4H, ArH), 7.47-7.43 (m, 3H, ArH), 5.26 (t, *J* = 7.7 Hz, 1H, CHI), 3.95 (d, *J* = 7.7 Hz, 2H, CH_2N_3).

^{13}C NMR : 137.24, 133.08, 132.88, 128.93, 127.88, 127.63, 126.60, 126.57, 126.11, 125.03, 58.26, 28.42.

2-Azido-1-iodo-1-phenylpropane (23)

A mixture of *β*-methylstyrene (118 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature. After completion of the reaction it was processed as described earlier to afford **23** (131 mg, 46%) as a pale yellow oil (1:1 mixture of *syn* and *anti* isomers).

IR (neat) ν_{max} : 2983, 2100, 1458, 1259, 693 cm^{-1}.

^{1}H NMR : δ 7.42-7.25 (m, 10H, ArH), 4.96 (d, *J* = 8.0 Hz, 1H, CHI), 4.90 (d, *J* = 7.7 Hz, 1H, CHI), 3.97-3.76 (m, 2H, CHN_3), 1.52 (d, *J* = 6.4 Hz, 3H, CH_3), 1.23 (d, *J* = 6.4 Hz, 3H, CH_3).

^{13}C NMR : δ 140.69, 140.45, 128.82, 128.73, 128.52, 128.46, 128.16, 127.85, 63.73, 63.21, 37.18, 36.27, 19.92, 18.41.

GC-MS (*m/z*) : 217 [M^+-CHN_3Me] (30), 160 (2), 127 (30), 117 (60), 91 (100).

1-Azido-2-iodo-1-methoxy-2-phenylethane (25)

A mixture of *β*-methoxystyrene (134 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature. After completion of the reaction the mixture was

worked up as usual and the residue purified by column chromatography using hexane as eluent to afford **25** (172 mg, 57%) as a pale yellow oil (1:1 mixture of *syn* and *anti* isomers).

IR (neat) ν_{max} : 2934, 2834, 2106, 1452, 1209, 1110 cm^{-1}.

^1H NMR : δ 7.51-7.25 (m, 10H, ArH), 5.09 (m, 2H, CHI), 4.61 (m, 2H, CHN_3), 3.56 (s, 3H, OMe), 3.47 (s, 3H, OMe).

^{13}C NMR : δ 138.95, 138.13, 134.15, 133.88, 129.09, 128.64, 128.38, 128.22, 57.49, 57.43, 56.97, 31.83, 31.62.

***trans*-1-Azido-2-iodo-acenaphthene (27)**

A mixture of acenaphthylene (75 mg, 0.49 mmol), sodium azide (33 mg, 0.5 mmol) and sodium iodide (75 mg, 0.5 mmol) in methanol (2 mL) was treated with a solution of CAN (564 mg, 1.03 mmol) in methanol (6 mL) at ice temperature for 30 minutes. The reaction mixture was worked up as usual and the residue purified by column chromatography using hexane as eluent to afford **27** (44 mg, 28%) as a pale yellow oil.

IR (neat) ν_{max} : 3046, 2093, 1489, 1240, 811, 774 cm^{-1}.

^1H NMR : δ 7.83-7.23 (m, 6H, ArH), 5.77 (s, 1H, CHI), 5.64 (s, 1H, CHN_3).

^{13}C NMR : δ 143.15, 137.31, 134.97, 130.96, 128.73, 128.22, 125.93, 124.99, 122.17, 121.42, 75.15, 25.62.

***trans/cis*-1-Azido-2-iodocyclohexane (29)**[9]

A mixture of cyclohexene (82 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature for 30 minutes. Usual work-up and purification of the product

afforded **29** (150 mg, 60%) as a colorless oil (2:3 mixture of *cis* and *trans* isomers).

IR (neat) ν_{max} : 2940, 2859, 2093, 1446, 1247, 1159 cm^{-1}.

