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

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

BY

JESSYMOL MATHEW

REGIONAL RESEARCH LABORATORY (C S I R)
TRIVANDRUM-695 019, INDIA

FEBRUARY 1995

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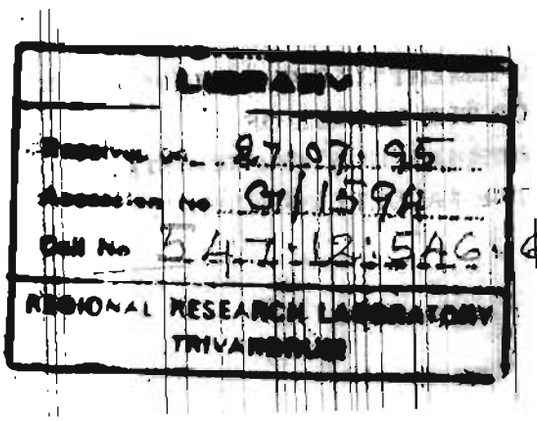

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DECLARATION

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me at the Regional Research Laboratory, Trivandrum, under the supervision of **Dr. G. Vijay Nair** and the same has not been submitted elsewhere for any other degree.

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CERTIFICATE

Certified that the work contained in this thesis entitled "**NOVEL CARBON-CARBON BOND FORMING REACTIONS MEDIATED BY CERIUM(IV) AMMONIUM NITRATE**" has been carried out by Ms. **Jessymol Mathew** under my supervision and the same has not been submitted elsewhere for any other degree.

G. Vijay Nair

G. VIJAY NAIR

THESIS SUPERVISOR

February 1995

ACKNOWLEDGEMENTS

It is with great pleasure that I place on record my deep sense of gratitude and indebtedness to my research supervisor, Dr. G. Vijay Nair, for his inspiring guidance, constant encouragement and helpful discussions.

I am grateful to Dr. A.D. Damodaran, Director, RRL, Trivandrum, for providing the necessary facilities to carry out this work.

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I would like to express my gratitude to Dr. Mangalam S. Nair for the help I received during the course of this work. All the members of the Organic Chemistry Division have been extremely helpful and cooperative and I am thankful to one and all of them. A special word of thanks to my friend Ms. Kanakamma, P.P. for her immense help and constant support throughout my stay at RRL. I take this opportunity to thank Mr. T. K. Sasikumar, Mr. J. S. Dileepkumar, Dr. George Thomas and Mr. K. J. Thomas for their help in recording NMR and mass spectra and Ms. Susan Alexander, Ms. R. L. Bindu and Mr. K. V. Radhakrishnan for their help in completing some of the experiments reported in this thesis. I am thankful to Dr. Abraham Thomas for proof reading the thesis. Also, I wish to thank all the members of the Photochemistry Research Unit for their help during the course of this work.

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JESSYMOL MATHEW

CONTENTS

PREFACE

Carbon-carbon bond forming reactions are of fundamental importance in Organic Synthesis. A vast array of synthetic methods involving polar, radical or pericyclic reactions are available for C-C bond formation. Among these, the radical processes have received the least attention due to the erroneous notion that radical reactions lack selectivity and are uncontrollable. However, the situation changed during the past decades, largely due to a better understanding of the structure and reactivity of many elementary classes of organic radicals and the demonstration by Stork and others that radical methodology can provide a powerful alternative to ionic reactions in the construction of complex and highly functionalized organic compounds. Today, there is widespread appreciation of the potential offered by radical processes and these are perceived to add a new dimension to Organic Synthesis.

Among the various procedures developed for the generation of radicals, the oxidative process mediated by $Mn(OAc)_3$ has received considerable attention. Eventhough cerium salts such as cerium(IV) ammonium nitrate (CAN) has been shown to offer some advantages over $Mn(OAc)_3$, the potential of Ce(IV) reagents in C-C bond forming reactions has not been tapped adequately. Therefore a detailed investigation was carried out to explore the synthetic utility of CAN and the results obtained are presented in the thesis entitled "Novel Carbon-Carbon Bond Forming Reactions Mediated by Cerium(IV) Ammonium Nitrate". The thesis is divided into four chapters. Relevant references are given at the end of each chapter.

A brief account of the developments in the chemistry of radical reactions in general and Ce(IV) mediated reactions in particular, from the vantage point of organic synthesis, forms the subject matter of Chapter 1.

The second chapter details a facile, experimentally simple and efficient procedure for the CAN mediated oxidative addition of 1,3-dicarbonyl compounds to alkenes. A comparative study of these reactions with $Mn(OAc)_3$ which indicates the superiority of CAN in terms of experimental simplicity and higher yields of products is also described.

The CAN mediated addition of dimethyl malonate to styrene and ring substituted styrenes led to some novel and remarkable results and these are discussed in the third chapter.

Chapter four deals with the synthesis of spirodihydrofurans along with some miscellaneous reactions mediated by CAN. These include oxidative addition reactions of 1,3-dicarbonyl compounds to dienes and acetylenes, attempted intramolecular radical cyclizations and oxidative additions of 2-acetyl- and 2-carboethoxycyclohexanones.

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

CHAPTER 1

FREE RADICAL CARBON-CARBON BOND FORMING REACTIONS IN ORGANIC SYNTHESIS

1.1. Introduction

Formation of carbon-carbon bond is of pivotal importance in Organic Synthesis. During the past forty years, there have been dramatic developments in the design of novel synthetic methods for the construction of C-C bonds. These methods involve such diverse reactions as alkylation and acylation of enolates and enamines, nucleophilic additions to carbonyls and activated alkenes, transition metal mediated additions, photochemical and carbene reactions. Many of these processes often suffer from competing side reactions brought about by incompatible functional groups.

The addition of a carbon centred radical to a π-bond to form a σ-bond and a new radical is a fundamental organic reaction that has been exploited by polymer chemists for the synthesis of new materials. On the other hand, synthetic organic chemists have rarely employed free radical C-C bond forming reactions in the synthesis of complex organic compounds. During the past few years, however, free radical reactions have gained popularity and organic chemists have begun to use inter- and intramolecular radical reactions to achieve useful synthetic transformations. A brief account of the developments in the chemistry

of free radical reactions from the vantage point of organic synthesis is presented in the next few pages.

Ever since Gomberg[1] first investigated the formation and reactions of triphenylmethyl radical in 1900, free radical species have been known to be the reactive intermediates in a large number of chemical reactions. The first description of the application of radicals in organic synthesis is the phenylation of aromatic compounds in presence of benzoyl peroxide reported by Hey and Waters[2] in 1937. Later, Kharasch[3] has shown that the anti-Markovnikov addition of hydrogen bromide to alkenes proceeds through radical intermediate. In the following years, Mayo, Walling and Lewis[4] applied the rules of radical copolymerization to synthesize polymers of industrial importance. Most of the fundamental principles governing organic radical reactions emerged as a result of the research in radical mediated polymerizations and the mechanistic studies carried out by Kharasch[5]. Subsequent elucidation of the kinetics and thermodynamics of hexenyl radical[6] cyclizations, Stork's report of the cyclization of ketyls[7] and the emergence of tin hydrides as useful reagents[8], all contributed significantly to the development of the field. By 1970, radical allylations with allyl stannanes were described[9] and Julia[10] demonstrated many elegant examples of ring forming reactions of radicals. The oxidative process for radical generation with manganese(III) acetate[11,12] and other transition metal salts[13] introduced during the same period was another important achievement. Mention may also be made of certain classical name reactions like Kolbe electrolysis[14], Barton reaction[15] and Hofmann-Löffler-Freytag reaction[16] that are now recognized to involve the intermediacy of radicals. Another important radical reaction that came out later was the Giese reaction[17]. Even after all these developments,

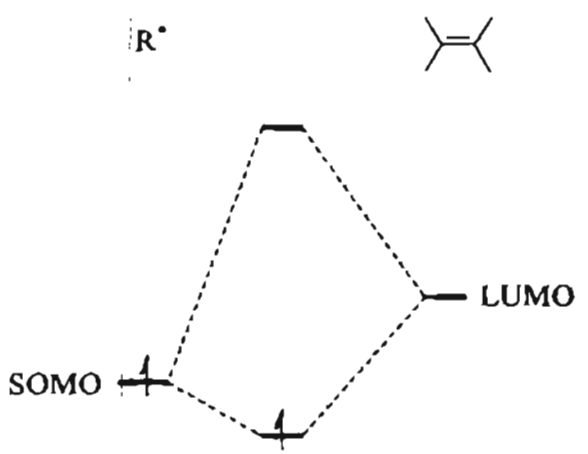
free radical reactions continued to be considered by most organic chemists as erratic and prone to give intractable mixtures.

However, during the past decade, free radical methodology was brought to limelight by the conceptualization and demonstration by Stork that the controlled formation[18] as well as addition of vinyl radicals to alkenes offers a unique and powerful method for complex carbocyclic construction[19]. This work and the demonstration by others coupled with the understanding of the structure and reactivity of many elementary classes of radicals led to the widespread use of radical methodology in organic synthesis[20]. The potential offered by radical processes is dramatically illustrated in the total synthesis of a number of complex natural products[20f,21].

It is now widely accepted that radical reactions even with highly complex substrates can be conducted selectively and efficiently. These reactions often provide advantages over the alternative ionic processes, the principal one being the avoidance of protecting groups for alcohols, amines and related functional groups. Also, radical reactions are ideally suited for the construction of quaternary and neopentyl centres. Unless a substrate or reagent contains an acidic or basic site, the conditions for most radical reactions are neutral. Thus side reactions like base catalysed epimerization are rarely a problem. In contrast to ionic intermediates, most radicals are inert to reactions that involve β-bond fragmentation. Another advantage is that carbon centred radicals can add to electron rich and electron deficient alkenes, allenes and acetylenes. These characteristics as well as the fact that radical reactions can accomplish many transformations that are difficult to achieve by conventional methods contribute to the importance of such reactions.

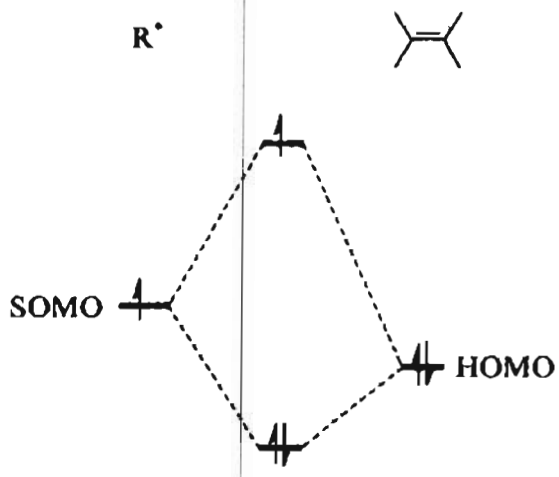
The addition of carbon centred radicals to double and triple bonds is a very useful C-C bond forming reaction in which a new sigma bond is formed at the expense of a pi bond. The appropriate matching of reactivity of a radical and an *acceptor is important* for the success of an addition reaction. Radicals are often classified according to their rates of reactions with alkenes. Those radicals that react more rapidly with electron poor alkenes than with electron rich ones are called nucleophilic radicals. Conversely, those that react more rapidly with electron rich alkenes than with electron poor ones are called electrophilic radicals.

The rate of addition of a radical to an alkene can be described by frontier molecular orbital (FMO) theory[22]. The singly occupied molecular orbital (SOMO) of the radical interacts with the lowest unoccupied molecular orbital (LUMO) or the highest occupied molecular orbital (HOMO) of the C-C multiple bond. Nucleophilic radicals have high lying SOMO and hence interacts preferentially with the LUMO of the alkene. Electron withdrawing substituents on the alkene lower the LUMO energy and hence increase the rate of addition by reducing the SOMO-LUMO energy gap.



Orbital interaction between a nucleophilic radical and an electron poor alkene

On the other hand, radicals with electron withdrawing substituents have low SOMO energy and SOMO-HOMO interaction occurs. These radicals react like electrophiles and electron donating substituents on the alkenes increase the rate of addition.



Orbital interaction between an electrophilic radical and an electron rich alkene

A number of procedures involving chemical[20], electrochemical[23] and photochemical methods[15,20e,24] have been developed for the generation of radicals. Some of the important chemical methods include metal hydride mediated reactions[20,25], fragmentation reactions[20a,26], and atom transfer reactions[20,27]. Recent efforts in this area have focussed on the use of transition metal salts for the generation of radicals. Oxidative methods mediated by Mn(III), Co(II), Cu(II), Ag(I) and V(V) are the most widely explored[13,20,28,29]. The main difference of oxidative methods from the traditional approaches is the dual role the metal oxidants play in these reactions. Initial one electron oxidation of the carbonyl compound generates the educt radical. Addition to an alkene now gives

the adduct radical that is more susceptible to oxidation. Products are often derived from the intermediate cation by inter- or intramolecular capture or by the loss of a proton to form an alkene. Hence, the products of metal mediated reactions significantly differ from peroxide or light initiated radical processes.

Metal ions like Mn(III) and Cu(II) generate carbon centred radicals from substrates which have one or more electron withdrawing groups. Thus, electrophilic educt radicals are formed which are not easily oxidised but can add efficiently to electron rich alkenes. Among the metal oxidants, a unique place is occupied by manganese(III) acetate providing a number of novel approaches to the synthesis of different classes of organic compounds[29]. Despite its growing importance, especially in natural product synthesis, the formation of side products often limit its use.

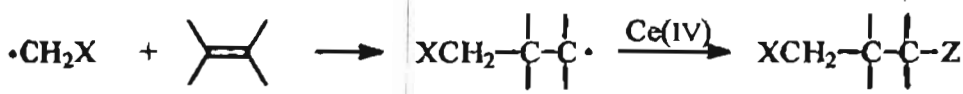
Naturally, there has been continuing interest in developing newer reagents and methods for generating radicals. Salts of other metals with stable oxidation states and suitable oxidation potentials can be expected to behave in an analogous manner. The pioneering work of Heiba and Dessau[30-33] has shown that Ce(IV) salts can be used for the generation of electrophilic carbon radicals. The low cost and toxicity of cerium reagents combined with their solubility in a variety of organic solvents like acetonitrile, methanol and tetrahydrofuran make these reagents attractive in organic synthesis. Cerium(IV) compounds, particularly cerium(IV) ammonium nitrate (CAN), have been extensively used for a variety of oxidative transformations. But there are only very few reports on their use in oxidative coupling reactions. These reports indicate the enhanced reactivity and general superiority of Ce(IV) reagents over the more frequently used Mn(III) salts. A brief review of the applications of Ce(IV) reagents in the construction of carbon-carbon bonds is presented in the next section.

1.2. Carbon-Carbon Bond Forming Reactions Mediated by Cerium(IV) Reagents : A Review

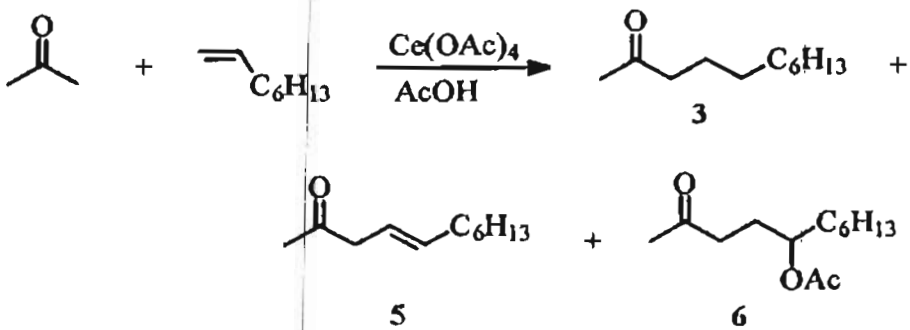
In recent years, the addition reactions of carbon centred radicals to alkenes mediated by one electron oxidants have attracted the attention of several research groups[28,29] as a very efficient method for the synthesis of a variety of useful compounds. As pointed out in Section 1.1, most of the work in this area involved the use of manganese(III) acetate as the oxidant. However, $Mn(OAc)_3$ is not always reliable and therefore it is of interest to explore the use of other oxidants.

The use of Ce(IV) salts for the generation of carbon centred radicals began with the initial work of Heiba and Dessau[30] in 1971. They have shown that electrophilic carbon radicals like $\cdot CH_2X$ and $\cdot CHXY$ (X and Y are electron withdrawing groups) generated by metal ions like Mn(III) and Ce(IV) which are one electron oxidants can react with alkenes to give addition products as shown below (Z is the ligand of the metal or conjugate base of the solvent).

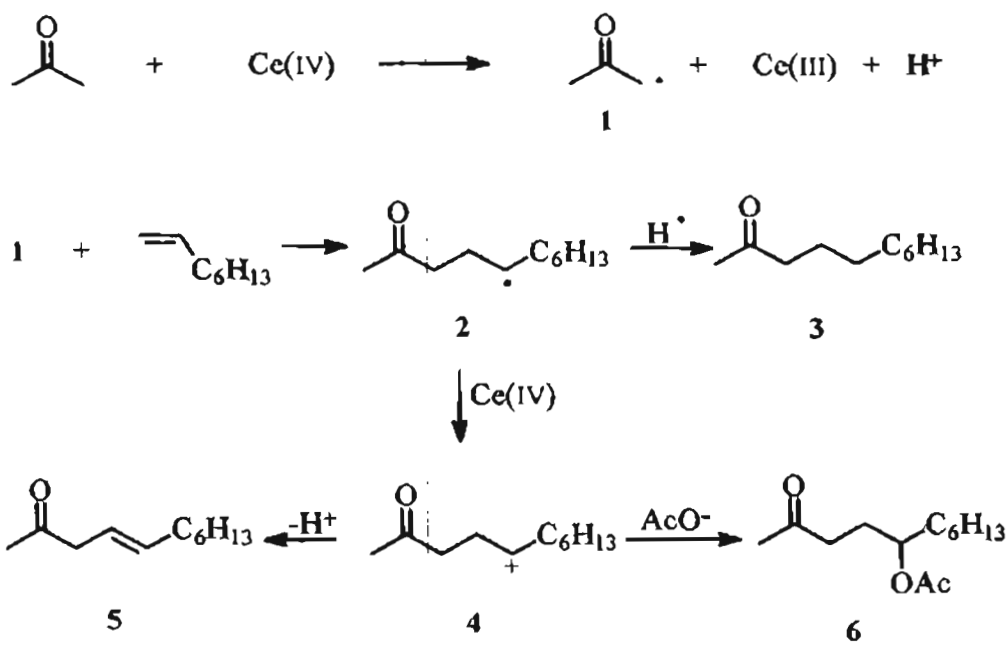
$$CH_3X + Ce(IV) \longrightarrow \cdot CH_2X + Ce(III) + H^+$$



Thus acetone reacts with 1-octene in the presence of cerium(IV) acetate to give the saturated ketone **3**, unsaturated ketone **5** and ketoacetate **6**.

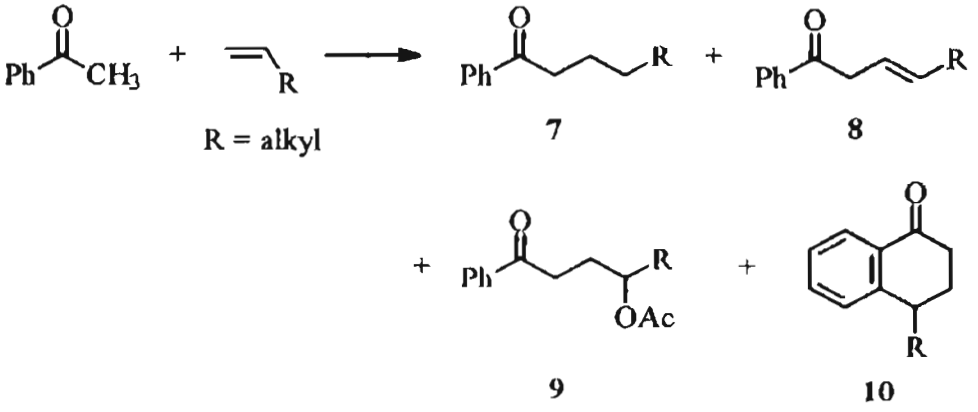


The formation of these products can be explained by the mechanism shown in Scheme 1. The initial step involves the oxidation of the ketone by Ce(IV) ion leading to the α-keto radical **1**. The radical rapidly adds to the olefin forming a secondary alkyl radical **2** which can either abstract a hydrogen atom from the solvent forming the saturated ketone **3** or undergo oxidation by the higher valent metal ion to the unsaturated ketone **5** and the ketoacetate **6**. The initially formed α-keto radical **1** is not easily oxidised due to the electron withdrawing character of the carbonyl group whereas the secondary alkyl radical **2**, formed by the addition of **1** to the olefin is readily oxidised by the metal ion.

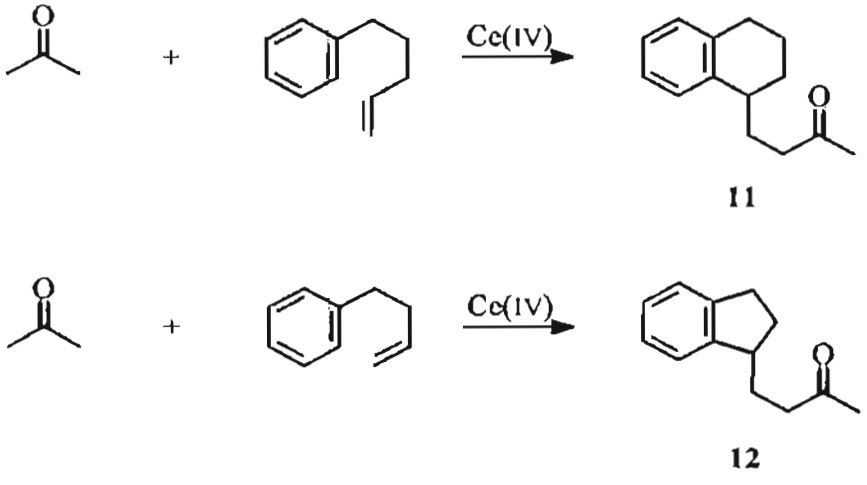


Scheme 1

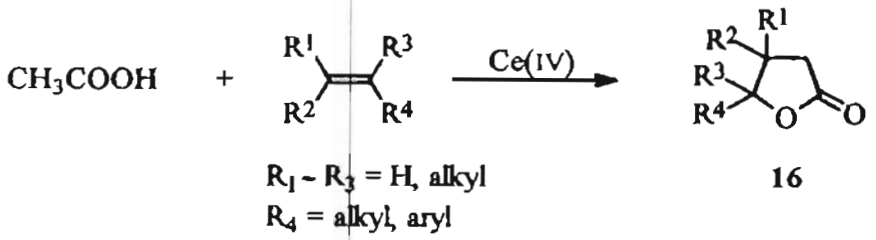
When an aryl ketone such as acetophenone was used, in addition to the three expected products **7**, **8** and **9**, a new product α-tetralone **10** was obtained[31], presumably by the addition of the intermediate radical to the benzene ring.



Another variation of the reaction *viz.* the synthesis of cyclized products **11** and **12** is shown in the following equations[31].



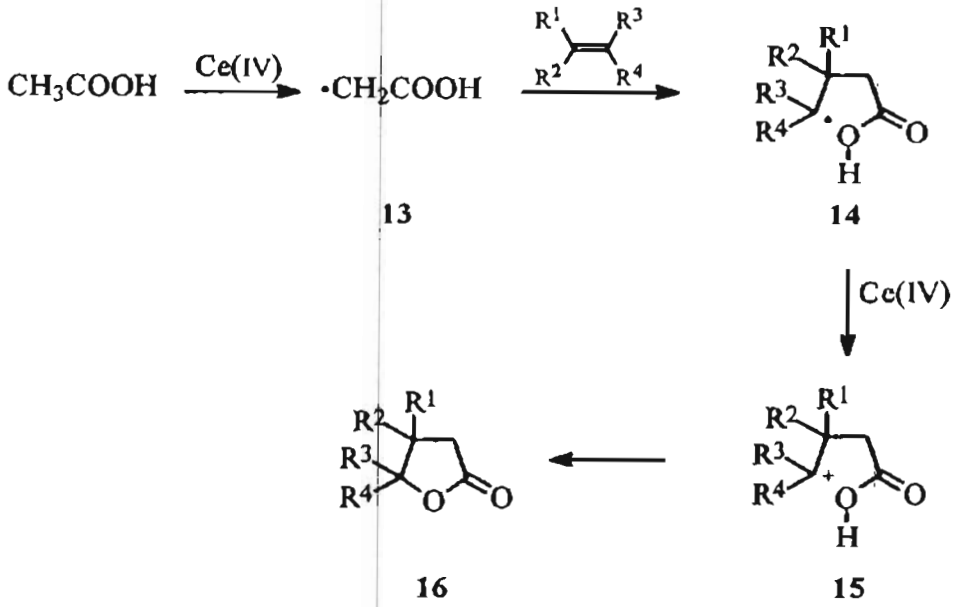
Cerium(IV) salts especially cerium(IV) acetate and cerium(IV) ammonium nitrate have been successfully used for the one step synthesis of γ-lactones from olefins and carboxylic acids[32,33].