^1H NMR : δ 4.54 (m, C<u>H</u>I), 3.96-3.93 (m, C<u>H</u>I), 3.54-3.49 (m, C<u>H</u>N_3), 3.23 (brs, C<u>H</u>N_3), 2.47-1.23 (m, C<u>H_2</u>).

^{13}C NMR : δ 67.19, 63.15, 38.42, 36.86, 34.50, 33.28, 31.94, 29.27, 27.05, 24.03, 23.87, 22.23.

GC-MS (*m/z*) : 251 (M^+, 8), 127 (20), 81 (12), 69 (100).

1-Azido-2-iodooctane (31)

A mixture of 1-octene (112 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature. After completion of the reaction the mixture was subjected to the usual work-up and purification to afford **31** (103 mg, 37%) as a colorless oil.

IR (neat) ν_{max} : 2927, 2100, 1458, 1253 cm^{-1}.

^1H NMR : δ 4.10-4.05 (m, 1H, C<u>H</u>I), 3.75 (dd, J = 12.7, 5.9 Hz, 1H, C<u>H_2</u>N_3), 3.61 (dd, J = 12.7, 7.1 Hz, 1H, C<u>H_2</u>N_3), 1.76 (t, J = 7.1 Hz, 2H, C<u>H_2</u>), 1.30-1.25 (m, 8H, C<u>H_2</u>), 0.89 (brs, 3H, C<u>H_3</u>).

^{13}C NMR : δ 59.00, 37.11, 31.99, 31.59, 29.18, 28.41, 22.57, 14.08.

GC-MS (*m/z*) : 281 (M^+, 2), 155 (20), 127 (30), 97 (15), 84 (37), 70 (50), 55 (100).

Iodoazide 2[9]

A mixture of carvone (75.5 mg, 0.5 mmol), sodium azide (33 mg, 0.5 mmol) and sodium iodide (75 mg, 0.5 mmol) in methanol (2 mL) was treated with a solution of CAN (576 mg, 1.05 mmol) in methanol (5 mL) at ice temperature. After completion of the reaction the mixture was subjected to the usual work-up and purification to afford **2** (103 mg, 64%) as a colorless oil (1:1 mixture of isomers).

IR (neat) ν_{max} : 2927, 2100, 1676, 1434, 1365, 1110, 886 cm^{-1}.

^1H NMR : δ 6.72 (m, 1H, olefinic), 3.85-3.83 (m, 2H), 2.64-2.31 (m, 4H), 2.00 (d, J = 1.5 Hz, 3H, C$\underline{H}_3$), 1.78 (s, 3H, C$\underline{H}_3$), 1.54-1.48 (m, 1H).

^{13}C NMR : δ 197.35, 197.18, 142.88, 135.30, 135.18, 62.77, 57.59, 43.80, 42.66, 42.02, 30.60, 30.50, 30.44, 29.83, 15.41.

Iodoazide 33

A mixture of α-pinene (136 mg, 1 mmol), sodium azide (65 mg, 1 mmol) and sodium iodide (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature. After completion of the reaction, the mixture was subjected to the usual work-up and purification to afford **33** (91 mg, 30%) as a pale yellow amorphous solid.

IR (KBr) ν_{max} : 2959, 2087, 1446, 1259 cm^{-1}.

^1H NMR : δ 4.30-4.25 (m, 1H), 4.04-3.99 (m, 1H), 2.60-2.49 (m, 1H), 2.37-2.26 (m, 1H), 1.84-1.74 (m, 2H), 1.30 (dd, J = 13.4, 4.6 Hz, 1H), 1.00 (s, 6H, C$\underline{H}_3$), 0.91 (s, 3H, C$\underline{H}_3$).

^{13}C NMR : δ 66.39, 52.62, 47.47, 43.97, 41.55, 35.45, 26.47, 19.83, 13.60.