$R_1 - R_3$ = H, alkyl
R_4 = alkyl, aryl

16

The proposed mechanism for lactone formation is presented in Scheme 2.



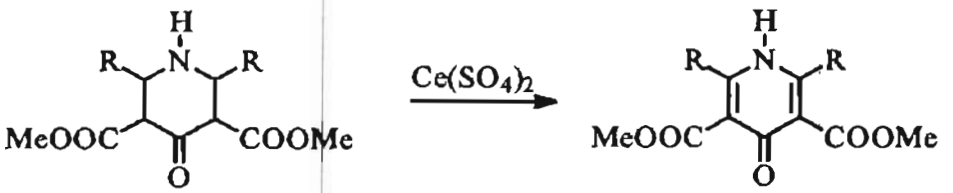
13 **14** **15** **16**

Scheme 2

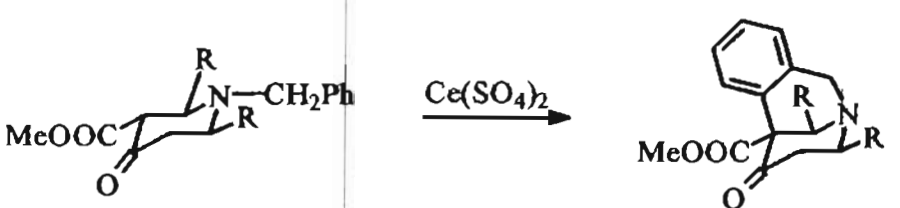
The initially formed carboxymethyl radical **13** adds to the olefin to give the radical **14** which is rapidly oxidised to the carbocation **15**. The latter then undergoes cyclization to give the lactone **16**.

Dimethyl ester of 2,6-disubstituted-4-piperidone-3,5-dicarboxylic acid was known to undergo oxidation to the pyridone **17** on reaction with cerium(IV) sulfate[34]. However, the corresponding reaction of 1-benzyl-2,6-disubstituted-4-

piperidone-3-carboxylic acid methyl ester afforded the cyclized product **18** in very low yield[35].



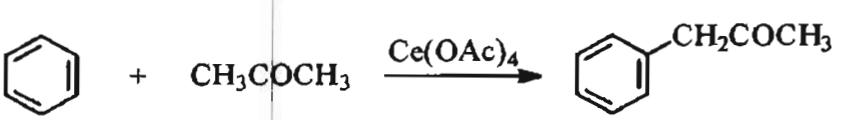
R = alkyl **17**



R = alkyl **18**

The free radical aromatic nitromethylation[36] and acetonylation[37] mediated by CAN have been reported to afford high yields of products.

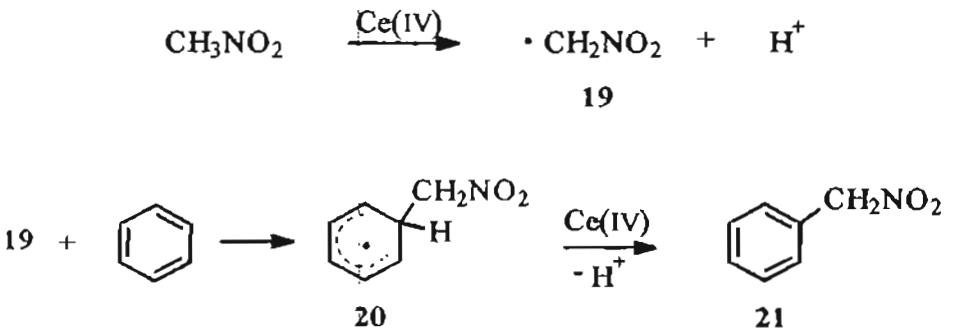
21



22

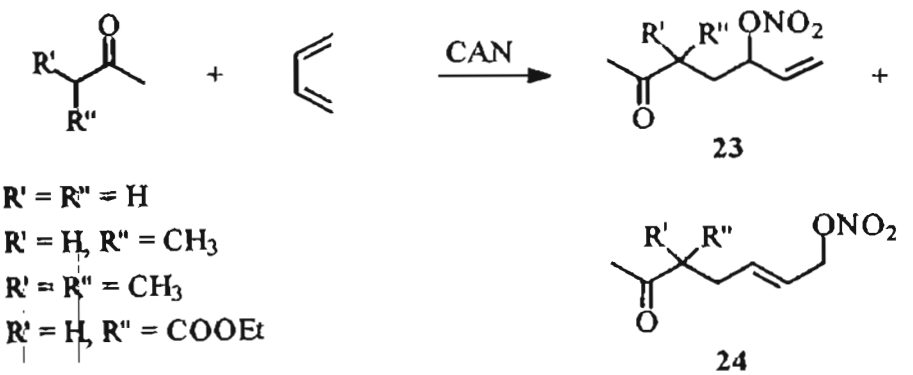
The mechanism of the reaction illustrated for the nitromethylation involves the oxidation of nitromethane to generate the radical **19**, attack of the

latter radical on the arene to produce a σ-radical complex **20** and its subsequent rearomatization to furnish the final product **21** (Scheme 3).

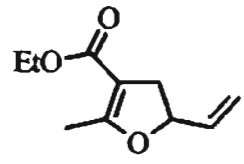


Scheme 3

Baciocchi and Ruzziconi have carried out CAN mediated 1,2- and 1,4-additions of carbonyl compounds such as acetone, 2-butanone, 3-methyl-2-butanone and ethyl acetoacetate to 1,3-butadiene[38].

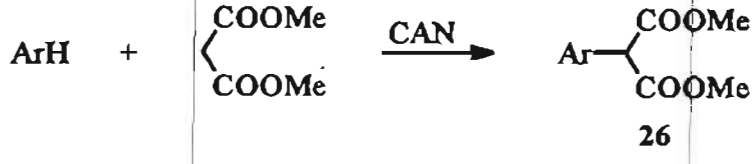


The 1,2-adduct formed in the case of ethyl acetoacetate was unstable and it underwent cyclization to **25**.



25

Aromatic compounds[39] and heteroaromatic compounds[40] undergo facile malonylation on reaction with malonyl radicals# generated by cerium(IV) ammonium nitrate and cerium(IV) sulfate respectively.



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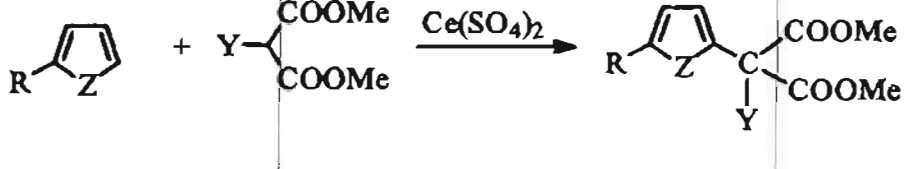
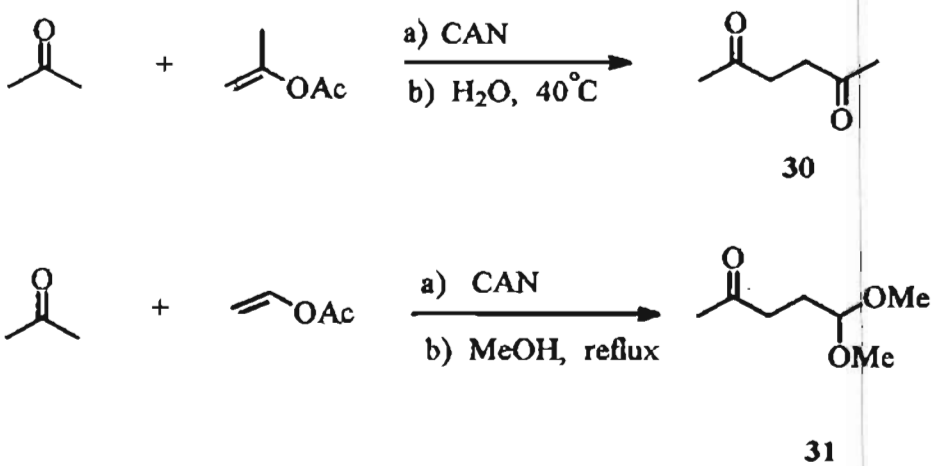


R = H, CH_3 Y = H, CH_2Ph, **27**

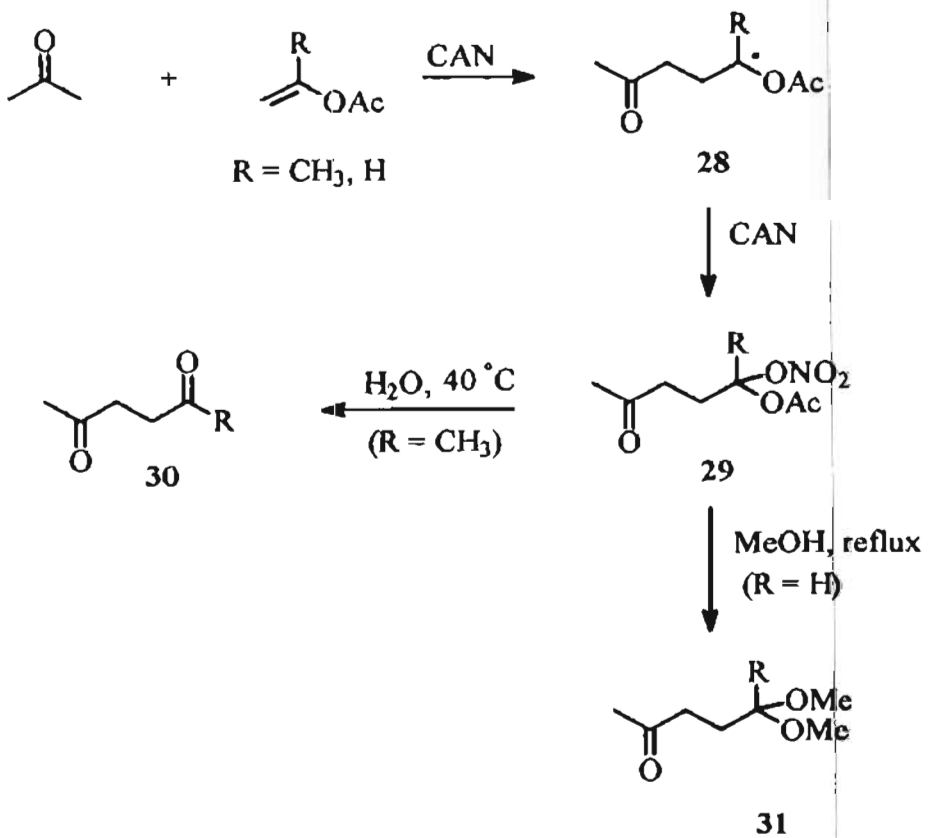
Z = O, S COOEt

1,4-diketones and 4-ketoaldehyde dimethyl acetals have been synthesized[41] in good yields by the CAN mediated addition of ketones to isopropenyl and vinyl acetates. Thus, the reaction of acetone with isopropenyl and vinyl acetate gave the diketone **30** and the dimethyl acetal **31** respectively.

An accurate description of this species would be 1,1-dicarbomethoxy methyl radical. However, for the sake of convenience, the term 'malonyl radical' is used throughout this thesis.

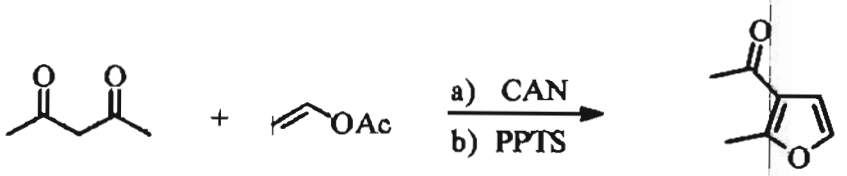


In this reaction, the nitrate adduct **29** is initially formed, from the radical **28** which gets converted to **30** and **31** as shown in Scheme 4.



Scheme 4

Similar reaction of acetylacetone and ethyl acetoacetate with vinyl acetate[42] gave 3-acetyl- and 3-carboethoxyfurans **32** and **33**.



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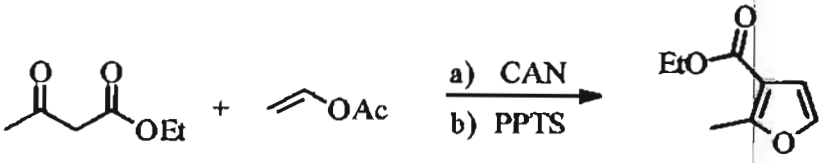
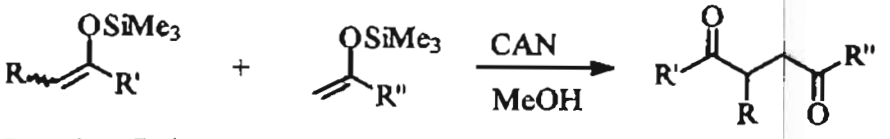


33

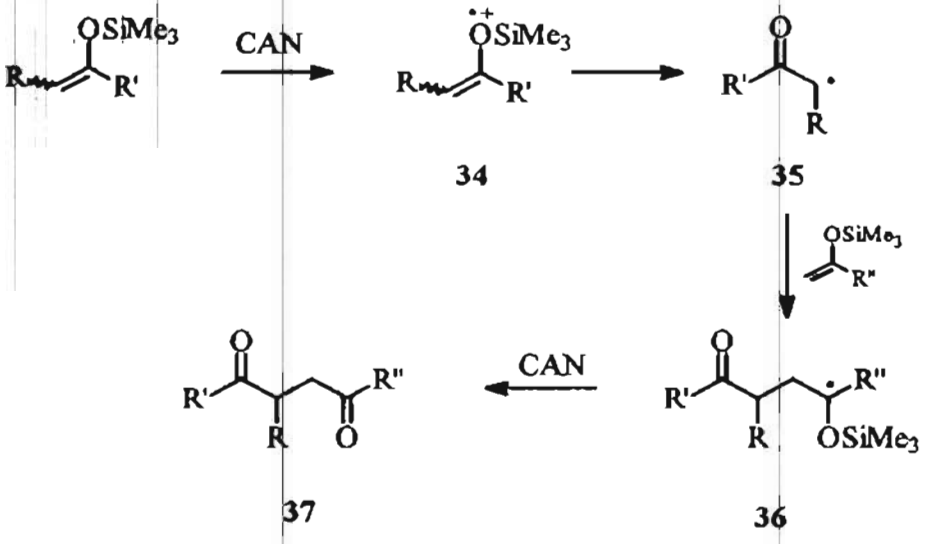
The synthesis of unsymmetrical 1,4-diketones have been achieved by the oxidative cross coupling between 1,2-disubstituted and 1-substituted trimethyl-silyl enol ethers[43].



R = R' = alkyl R'' = CH_3

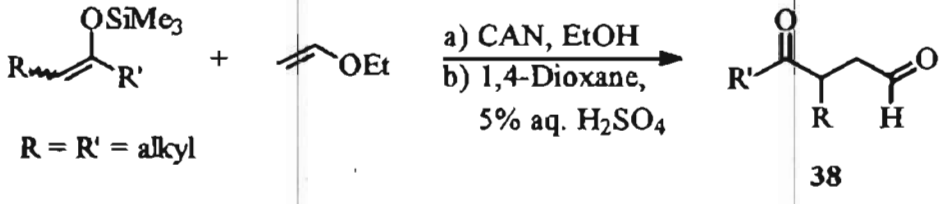
37

The success of the reaction rests on the relative ease of oxidation of the 1,2-disubstituted silyl enol ether *vis a vis* the 1-substituted one. CAN preferentially reacts with the former giving the electrophilic α-oxocarbon radical **35**, presumably through the radical cation **34**. The radical **35** now adds easily to the terminal double bond of electron rich 1-substituted silyl enol ether. The newly formed radical **36** is oxidised by CAN to give eventually the 1,4-dicarbonyl compound **37** (Scheme 5).



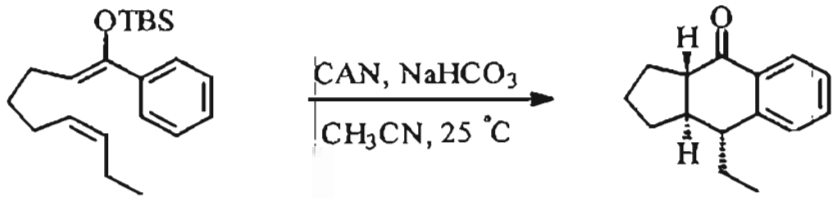
Scheme 5

A convenient synthesis of 4-oxoaldehydes[44] by the oxidative addition of 1,2-disubstituted trimethylsilyl enol ethers to ethyl vinyl ether has also been reported.



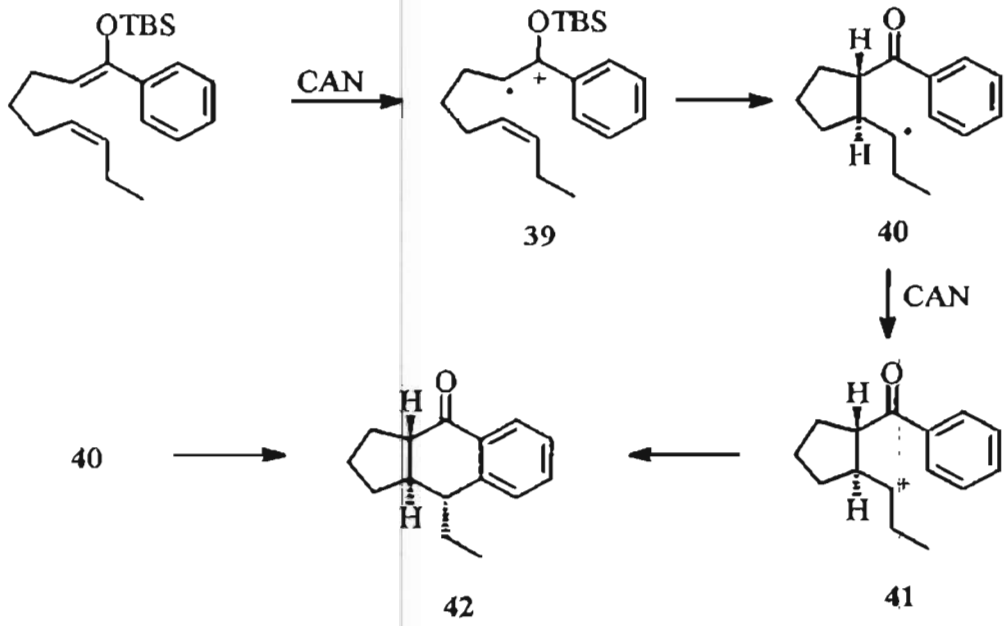
If acidification is omitted the diethyl acetal of the aldehyde is obtained along with small amounts of **38**.

An isolated report on the oxidative cyclization of unsaturated silyl enol ethers of aryl ketones with CAN in the presence of sodium bicarbonate to provide tricyclic ketones have appeared[45].



42

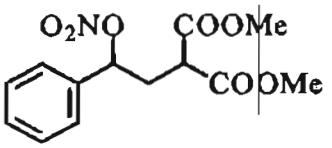
It is proposed that the reaction involves the initial formation of the cation radical **39** which adds to the double bond to give **40**. Cyclization to afford the tetralone **42** can occur at the cation or radical oxidation state as shown in Scheme 6.



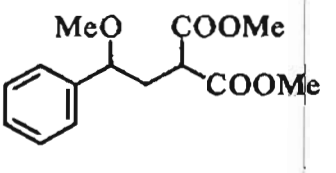
Scheme 6

The CAN mediated addition of dimethyl malonate to styrene# leading to the adducts **43** and **44** has been reported[46].

It should however be pointed out that we have obtained results that are significantly different and these are described in Chapter 3.

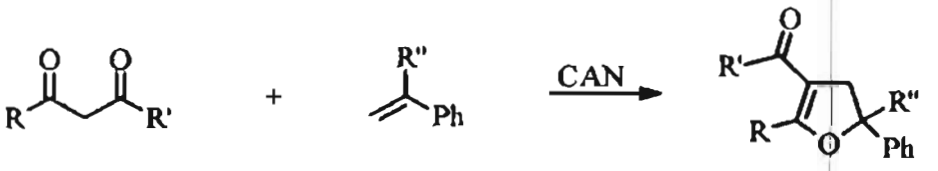


43



44

Acetylacetone and ethyl acetoacetate have been reported to undergo addition to substituted styrenes to afford dihydrofurans[47].



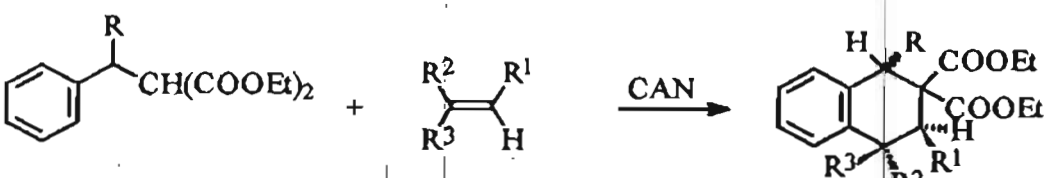
R = CH_3

R' = CH_3, OCH_3

R" = H, alkyl

45

The oxidation of substituted diethyl α-benzylmalonate by CAN in the presence of substituted olefins produced highly functionalized tetrahydronaphthalenes[48].



R = H, alkyl

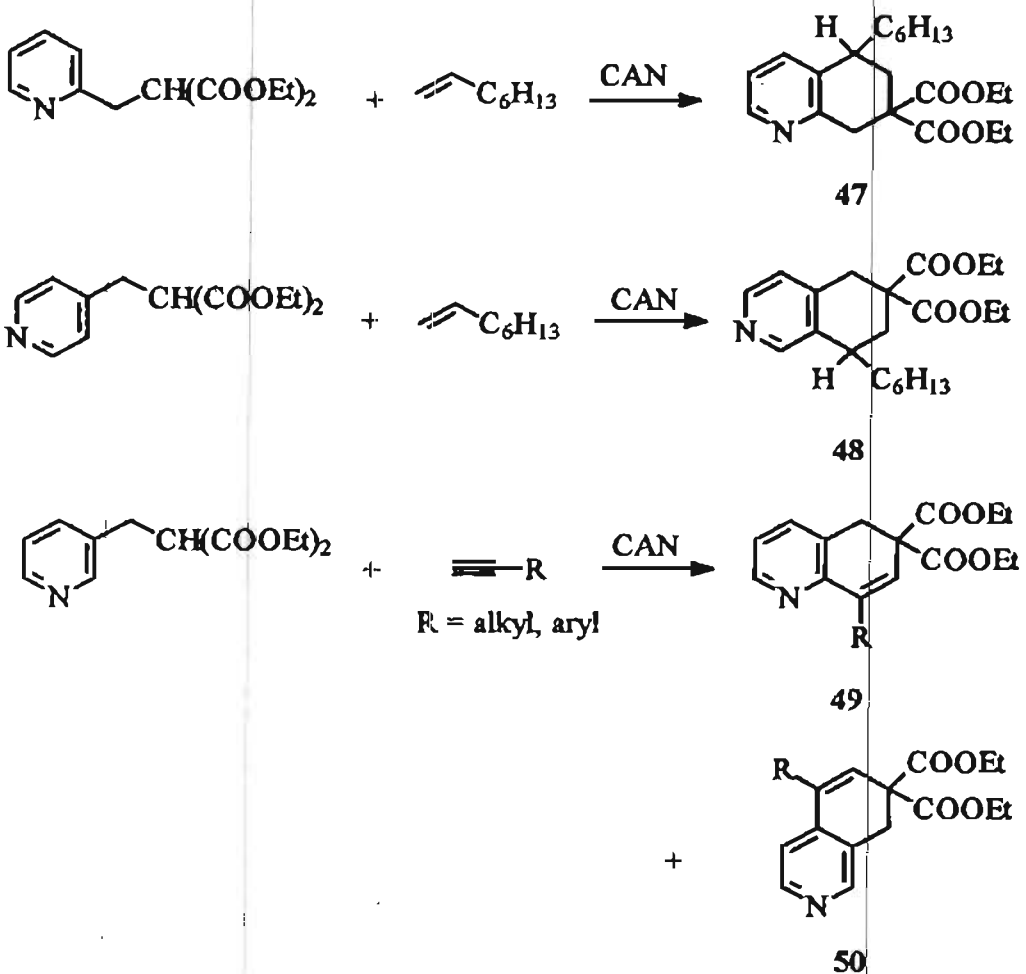
R_1 = H, CH_3

R_2 = CN, OAc, aryl etc

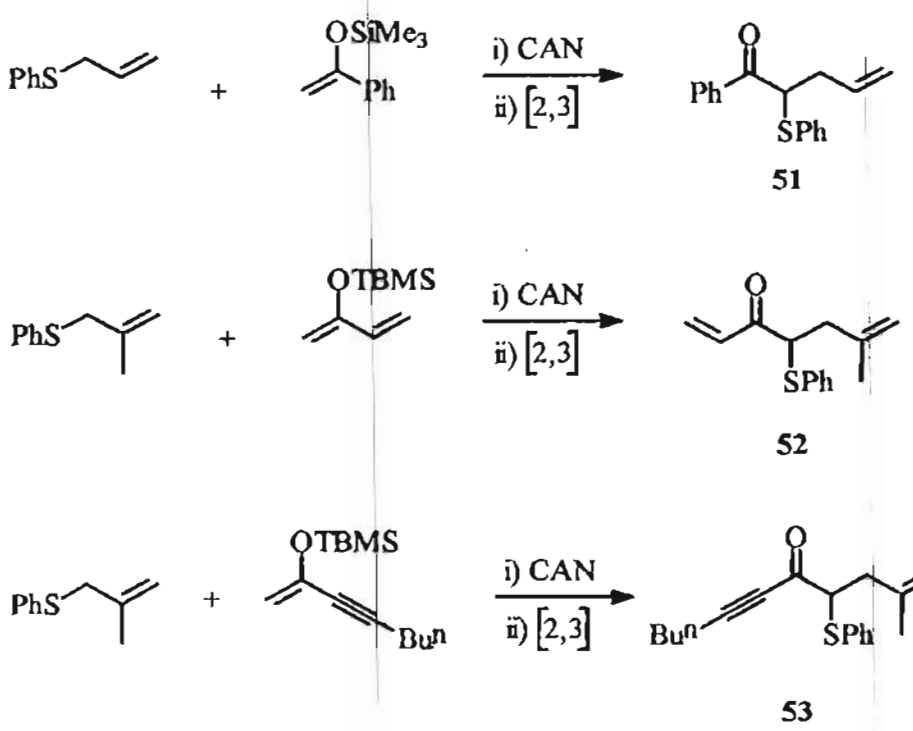
R_3 = H, CN, COOMe etc

46

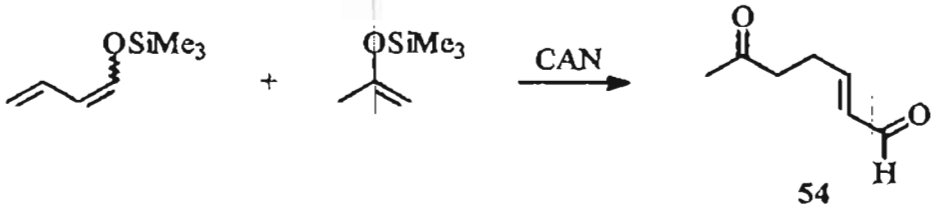
Similar oxidation[49] of diethyl (pyridylmethyl)malonates in the presence of alkenes and alkynes afforded substituted tetra- or dihydroquinolines and/or isoquinolines, **47-50**.



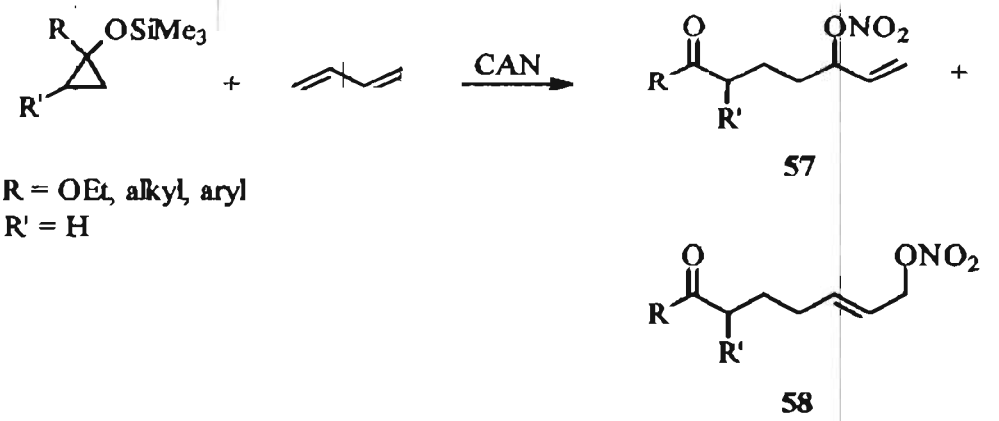
The cation radicals generated from allyl phenyl sulfides react with silyl enol ether, siloxy diene and siloxy enyne to give α-phenylthio-γ,δ-unsaturated ketones **51-53**. Presumably the reactions occur *via* the nucleophilic addition of silyl enol ethers to the sulfur cation radicals and the successive [2,3] sigmatropic rearrangement[50].



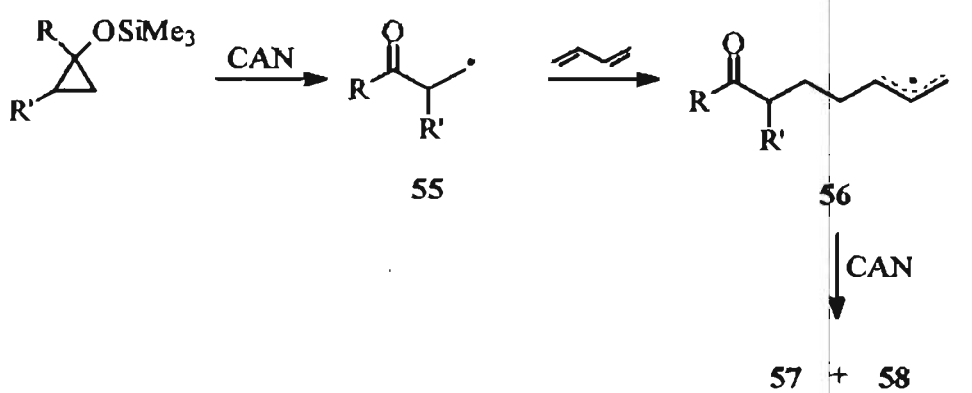
γ-Selectivity[51] was observed in the CAN mediated oxidative addition of silyl dienol ethers to silyl enol ethers.



Recent investigations of Ruzziconi[52] have shown that, like enol derivatives, silyloxy cyclopropanes can be easily oxidised by CAN. Accordingly, when trimethylsilyloxy cyclopropane was reacted with CAN in the presence of 1,3-butadiene, a mixture of 1,2- and 1,4-nitrooxy adducts **57** and **58** in nearly equimolar amount was obtained.



The overall process could be rationalized by considering that the oxidation of trimethylsilyloxy cyclopropane by CAN generates the allyl radical **56**. The latter then undergoes a fast oxidation by CAN leading to a mixture of 1,2- and 1,4-nitrooxy adducts **57** and **58** probably through a ligand transfer process (Scheme 7).



Scheme 7

It is evident from the foregoing discussion that the potential of cerium(IV) reagents in C-C bond forming reactions has not been exploited adequately. We have therefore carried out an extensive investigation in this area and our results are described in the subsequent chapters of this thesis.

1.3. References

1. (a) Gomberg, M. *J. Am. Chem. Soc.* **1900**, *22*, 757. (b) Gomberg, M. *Chem. Ber.* **1900**, *33*, 3150.
2. Hey, D. H.; Waters, W. A. *Chem. Rev.* **1937**, *21*, 169.
3. Kharasch, M. S.; Margolis, E. T.; Mayo, F. R. *J. Org. Chem.* **1937**, *2*, 393.
4. (a) Mayo, F. R.; Lewis, F. M. *J. Am. Chem. Soc.* **1944**, *66*, 1594. (b) Mayo, F. R.; Lewis, F. M.; Walling, C. *Discuss. Faraday Soc.* **1947**, *2*, 285.
5. Kharasch, M. S.; Jensen, E. V.; Urry, W. H. *Science* **1945**, *102*, 128.
6. Walling, C.; Huyser, E. S. *Org. React.* **1963**, *13*, 91.
7. Stork, G.; Malhotra, S.; Thompson, H.; Uchibayashi, M. *J. Am. Chem. Soc.* **1965**, *87*, 1148.
8. Kuivila, H. G. *Acc. Chem. Res.* **1968**, *1*, 299.
9. (a) Kosugi, M.; Kurino, K.; Takayama, K.; Migita, T. *J. Organomet. Chem.* **1973**, *56*, C11. (b) Grignon, J.; Pereyre, M. *J. Organomet. Chem.* **1973**, *61*, C33.
10. (a) Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386. (b) Julia, M. *Pure and Appl. Chem.* **1974**, *40*, 553.
11. Bush, J. B. Jr.; Finkbeiner, H. *J. Am. Chem. Soc.* **1968**, *90*, 5903.
12. Heiba, E. I.; Dessau, R. M.; Koehl, W. J. *J. Am. Chem. Soc.* **1968**, *90*, 5905.
13. (a) Jackson, A. H.; Martin, J. A. *J. Chem. Soc., Chem. Commun.* **1965**, 420. (b) Minisci, F. *Acc. Chem. Res.* **1975**, 165. (c) Nikishin, G. I.; Vinogradov, M. G.; Verenchikov, S. P. *Bull. Acad. Sci. USSR* **1969**, 1698. (d) Kauffmann, T.; Berger, D. *Chem. Ber.* **1968**, *101*, 3022. (e) Maryanoff, C. A.; Maryanoff, B. E.; Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 5839.

14. Kolbe, H. *Ann.* **1849**, *69*, 257. (b) Weedon, B. C. L. *Advances in Organic Chemistry, Methods and Results*; Interscience: New York, 1960; Vol.1, p. 1

15. (a) Barton, D. H. R. *Pure and Appl. Chem.* **1968**, *16*, 1. (b) Hesse, R. H. *Adv. in Free Radical Chem.* **1969**, *3*, 83.

16. Wolf, M. E. *Chem. Rev.* **1963**, *63*, 55.

17. (a) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 553. (b) Giese, B.; Kretzschmar, G. *Chem. Ber.* **1984**, *117*, 3175.

18. (a) Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321. (b) Stork, G.; Mook, R. Jr. *J. Am. Chem. Soc.* **1983**, *105*, 3720. (c) Stork, G. *Current Trends in Organic Synthesis;* Nozaki, H., Ed.; Pergamon: Oxford, 1983; p. 359.

19. (a) Stork, G.; Baine, N. H. *Tetrahedron Lett.* **1985**, *26*, 5927. (b) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765. (c) Stork, G. *Selectivity - A Goal for Synthetic Efficiency*; Bartman, W.; Trost, B. M., Ed.; Verlag Chemie: Weinheim, 1981; p. 281.

20. For excellent reviews on the use of radicals in organic synthesis see: (a) Giese B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: Oxford, 1986. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Curran, D. P. *Synthesis* **1988**, 417 (Part 1); **1988**, 489 (part 2). (d) Baciocchi, E.; Ruzziconi, R. *Free Radicals in Synthesis and Biology*; Minisci, F., Ed.; Kluwer: Dordrecht, 1989; p. 155. (e) Barton, D. H. R. *Aldrichimica Acta* **1990**, *23*, 3. (f) Curran, D. P.; Jasperse, C. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (g) Curran, D. P. *Comprehensive Organic Synthesis;* Trost, B. M.; Fleming, I., Ed.; Pergamon: New York, 1991; Vol. 4, p. 715 . (h) Beckwith, A. L. J. *Chem. Soc. Rev.* **1993**, 143.

21. Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303.

22. Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976.

23. (a) Knolle, J.; Schäfer, H. J. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 758. (b) Becking, L.; Schäfer, H. J. *Tetrahedron Lett.* **1988**, *29*, 2801. (c) Schäfer, H. J. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 911.

24. (a) Barton, D. H. R.; Crich, D.; Kretzschmar, G. *Tetrahedron Lett.* **1984**, *25*, 1055. (b) Cowan, D. O.; Drisko, R. L. *Elements of Organic Photochemistry*; Plenum: New York, 1976.

25. (a) Burke, S. D.; Fobare, W. F.; Armistead, D. M. *J. Org. Chem.* **1982**, *47*, 3348. (b) Giese, B.; Dupuis, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 622. (c) Adlington, R. M.; Baldwin, J .E.; Basak A.; Kozyrod, R. P. *J. Chem. Soc., Chem. Commun.* **1983**, 944.

26. (a) Russell, G. A.; Tashtoush, H. I.; Ngoviwatchai, P. *J. Am. Chem. Soc.* **1984**, *106*, 4622. (b) Toru, T.; Yamada, Y.; Ueno. T.; Maekawa, E.; Ueno, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4815.

27. Curran, D. P. *Free Radicals in Synthesis and Biology*; Minisci, F., Ed.; Kluwer: Dordrecht, 1989; p. 37.

28. De Klein, W. J. *Organic Synthesis by Oxidation with Metal Compounds*; Mijs, W. J.; de Jonge, C. R. H., Ed.; Plenum: New York, 1986; p. 261.

29. (a) Melikyan, G. G. *Synthesis* **1993**, 833. (b) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.

30. Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 524.

31. Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1972**, *94*, 2888.

32. Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 995.

33. Heiba, E. I.; Dessau, R. M.; Rodewald, P. G. *J. Am. Chem. Soc.* **1974**, *96*, 7977.

34. Müller, E.; Haller, R.; Merz, K. W. *Chem. Ber.* **1966**, *99*, 445.

35. Haller, R.; Kohlmorgen, R.; Hansel, W. *Tetrahedron Lett.* **1973**, *15*, 1205.

36. Kurz, M. E., Ngoviwatchai, P. *J. Org. Chem.* **1981**, *46*, 4672.

37. Kurz, M. E., Baru, V.; Nguyen, P. N. *J. Org. Chem.* **1984**, *49*, 1603.

38. Baciocchi, E.; Ruzziconi, R. *J. Org. Chem.* **1986**, *51*, 1645.

39. Baciocchi, E.; Ruzziconi, R., Aira, D. D. *Tetrahedron Lett.* **1986**, *27*, 2763.

40. Weinstock, L. M.; Corley, E.; Abramson, N. L.; King, A. O.; Karady, S. *Heterocycles* **1988**, *27*, 2627.

41. Baciocchi, E.; Civatarese, G.; Ruzziconi, R. *Tetrahedron Lett.* **1987**, *28*, 5357.

42. Baciocchi, E.; Ruzziconi, R. *Synth. Commun.* **1988**, *18*, 1841.

43. Baciocchi, E.; Casu, A.; Ruzziconi, R. *Tetrahedron Lett.* **1989**, *30*, 3707.

44. Baciocchi, E.; Casu, A.; Ruzziconi, R. *Synlett* **1990**, 679.

45. Snider, B. B.; Kwon, T. *J. Org. Chem.* **1990**, *55*, 4786.

46. Baciocchi, E.; Giese, B.; Farshchi, H.; Ruzziconi, R. *J. Org. Chem.* **1990**, *55*, 5688.

47. Baciocchi, E.; Ruzziconi, R. *J. Org. Chem.* **1991**, *56*, 4772.

48. Citterio, A.; Sebastiano, R.; Marion, A. *J. Org. Chem.* **1991**, *56*, 5328.

49. Citterio, A.; Sebastiano, R.; Carvayal, M. C. *J. Org. Chem.* **1991**, *56*, 5335.

50. Narasaka, K.; Okauchi, T. *Chem. Lett.* **1991**, 515.

51. Paolobelli, A. B.; Latini, D.; Ruzziconi, R. *Tetrahedron Lett.* **1993**, *34*, 721.

52. Paolobelli, A. B.; Gioacchini, F.; Ruzziconi, R. *Tetrahedron Lett.* **1993**, *34*, 6333.

CHAPTER 2

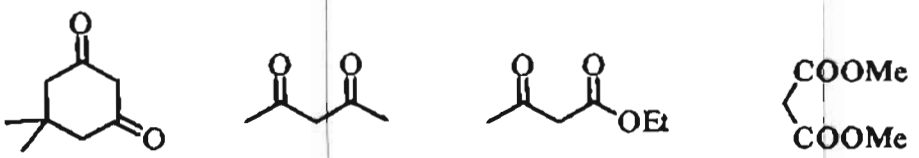
CERIUM(IV) AMMONIUM NITRATE MEDIATED OXIDATIVE ADDITION OF 1,3-DICARBONYL COMPOUNDS TO ALKENES

2.1. Introduction

The resurgence of interest in the use of radicals[1-5] in carbon-carbon bond forming reactions has spurred considerable work in developing novel methods for the generation of carbon centred radicals[6]. Among the metal salts such as $TiCl_3$, $Mn(OAc)_3$, $Co(OAc)_2$, $FeCl_3$ and $CuCl_2$ used for the generation of radicals, $Mn(OAc)_3$ has received the most attention[6-8]. In spite of its widespread use, $Mn(OAc)_3$ is not always reliable and some procedural problems have been associated with this reagent[7]. Therefore it is of interest to explore the use of other one electron oxidants. The pioneering work of Heiba and Dessau[9,10] and the subsequent investigations of Kurz[11,12] and Baciocchi[13-17] have demonstrated the usefulness of Ce(IV) reagents for the generation of carbon centred radicals.

There are reports on the formation of dihydrofurans[18-24] by $Mn(OAc)_3$, $Co(OAc)_2$, $CuCl_2$, $Hg(OAc)_2$, $Tl(OAc)_3$, $Pb(OAc)_4$ and PbO_2 mediated reactions of enolizable ketones and alkenes. Similarly CAN mediated addition of acetyl-acetone and ethyl acetoacetate to ring substituted styrenes[25] has also been reported to give dihydrofurans. However there has been no systematic investigation of Ce(IV) mediated generation of radicals and their addition to cyclic and acyclic alkenes, particularly unactivated ones (see Section 1.2). We have therefore undertaken a detailed study of Ce(IV) mediated oxidative addition of active methylene compounds to such systems. In view of the solubility in common

organic solvents such as acetonitrile, methanol and tetrahydrofuran, the Ce(IV) reagent of choice has been CAN. The dicarbonyl compounds chosen for our study are dimedone (**1**), acetylacetone (**2**), ethyl acetoacetate (**3**) and dimethyl malonate (**4**). The results of these investigations are described in the Sections 2.2.1 and 2.2.2. A comparative study of these reactions with $Mn(OAc)_3$ forms the subject matter of Section 2.2.3.

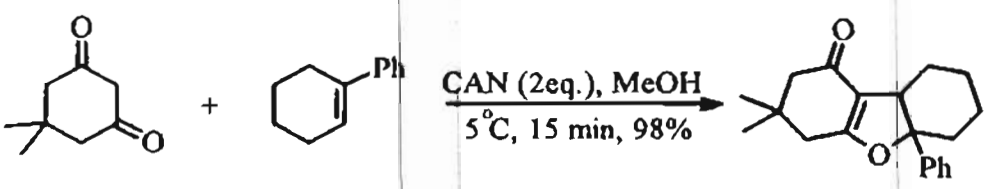


1 **2** **3** **4**

2.2. Results and Discussion

2.2.1. A Facile Synthesis of Dihydrofurans by CAN Mediated Oxidative Addition Reactions

CAN mediated addition of the dicarbonyl compounds **1-3** to cyclic and acyclic alkenes occurs rapidly to afford 4,5-dihydrofurans in high yields. The following example is illustrative for the formation of dihydrofuran.

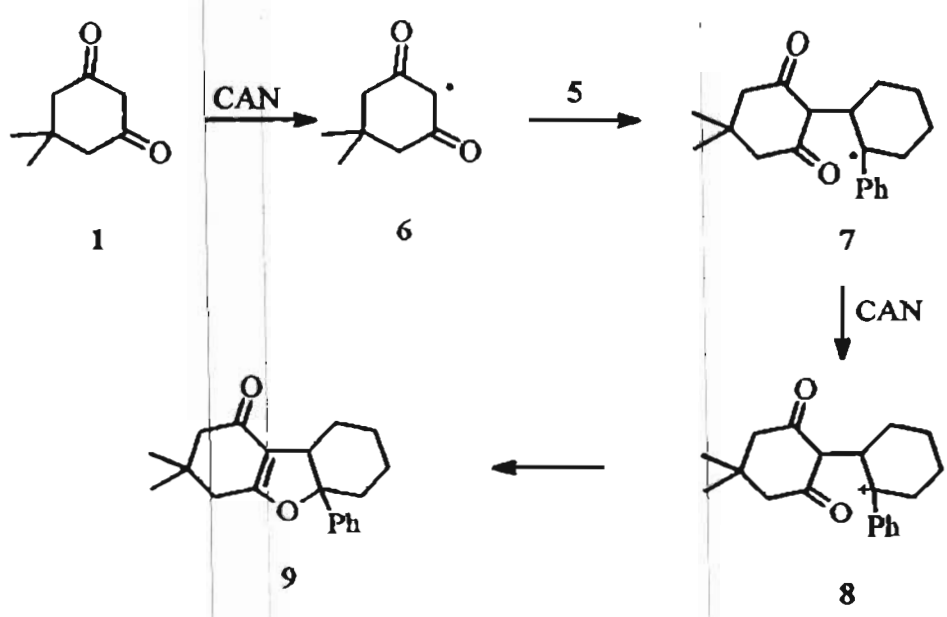


1 **5** **9**

The structure of **9** was assigned on the basis of its IR and NMR spectral data. The IR spectrum showed carbonyl absorption at 1633 cm^{-1}. In the ^1H

NMR spectrum, the aromatic protons resonated as a multiplet centred at δ 7.32 and the methine proton resonated as a triplet at δ 3.44. The spectrum also contained two singlets at δ 1.14 and 1.08 due to the protons of two $-CH_3$ groups. The characteristic resonances at δ 194.9, 174.6, 114.9 and 94.1 in the ^{13}C NMR spectrum further confirmed the structure **9**.

In all the cases studied, two equivalents of CAN are required for the completion of the reaction. If less than two equivalents are used, a proportional amount of alkene is left unreacted. While the mechanistic details of the reaction remain unclear, a rationalization along the following lines (Scheme 1) may be made. The first step involves the CAN mediated generation of the radical **6** from dimedone, which is immediately trapped by **5** giving the intermediate radical **7**. In the second step, the radical **7** is oxidised to the cation **8** by the second equivalent of CAN. The latter then undergoes cyclization to afford the dihydrofuran **9**.

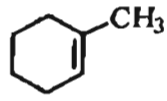
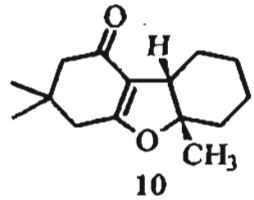
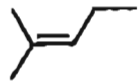
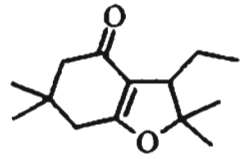
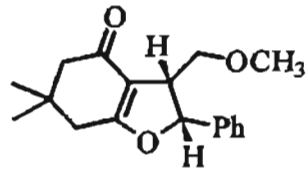
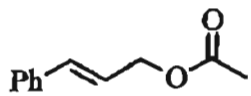
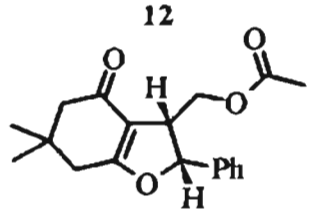
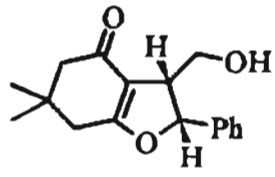
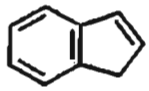
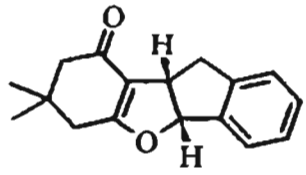


Scheme 1

It should however be pointed out that an alternate mechanism that excludes cation formation cannot be ruled out.