GC-MS (*m/z*) : 305 (M^+, 3), 254 (2), 150 (25), 127 (15), 123 (40), 109 (45), 81 (100), 67 (40).

4.2 CAN Mediated Iodothiocyanation of Alkenes

4.2.1 Introduction

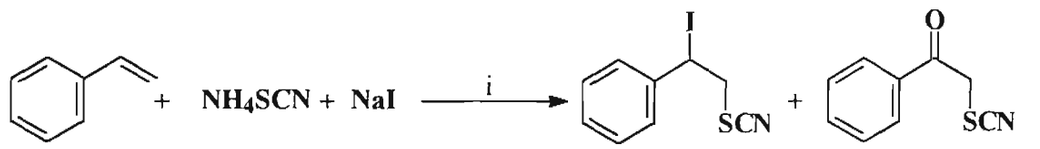
Earlier investigations in our laboratory have shown that CAN mediates a facile addition of thiocyanate to arylalkenes leading to the formation of dithiocyanates[13] or phenacyl thiocyanates.[14] Prompted by the interesting results obtained in the case of azidoiodination reaction it was decided to explore the corresponding iodothiocyanation reactions using NH_4SCN/ NaI/ CAN reagent combination in methanol.

The available method for the preparation of iodothiocyanates involves the use of iodine thiocyanate, which in turn is prepared either by the reaction of thermally unstable thiocyanogen with iodine,[15] or by the reaction of KSCN and iodine(I) chloride or iodine in polar solvents like tetremethylene sulfone (sulfolan).[16]

It is noteworthy that the iodothiocyanates on treatment with $BF_3.OEt_2$ undergo rearrangement to afford iodoisothiocyanates[16], which are precursors of heterocyclic compounds like thiazolidin-2-ones and 2-amino-2-thiazolines.[17]

4.2.2 Results and Discussion

Our initial experiment involved the reaction of styrene with NH_4SCN, NaI and CAN in methanol to afford the iodothiocyanate **36** as the major product along with phenacyl thiocyanate **37** (Scheme 14).



7 **36** (42%) **37** (20%)

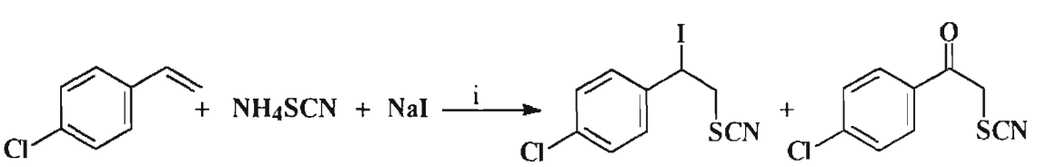
i. CAN, MeOH, 0 °C, 30 min

Scheme 14

The structure of the product **36** was ascertained from its spectral data.[16] In the IR spectrum, the absorption due to -SCN group was visible at 2155 cm^{-1}. In the ^{1}H NMR spectrum, the benzylic proton resonated at δ 5.30 as a double doublet (J = 10.8, 5.5 Hz). The $\underline{CH_2}SCN$ protons appeared as two double doublets at δ 3.94 (J = 13.0, 5.5 Hz) and δ 3.69 (J = 13.0, 10.8 Hz). In the ^{13}C NMR spectrum, the -SCN carbon was discernible at δ 110.24 and CHI carbon resonated at δ 25.49. All other NMR signals were in agreement with the assigned structure.

The IR spectrum of **37** showed the characteristic absorption for -SCN and carbonyl groups at 2155 and 1676 cm^{-1}. Its identity was further confirmed by comparing its melting point with that reported in the literature.[18]

A similar reaction was observed in the case of 4-chlorostyrene (Scheme 15).