Dimedone reacts similarly with a number of alkenes and the results are summarized in Table 1.

Table 1. CAN Mediated Addition of Dimedone to Alkenes

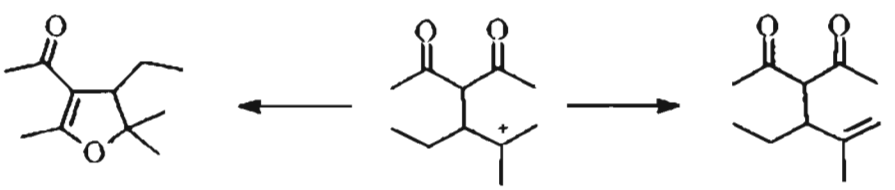
Entry	Alkene	Product	Yield (%)
1		 **10**	57
2		 **11**	60
3		 **12**	65
4		 **13**	45
5		 **14**	55
6		 **15**	63

The coupling constant (*J*) values for the proton geminal to the phenyl group in the products **12, 13** and **14** are in the range 5.0-7.1 Hz. These values are indicative of a *cis*-stereochemistry[26]. Also, similar dihydrofurans synthesized by $Co(OAc)_2$ mediated reactions have been reported to have *cis*-stereochemistry[19].

Just like dimedone, acetylacetone (**2**) also reacts with alkenes to afford 4,5-dihydrofurans **16-18**. However, in the case of 2-methyl-2-pentene, in addition to the dihydrofuran **20**, a second product **21** was isolated.

The IR and NMR spectra revealed the structure of **21**. The IR spectrum exhibited a strong absorption at 1706 cm^{-1} (>C=O). In the ^1H NMR spectrum, the olefinic protons resonated at δ 4.75. The two methine protons were observed at δ 3.75 (d, 1 H) and 2.78 (m, 1 H). The two singlets at δ 2.11 and 2.01 were assigned to the acetyl protons. The carbonyl carbons appeared at δ 204.1 and 203.4 in the ^{13}C NMR spectrum. The two signals at δ 143.2 and 114.8 were attributed to the two olefinic carbons. The molecular ion peak at *m/z* 182 in the mass spectrum was also in agreement with the proposed structure.

The formation of **21** further supports the mechanistic pathway described in Scheme 1. Analogous to the cation **8**, in this case, the cation **19** is formed after the addition of the radical from acetylacetone to 2-methyl-2-pentene and the subsequent oxidation of the resulting radical. The cation **19** can cyclize to give the dihydrofuran **20** or loss a proton to afford **21** (Scheme 2).

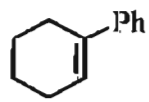
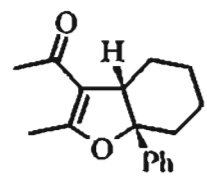
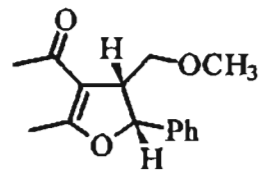
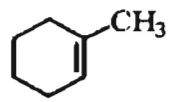
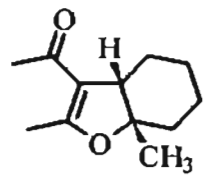
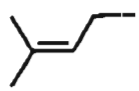
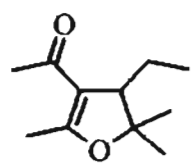
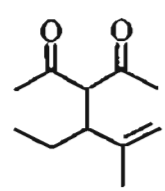


20 19 21

Scheme 2

The reactions of acetylacetone with various alkenes are shown in Table 2.

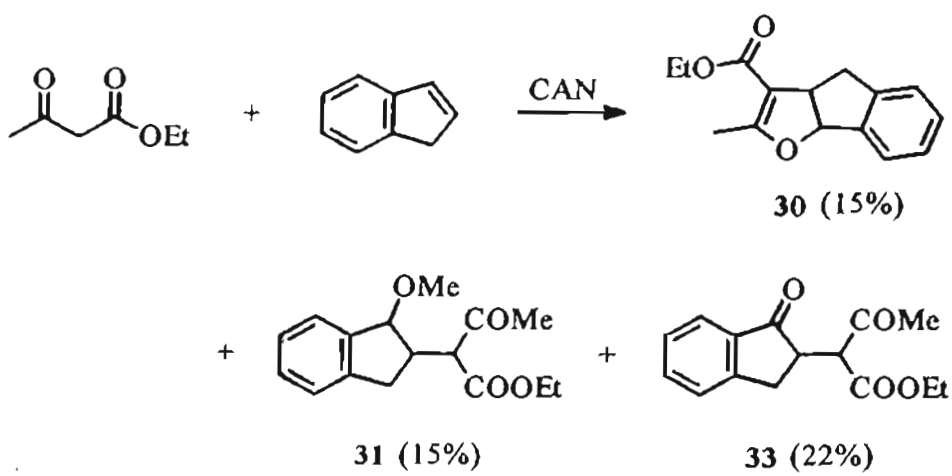
Table 2. CAN Mediated Addition of Acetylacetone to Alkenes

Entry	Alkene	Product	Yield (%)
1		 **16**	96
2		 **17**	58
3		 **18**	40
4		 **20**	60
		 **21**	16

In the product 17, the observed J value for the proton geminal to the phenyl group is 3.7 Hz. This is much lower than the corresponding value for the

product **12**. However, it is in line with the *J* value calculated by MMX programme (i.e. 2.3 Hz) for the *cis*-product. Therefore, *cis*-stereochemistry has been suggested for the dihydrofuran derivatives in Table 2.

The reaction of ethyl acetoacetate with 1-phenyl-1-cyclohexene, 1-methyl-1-cyclohexene and cinnamyl methyl ether furnished only 4,5-dihydrofurans (**22-24**). 2-Methyl-2-pentene and indene reacted differently. Thus 2-methyl-2-pentene afforded **26** in 20% yield along with the dihydrofuran **25** (Table 3). CAN mediated addition of ethyl acetoacetate to indene afforded two products **31** and **33** in addition to the dihydrofuran **30**. The reaction can be represented as shown below.



30 (15%)

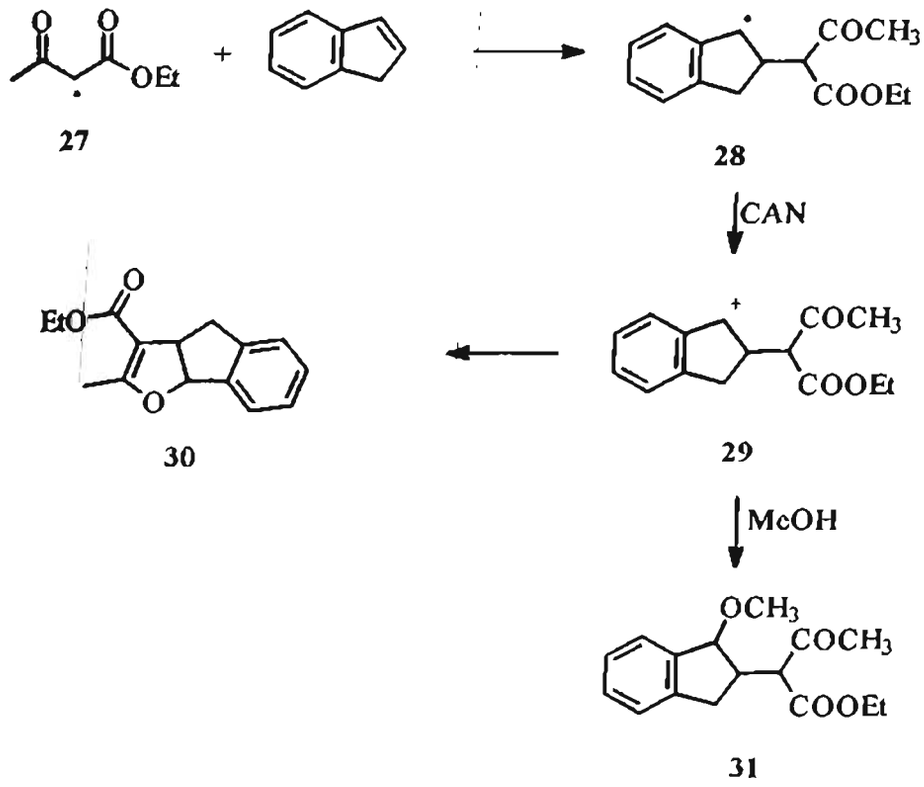
31 (15%) **33** (22%)

*The products **31** and **33** were characterized on the basis of their spectral* data. The ^{1}H and ^{13}C NMR spectra revealed that both the products were mixture of isomers. The IR spectrum of **31** contained carbonyl absorptions at 1745 and 1716 cm^{-1}. In the ^{1}H NMR spectrum, the proton geminal to the methoxy group appeared at δ 4.63. The methoxy protons resonated as a singlet at δ 3.38. The singlets at δ 2.22 and 2.19 were attributed to the acetyl protons of the two isomers. In the ^{13}C NMR spectrum two carbonyl carbons were observed at δ

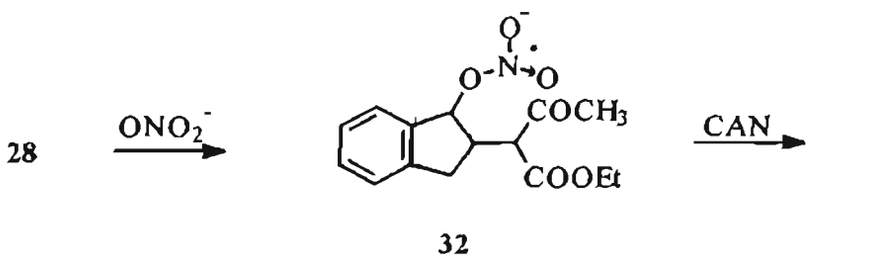
201.8 and 201.4 and the ester carbonyls resonated at δ 168.4 and 168.3. The signals due to aromatic carbons were visible in the range δ 141.3-124.1 and the carbon bearing the methoxy group appeared at δ 86.7 and 86.5 for the two isomers. In the IR spectrum of **33**, two carbonyl absorptions were observed at 1714 and 1613 cm^{-1}. The ^1H NMR spectrum contained $-COCH_3$ proton resonances at δ 2.42 and 2.26. Also the signals due to the methyl group of $-CH_2CH_3$ appeared as triplets at δ 1.32 and 1.06. The ^{13}C NMR spectrum showed four carbonyl resonances at δ 205.43, 205.13, 202.34 and 201.55 and two ester carbonyls at δ 168.24 and 168.22.

A tentative mechanism which will rationalize the formation of the products **30**, **31** and **33** is shown in Scheme 3. The radical **27**, generated by CAN from ethyl acetoacetate, undergoes addition to indene giving the benzylic radical **28**. This radical can either be oxidised to the cation **29** or be trapped by NO_3^- to form the unstable radical anion **32**. The former cyclizes to the dihydrofuran **30** or gets converted to **31** by methanol addition. Oxidative fragmentation of **32** would lead to the ketone **33**.

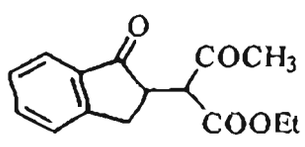
The results obtained in the reactions of ethyl acetoacetate with various alkenes are presented in Table 3. The dihydrofuran derivatives **22-25** have been assigned *cis*-stereochemistry. This is based on the fact that the observed coupling constant value for the proton geminal to the phenyl group in the product **24** (5.0 Hz) is very close to the value calculated for the *cis*-product (5.3 Hz) by the MMX programme.



27 28 29 30 31



32

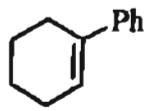
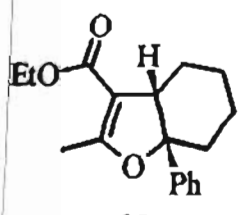
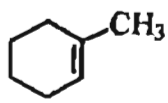
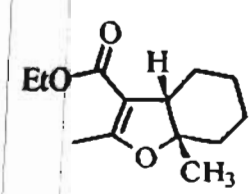
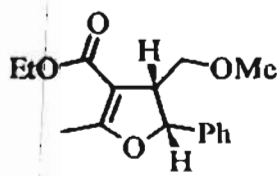
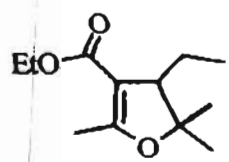
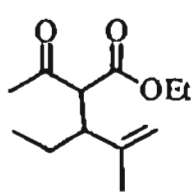


+ H^+ + NO_2^- + Ce(III)

33

Scheme 3

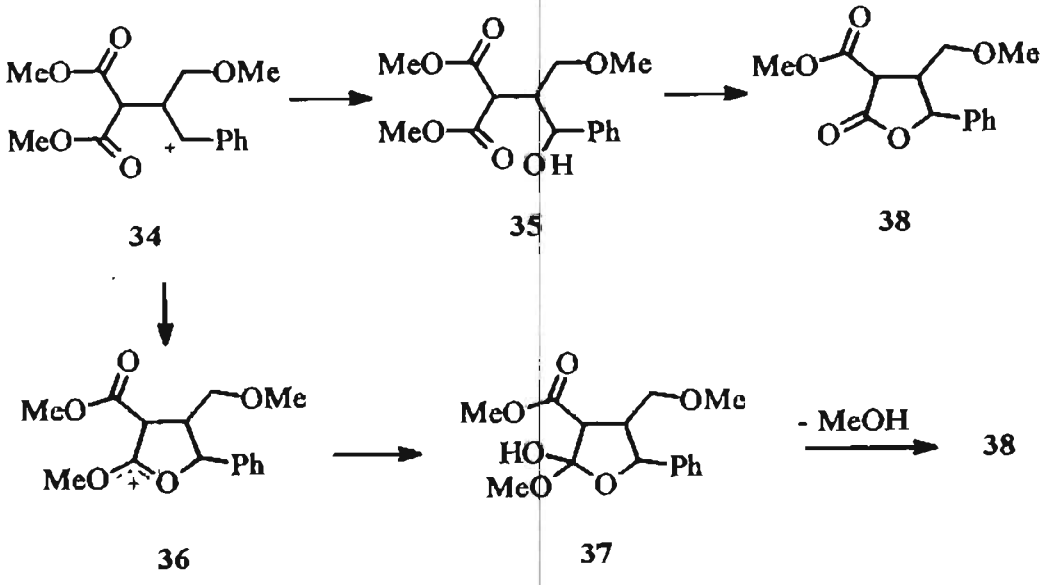
Table 3. CAN Mediated Addition of Ethyl Acetoacetate to Alkenes

Entry	*Alkene*	Product	Yield (%)
1		 **22**	40
2		 **23**	38
3		 **24**	65
4		 **25**	37
		 **26**	20

2.2.2. Oxidative Addition of Dimethyl Malonate to Alkenes

Unlike dimedone and acetylacetone, dimethyl malonate reacted differently with most of the alkenes. For example, when dimethyl malonate was reacted with cinnamyl methyl ether and 1-phenyl-1-cyclohexene under the same conditions described earlier, instead of the addition of malonyl radical to the alkenes, the latter underwent oxidation. However, addition to both these alkenes occurred when the experiment was carried out in aqueous methanol. Thus, the reaction of dimethyl malonate and cinnamyl methyl ether afforded the lactone **38** in 58% yield. Its IR spectrum showed two carbonyl absorptions at 1790 and 1743 cm^{-1}. The ^1H NMR spectrum exhibited a signal at δ 5.20 which could be attributed to the proton geminal to the lactone ring oxygen atom. The characteristic carbon resonances at δ 170.4, 167.1 and 81.1 also helped to confirm the structure **38**.

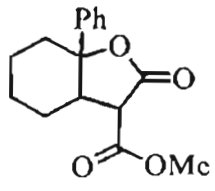
The formation of the lactone **38** can be explained as follows.



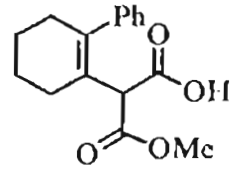
Scheme 4

The initial addition of malonyl radical to cinnamyl methyl ether followed by oxidation would produce the cation **34**. Since the reaction is done in aqueous *methanol*, **34** would be easily converted to **35** which on loss of methanol would furnish **38**. Alternatively, **37** formed from **34** *via* the *stabilized* cation **36** can loose methanol to afford **38** (Scheme 4).

The oxidative addition of dimethyl malonate to 1-phenyl-1-cyclohexene led to an inseparable mixture of **39** and **40**. IR and NMR spectral data showed the presence of these two products. Thus the IR spectrum contained two carbonyl *absorptions at 1784 and 1743* cm^{-1}. The carboxylic acid proton appeared at δ 9.75 *in the* ^1H *NMR spectrum*. Further, the methoxy protons of the ester groups appeared as sharp singlets at δ 3.67 and 3.56. There were four *signals* due to carbonyl carbon in the ^{13}C NMR spectrum at δ 170.5, 170.2, 167.5 and 166.7.



39



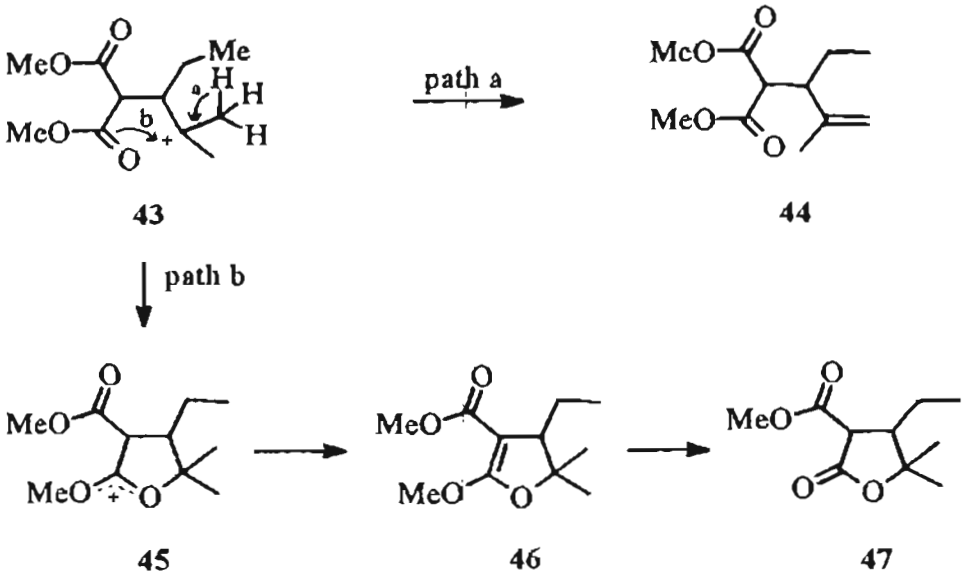
40

The mechanism given in Scheme 4 also explains the formation of **39**. It is assumed that **40** is formed from **39** *via* the lactone ring opening.

Analogous to the reaction of ethyl acetoacetate and indene, the reaction of dimethyl malonate with the latter in methanol afforded **41** and **42**. The formation of these products also can be explained by the mechanism depicted in Scheme 3.

CAN mediated addition of dimethyl malonate to 2-methyl-2-pentene afforded the products **44** and **47**. The mechanistic pathways suggested for this reaction are shown in Scheme 5. The addition of malonyl radical to 2-methyl-

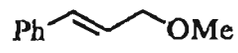
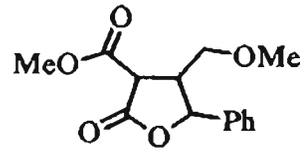
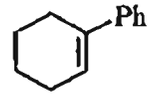
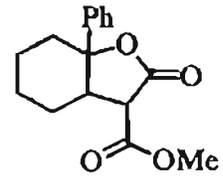
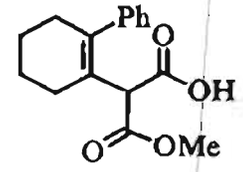
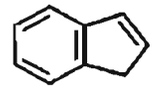
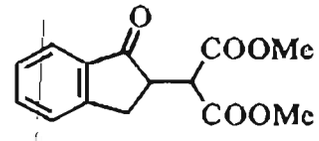
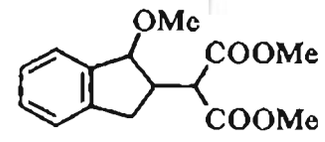
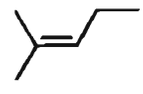
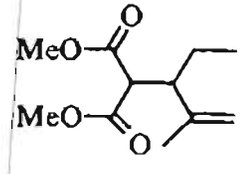
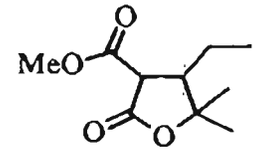
2-pentene and the oxidation of the resulting radical by CAN would give the cation **43**. This cation would eliminate a proton to give the alkene **44** (path a) as in the reactions of acetylacetone or ethyl acetoacetate with 2-methyl-2-pentene. Alternatively, the cation **43** can undergo cyclization to afford **45** (path b) which can loose a proton to furnish the dihydrofuran **46**. The latter on work-up will be converted to the product **47**.



Scheme 5

The results of the reactions of dimethyl malonate described above are shown in Table 4.

Table 4. CAN Mediated Addition of Dimethyl Malonate to Alkenes

Entry	Alkene	Product (yield)
1		 **38** (58%)
2		 +  **39** **40** (43%)
3		  **41** (17%) **42** (32%)
4		  **44** (20%) **47** (41%)

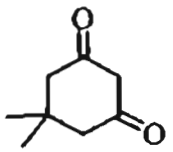
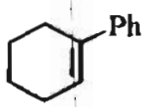
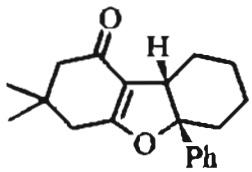
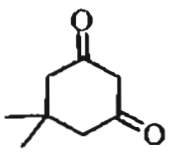
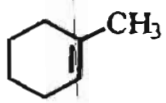
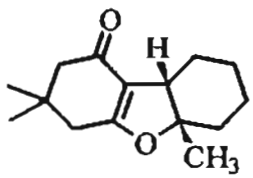
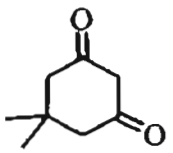
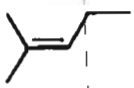
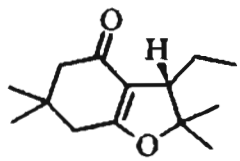
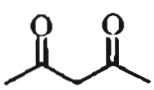
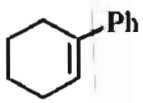
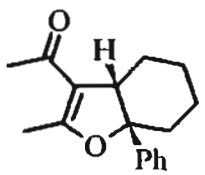
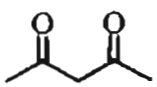
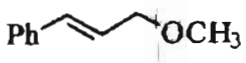
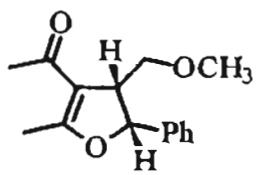
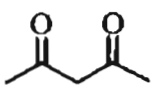
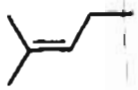
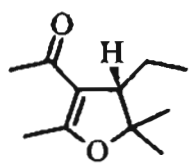
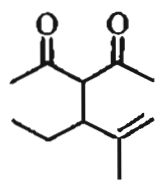
2.2.3. Oxidative Addition of 1,3-Dicarbonyl Compounds to Alkenes Mediated by CAN and $Mn(OAc)_3$: A Comparative Study

It is evident from the foregoing section that CAN mediated oxidative addition of 1,3-dicarbonyl compounds to unactivated alkenes provides a facile, convenient and simple method for carbon-carbon bond formation. Even though $Mn(OAc)_3$ mediated radical additions have been studied in detail, no

comparative data on CAN mediated reactions *vis a vis* $Mn(OAc)_3$ exist. We have therefore investigated some of the reactions discussed in Section 2.2.1 with $Mn(OAc)_3$ instead of CAN. The results are summarized in Table 5. Although, occasionally ethanol and methanol have been used as solvents for $Mn(OAc)_3$ mediated reactions[27], in our experience no reaction occurred between dicarbonyl compounds and alkenes even in refluxing ethanol. However, the reaction took place in refluxing glacial acetic acid. It is noteworthy that most of the corresponding CAN mediated reactions proceed well in methanol at 5°C. Table 5 clearly shows that the CAN mediated reactions consistently lead to higher yields of products.