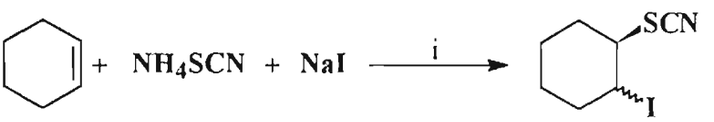
12 **38** (33%) **39** (16%)

i. CAN, MeOH, 0 °C, 30 min

Scheme 15

As usual, the structures of the products **38** and **39**[19] were established on the basis of spectral data. The GC-MS of **38** displayed a peak at *m/z* 138 corresponding to the loss of -SCN and iodine.

In order to examine the applicability of this reaction to aliphatic alkenes we exposed cyclohexene and 1-octene to NH_4SCN, NaI, CAN reagent combination in methanol. Cyclohexene under the above reaction conditions afforded the 1-iodo-2-thiocyanate in 57% yield as a 1:4 mixture of *cis* and *trans* isomers (Scheme 16). The ratio of the inseparable mixture was determined from the ^1H NMR spectrum.



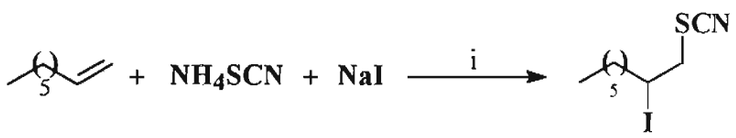
28 **40**

i. CAN, MeOH, 0 °C, 30 min, 57%.

Scheme 16

In the IR spectrum of **40**,[16] the -SCN absorption was visible as a sharp peak at 2149 cm^{-1}. The -C<u>H</u>I protons of the isomers gave rise to multiplets centered at δ 4.29 and 4.08. The C<u>H</u>SCN protons also resonated as multiplets centered at δ 3.45 and 3.23. In the ^{13}C NMR spectrum, the -SCN carbon appeared at δ 110.16. GC-MS displayed the molecular ion peak at *m/z* 267. All other signals were in agreement with the assigned structure.

A similar reaction occurred with 1-octene to afford the iodothiocyanate **41** in poor yield (Scheme 17).



30 **41**

i. CAN, MeOH, 0 °C, 30 min, 12%

Scheme 17

The IR spectrum of **41** showed the characteristic absorption of -SCN at 2155 cm^{-1}. In the ^{1}H NMR spectrum, the C<u>H</u>I and C<u>H</u>$_2$SCN protons resonated as multiplets in the region δ 4.31-4.22 and 3.73-3.38 respectively. In the ^{13}C NMR spectrum, the -SCN carbon was discernible at δ 110.90. All other NMR signals were in agreement with the proposed structure.

In conclusion, we have encountered a novel and experimentally simple route to iodothiocyanates. Further investigations aimed at determining the scope and limitations of this reaction and optimizing the reaction conditions are currently being pursued by other members of the research group.

4.2.3 Experimental

1-Iodo-1-phenyl-2-thiocyanatoethane (36) and

2-Thiocyanatoacetophenone (37)

To a mixture of styrene (104 mg, 1 mmol), NH_4SCN (76 mg, 1 mmol) and NaI (149 mg, 1 mmol) in methanol (2 mL), a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) was added dropwise at 0 °C. After completion of the reaction, the mixture was diluted with water (100 mL) and extracted using dichloromethane (4 X 25 mL). The combined organic extract

was washed successively with water and saturated brine, dried (anhydrous Na_2SO_4) and concentrated in *vacuo*. The crude residue was subjected to column chromatography using hexane-ethyl acetate (95:5) as eluent to afford **36** (122 mg, 42%) as a pale yellow oil. Further elution using hexane-ethyl acetate (90:10) afforded **37** (35 mg, 20%) as a colorless solid.

Product 36[16]

IR (neat) ν_{max} : 3033, 2155, 1452, 1104, 693 cm^{-1}.

^1H NMR : δ 7.39-7.33 (m, 5H, ArH), 5.30 (dd, J = 10.8, 5.5 Hz, 1H, CHI), 3.94 (dd, J = 13.0, 5.5 Hz, 1H, CH_2SCN), 3.69 (dd, J = 13.0, 10.8 Hz, 1H, CH_2SCN).

^{13}C NMR : δ 139.58, 129.12, 128.84, 127.39, 110.24, 42.87, 25.49.

Product 37

Recrystallized from dichloromethane-hexane; mp 71-72 °C (lit.,[18] mp 72 °C).

IR (neat) ν_{max} : 2934, 2155, 1676, 1446, 1203, 998 cm^{-1}.

^1H NMR : δ 7.95-7.92 (m, 2H, ArH), 7.66 (t, J = 7.3 Hz, 1H, ArH), 7.55-7.40 (m, 2H, ArH), 4.74 (s, 2H, CH_2SCN).

1-(4'-chlorophenyl)-1-Iodo--2-thiocyanatoethane (38) and 4'-Chloro-2-thiocyanatoacetophenone (39)

A mixture of 4-chlorostyrene (138 mg, 1 mmol), NH_4SCN (76 mg, 1 mmol) and NaI (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature. After completion of the reaction the reaction mixture was processed as described earlier to afford **38** (105 mg, 33%) as a pale yellow oil and **39** (34 mg, 16%) as a colorless crystalline solid.

Product 38

IR (neat) ν_{max} : 2921, 2155, 1589, 1483, 1085, 823 cm^{-1}.

^1H NMR : δ 7.41-7.34 (m, 4H, ArH), 5.26 (dd, *J* = 11.0, 5.4 Hz, 1H, CHI), 3.94 (dd, *J* = 13.4, 5.4 Hz, 1H, CH_2SCN), 3.63 (dd, *J* = 11.0, 13.4 Hz, 1H, CH_2SCN).

^{13}C NMR : δ 138.23, 134.99, 129.46, 128.82, 110.17, 42.65, 24.13.

GC-MS (*m/z*) : 138 [M^+-SCN-I] (100), 127 (2), 103 (74), 77 (40).

Product 39

Recrystallized from dichloromethane-hexane; mp 135 °C (lit.,[19] mp 135 °C).

IR (neat) ν_{max} : 3095, 2983, 2155, 1670, 1589, 1203 cm^{-1}.

^1H NMR : δ 7.89 (d, *J* = 8.5 Hz, 2H, ArH), 7.51 (d, *J* = 8.5 Hz, 2H, ArH), 4.70 (s, 2H, CH_2SCN).

^{13}C NMR : δ 189.49, 141.59, 132.37, 129.86, 129.75, 111.27, 42.72.

***trans/cis*-1-iodo-2-thiocyanatocyclohexane 40**[16]

A mixture of cyclohexene (82 mg, 1 mmol), NH_4SCN (78 mg, 1 mmol) and NaI (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature. After completion of the reaction the mixture was worked up as usual and the product purified by silica gel column chromatography using hexane-ethyl acetate (95:5) as eluent to afford **40** (152 mg, 57%) as a colorless oil (1:4 mixture of *cis* and *trans* isomers).

IR (neat) ν_{max} : 2940, 2859, 2149, 1446, 1153, 973 cm^{-1}.

^{1}H NMR : δ 4.31-4.26 (m, C<u>H</u>I), 4.10-4.05 (m, C<u>H</u>I), 3.50-3.40 (m, C<u>H$_2$</u>SCN), 3.23 (m, C<u>H$_2$</u>SCN), 2.50-1.31 (m, 8H, CH_2).

^{13}C NMR : δ 110.16, 56.69, 55.43, 38.39, 37.42, 34.98, 32.60, 31.90, 30.01, 26.87, 26.12, 24.64, 23.35.

GC-MS (*m/z*) : 267 M^+ (5), 254 (5), 209 (1), 140 (12), 127 (20), 98 (4), 81 (100).