Thus in terms of the mildness of the procedure, experimental simplicity and higher yields of products, CAN appears to be superior to the more commonly used $Mn(OAc)_3$.

Table 5. Oxidative Addition of 1,3-Dicarbonyl Compounds to Alkenes Mediated by CAN and $Mn(OAc)_3$

Entry	Dicarbonyl Compound	Alkene	Product	Yield (%)
1				98 (84)
2				58 (47)
3				60 (41)
4				96 (83)
5				85 (54)
6				60 (39)
				16 (8)

Yields obtained with $Mn(OAc)_3$ mediated reactions are given in paranthesis

2.3. Experimental

Melting points were determined on a Büchi-530 melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 882 infrared spectrophotometer. Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded on Varian Unity-400, Nicolet GE-300, Varian XL-200, Jeol EX-90 and Hitachi R 24B-60 NMR spectrometer using chloroform-*d* or carbon tetrachloride as solvent. The chemical shifts are given in δ scale with tetramethylsilane as internal standard. The abbreviations s, d, dd, t, m and brs refer to singlet, doublet, doublet of doublet or double doublet, triplet, multiplet and broad singlet respectively. Mass spectra were recorded on Finnigan MAT 1020 B and Hewlett Packard 5890 mass spectrometers. The relative intensities of the *m/z* values (in percentage) are given in paranthesis. Elemental analyses were performed on a Hewlett Packard 185-B CHN analyser.

Commercial grade solvents were used for column chromatography and were distilled before use. Petroleum ether refers to the fraction boiling between 60-80°C. Column chromatography was done using 100-200 mesh silica gel and appropriate mixture of petroleum ether and ethyl acetate for elution. Analytical thin layer chromatography (TLC) was performed on home made plates using silica gel G or GF_{254} containing 13% calcium sulfate as binder. All reactions were monitored by TLC employing appropriate solvent systems for development and the developed plates were visualized by exposure to iodine vapour or UV light.

CAN, dimedone, 1-methyl-1-cyclohexene and 2-methyl-2-pentene purchased from Aldrich were used as such. 1-Phenyl-1-cyclohexene and indene obtained from Aldrich were purified by column chromatography before use. Acetylacetone, ethyl acetoacetate, dimethyl malonate and cinnamyl alcohol were

purchased from local sources. Cinnamyl methyl ether and cinnamyl acetate were prepared by the reported procedure[28].

Synthesis of Dihydrofurans: General Procedure

A solution of CAN (2.52 g, 4.6 mmol) in methanol (20 mL) was added dropwise to an ice-cooled, stirred mixture of the dicarbonyl compound **1**, **2** or **3** (2.4 mmol) and alkene (2.0 mmol) in methanol (10 mL). In most of the cases the reddish brown colour of CAN disappeared by the time the addition was over (*ca.* 15 min). In the remaining cases it took *ca.* 30-45 min for the completion of the reaction. The mixture after decolourisation was diluted with water (150 mL) and extracted with dichloromethane (3 x 40 mL). The combined organic extracts were washed with water, then with brine, dried over anhydrous Na_2SO_4 and evaporated. The residue obtained was subjected to chromatography on silica gel column. Elution with 10% ethyl acetate in petroleum ether (unless otherwise specified) afforded the dihydrofuran derivative.

3,3-Dimethyl-5a-phenyl-1,2,3,4,5a,6,7,8,9,9a-decahydrodibenzofuran-1-one (9)

A mixture of dimedone (0.336 g, 2.4 mmol) and 1-phenyl-1-cyclohexene (0.316 g, 2.0 mmol) was treated with CAN (2.52 g, 4.6 mmol) as described in the general procedure to afford **9** (0.579 g, 98%) as a colourless viscous liquid.

IR (CH_2Cl_2) ν_{max} : 2959, 2872, 1633, 1401, 1239 cm^{-1}.

^1H NMR (300 MHz) : δ 7.39-7.24 (m, 5 H, ArH), 3.44 (t, J = 5.1 Hz, 1 H, >C<u>H</u>CH_2-), 2.39 (d, J = 1.4 Hz, 2 H), 2.19 (s, 2 H), 2.02-1.91 (m, 4 H, -CH_2-), 1.65-1.44 (m, 4H, -CH_2-), 1.14 (s, 3 H, -CH_3), 1.08 (s, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 194.9, 174.6, 146.2, 128.6, 127.1, 124.3, 114.9, 94.1, 51.2, 44.4, 37.8, 33.5, 33.2, 28.5, 27.9, 23.8, 17.5.

EI-MS *m/z* : 296 (M^+, 100), 279 (10), 205 (16), 185 (15), 169 (10), 157 (75), 130 (60).

3,3,5a-Trimethyl-1,2,3,4,5a,6,7,8,9,9a-decahydrodibenzofuran-1-one (10)

The reaction of dimedone (0.420 g, 3.0 mmol) and 1-methyl-1-cyclohexene (0.240 g, 2.5 mmol) with CAN (3.15 g, 5.75 mmol) as described in the general procedure afforded **10** (0.331 g, 57%) as a colourless viscous liquid.

IR (CH_2Cl_2) ν_{max} : 2943, 2874, 1631, 1405, 1239 cm^{-1}.

^1H NMR (300 MHz) : δ 2.85 (t, J = 5.6 Hz, 1 H, >C<u>H</u>CH_2-), 2.25 (d, J = 1.3 Hz, 2 H), 2.22 (s, 2 H), 1.87-1.59 (m, 4 H), 1.49-1.38 (m, 4 H), 1.35 (s, 3 H, -CH_3), 1.10 (s, 6 H, -CH_3).

^{13}C NMR (75.5 MHz) : δ 194.98, 175.38, 115.26, 91.88, 51.21, 43.71, 38.18, 34.01, 32.11, 29.02, 28.27, 27.22, 24.15, 18.56.

GC-MS *m/z* : 234 (M^+, 100), 219 (72), 201 (41), 191(38), 166 (43), 154 (49), 135 (48), 122 (30).

3-Ethyl-2,2,6,6-tetramethyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one (11)

The oxidative addition of dimedone (0.420 g, 3.0 mmol) to 2-methyl-2-pentene (0.211 g, 2.5 mmol) in presence of CAN (3.15 g, 5.75 mmol) was carried out following the general procedure. Pure product **11** (0.334 g, 60%) was obtained as a pale yellow oil.

IR (CH_2Cl_2) ν_{max} : 2964, 2932, 1644, 1395, 1252 cm^{-1}.

^1H NMR (60 MHz) : δ 2.81-2.40 (m, 1 H, >C<u>H</u>CH_2-), 2.25 (s, 2 H), 2.12 (s, 2 H), 1.75-1.50 (m, 2 H), 1.35 (s, 6 H, -CH_3), 1.13 (s, 6 H, -CH_3), 0.89-0.69 (m, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 194.1, 173.9, 114.5, 92.2, 50.8, 48.5, 37.4, 32.5, 29.2, 28.1, 27.5, 21.4, 21.1, 11.5.

HRMS exact mass calcd for $C_{14}H_{22}O_2$: 222.1619 (M^+)

Found : 222.1613.

6,6-Dimethyl-3-methoxymethyl-2-phenyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one (12)

A mixture of dimedone (0.420 g, 3.0 mmol) and cinnamyl methyl ether (0.371 g, 2.5 mmol) on reaction with CAN (3.15 g, 5.75 mmol) as described in the general procedure furnished 12 (0.465 g, 65%) as a pale yellow oil.

IR (CH_2Cl_2) ν_{max} : 2965, 1638, 1402, 1221, 1121 cm^{-1}.

^1H NMR (60 MHz) : δ 7.02 (s, 5 H, ArH), 5.41 (d, J = 6.0 Hz, 1 H, >C<u>H</u>Ph), 3.60-3.32 (m, 2 H, -OCH_2-), 3.21 (s, 4 H, -O<u>C</u>H_3, >C<u>H</u>CH_2-), 2.20 (s, 2 H), 2.02 (s, 2 H), 1.05 (s, 6 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 193.5, 176.2, 140.3, 128.1, 127.5, 124.5, 110.4, 89.1, 72.2, 59.3, 50.8, 48.9, 37.6, 33.4, 28.0, 27.5.

GC-MS *m/z* : 286 (M^+, 18), 271 (12), 254 (48), 241 (100), 199 (35), 165 (18), 157 (29), 128 (25).

3-Acetyloxymethyl-6,6-dimethyl-2-phenyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one (13)

A mixture of dimedone (0.336 g, 2.4 mmol) and cinnamyl acetate (0.352 g, 2.0 mmol) was reacted with CAN (2.52 g, 4.6 mmol) as described in the general procedure to afford **13** (0.282 g, 45%) as a pale yellow oil.

IR (CH_2Cl_2) ν_{max} : 2963, 1744, 1639, 1619, 1403, 1230 cm^{-1}.

^1H NMR (60 MHz) : δ 7.11 (s, 5 H, ArH), 5.35 (d, J = 5.0 Hz, 1 H, >C<u>H</u>Ph), 4.42-4.10 (m, 2 H, -OCH_2-), 3.45-3.25 (m, 1 H, >C<u>H</u>CH_2-), 2.32 (s, 2 H), 2.10 (s, 2 H), 1.91 (s, 3 H, -$COCH_3$), 1.10 (s, 6 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 194.4, 176.7, 140.7, 128.5, 127.9, 125.2, 110.9, 89.5, 72.6, 58.7, 51.1, 48.60, 37.8, 34.0, 28.6, 28.2.

GC-MS *m/z* : 271 (M^+-$COCH_3$, 10), 254 (46), 241 (100), 199 (35), 165 (18), 157 (28), 128 (25), 115 (46).

6,6-Dimethyl-3-hydroxymethyl-2-phenyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one (14)

The reaction of dimedone (0.420 g, 3.0 mmol) and cinnamyl alcohol (0.335 g, 2.5 mmol) with CAN (3.15 g, 5.75 mmol) as described in the general procedure furnished **14** (0.353 g, 52%) as a colourless viscous liquid.

IR (CH_2Cl_2) ν_{max} : 3393, 2964, 1624, 1425, 1228 cm^{-1}.

^1H NMR (60 MHz) : δ 7.11 (s, 5 H, ArH), 5.30 (d, J = 7.1 Hz, >C<u>H</u>Ph), 4.32 (brs, 1 H, -OH), 3.50 (d, J = 6.0 Hz, 2 H, -C<u>H</u>$_2$OH), 3.32-3.03 (m, 1 H, >C<u>H</u>CH_2OH), 2.25 (s, 2 H), 2.08 (s, 2 H), 1.0 (s, 6 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 195.9, 177.8, 139.9, 128.5, 128.1, 125.3, 113.4, 88.5, 63.5, 51.1, 50.3, 37.5, 34.2, 28.3.

GC-MS *m/z* : 272 (M^+, 10), 254 (12), 241 (100), 199 (40), 185 (30), 166 (90), 157 (25), 128 (40).

Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.96; H, 7.41

Found : C, 74.95; H, 7.39.

Dihydrofuran 15

A mixture of dimedone (0.336 g, 2.4 mmol) and indene (0.232 g, 2.0 mmol) on reaction with CAN (2.52 g, 4.6 mmol) afforded the dihydrofuran **15** (0.321 g, 63%) as a colourless viscous liquid.

IR (CH_2Cl_2) ν_{max} : 2963, 2894, 1631, 1400, 1219 cm^{-1}.

^1H NMR (60 MHz) : δ 7.52-7.10 (m, 4 H, ArH), 6.12 (d, J = 8.9 Hz, 1 H, >CHO-), 4.10-3.72 (m, 1 H, >C<u>H</u>CH_2-), 3.30-2.95 (m, 2 H), 2.15 (s, 2 H), 2.0 (s, 2 H), 1.15 (s, 3 H, -CH_3), 0.90 (s, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 193.9, 174.4, 142.3, 138.8, 129.0, 126.4, 125.1, 124.9, 114.2, 93.1, 50.3, 41.1, 37.1, 36.4, 33.2, 28.5, 27.8

GC-MS *m/z* : 254 (M^+, 100), 198 (20), 170 (20), 156 (5), 128 (7).

3-Acetyl-2-methyl-7a-phenyl-3a,4,5,6,7,7a-hexahydrobenzofuran (16)

The reaction of CAN (3.15 g, 5.75 mmol) with a mixture of acetylacetone (0.30 g, 3.0 mmol) and 1-phenyl-1-cyclohexene (0.396 g, 2.5 mmol) as described

in the general procedure afforded **16** as a pale yellow viscous liquid (0.614 g, 96%).

IR (CH_2Cl_2) ν_{max} : 2942, 1669, 1624, 1599, 1386 cm^{-1}.

^1H NMR (60 MHz) : δ 7.05 (s, 5 H, ArH), 3.17 (t, J = 5.9 Hz, 1 H, >C<u>H</u>CH_2-), 2.15 (s, 3 H, -CH_3), 1.90 (s, 3 H, -$COCH_3$), 1.61-1.12 (m, 8 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 194.1, 166.5, 147.2, 128.3, 126.8, 124.1, 118.5, 90.0, 46.9, 34.1, 28.9, 26.8, 19.3, 18.8, 15.2.

EI-MS *m/z* : 256 (M^+, 20), 238 (11), 213 (38), 195 (32), 156 (28), 141 (20), 129 (30).

Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86

Found : C, 79.58; H, 7.85.

3-Acetyl-4-methoxymethyl-2-methyl-5-phenyl-4,5-dihydrofuran (17)

A mixture of acetylacetone (0.240 g, 2.4 mmol) and cinnamyl methyl ether (0.296 g, 2.0 mmol) was treated with CAN (2.52 g, 4.6 mmol) as described in the general procedure to afford **17** (0.284 g, 58%) as a pale yellow oil.

IR (CH_2Cl_2) ν_{max} : 2940, 1630, 1600, 1400, 1230 cm^{-1}.

^1H NMR (300 MHz) : δ 7.41-7.26 (m, 5 H, ArH), 5.49 (d, J = 3.7 Hz, 1 H, >C<u>H</u>Ph), 3.66-3.64 (t, J = 5.9 Hz, 1 H, >C<u>H</u>CH_2-), 3.48-3.41 (m, 2 H, -C<u>H</u>$_2OCH_3$), 3.39 (s, 3 H, -OCH_3), 2.36 (s, 3 H, -CH_3), 2.26 (s, 3 H, -$COCH_3$).

^{13}C NMR (75.5 MHz) : δ 193.84, 168.63, 141.20, 128.57, 127.92, 125.07, 113.03, 86.19, 73.81, 58.92, 51.97, 29.26, 15.58.

EI-MS *m/z* : 246 (M^+, 10), 214 (8), 201 (100), 155 (27), 129 (8), 121 (12), 115 (12).

3-Acetyl-2,7a-dimethyl-3a,4,5,6,7,7a-hexahydrobenzofuran (18)

The reaction of acetylacetone (0.30 g, 3.0 mmol) and 1-methyl-1-cyclohexene (0.240 g, 2.5 mmol) with CAN (3.15 g, 5.75 mmol) as described in the general procedure furnished **18** (0.151 g, 40%) as a colourless oil.

IR (CH_2Cl_2) ν_{max} : 2939, 1665, 1614, 1593, 1385, 1249 cm^{-1}.

^1H NMR (60 MHz) : δ 2.77-2.52 (m, 1 H, >C<u>H</u>CH_2-), 2.13 (s, 3 H, -CH_3), 2.08 (s, 3 H, -$COCH_3$), 1.87-1.29 (m, 8 H, -CH_2-), 1.22 (s, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 193.7, 166.5, 117.8, 86.4, 45.8, 31.5, 28.5, 26.5, 26.1, 19.5, 14.9.

EI-MS *m/z* : 194 (M^+, 72), 179 (38), 161 (90), 151 (60), 137 (35), 133 (100), 123 (65).

Oxidative Addition of Acetylacetone to 2-Methyl-2-pentene

A mixture of acetylacetone (0.30 g, 5.0 mmol) and 2-methyl-2-pentene (0.250 g, 3.25 mmol) was reacted with CAN (3.15 g, 5.75 mmol) as described in the general procedure. The residue obtained on careful chromatography using ethyl acetate in petroleum ether (2% and 3% respectively) as eluent furnished **21** (0.075 g, 16%) and **20** (0.272 g, 60%) as colourless oils.

3-Acetyl-4-ethyl-2,5,5-trimethyl-4,5-dihydrofuran (20)

IR (neat) ν_{max} : 2979, 1630, 1386, 1276 cm^{-1}.

^{1}H NMR (90 MHz) : δ 2.72 (t, J = 5.4 Hz, 1 H, >C<u>H</u>CH_2-), 2.23 (s, 3 H, -CH_3), 2.18 (s, 3 H, -CH_3), 1.71-1.48 (m, 2 H, -CH_2-), 1.39 (s, 3 H, -CH_3), 1.31 (s, 3 H, -CH_3), 0.87 (t, J = 7.2 Hz, 3 H, -$CH_2C\underline{H}_3$).

^{13}C NMR (22.4 MHz) : δ 194.3, 165.9, 117.3, 88.3, 51.7, 29.1, 28.9, 22.6, 21.6, 15.4, 11.7.

GC-MS *m/z* : 182 (M^+, 26), 167 (8), 153 (65), 149 (8), 139 (10), 125 (10), 111 (100).

3-[3'-(2'-Methyl-pent-1'-enyl)]pentane-2,4-dione (21)

IR (neat) ν_{max} : 2972, 1706, 1360, 1157 cm^{-1}.

^{1}H NMR (90 MHz) : δ 4.75 (d, J = 7.9 Hz, 2 H, olefinic), 3.75 (d, J = 11.6 Hz, 1 H), 2.92-2.64 (m, 1 H, >C<u>H</u>CH_2-), 2.11 (s, 3 H, -$COCH_3$), 2.01 (s, 3 H, -$COCH_3$), 1.54 (s, 3 H, -CH_3), 1.27-1.09 (m, 2 H, -CH_2-), 0.71 (t, J = 8.2 Hz, 3 H, -$CH_2C\underline{H}_3$).

^{13}C NMR (22.4 MHz) : δ 204.1, 203.4, 143.2, 114.8, 48.8, 30.3, 29.6, 23.5, 18.6, 11.2.

GC-MS *m/z* : 182 (M^+, 5), 164 (7), 153 (12), 139 (50), 121 (32), 111 (100).

2-Methyl-7a-phenyl-3a,4,5,6,7,7a-hexahydrobenzofuran-3-carboxylic acid ethyl ester (22)

A mixture of ethyl acetoacetate (0.390 g, 3.0 mmol) and 1-phenyl-1-cyclohexene (0.396 g, 2.5 mmol) was treated with CAN (3.15 g, 5.75 mmol)

as described in the general procedure to afford **22** (elution with 2% ethyl acetate in petroleum ether, 0.262 g, 40%) as a colourless viscous liquid.

IR (CH_2Cl_2) ν_{max} : 2952, 1679, 1651, 1451, 1381, 1242 cm^{-1}.

^1H NMR (60 MHz) : δ 7.23-6.88 (m, 5 H, ArH), 3.95 (q, J = 7.1 Hz, 2 H, $-OC\underline{H}_2CH_3$), 3.17 (t, J = 4.9 Hz, 1 H, $>C\underline{H}CH_2-$), 2.17 (s, 3 H, $-CH_3$), 2.0-1.41 (m, 8 H), 1.12 (t, J = 7.1 Hz, 3 H, $-CH_2C\underline{H}_3$).

^{13}C NMR (22.4 MHz) : δ 167.1, 165.8, 147.4, 127.9, 126.5, 124.1, 107.2, 89.5, 58.5, 47.2, 34.1, 26.2, 19.0, 18.3, 14.2.

GC-MS *m/z* : 286 (M^+, 5), 244 (77), 212 (20), 197 (31), 169 (76), 156 (100), 141 (70), 115 (50).

Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74

Found : C, 75.56; H, 7.75.

2,7a-Dimethyl-3a,4,5,6,7,7a-hexahydrobenzofuran-3-carboxylic acid ethyl ester (23)

The reaction of ethyl acetoacetate (0.390 g, 3.0 mmol) and 1-methyl-1-cyclohexene (0.250 g, 2.5 mmol) with CAN (3.15 g, 5.75 mmol) as described in the general procedure furnished **23** (elution with 2% ethyl acetate in petroleum ether, 0.211 g, 38%) as a colourless oil.

IR (CH_2Cl_2) ν_{max} : 2940, 1695, 1352, 1339, 1108 cm^{-1}.

^1H NMR (60 MHz) : δ 4.12 (q, J = 7.2 Hz, 2 H, $-OCH_2-$), 2.65 (t, J = 6.9 Hz, 1 H, $>C\underline{H}CH_2-$), 2.05 (s, 3 H, $-CH_3$), 1.80-1.05 (m, 14 H).

^{13}C NMR (22.4 MHz) : δ 167.7, 162.0, 107.9, 87.5, 59.1, 50.5, 46.4, 32.1, 27.2, 26.1, 19.0, 14.6, 14.1.

GC-MS *m/z* : 224 (M^+, 16), 206 (5), 195 (7), 182 (26), 163 (10), 151 (22), 135 (55), 122 (24), 107 (30), 94 (100).

4-Methoxymethyl-2-methyl-5-phenyl-4,5-dihydrofuran-3-carboxylic acid ethyl ester (24)

The reaction of ethyl acetoacetate (0.390 g, 3.0 mmol) and cinnamyl methyl ether (0.372 g, 2.5 mmol) with CAN (3.15 g, 5.75 mmol) as described in the general procedure furnished **24** (elution with 5% ethyl acetate in petroleum ether, 0.454 g, 65%) as a pale yellow oil.

IR (CH_2Cl_2) ν_{max} : 2935, 1669, 1649, 1383, 1218 cm^{-1}.

^{1}H NMR (60 MHz) : δ 7.01 (s, 5 H, ArH), 5.25 (d, J = 5.0 Hz, 1 H, >C<u>H</u>Ph), 3.92 (q, J = 7.2 Hz, 2 H, -O<u>C</u>H_2-), 3.40-3.15 (m, 3 H, >C<u>H</u>C<u>H</u>$_2$-), 3.12 (s, 3 H, -O<u>C</u>H_3), 2.11 (s, 3 H, -<u>C</u>H_3), 1.03 (t, J = 7.2 Hz, 3 H, -CH$_2$C<u>H</u>$_3$).

^{13}C NMR (22.4 MHz) : δ 168.8, 164.9, 141.7, 128.1, 127.3, 124.5, 101.2, 86.1, 73.3, 59.1, 58.2, 51.3, 49.5, 13.9.

EI-MS *m/z* : 276 (M^+, 26), 244 (5), 231 (38), 203 (10), 158 (30), 115 (28).

Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30

Found : C, 69.65; H, 7.30.

Oxidative Addition of Ethyl Acetoacetate to 2-Methyl-2-pentene

A mixture of ethyl acetoacetate (0.390 g, 3.0 mmol) and 2-methyl-2-pentene (0.210 g, 2.5 mmol) was treated with CAN (3.15 g, 5.75 mmol) as described in the general procedure. The residue obtained on column chromatography using ethyl acetate in petroleum ether (2% and 3% respectively) as eluent afforded **25** (0.195 g, 37%) and **26** (0.106 g, 20%) as colourless oils.

4-Ethyl-2,5,5-trimethyl-4,5-dihydrofuran-3-carboxylic acid ethyl ester (25)

IR (CH_2Cl_2) ν_{max} : 2979, 1705, 1645, 1376, 1192 cm^{-1}.

^1H NMR (60 MHz) : δ 4.03 (q, J = 7.1 Hz, 2 H, $-OCH_2-$), 2.73-2.40 (m, 1 H, $>C\underline{H}CH_2-$), 2.12 (s, 3 H, $-CH_3$), 1.70-1.12 (m, 8 H), 0.85 (t, J = 7.1 Hz, 6 H, $-CH_2C\underline{H_3}$).

^{13}C NMR (22.4 MHz) : δ 166.2, 166.1, 105.3, 87.8, 58.3, 51.1, 29.6, 22.2, 21.1, 14.2, 13.8, 11.6.