2-Iodo-1-thiocyanatoctane 41

A mixture of 1-octene (112 mg, 1 mmol), NH_4SCN (76 mg, 1 mmol) and NaI (149 mg, 1 mmol) in methanol (2 mL) was treated with a solution of CAN (1.151 g, 2.1 mmol) in methanol (10 mL) at ice temperature. After completion of the reaction, the mixture was worked up as usual and the product purified by silica gel column chromatography using hexane-ethyl acetate (95:5) as eluent to afford **41** (35 mg, 12%) as a colorless oil.

IR (neat) ν_{max} : 2934, 2155, 1639, 1458 cm^{-1}.

^{1}H NMR : δ 4.31-4.22 (m, 1H, C<u>H</u>I), 3.73-3.38 (m, 2H, C<u>H$_2$</u>SCN), 1.89-0.91 (m, 13H).

^{13}C NMR : δ 110.90, 43.24, 37.75, 34.21, 30.56, 29.17, 28.30, 22.57, 14.09.

4.3 References

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SUMMARY

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

A brief account of the development of radical reactions followed by a survey of the literature on the synthetic applications of CAN, mainly in carbon-heteroatom bond forming reactions, form the subject matter of chapter 1. A definition of the research problem has also been presented.

Chapter 2 deals with the CAN mediated addition of azide to α,β-unsaturated carbonyl compounds and their further chemical transformations. The α,β-unsaturated carbonyl compounds selected for our study are cinnamic acids (**15**, **17**, **19**, **21** and **23**), cinnamic esters (**27**, **29**, **31**, **33**, **35**, **37**, **39**, **42**, **45** and **48**), benzylidene acetones (**56**, **72**, **74** and **76**), chalcones (**78** and **80**), dibenzylidene acetone **82** and cinnamamide **59**. CAN mediated oxidative addition of azide to cinnamic acids in dry acetonitrile under deoxygenated atmosphere afforded the corresponding α-azido-β-nitrato acids. The cinnamic esters **27**, **29**, **31**, **33**, **35** and **37** afforded the α-azido-β-nitrato esters as the only isolable products. Azidonitrates were found to be mixture of *syn* and *anti* isomers. Cinnamic ester **39** afforded the α-azido-β-nitrato ester **40** and α-azido-β-hydroxy ester **41**. Cinnamic ester **42** afforded the α-azidocinnamate **43** and α-azido-β-hydroxy ester **44** under the usual reaction conditions. Benzylidene acetone **56** afforded the azidonitrate **57**, α-azido-α,β-unsaturated ketone **58** and phenacyl azide **14** under deoxygenated atmosphere, whereas **14** was the major product under

oxygen atmosphere. Cinnamamide **59** also afforded the α-azido-β-nitrato amide **60** in very good yield. In the second part of this chapter, the chemical transformations of α-azido-β-nitrates are described. Sequential treatment of cinnamic acids (**15**, **17**, **19** and **21**) with NaN_3/CAN in dry acetonitrile followed by sodium acetate in dry acetone afforded the β-azidostyrenes **61-64** in moderate to good yields. Cinnamic esters (**27**, **29**, **31**, **33**, **37**, **39** and **48**) under these reaction conditions afforded corresponding α-azidocinnamates **65-71** in good yields; the latter are precursors of indoles and azirines. α,β-Unsaturated ketones (**56**, **72**, **74**, **76**, **78**, **80** and **82**) also underwent similar reaction to afford the α-azido-α,β-unsaturated ketones **58**, **73**, **75**, **77**, **79**, **81** and **83** respectively in good yields. A mechanistic rationalization of the various reactions observed is provided in this chapter.