HRMS exact mass calcd for $C_{12}H_{20}O_3$: 212.1412 (M^+)

Found : 212.1402.

2-[3'-(2'-Methyl-pent-1'-enyl)]-3-oxo-butanoic acid ethyl ester (26)

This product is a mixture of isomers.

IR (CH_2Cl_2) ν_{max} : 2973, 1740, 1719, 1369, 1176 cm^{-1}.

^1H NMR (90 MHz) : δ 4.84-4.75 (m, 2 H, olefinic), 4.11 (q, J = 7.3 Hz, 2 H, $-OCH_2-$), 3.51 (dd, J = 2.4, 2.2 Hz, 2 H), 2.92-2.61 (m, 1 H, $>C\underline{H}CH_2-$), 2.20 (s, $-COCH_3$), 2.15

(s, -$COCH_3$), 1.65-1.54 (m, 2 H), 1.36-1.08 (m, 6 H, -CH_3), 0.91-0.66 (m, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 202.3, 202.1, 168.7, 168.1, 143.3, 114.4, 114.2, 84.8, 64.3, 61.1, 60.9, 48.4, 48.1, 29.1, 27.9, 23.5, 23.4, 18.7, 18.5, 13.9, 13.8, 11.2, 11.0.

HRMS exact mass calcd for $C_{12}H_{20}O_3$: 212.1412 (M^+)
Found : 212.1404.

Oxidative Addition of Ethyl Acetoacetate to Indene

A mixture of ethyl acetoacetate (0.311 g, 2.4 mmol) and indene (0.230 g, 2.0 mmol) was treated with CAN (2.52 g, 4.6 mmol) as described in the general procedure. After 30 min the reaction mixture was not decolourised. But the TLC analysis showed that indene was absent in the mixture and hence it was worked up. The residue on column chromatography using 5% ethyl acetate in petroleum ether as eluent afforded **30** (pale yellow oil, 0.075 g, 15%). Further elution with 10% ethyl acetate in petroleum ether furnished **31** (0.155 g, 15%) and **33** (0.117 g, 22%) as pale yellow oils.

Dihydrofuran 30

IR (CH_2Cl_2) ν_{max} : 2944, 1698, 1646, 1387, 1253 cm^{-1}.

^1H NMR (60 MHz) : δ 7.40-6.91 (m, 4 H, ArH), 5.75 (d, J = 9.0 Hz, 1 H, >CHO-), 4.02 (q, J =7.2 Hz, 2 H, -OCH_2-), 3.83-3.63 (m, 1 H, >C<u>H</u>CH_2-), 3.35-3.02 (m, 2 H, -CH_2-), 2.10 (s, 3 H, -CH_3), 1.23 (t, J = 7.2 Hz, 3 H, -CH_2C<u>H</u>$_3$).

^{13}C NMR (75.5 MHz) : δ 167.88, 166.30, 143.41, 140.61, 129.75, 127.22, 125.85, 125.62, 106.57, 90.10, 59.61, 45.46, 39.29, 14.75, 14.63.

HRMS exact mass calcd for $C_{15}H_{16}O_3$: 244.1099 (M^+)

Found : 244.1076.

2-[2'-(1'-Methoxyindan)]-3-oxobutanoic acid ethyl ester (31)

This product is a mixture of isomers.

IR (neat) ν_{max} : 2940, 1745, 1716, 1465, 1360 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.42-7.11 (m, 4 H, ArH), 4.63 (dd, J = 5.3, 4.4 Hz, 1 H, >C<u>H</u>OCH_3), 4.08 (q, J = 7.3 Hz, 2 H, -OCH_2-), 3.50-3.42 (m, 1 H), 3.38 (s, 3 H, -OCH_3), 3.24-3.14 (m, 2 H, -CH_2-), 2.66-2.37 (m, 1 H, >CH-), 2.22 (s, -$COCH_3$), 2.19 (s, -$COCH_3$), 1.19 (m, -$CH_2C\underline{H}_3$).

: δ 201.8, 201.4, 168.4, 168.3, 141.3, 141.2, 140.9, 140.8, 128.1, 127.9, 126.1, 124.5, 124.1, 86.7, 86.5, 62.4, 62.1, 60.8, 55.9, 55.3, 44.2, 43.2, 34.1, 33.7, 28.5, 28.2, 13.4.

GC-MS *m/z* : 246 (MH^+- OCH_3 , 25), 198 (92), 170 (30), 155 (50), 128 (100).

2-[2'-(Indan-1'-one)]-3-oxobutanoic acid ethyl ester (33)

This product is a mixture of isomers.

IR (CH_2Cl_2) ν_{max} : 2989, 1714, 1613, 1368, 1287 cm^{-1}.

^1H NMR (300 MHz) : δ 7.65-7.30 (m, 8 H, ArH), 4.34-4.04 (m, 6 H), 3.48-3.01 (m, 6 H), 2.42 (s, 3 H), 2.26 (s, 3 H), 1.32 (t, J = 7.2 Hz, 3 H, $-CH_2C\underline{H}_3$), 1.06 (t, J = 7.2 Hz, 3 H, $-C\underline{H}_2CH_3$).

^{13}C NMR (75.5 MHz) : δ 205.43, 205.13, 202.34, 201.55, 168.24, 168.22, 153.33, 153.25, 135.01, 134.01, 127.02, 126.62, 124.11, 61.93, 61.73, 59.48, 59.15, 46.97, 46.42, 31.14, 31.05, 30.31, 29.83, 14.28, 13.96.

GC-MS *m/z* : 261 (MH^+, 100), 247 (10), 189 (26), 173 (5), 145 (8), 131 (44).

4-Methoxymethyl-2-oxo-5-phenyl-tetrahydrofuran-3-carboxylic acid methyl ester (38)

A mixture of cinnamyl methyl ether (0.220 g, 1.5 mmol) and dimethyl malonate (0.237 g, 1.8 mmol) was dissolved in methanol (5 mL). A solution of CAN (1.89 g, 3.45 mmol) in water (15 mL) was added dropwise and stirred in an ice-bath for 1 h and further stirred at room temperature for 2 h. The reaction mixture was worked up and the residue was subjected to column chromatography. Elution with petroleum ether-chloroform-ethyl acetate mixture (16:3:1) furnished **38** (0.230 g, 58%) as a colourless viscous liquid.

IR (CH_2Cl_2) ν_{max} : 2936, 1790, 1743, 1459, 1269 cm^{-1}.

^1H NMR (60 MHz) : δ 7.25 (s, 5 H, ArH), 5.20 (d, J = 9.9 Hz, 1 H, >C$\underline{H}$Ph), 3.85-3.58 (m, 4 H), 3.52-2.95 (m, 6 H).

^{13}C NMR (22.4 MHz) : δ 170.4, 167.1, 136.8, 128.9, 128.1, 125.7, 81.1, 68.3, 58.2, 51.6, 49.4, 48.1.

GC-MS *m/z* : 264 (M^+, 5), 232 (6), 219 (3), 200 (7), 173 (30), 163 (30), 105 (100).

Oxidative Addition of Dimethyl Malonate to 1-Phenyl-1-cyclohexene

A mixture of dimethyl malonate (0.330 g, 2.5 mmol) and 1-phenyl-1-cyclohexene (0.475 g, 3.0 mmol) was dissolved in methanol (10 mL). A solution of CAN (3.15 g, 5.75 mmol) in water (25 mL) was added dropwise and stirred in an ice-bath for 1 h and then at room temperature for 1 h. The reaction mixture was worked up and the product purified by column chromatography. Elution with 10% ethyl acetate in petroleum ether afforded a mixture of **39** and **40** (0.289 g, 43%) as a pale yellow viscous liquid.

IR (CH_2Cl_2) ν_{max} : 2950, 1784, 1743, 1451, 1169 cm^{-1}.

^1H NMR (60 MHz) : δ 9.75 (s, -COOH), 8.11-7.82 (m, ArH), 7.50-7.21 (m, ArH), 3.67 (s, $-COOCH_3$), 3.56 (s, $-COOCH_3$), 3.30-2.80 (m, >CH-), 2.60-1.20 (m, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 170.5, 170.2, 167.5, 166.7, 143.2, 142.0, 133.1, 128.8, 128.6, 128.1, 127.8, 125.2, 124.4, 86.1

Oxidative Addition of Dimethyl Malonate to Indene

A solution of CAN (3.15 g, 5.75 mmol) in methanol (30 mL) was added dropwise to an ice-cooled mixture of dimethyl malonate (0.330 g, 2.5 mmol) and indene (0.350 g, 3.0 mmol) in methanol (10 mL). The reaction mixture was stirred at this temperature for 1 h and then at room temperature for 2 h. Worked up by the usual procedure and the residue was purified by column

chromatography. Elution with 10% ethyl acetate in petroleum ether afforded **41** (0.110 g, 17%) and **42** (0.221 g, 32%) as pale yellow oils.

2-[2'-(Indan-1'-one)]propanedioic acid dimethyl ester (41)

IR (CH_2Cl_2) ν_{max} : 2959, 1742, 1726, 1613, 1439, 1263 cm^{-1}.

^1H NMR (300 MHz) : δ 7.80-7.39 (m, 4 H, ArH), 4.20-4.14 (m, 1 H), 3.82 (s, 3 H, $-COOCH_3$), 3.68 (s, 3 H, $-COOCH_3$), 3.48-3.34 (m, 1 H), 3.28-3.21 (m, 2 H, $-CH_2-$).

^{13}C NMR (75.5 MHz) : δ 204.43, 169.18, 168.28, 153.30, 135.06, 127.70, 126.63, 124.24, 52.90, 52.72, 51.72, 46.77, 30.94.

HRMS exact mass calcd for $C_{14}H_{14}O_5$: 262.0841 (M^+)

Found : 262.0823.

2-[2'-(1'-Methoxyindan)]propanedioic acid dimethyl ester (42)

IR (CH_2Cl_2) ν_{max} : 2958, 1757, 1736, 1439, 1269 cm^{-1}.

^1H NMR (300 MHz) : δ 7.41-7.20 (m, 4 H, ArH), 4.78 (d, J = 6.0 Hz, 1H, $>C\underline{H}OCH_3$), 3.74 (s, 3 H, $-COOCH_3$), 3.72 (s, 3 H, $-COOCH_3$), 3.52-3.48 (m, 1 H), 3.44 (s, 3 H, $-OCH_3$), 3.36-3.28 (m, 1 H), 3.16-3.06 (m, 2 H, $-CH_2-$).

^{13}C NMR (75.5 MHz) : δ 169.09, 168.99, 141.99, 128.81, 126.90, 125.21, 125.16, 87.28, 56.26, 54.51, 52.56, 44.53, 34.69.

HRMS exact mass calcd for $C_{15}H_{18}O_5$: 278.1154 (M^+)

Found : 278.1148.

Oxidative Addition of Dimethyl Malonate to 2-Methyl-2-pentene

A solution of CAN (3.15 g, 5.75 mmol) in methanol (30 mL) was added to an ice-cooled mixture of dimethyl malonate (0.330 g, 2.5 mmol) and 2-methyl-2-pentene (0.252 g, 3.0 mmol) in methanol (10 mL). The reaction mixture was stirred in the ice-bath for 1 h and at room temperature for 3 h. Worked up and the residue was subjected to column chromatography. Elution with 10% ethyl acetate in petroleum ether furnished **44** (0.103 g, 20%) and **47** (0.206 g, 41%) as pale yellow oils.

2-[3'-(2'-Methyl-pent-1'-enyl)]propanedioic acid dimethyl ester (44)

IR (CH_2Cl_2) ν_{max} : 2964, 1763, 1743, 1439, 1260 cm^{-1}.

^1H NMR (60 MHz) : δ 4.70 (m, 2 H, olefinic), 3.62 (s, 3 H, $-COOCH_3$), 3.50 (s, 3 H, $-COOCH_3$), 3.35-3.21 (m, 1 H), 2.91-2.40 (m, 1 H), 1.85 (s, 3 H, $-CH_3$), 1.52-1.20 (m, 2 H, $-C\underline{H}_2CH_3$), 0.90 (t, J = 7.0 Hz, 3 H, $-CH_2C\underline{H}_3$).

^{13}C NMR (22.4 MHz) : δ 168.8, 168.1, 143.2, 114.5, 56.1, 52.3, 48.2, 23.3, 18.8, 11.2.

HRMS exact mass calcd for $C_{11}H_{18}O_4$: 214.1205 (M^+)

Found : 214.1252.

5,5-Dimethyl-4-ethyl-2-oxofuran-3-carboxylic acid methyl ester (47)

IR (CH_2Cl_2) ν_{max} : 2960, 1790, 1748, 1465, 1263 cm^{-1}.

^1H NMR (300 MHz) : δ 3.82 (s, 3 H, $-COOCH_3$), 3.38 (d, J = 12.1 Hz, 1 H, $>C\underline{H}COOCH_3$), 2.71-1.62 (m, 1 H, $>C\underline{H}CH_2-$),

1.60-1.42 (m, 5 H, $-C\underline{H}_2CH_3$, $-C\underline{H}_3$), 1.26 (s, 3 H, $-CH_3$), 0.93 (t, J = 7.4 Hz, 3 H, $-CH_2C\underline{H}_3$).

^{13}C NMR (75.5 MHz) : δ 170.69, 169.02, 86.13, 53.56, 53.01, 51.65, 27.86, 22.68, 22.60, 12.62.

HRMS exact mass calcd for $C_{10}H_{16}O_4$: 200.1048 (M^+)

Found : 200.1026.

Preparation of Dihydrofurans Mediated by $Mn(OAc)_3$: General Procedure

A mixture of the dicarbonyl compound (1.0 mmol), alkene (1.2 mmol) and $Mn(OAc)_3$ (2.3 mmol) in acetic acid (15 mL) was refluxed until the brown colour of $Mn(OAc)_3$ disappeared (15 min). It was cooled, diluted with water (100 mL) and extracted with ether (3 x 75 mL). The combined organic extracts were repeatedly washed with $NaHCO_3$ and then with water, dried and evaporated. The residue obtained on column chromatography using 10% ethyl acetate in petroleum ether as eluent afforded the dihydrofuran.

3,3-Dimethyl-5a-phenyl-1,2,3,4,5a,6,7,8,9,9a-decahydrodibenzofuran-1-one (9)

The reaction of a mixture of dimedone (0.140 g, 1.0 mmol), and 1-phenyl-1-cyclohexene (0.189 g, 1.2 mmol) with $Mn(OAc)_3$ (0.804 g, 3.0 mmol) according to the general procedure furnished **9** (0.250 g, 84%).

3,3,5a-Trimethyl-1,2,3,4,5a,6,7,8,9,9a-decahydrodibenzofuran-1-one (10)

A mixture of dimedone (0.140 g, 1.0 mmol) and 1-methyl-1-cyclohexene (0.115 g, 1.2 mmol) was treated with $Mn(OAc)_3$ (0.616 g, 2.3 mmol) as described in the general procedure. The product **10** was obtained in 47% yield (0.112 g).

3-Ethyl-2,2,6,6-tetramethyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one (11)

The reaction of a mixture of dimedone (0.210 g, 1.5 mmol) and 2-methyl-2-pentene (0.150 g, 1.8 mmol) with $Mn(OAc)_3$ (0.925 g, 3.45 mmol) as described in the general procedure afforded **11** (0.141 g, 41%).

3-Acetyl-2-methyl-7a-phenyl-3a,4,5,6,7,7a-hexahydrobenzofuran (16)

A mixture of acetylacetone (0.240 g, 2.4 mmol) and 1-phenyl-1-cyclohexene (0.316 g, 2.0 mmol) was treated with $Mn(OAc)_3$ (1.23 g, 4.6 mmol) according to the general procedure to give **16** (0.430 g, 84%).

3-Acetyl-4-methoxymethyl-2-methyl-5-phenyl-4,5-dihydrofuran (17)

The reaction of a mixture of acetylacetone (0.140 g, 1.38 mmol) and cinnamyl methyl ether (0.172 g, 1.15 mmol) with $Mn(OAc)_3$ (0.710 g, 2.65 mmol) as described in the general procedure furnished **17** (0.153 g, 54%).

Oxidative Addition of Acetylacetone to 2-Methyl-2-pentene

The reaction of a mixture of acetylacetone (0.20 g, 2.0 mmol) and 2-methyl-2-pentene (0.202 g, 2.4 mmol) with $Mn(OAc)_3$ (1.23 g, 4.6 mmol) according to the general procedure furnished 3-acetyl-4-ethyl-2,5,5-trimethyl-4,5-dihydrofuran (**20**, 0.141 g, 39%) and 3-[3'-(2'-methyl-pent-1'-enyl)]pentane-2,4-dione (**21**, 0.03 g, 8%).

2.4. References

1. (a) Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321. (b) Stork, G.; Baine, N. H. *Tetrahedron Lett.* **1985**, *26*, 5927.
2. (a) Stork, G.; Mook, R. Jr., *J. Am. Chem. Soc.* **1983**, *105*, 3720. (b) Stork, G. *Vinyl and β-Alkoxy Radicals in Organic Synthesis*; Nozaki, H., Ed.; Pergamon Press: Oxford, 1983; p. 359. (c) Stork, G. *Selectivity: A Goal for Synthetic Efficiency*; Bartman, W.; Trost, B. M., Ed.; Verlag Chemie: Weinheim, 1984; p. 281.
3. Beckwith, A. L. J.; Ingold, K. U. *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; p. 161.
4. (a) Julia, M. *Pure and Appl. Chem.* **1967**, *15*, 167. (b) Julia, M. *Acc. Chem. Res.* **1971**, *4*, 386. (c) Julia, M. *Pure and Appl. Chem.* **1974**, *40*, 553.
5. Giese, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 553.
6. For reviews on the generation and use of radicals in organic synthesis see: (a) Giese, B. *Radicals in Organic Synthesis : Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, 1986. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Curran, D. P.; *Synthesis* **1988**, 417, (Part 1); 489, (Part 2). (d) Barton, D. H. R. *Aldrichimica Acta* **1990**, *23*, 3. (e) Curran, D. P.; Jasperse, C. P.; Fevig, T. L. *Chem. Rev.* **1991**, 1237. (f) Beckwith, A. L. J. *Chem. Soc. Rev.* **1993**, 143.
7. Melikyan, G. G. *Synthesis* **1993**, 833.
8. Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.
9. (a) Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 524. (b) Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 995.
10. Heiba, E. I.; Dessau, R. M. *J. Am. Chem. Soc.* **1974**, *96*, 7977.
11. Kurz, M. E.; Ngoviwatchai, P. *J. Org. Chem.* **1981**, *46*, 4672.

12. Kurz, M. E.; Baru, V.; Nguyen, P. N. *J. Org. Chem.* **1984**, *49*, 1603.

13. Baciocchi, E.; Aira, D. D.; Ruzziconi, R. *Tetrahedron Lett.* **1986**, *27*, 2763.

14. Baciocchi, E.; Ruzziconi, R. *Synth. Commun.* **1988**, *18*, 1841.

15. Baciocchi, E.; Casu, A.; Ruzziconi, R. *Tetrahedron Lett.* **1989**, *30*, 3707.

16. Baciocchi, E.; Casu, A.; Ruzziconi, R. *Synlett* **1990**, 679.

17. Baciocchi, E.; Civatarese, G.; Ruzziconi, R. *Tetrahedron Lett.* **1987**, *28*, 5357.

18. Heiba, E. I.; Dessau, R. M. *J. Org. Chem.* **1974**, *39*, 3456.

19. (a) Iqbal, J.; Kumar, T. K. P.; Manogaran, S. *Tetrahedron Lett.* **1989**, *30*, 4701. (b) Tarakeshwar, P.; Iqbal, J.; Manogaran, S. *Tetrahedron* **1991**, *47*, 297. (c) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Tetrahedron* **1991**, *47*, 6457. (d) Bhatia, B.; Punniyamurthy, T.; Iqbal, J. *J. Org. Chem.* **1993**, *58*, 5518. (e) Bhatia, S.; Punniyamurthy, T.; Iqbal, J.; Bhatia, B. *Tetrahedron* **1993**, *49*, 6101.

20. Vinogradov, M. G.; Kondorsky, A. E.; Nikishin, G. I. *Synthesis* **1980**, 60.

21. Ichikawa, K.; Itoh, O.; Kawamura, T.; Fujiwara, M.; Ueno, T. *J. Org. Chem.* **1966**, *31*, 447.

22. Ichikawa, K.; Uemura, S.; Sugitha, T. *Tetrahedron* **1966**, *22*, 407.

23. Ichikawa, K.; Uemura, S. *J. Org. Chem.* **1967**, *32*, 493.

24. Hajek, M.; Silhavy, P.; Malek, J. *Tetrahedron Lett.* **1974**, 3193.

25. Baciocchi, E.; Ruzziconi, R. *J. Org. Chem.* **1991**, *56*, 4772.

26. Dauzonne, D.; Demerseman, P. *J. Heterocyclic Chem.* **1990**, *27*, 1581.

27. Snider, B. B.; Merritt, J. E.; Dombroski, M. A.; Buckman, B. O. *J. Org. Chem.* **1991**, *56*, 5544.

28. Green, T. W. *Protective Groups in Organic Synthesis;* Wiley-Interscience: 1980; p. 14, 53.

CHAPTER 3

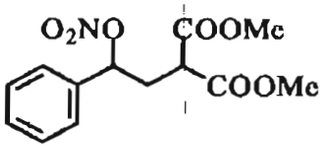
CERIUM(IV) AMMONIUM NITRATE MEDIATED OXIDATIVE ADDITION OF DIMETHYL MALONATE TO STYRENES

3.1. Introduction

In the previous chapter, we have demonstrated a facile and experimentally simple procedure for the oxidative addition of 1,3-dicarbonyl compounds to alkenes mediated by CAN. Dihydrofurans were obtained in good yields when dimedone, acetylacetone and ethyl acetoacetate were reacted with a variety of activated and unactivated alkenes, both cyclic and acyclic. The corresponding reactions of dimethyl malonate led to lactones in most of the cases. The reaction of dimethyl malonate as well as ethyl acetoacetate with indene, which furnished some very interesting products is an exception. In continuation of these studies, we decided to investigate the oxidative addition of dimethyl malonate to styrenes.

A survey of the literature revealed that malonyl radical generated by CAN is known to undergo substitution reactions with aromatic[1] and heteroaromatic[2] compounds. Recently it has been reported that the oxidation of substituted α-benzylmalonate in presence of olefins afforded highly functionalized tetrahydronaphthalenes[3]. Similar oxidative addition of diethyl (pyridylmethyl)-malonates to alkenes and alkynes furnished substituted tetra- or dihydroquinolines and/or isoquinolines[4]. Spirocyclohexadiene derivatives were also isolated in some cases[5].

While surveying the literature, we became intrigued by the 1990 report[6] of Baciocchi *et al* claiming that the addition of dimethyl malonate to styrene in presence of CAN afforded exclusively the nitrate **10** and the methoxy compound **11**. It was felt that the claim was not adequately supported by experimental data. For example, products were not isolated and spectral data were reported only for the crude products. Furthermore, an unprecedented reaction, i.e. the transformation of **11** to a cyclopropane derivative on refluxing in methanol, has been invoked to support the claim. Therefore we decided to reinvestigate this reaction[#]. We have now obtained results that are significantly different and these are presented in this chapter.