The third chapter is concerned with CAN mediated addition of thiocyanate to arenes and dienes. The arenes selected for our study are indoles (**31**, **32**, **34**, **36** and **40**), pyrroles (**42** and **44**), thiophene **45**, aromatic amines (**25**, **49**, **51**, **53** and **55**) and veratrole **14**. Indoles (**31**, **32**, **34** and **36**) on reaction with NH_4SCN and CAN in methanol afforded the 3-thiocyanated products in excellent yields. 3-Methylindole **40** afforded the 2-oxo-3-thiocyanatoindole **41** in low yield. Pyrroles **42** and **44** afforded the 2-thiocyanated products **43** and **10** respectively in very good yields. Thiophene **45** afforded the 2-thiocyanated product in low yield. In the case of anilines, *p*-thiocyanated products were isolated in moderate to good yields. Reaction of *N,N*-dimethylaniline **25** in acetonitrile afforded the *o*-nitro-*p*-thiocyanated product **58** in moderate yield. In the case of the alkoxybenzene **14**, formation of thiocyanated product was not observed. In the second part of this chapter, thiocyanation of dienes using NH_4SCN/CAN reagent combination in acetonitrile was investigated. Diene **60** afforded the 1,4-dithiocyanated product **61** as the only isolable product. In the case of

dienes **62**, **68**, **70**, **72** and **74**, the dithiocyanate formed underwent [3,3] sigmatropic rearrangement to afford the isothiocyanato-thiocyanates. Dienes **76** and **78** afforded the γ-thiocyanato-α,β-unsaturated carbonyl compounds **77** and **79** respectively.

Chapter 4 is divided into two sections. In the first section, a facile one-pot azidoiodination of alkenes using NaN_3/NaI/CAN reagent combination in methanol is discussed. The reaction was investigated with arylalkenes (**7**,**10**, **12**, **14**, **20**, **22**, **24** and **26**), cyclic alkenes (**28** and **32**), aliphatic alkene **30** and carvone **1**. The azidoiodination proceeded with high regioselectivity and the products were isolated in moderate to good yields. α-Pinene **32** under similar reaction conditions afforded the rearranged product **33**. In the second part of this chapter, a preliminary investigation of the corresponding iodothiocyanation reaction was carried out using NH_4SCN/NaI/CAN reagent combination in methanol. Styrenes **7** and **12** afforded the iodothiocyanates **36** and **38** respectively in moderate yields along with the corresponding phenacyl thiocyanates. Cyclohexene afforded the iodothiocyanate **40** in good yield. In the case of 1-octene, the iodothiocyanated product **41** was isolated in low yield.

In conclusion, it has been clearly demonstrated that CAN is an excellent reagent for carbon-heteroatom bond forming reactions. It is anticipated that the results of our investigations will lead to wider acceptance of CAN in organic synthesis.

LIST OF PUBLICATIONS

1. Nair, V.; **George, T. G.**; Nair, L. G.; Panicker, S. B. *"A Direct Synthesis of Arylthiocyanates Mediated by Cerium(IV) Ammonium Nitrate."* **Tetrahedron Lett. 1999**, *40*, 1195.
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3. Nair, V.; Sheeba, V.; Panicker, S. B.; **George, T.G.**; Rajan, R.; Balagopal, L.; Vairamani, M.; Prabhakar, S. *"Cerium(IV) Ammonium Nitrate Induced Dimerization of Methoxystyrenes"* **Tetrahedron 2000**, 56, 0000.
4. Nair, V.; **George, T. G.** *"A Novel Synthesis of α-Azidocinnamates, α-Azido-α,β-unsaturated ketones and β-Azidostyrenes Mediated by Cerium(IV) Ammonium Nitrate."* **Tetrahedron Lett. 2000**, *41*, 0000.
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6. Nair, V.; **George, T. G.** *"Cerium(IV) Ammonium Nitrate Mediated Addition of Thiocyanate to Dienes."* **Synth. Commun.** (To be communicated).
7. Nair, V.; **George, T. G**. *"A Facile Synthesis of Iodoazides Mediated by Cerium(IV) Ammonium Nitrate"* **Synlett** (To be communicated).

POSTERS PRESENTED AT SYMPOSIA

1. Nair, V.; Mathew, J.; Nair, L. G.; Panicker, S. B.; Sheeba, V.; **George, T. G**. *"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.
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