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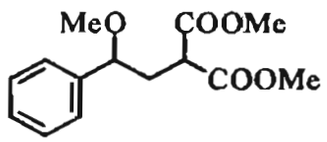

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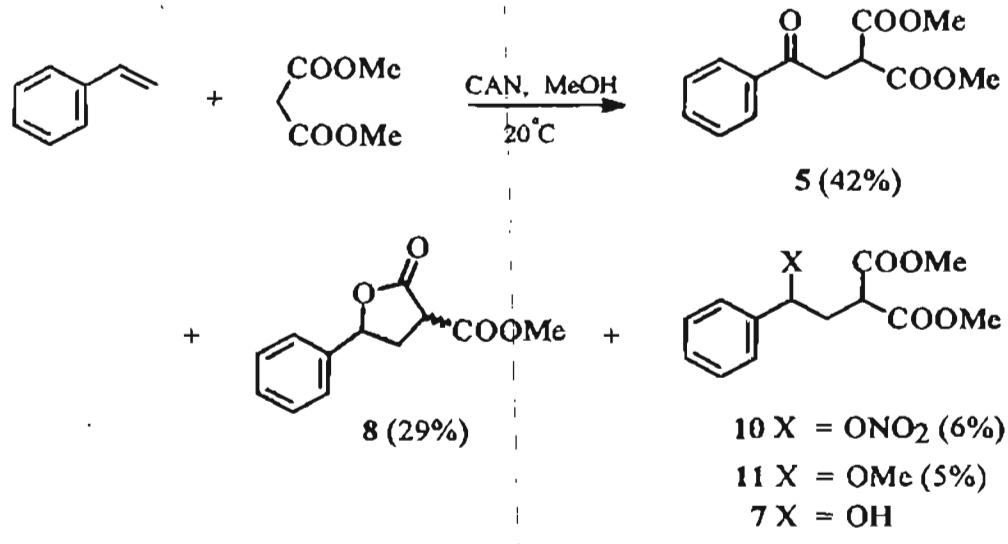
3.2. Results and Discussion

The procedure for the addition of dimethyl malonate to styrene reported by Baciocchi[6] is as follows: A solution of CAN in methanol was treated with dimethyl malonate and excess of styrene in the same solvent at 20°C for 40 min. The methanolic solution was poured into water and extracted with diethyl ether. The collected extracts were washed with water, dried and the solvent was evaporated. The ^{1}H NMR spectrum of the crude product showed the presence of

In our correspondence with Dr. Baciocchi we were unable to obtain any satisfactory response.

[2-(nitrooxy)-2-phenylethyl]propanedioic acid dimethyl ester (**10**) in 69% yield and (2-methoxy-2-phenylethyl)propanedioic acid dimethyl ester (**11**) in 24% yield.

We have repeated the experiment precisely under the conditions described above. The ^1H NMR spectrum of the crude product contained the characteristic proton signals (C_6H_5CO-) of the product **5** in addition to the signals corresponding to **10** and **11**. The IR spectrum of the crude product had a strong absorption at 3540 cm^{-1}. This indicated the presence of **7** along with **5**, **10** and **11**. Isolation of the products was achieved by chromatography on silica gel column. Elution with ethyl acetate in petroleum ether (5%, 10% and 15%) afforded **10** and **11** as a mixture whereas **5** and **8** were obtained pure in 42% and 29% yields respectively. It was necessary to resort to MPLC for the separation of **10** and **11**. Elution with CH_2Cl_2 and ethyl acetate afforded **10** and **11** respectively in 6% and 5% yields. The carbinol **7** is unstable and it lactonizes to **8** on standing or on silica gel column during chromatography. However it can be isolated by very careful and rapid column chromatography (elution with 20% ethyl acetate in petroleum ether). Thus the reaction can be represented as shown below.



It may be emphasized that our results are consistently reproducible and that the earlier workers did not isolate the products of the reaction.

The structures of the products **5**, **7**, **8**, **10** and **11** were assigned with the aid of IR, ^{1}H NMR and ^{13}C NMR spectral data. The IR spectrum of **5** displayed carbonyl absorptions at 1749 (-COOMe) and 1689 cm^{-1} (C_6H_5CO-). The ^{1}H NMR spectrum with two multiplets centred at δ 7.96 and 7.50 which correspond to the five aromatic protons in the ratio 2:3 clearly indicates the presence of C_6H_5CO- group. The protons of the two methoxy groups resonated as a singlet at δ 3.77. In the ^{13}C NMR spectrum, the two carbonyl carbons of the keto- and the ester groups appeared at δ 196.4 and 169.1 respectively. The mass spectrum of **5** showed molecular ion peak at *m/z* 250 which was also in agreement with the proposed structure.

The IR spectrum of **7** contained a strong absorption at 3528 cm^{-1} indicating the presence of a hydroxyl group, while the carbonyl absorption was observed at 1733 cm^{-1}. In the ^{1}H NMR spectrum, the aromatic protons resonated as a singlet at δ 7.20 and the proton attached to the carbon bearing the -OH group appeared at δ 4.71 as a multiplet. The protons of the two methoxy groups were seen as singlets at δ 3.73 and 3.60. The two ester carbonyls appeared at δ 169.9 in the ^{13}C NMR spectrum. Further, the signal at δ 71.4 corresponding to the carbon bearing the -OH group is confirmatory for the structure **7**.

The product **8** was obtained as an inseparable mixture of *cis-trans* isomers. The IR spectrum exhibited two strong absorptions at 1783 and 1741 cm^{-1} characteristic of γ-lactone and ester group respectively. In the ^{1}H NMR spectrum, the aromatic protons were observed as a multiplet centred at δ 7.28. The single proton geminal to the phenyl group appeared as a triplet at δ 5.63 and a doublet of doublet at δ 5.36 for the two isomers. The protons of the methoxy groups

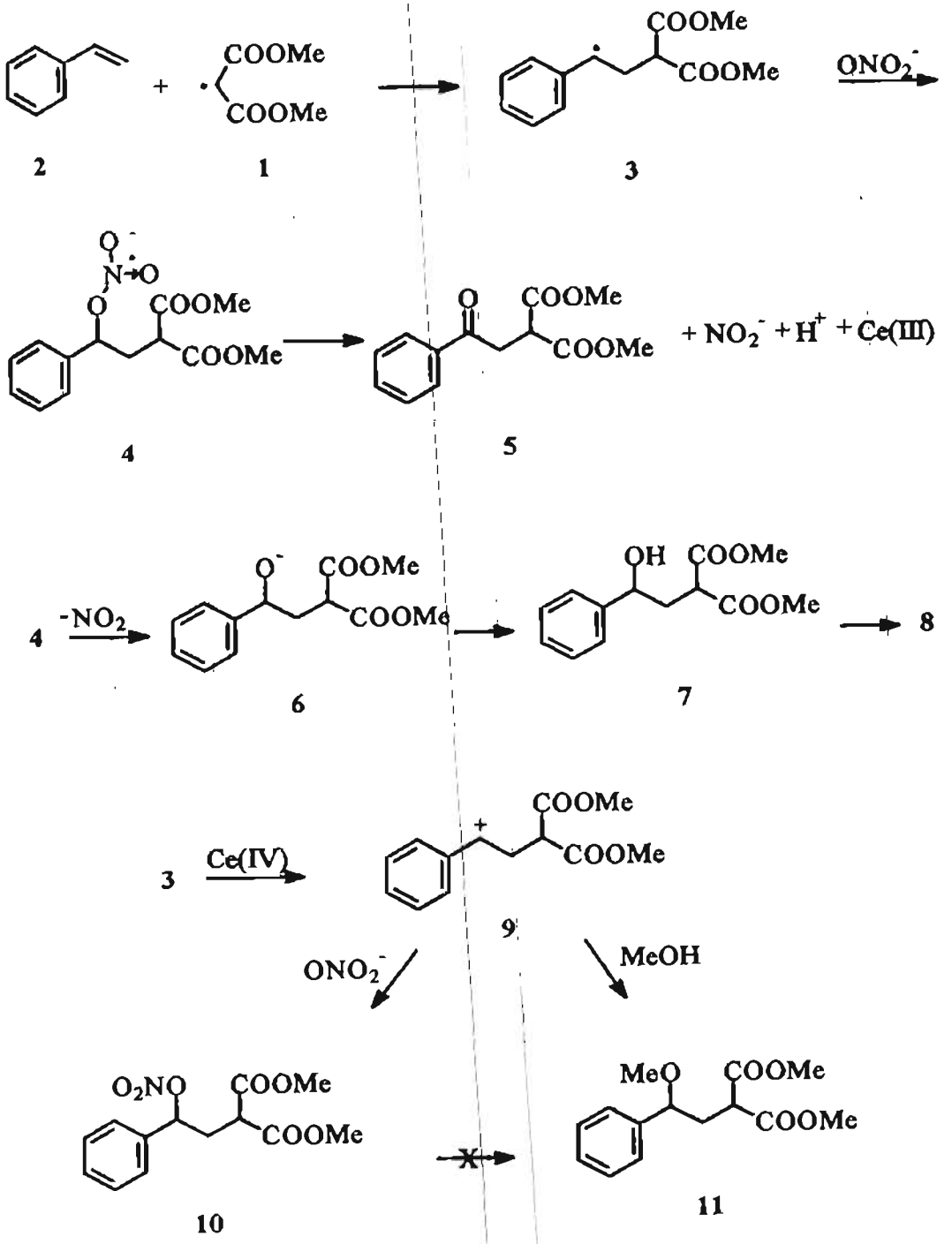
resonated as singlets at δ 3.76 and 3.74. Apart from these, the methine proton and the methylene protons could be seen as multiplets centred at δ 3.63 and 2.65. The presence of γ-lactone was further confirmed from the ^{13}C NMR spectrum with a resonance at δ 171.3. The ester carbonyls of the two isomers were identified at δ 167.9 and 167.8 and the lactone ring carbon bearing the phenyl group appeared as two signals at δ 80.3 and 79.8.

The IR spectrum of **10** exhibited a strong absorption at 1639 cm^{-1} due to the -N=O asymmetric stretching in addition to the strong carbonyl absorptions at 1759 and 1740 cm^{-1}. Another absorption was observed at 1278 cm^{-1} which could be attributed to the -N=O symmetric stretching. In the ^{1}H NMR spectrum, the aromatic protons resonated as a singlet at δ 7.40. Another signal which appeared as a doublet of doublet at δ 5.93 corresponds to the proton attached to the carbon bearing the $-ONO_2$ group. The protons of the methoxy groups appeared as singlets at δ 3.78 and 3.77. The ^{13}C NMR spectrum with the carbonyl carbon at δ 169.4 and the characteristic signal at δ 82.9 due to the carbon bearing the $-ONO_2$ group further confirmed the structure assigned for **10**.

In the IR spectrum of **11**, the carbonyl absorptions were observed at 1755 and 1743 cm^{-1}. The aromatic protons resonated as a multiplet centred at δ 7.28 in the ^{1}H NMR spectrum. The proton geminal to the methoxy group appeared as a doublet of doublet at δ 4.16. The protons of the three methoxy groups were identified at δ 3.74, 3.72 and 3.18. The resonances in the ^{13}C NMR spectrum at δ 169.8 and 169.6 were due to the two ester groups. The carbon bearing the methoxy group resonated at δ 81.3. Thus, all the spectral data were in complete agreement with the proposed structure **11**.

A tentative mechanism which will rationalize these results can be depicted as follows: The addition of malonyl radical **1**, generated by CAN, to styrene would

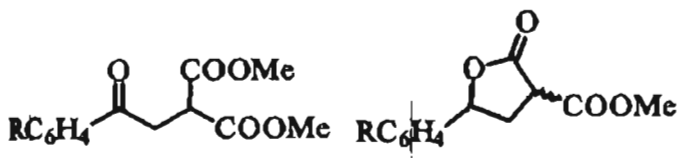
give the benzylic radical **3** which gets trapped by NO_3^- to form the unstable radical anion **4**. The oxidative fragmentation of **4** would lead to the ketone **5**. The direct fragmentation of **4** followed by protonation of the resulting alkoxide would give the carbinol **7**, the precursor for the lactone **8**. The mechanism for the formation of the nitrate **10** can involve either the oxidation of **4** or the trapping of the benzylic cation **9**, resulting from the oxidation of the radical **3**, by NO_3^-. Similarly **9** can be trapped by methanol to afford **11**. The formation of **11** by solvolysis of **10** is less likely since the only product isolated in the attempted methanolysis of **10** was the lactone **8**. Although benzylic alcohols are known to undergo oxidation to ketones by Ce(IV), such a pathway can be excluded in the formation of **5** as our attempts to convert the carbinol **7** to **5** by CAN have not been successful. Also, in all likelihood the ketone **5** is not derived from **11** as attempted oxidation of **11** failed to afford **5**. Whether the methanol used is dry or not does not have any bearing on product distribution. This rules out the possibility of formation of the carbinol **7** by the attack of water on the cation **9**. The mechanistic rationale described above is illustrated by the following scheme.

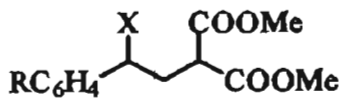

COOMe
COOMe
2
1
3
ONO_2^-
$+ NO_2^- + H^+ + Ce(III)$
4
5
$-NO_2$
6
7
8
Ce(IV)
9
ONO_2^-
MeOH
O_2NO
10
MeO
11
X

Scheme 1

In the procedure described above, large excess of styrene (4.4 equiv.) was used. Actually this is not needed for the completion of the reaction. The experiment was repeated under the conditions which we have used for the addition of dicarbonyl compounds like dimedone and acetylacetone to alkenes (see Section 2.3). Thus an ice-cooled solution of dimethyl malonate and styrene (in the ratio 1:1.2) in methanol was subjected to dropwise treatment with CAN (2.3 equiv.) also in the same solvent. Slowly the reaction mixture was warmed to ambient temperature and stirred until the brown colour of CAN disappeared (4 h). Processing of the reaction mixture followed by chromatography on silica gel column afforded products **5**, **8**, **10** and **11** in 43%, 30%, 5% and 8% yields respectively. Evidently, when compared with the results of the earlier experiment there is no appreciable change in the product distribution. Therefore we have adopted the latter procedure for reactions with substituted styrenes.

The addition of dimethyl malonate to 4-chloro-, 4-methyl- and 3-methyl substituted styrenes furnished products analogous to those obtained in the reaction with unsubstituted styrene (Scheme 2). In the case of 3-chlorostyrene, the corresponding reaction afforded only the ketone **24** and the lactone **25** in 42% and 14% yields respectively. 3-Nitrostyrene on the other hand furnished the ketone **26** and the nitrate **27**. The reaction of 4-nitrostyrene led to the ketone **28** along with some polymeric products which were not characterized.

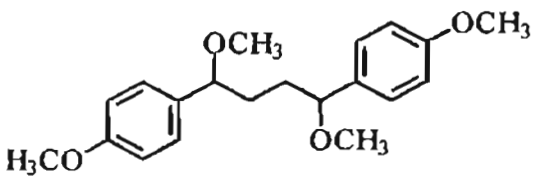




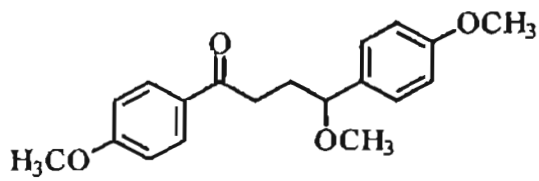
12 R = 4-Cl (30%)	**13** R = 4-Cl (25%)	**14** R = 4-Cl, X = ONO_2 (13%) **15** R = 4-Cl, X = OMe (4%)
16 R = 4-Me (14%)	**17** R = 4-Me (16%)	**18** R = 4-Me, X = ONO_2 (4%) **19** R = 4-Me, X = OMe (6%)
20 R = 3-Me (43%)	**21** R = 3-Me (25%)	**22** R = 3-Me, X = ONO_2 (7%) **23** R = 3-Me, X = OMe (8%)
24 R = 3-Cl (42%)	**25** R = 3-Cl (14%)	—
26 R = 3-NO_2 (32%)	—	**27** R = 3-NO_2, X = ONO_2 (24%)
28 R = 4-NO_2 (17%)	—	—

Scheme 2

When 4-methoxystyrene was used in this reaction, instead of the addition of malonyl radical to the styrene, the latter underwent oxidative coupling leading to **34** and **36**.



34



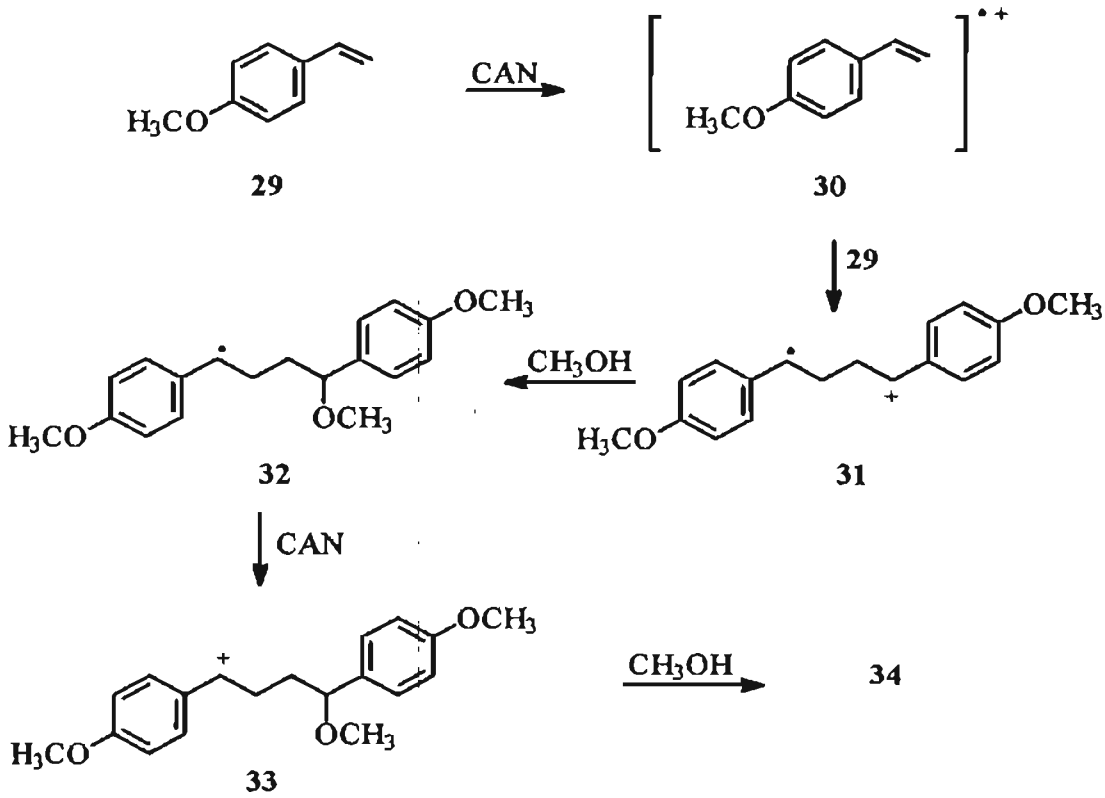
36

The products **34** and **36** were characterized by spectral analysis. The ^{1}H NMR spectrum of **34** provided convincing evidence that it is a symmetrical product. The aromatic protons appeared as two doublets at δ 7.04 and 6.74. Two sets of methoxy protons were seen as singlets at δ 3.69 and 3.03. The 10 line ^{13}C NMR spectrum confirmed that C_2 symmetry had been maintained. Also the resonances at δ 83.83 due to >C̲HOMe and at δ 56.59 and 55.47 due to -OC̲H$_3$ were highly diagnostic and enabled us to assign the structure **34**. In the IR spectrum of **36** carbonyl absorption was observed at 1676 cm^{-1}. The ^{1}H NMR spectrum, apart from the aromatic resonances at δ 7.84, 7.16 and 6.82, contained a characteristic signal at δ 4.10 (>C̲HOCH$_3$). Three singlets were observed at δ 3.79, 3.74 and 3.12 and these were attributed to the protons of the three methoxy groups. The presence of a signal at δ 82.74 due to the carbon bearing methoxy substituent and three methoxy carbons at δ 56.68, 55.66 and 55.49 further confirmed the structural formulation **36**.

The formation of the products **34** and **36** can be explained as follows. Methoxystyrene undergoes oxidation by CAN to generate the radical cation **30** which can add to another molecule of methoxystyrene and this would lead to the intermediate structure **31**[#]. Methanol addition to **31** followed by oxidation would

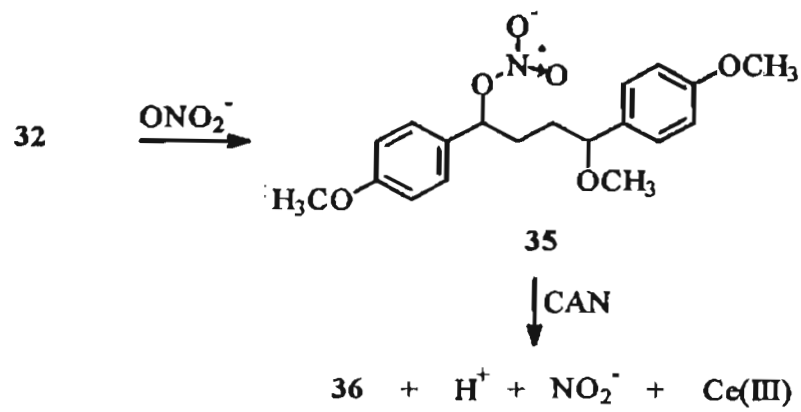
#Radical cation mediated dimerization of 4-methoxystyrene has been reported recently[7].

afford the cation **33**. Trapping of the intermediate **33** by methanol would furnish the product **34** (Scheme 3).



Scheme 3

Alternatively, the radical **35** can be formed by the addition of NO_3^- to the radical **32**. Oxidative fragmentation of **35** would lead to the product **36** (Scheme 4).



Scheme 4

3.3. Experimental

A general description of the experimental techniques and instruments used for spectral recordings is given in Chapter 2 (Section 2.3).

Dry THF was obtained by distillation over sodium-benzophenone ketyl. NaH used was a 50% suspension in mineral oil. Styrene and 3-methylstyrene purchased from Aldrich were used directly. 4-Chloro-, 3-chloro-, 4-methyl-, 4-nitro-, 3-nitro- and 4-methoxystyrenes were prepared from the corresponding aldehydes by Wittig reaction.

Oxidative Addition of Dimethyl Malonate to Styrene (Reported Procedure)[6]

CAN (4.98 g, 9.1 mmol) was dissolved in methanol (90 mL) and stirred at 20°C. To this was added styrene (2.08 g, 20 mmol) and dimethyl malonate (0.594 g, 4.5 mmol) in 10 mL methanol and stirred for 40 min. The methanolic solution was poured into water (250 mL) and extracted with diethyl ether

(3 x 100 mL). The collected extracts were washed with water, dried over anhydrous sodium sulfate and the solvent was evaporated. The residue on column chromatography using 5%, 10% and 15% ethyl acetate in petroleum ether as eluent afforded **10** and **11** as a mixture and pure products (2-oxo-2-phenyl-ethyl)propanedioic acid dimethyl ester (**5**, 0.470 g, 42%) and 2-oxo-5-phenyl-tetrahydrofuran-3-carboxylic acid methyl ester[8] (**8**, 0.287 g, 29%) respectively. MPLC separation using dichloromethane and ethyl acetate as eluent furnished [2-(nitrooxy)-2-phenylethyl]propanedioic acid dimethyl ester (**10**, 0.075 g, 6%) and (2-methoxy-2-phenylethyl)propanedioic acid dimethyl ester (**11**, 0.065 g, 5%).

Oxidative Addition of Dimethyl Malonate to Styrene (Modified Procedure)

Dimethyl malonate (0.990 g, 7.5 mmol) and styrene (0.937 g, 9.0 mmol) were dissolved in methanol (50 mL) and stirred in an ice-bath. To this was added a solution of CAN (9.45 g, 17.25 mmol) in methanol (120 mL) dropwise. The reaction mixture was stirred at this temperature for 2 h and then at RT for 2 h. Methanol was evaporated *in vacuo* and the residue was extracted with CH_2Cl_2 (3 x 100 mL) after diluting with water (150 mL). The combined organic extracts were washed with water, dried and evaporated. Column chromatography of the residue as described above afforded **5** (0.811 g, 43%), **8** (0.497 g, 30%), **10** (0.118 g, 5%) and **11** (0.156 g, 8%).

(2-Oxo-2-phenylethyl)propanedioic acid dimethyl ester (5)

IR (CH_2Cl_2) ν_{max} : 2960, 1749, 1689, 1443, 1285 cm^{-1}.

^1H NMR (90 MHz) : δ 8.02-7.91 (m, 2 H, ArH), 7.58-7.43 (m, 3 H, ArH), 4.10-4.01 (m, 1 H, >CH-), 3.77 (s, 6 H, $-COOCH_3$), 3.67-3.48 (m, 2 H, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 196.4, 169.1, 135.5, 133.2, 128.4, 127.9, 52.5, 46.2, 37.1.

GC-MS *m/z* : 250 (M^+, 5), 232 (10), 219 (6), 187 (8), 159 (7), 145 (5), 105 (100).

Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64

Found : C, 62.50; H, 5.66.

2-Oxo-5-phenyl-tetrahydrofuran-3-carboxylic acid methyl ester (8)

This product is a mixture of *cis-trans* isomers.

IR (CH_2Cl_2) ν_{max} : 2961, 1783, 1741, 1459 cm^{-1}.

^1H NMR (300 MHz) : δ 7.33-7.23 (m, 5 H, ArH), 5.63 (t, J = 7.2 Hz), 5.36 (dd, J = 10.2, 6.2 Hz), 3.76 (s, $-COOCH_3$), 3.74 (s, $-COOCH_3$), 3.72-3.54 (m, 1 H, $>CHCOOCH_3$), 3.01-2.30 (m, 2 H, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 171.3, 167.9, 167.8, 138.4, 137.8, 128.7, 128.6, 128.5, 125.6, 125.1, 80.3, 79.8, 53.0, 52.8, 47.4, 46.6, 34.7, 34.5.

GC-MS *m/z* : 220 (M^+, 20), 192 (25), 160 (20), 145 (12), 120 (20), 105 (70), 87 (100).

Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49

Found : C, 65.32; H, 5.48.

[2-(Nitrooxy)-2-phenylethyl]propanedioic acid dimethyl ester (10)

IR (CH_2Cl_2) ν_{max} : 2962, 1759, 1740, 1639, 1440, 1278 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.40 (s, 5 H, ArH), 5.93 (dd, J = 8.0, 6.2 Hz, 1 H, >CHONO$_2$), 3.78 (s, 3 H, -COOCH$_3$), 3.77 (s, 3 H, -COOCH$_3$), 3.64-3.48 (m, 1 H, >CH-), 2.64-2.45 (m, 2 H, -CH$_2$-).

^{13}C NMR (22.4 MHz) : δ 169.4, 137.1, 129.5, 129.0, 126.4, 82.9, 52.5, 48.3, 33.6.

GC-MS *m/z* : 234 (M$^+$-ONO$_2$-1, 10), 202 (15), 170 (60), 143 (10), 129 (15), 115 (100).

(2-Methoxy-2-phenylethyl)propanedioic acid dimethyl ester (11)

IR (CH_2Cl_2) ν_{max} : 2957, 1755, 1743, 1440 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.31-7.26 (m, 5 H, ArH), 4.16 (dd, J = 7.5, 5.9 Hz, 1 H, >C<u>H</u>OCH$_3$), 3.74 (s, 3 H, -COOCH$_3$), 3.72 (s, 3 H, -COOCH$_3$), 3.64-3.56 (m, 1 H, >CH-), 3.18 (s, 3 H, -OCH$_3$), 2.32-2.24 (m, 2 H, -CH$_2$-).

^{13}C NMR (22.4 MHz) : δ 169.8, 169.6, 141.0, 128.2, 127.8, 126.4, 81.3, 56.7, 52.3, 48.7, 37.2.

GC-MS *m/z* : 266 (M$^+$, 5), 251 (8), 235 (7), 219 (4), 135 (50), 121 (100), 115 (25).

Rapid column chromatography using 20% ethyl acetate in petroleum ether as eluent afforded (2-hydroxy-2-phenylethyl)propanedioic acid dimethyl ester (7).

(2-Hydroxy-2-phenylethyl)propanedioic acid dimethyl ester (7)

IR (CH_2Cl_2) ν_{max} : 3528, 2960, 1733, 1457 cm^{-1}.

^{1}H NMR (60 MHz) : δ 7.20 (s, 5 H, ArH), 4.82-4.60 (m, 1 H, >C<u>H</u>OH), 4.0 (brs, 1 H, -OH), 3.73 (s, 3 H, -$COOCH_3$), 3.60 (s, 3 H, -$COOCH_3$), 3.55-3.35 (m, 1 H), 2.25-2.05 (m, 2 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 169.9, 143.8, 128.2, 127.4, 125.5, 71.4, 52.5, 48.6, 37.3.

Preparation of Substituted Styrenes: General Procedure

NaH (3.0 g, *ca.* 66 mmol) was suspended in dry THF (50 mL). Triphenylmethylphosphonium iodide (20.2 g, 50 mmol) was added to it and refluxed for 1.5 h. Substituted benzaldehyde (33 mmol) dissolved in THF (25 mL) was added and stirred at 40-45°C for 1-2 h. The reaction mixture was cooled, diluted with water (200 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic extracts were washed with water, dried and evaporated. The residue was purified by column chromatography. Elution with petroleum ether afforded substituted styrene.

Oxidative Addition of Dimethyl Malonate to 4-Chlorostyrene

Dimethyl malonate (0.661 g, 5.0 mmol) and 4-chlorostyrene (0.866 g, 6.25 mmol) were dissolved in methanol (30 mL) and treated with CAN (6.31 g, 11.5 mmol) in methanol (80 mL) as described previously. Work-up and column chromatography furnished **12** (colourless viscous liquid, 0.435 g, 30%), **13** (colourless viscous liquid, 0.291 g, 23%), **14** (yellow oil, 0.220 g, 13%) and **15** (pale yellow oil, 0.06 g, 4%).

[2-(4'-Chlorophenyl)-2-oxoethyl]propanedioic acid dimethyl ester (12)

IR (CH_2Cl_2) ν_{max} : 2961, 1755, 1743, 1691, 1594, 1439 cm^{-1}.

^1H NMR (200 MHz) : δ 7.90 (d, J = 6.8 Hz, 2 H, ArH), 7.43 (d, J = 7.7 Hz, 2 H, ArH), 4.06 (t, J = 7.1 Hz, 1 H, >CH-), 3.77 (s, 3 H, $-COOCH_3$), 3.76 (s, 3 H, $-COOCH_3$), 3.59 (d, J = 7.1 Hz, $-CH_2-$).

^{13}C NMR (50 MHz) : δ 195.22, 169.23, 140.04, 134.39, 129.53, 129.01, 52.82, 46.78, 37.80.

GC-MS *m/z* : 284 (M^+, 5), 266 (6), 253 (4), 221 (10), 195 (6), 139 (100), 111 (25).

5-(4'-Chlorophenyl)-2-oxo-tetrahydrofuran-3-carboxylic acid methyl ester (13)

This product is a mixture of *cis-trans* isomers.

IR (neat) ν_{max} : 2963, 1788, 1745, 1356, 1161 cm^{-1}.

^1H NMR (90 MHz) : δ 7.45-7.20 (m, 4 H, ArH), 5.68 (t, J = 7.2 Hz), 5.42 (dd, J = 10.0, 6.4 Hz), 3.85 (s, $-COOCH_3$), 3.80 (s, $-COOCH_3$), 3.75-3.60 (m, 1 H, $>C\underline{H}COOCH_3$), 3.15-2.20 (m, 2 H, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 169.6, 166.3, 135.5, 135.0, 133.2, 127.5, 127.4, 125.6, 125.1, 77.6, 74.1, 51.7, 51.5, 45.9, 45.2, 33.2, 33.1.

GC-MS *m/z* : 254 (M^+, 10), 226 (8), 194 (9), 154 (15), 139 (35), 115 (30), 87 (100).

[2-(4'-Chlorophenyl)-2-(nitrooxy)ethyl]propanedioic acid dimethyl ester (14)

IR (neat) ν_{max} : 2961, 1754, 1741, 1642, 1441, 1279 cm^{-1}.

^1H NMR (90 MHz) : δ 7.30 (s, 4 H, ArH), 5.87 (dd, J = 8.0, 6.2 Hz, 1 H, $>CHONO_2$), 3.75 (s, 6 H, $-COOCH_3$), 3.60-3.35 (m, 1 H, >CH-), 2.65-2.35 (m, 2 H, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 168.5, 135.3, 134.9, 129.0, 127.6, 81.8, 52.6, 47.7, 33.1.

GC-MS *m/z* : 268 (M^+- ONO_2-1, 10), 236 (25), 204 (60), 155 (100), 149 (80).

[2-(4'-Chlorophenyl)-2-methoxyethyl]propanedioic acid dimethyl ester (15)

IR (neat) ν_{max} : 2957, 1755, 1743, 1438 cm^{-1}.

^1H NMR (90 MHz) : δ 7.31 (s, 4 H, ArH), 4.23-4.06 (m, 1 H, $>CHOCH_3$), 3.75 (s, 3 H, $-COOCH_3$), 3.71 (s, 3 H, $-COOCH_3$), 3.65-3.30 (m, 1 H, >CH-), 3.15 (s, 3 H, $-OCH_3$), 2.32-2.16 (m, 2 H, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 169.6, 169.5, 139.6, 128.6, 128.0, 127.8, 80.6, 56.7, 52.4, 48.5, 37.0.

GC-MS *m/z* : 300 (M^+, 4), 285 (5), 269 (7), 237 (4), 209 (10), 168 (45), 155 (100).

Oxidative Addition of Dimethyl Malonate to 4-Methylstyrene

To a mixture of dimethyl malonate (0.528 g, 4.0 mmol) and 4-methylstyrene (0.615 g, 5.2 mmol) dissolved in THF (50 mL), a solution of CAN (5.04 g, 9.2 mmol) in methanol (30 mL) was added dropwise and stirred till the reddish

brown colour of CAN disappeared (5°C→RT, 3 h). Worked up as described earlier. The residue on column chromatography afforded **16** (colourless viscous liquid, 0.151 g, 14%), **17** (colourless viscous liquid, 0.150 g, 16%), **18** (yellow oil, 0.051 g, 4%) and **19** (pale yellow oil, 0.064 g, 6%).

[2-(4'-Methylphenyl)-2-oxoethyl]propanedioic acid dimethyl ester (16)

IR (CH_2Cl_2) ν_{max} : 2960, 1758, 1741, 1693, 1439 cm^{-1}.

^1H NMR (200 MHz) : δ 7.86 (d, J = 8.2 Hz, 2 H, ArH), 7.25 (d, J = 7.9 Hz, 2 H, ArH), 4.07 (t, J = 7.1 Hz, 1 H, >CH-), 3.77 (s, 3 H, $-COOCH_3$), 3.76 (s, 3 H, $-COOCH_3$), 3.61 (d, J = 7.1 Hz, 2 H, $-CH_2-$), 2.41 (s, 3 H, $-CH_3$).

^{13}C NMR (50 MHz) : δ 195.96, 169.44, 144.39, 133.62, 129.33, 128.24, 52.74, 46.88, 37.77, 21.61.

GC-MS *m/z* : 264 (M^+, 5), 246 (4), 233 (5), 201 (7), 173 (4), 119 (100).

5-(4'-Methylphenyl)-2-oxo-tetrahydrofuran-3-carboxylic acid methyl ester (17)

This product is a mixture of *cis-trans* isomers.

IR (neat) ν_{max} : 2962, 1783, 1734, 1459, 1165 cm^{-1}.

^1H NMR (200 MHz) : δ 7.29-7.18 (m, 4 H, ArH), 5.67 (t, J = 7.2 Hz), 5.40 (dd, J = 10.2, 6.1 Hz), 3.83 (s, $-COOCH_3$), 3.81 (s, $-COOCH_3$), 3.75-3.68 (m, 1 H, >C<u>H</u>$COOCH_3$), 2.84-2.40 (m, 2 H, $-CH_2-$), 2.36 (s, 3 H, $-CH_3$).

^{13}C NMR (50 MHz) : δ 171.45, 168.08, 138.89, 138.65, 135.56, 134.93, 129.49, 125.92, 125.34, 80.61, 80.13, 53.15, 53.0, 47.75, 46.88, 34.87, 34.72, 21.14.

GC-MS *m/z* : 234 (M^+, 15), 219 (5), 206 (10), 191 (6), 174 (10), 159 (10), 147 (9), 131 (20), 119 (70).

[2-(4'-Methylphenyl)-2-(nitrooxy)ethyl]propanedioic acid dimethyl ester (18)

IR (neat) ν_{max} : 2960, 1754, 1743, 1638, 1442, 1277 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.25 (s, 4 H, ArH), 5.89 (dd, J = 8.0, 6.3 Hz, 1 H, >$CHONO_2$), 3.80 (s, 6 H, -$COOCH_3$), 3.62-3.44 (m, 1 H, >CH-), 2.61-2.45 (m, 2 H, -CH_2-), 2.38 (s, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 168.7, 139.2, 133.7, 129.5, 126.4, 82.7, 52.7, 48.0, 33.3, 21.1.

GC-MS *m/z* : 248 (M^+-ONO_2-1, 20), 216 (5), 189 (8), 158 (5), 129 (100).

[2-Methoxy-2-(4'-methylphenyl)ethyl]propanedioic acid dimethyl ester (19)

IR (neat) ν_{max} : 2956, 1755, 1741, 1440 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.15 (s, 4 H, ArH), 4.20-3.95 (m, 1 H, >C<u>H</u>OCH_3), 3.71 (s, 6 H, -$COOCH_3$), 3.55-3.25 (m, 1 H, >CH-), 3.14 (s, 3 H, -OCH_3), 2.31 (s, 3 H, -CH_3), 2.30-2.15 (m, 2 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 169.5, 169.3, 137.6, 137.1, 128.8, 126.1, 80.8, 56.2, 51.9, 48.3, 36.8, 20.6.

GC-MS *m/z* : 280 (M^+, 4), 265 (5), 249 (7), 233 (3), 217 (4), 201 (4), 185 (10), 148 (50), 135 (100).

Oxidative Addition of Dimethyl Malonate to 3-Methylstyrene

Dimethyl malonate (0.462 g, 3.5 mmol) and 3-methylstyrene (0.475 g, 4.02 mmol) dissolved in methanol (25 mL) was treated with CAN (4.41 g, 8.05 mmol) in methanol (55 mL) as described before. It was worked up and the residue was subjected to column chromatography. Pure products **20** (colourless viscous liquid, 0.40 g, 43%), **21** (colourless viscous liquid, 0.205 g, 25%), **22** (yellow oil, 0.074 g, 7%) and **23** (pale yellow oil, 0.079 g, 8%) were obtained.

[2-(3'-Methylphenyl)-2-oxoethyl]propanedioic acid dimethyl ester(20)

IR (neat) ν_{max} : 2961, 1742, 1691, 1440, 1161 cm^{-1}.

^1H NMR (90 MHz) : δ 7.85-7.71 (m, 4 H, ArH), 4.17-4.02 (m, 1 H, >CH-), 3.75 (s, 6 H, $-COOCH_3$), 3.70-3.55 (m, 2 H, $-CH_2-$), 2.41 (s, 3 H, $-CH_3$).

^{13}C NMR (22.4 MHz) : δ 196.2, 169.0, 138.1, 135.7, 133.9, 128.3, 128.2, 125.0, 52.4, 46.5, 37.6, 20.9.

GC-MS *m/z* : 264 (M^+, 4), 246 (5), 233 (3), 201 (10), 173 (5), 119 (100).

5-(3'-Methylphenyl)-2-oxo-tetrahydrofuran-3-carboxylic acid methyl ester (21)

IR (neat) ν_{max} : 2961, 1784, 1742, 1158 cm^{-1}.

^1H NMR (90 MHz) : δ 7.41-7.15 (m, 4 H, ArH), 5.66 (t, J = 7.3 Hz), 5.39 (dd, J = 10.0, 6.3 Hz), 3.80 (s, $-COOCH_3$), 3.79

(s, -$COOCH_3$), 3.77-3.61 (m, 1 H, >C<u>H</u>$COOCH_3$), 3.15-2.40 (m, 2 H, -CH_2-), 2.35 (s, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 171.4, 171.3, 167.8, 138.3, 138.2, 137.7, 129.3, 129.1, 128.4, 128.3, 126.1, 125.6, 122.6, 122.0, 80.3, 79.8, 52.8, 52.6, 47.4, 46.5, 34.7, 34.4, 21.0.

GC-MS *m/z* : 234 (M^+, 26), 206 (12), 174 (15), 159 (10), 146 (8), 131 (20), 119 (70), 87 (100).

[2-(3'-Methylphenyl)-2-(nitrooxy)ethyl]propanedioic acid dimethyl ester (22)

IR (neat) ν_{max} : 2961, 1754, 1743, 1640, 1440, 1278 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.30-7.15 (m, 4 H, ArH), 5.87 (dd, *J* = 7.9, 6.2 Hz, 1 H, >C<u>H</u>ONO_2), 3.79 (s, 6 H, -$COOCH_3$), 3.65-3.45 (m, 1 H, >CH-), 2.66-2.45 (m, 2 H, -CH_2-), 2.38 (s, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 168.5, 138.5, 136.5, 129.7, 128.5, 126.6, 123.1, 82.6, 52.5, 47.8, 33.2, 21.1.

[2-Methoxy-2-(3'-methylphenyl)ethyl]propanedioic acid dimethyl ester (23)

IR (neat) ν_{max} : 2957, 1752, 1741, 1440 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.36-7.05 (m, 4 H, ArH), 4.14 (dd, *J* = 7.6, 5.8 Hz, 1H, >C<u>H</u>OCH_3), 3.79 (s, 3 H, -$COOCH_3$), 3.75 (s, 3 H, -$COOCH_3$), 3.67-3.51 (m, 1 H, >CH-), 3.21 (s, 3 H, -OCH_3), 2.38 (s, 3 H, -CH_3), 2.35-2.21 (m, 2 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 169.4, 169.2, 140.5, 137.6, 128.1, 127.9, 126.6, 123.1, 80.9, 56.2, 51.9, 48.3, 36.7, 20.9.

GC-MS *m/z* : 280 (M^+, 3), 265 (4), 249 (6), 233 (2), 217 (4), 201 (3), 185 (10), 148 (50), 135 (100).

Oxidative Addition of Dimethyl Malonate to 3-Chlorostyrene

Dimethyl malonate (0.396 g, 3.0 mmol) and 3-chlorostyrene (0.498 g, 3.6 mmol) were dissolved in methanol (20 mL). This was subjected to the reaction with CAN (3.78 g, 6.9 mmol) in 50 mL methanol as described previously. Work-up by the usual procedure and column chromatography afforded **24** (0.361 g, 42%) and **25** (0.106 g, 14%) as colourless viscous liquids.

[2-(3'-Chlorophenyl)-2-oxoethyl]propanedioic acid dimethyl ester (24)

IR (neat) ν_{max} : 2960, 1757, 1693, 1435 cm^{-1}.

^1H NMR (90 MHz) : δ 7.90-7.77 (m, 2 H, ArH), 7.62-7.23 (m, 2 H, ArH), 4.03 (t, J = 7.5 Hz, 1 H, >CH-), 3.74 (s, 6 H, $-COOCH_3$), 3.55 (d, J = 7.5 Hz, 2 H, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 194.8, 168.8, 137.2, 134.6, 133.0, 129.7, 127.8, 125.8, 52.4, 46.3, 37.6.

GC-MS *m/z* : 284 (M^+, 5), 266 (7), 253 (6), 221 (12), 195 (8), 139 (100), 111 (30).

5-(3'-Chlorophenyl)-2-oxo-tetrahydrofuran-3-carboxylic acid methyl ester (25)

This product is a mixture of *cis-trans* isomers.

IR (neat) ν_{max} : 2963, 1788, 1745, 1356, 1161 cm^{-1}.

^1H NMR (90 MHz) : δ 7.42-7.18 (m, 4 H, ArH), 5.66 (t, J = 7.3 Hz), 5.48 (dd, J = 9.9, 6.4 Hz), 3.82 (s, $-COOCH_3$), 3.80 (s,

3 H, -$COOCH_3$), 3.74-3.63 (m, 1 H, -C<u>H</u>$COOCH_3$), 3.19-2.21 (m, 2 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 170.1, 167.7, 140.5, 140.0, 134.7, 134.6, 130.5, 128.8, 128.7, 125.7, 125.3, 123.7, 123.2, 79.4, 78.8, 53.1, 52.9, 47.2, 46.5, 34.6, 34.4.

GC-MS *m/z* : 254 (M^+, 12), 226 (8), 194 (10), 154 (12), 139 (45), 115 (32), 87 (100).

Oxidative Addition of Dimethyl Malonate to 3-Nitrostyrene

Dimethyl malonate (0.330 g, 2.5 mmol) and 3-nitrostyrene (0.447 g, 3 mmol) were dissolved in methanol (15 mL) and treated with CAN (3.15 g, 5.75 mmol) in methanol (20 mL). Work-up and column chromatography furnished **26** (yellow viscous liquid, 0.234 g, 32%) and **27** (yellow oil, 0.195 g, 24%).

[2-(3'-Nitrophenyl)-2-oxoethyl]propanedioic acid dimethyl ester (26)

IR (CH_2Cl_2) ν_{max} : 2962, 1702, 1537, 1354 cm^{-1}.

^{1}H NMR (300 MHz) : δ 8.94 (t, J = 1.9 Hz, 1 H, ArH), 8.59 (d, J = 2.2 Hz, 1 H, ArH), 8.57 (d, J = 2.2 Hz, 1 H, ArH), 8.46 (d, J = 1.2 Hz, 1 H, ArH), 4.26 (t, J = 7.0 Hz, 1 H, >CH-), 3.94 (s, 6 H, -$COOCH_3$), 3.81 (d, J = 7.0 Hz, 2 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 194.5, 168.9, 148.2, 136.8, 133.5, 130.2, 127.5, 122.5, 52.5, 46.7, 38.1.

[2-(Nitrooxy)-2-(3'-nitrophenyl)ethyl]propanedioic acid dimethyl ester (27)

IR (CH_2Cl_2) ν_{max} : 2960, 1740, 1646, 1532, 1273 cm^{-1}.

^1H NMR (300 MHz) : δ 8.34-8.30 (m, 2 H, ArH), 7.81-7.72 (m, 2 H, ArH), 6.08 (dd, J = 9.1, 5.1 Hz, 1 H, >$CHONO_2$), 3.92 (s, 3 H, -$COOCH_3$), 3.81 (s, 3 H, -$COOCH_3$), 3.65 (t, J = 7.1 Hz, 1 H, >CH-), 2.68-2.58 (m, 2 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 168.4, 148.8, 139.2, 132.1, 130.0, 124.0, 121.5, 81.6, 52.9, 47.48, 32.9.

Oxidative Addition of Dimethyl malonate to 4-Nitrostyrene

To a mixture of dimethyl malonate (0.396 g, 3.0 mmol) and 4-nitrostyrene (0.536 g, 3.6 mmol) dissolved in methanol (20 mL) was added a solution of CAN (3.78 g, 6.9 mmol) in methanol (50 mL) and stirred until the colour of the reaction mixture disappeared. It was worked up and the residue was subjected to column chromatography. Pure product **28** (0.15 g, 17%) was obtained as a yellow solid. Crystallization from petroleum ether-ethyl acetate mixture afforded fine needle shaped crystals, mp 116-118°C.

[2-(4'-Nitrophenyl)-2-oxoethyl]propanedioic acid dimethyl ester (28)

IR (KBr) ν_{max} : 2962, 1738, 1697, 1608, 1537, 1437 cm^{-1}.

^1H NMR (90 MHz) : δ 8.33 (d, J = 8.8 Hz, 2 H, ArH), 8.15 (d, J = 8.8 Hz, 2 H, ArH), 4.19 (t, J = 7.0 Hz, 1 H, >CH-), 3.81 (s, 6 H, -$COOCH_3$), 3.69 (d, J = 7.0 Hz, 2 H, -CH_2-).

^{13}C NMR (22.4 MHz) : δ 195.0, 168.8, 150.3, 140.2, 129.0, 123.7, 52.7, 46.5, 38.0.

Anal. Calcd for $C_{13}H_{13}O_7N$: C, 52.89; H, 4.44; N, 4.74

Found : C, 52.33; H, 4.36; N, 4.60.

Oxidative Addition of Dimethyl Malonate to 4-Methoxystyrene

A solution of CAN (3.78 g, 6.9 mmol) in methanol (25 mL) was added dropwise to an ice-cooled mixture of dimethyl malonate (0.390 g; 3.0 mmol) and 4-methoxystyrene (0.442 g, 3.3 mmol) in methanol (20 mL) and stirred for 1 h. The reaction mixture was worked up and the residue was purified by column chromatography. Pure products **34** (colourless solid, 0.202 g, 20%) and **36** (0.063 g, 6%) were obtained. Crystallization of **34** from petroleum ether-ethyl acetate mixture afforded colourless needle shaped crystals, mp 98-100°C.

1,4-Bis(methoxy-4'-methoxyphenyl)butane (34)

IR (KBr) ν_{max} : 2961, 1615, 1250, 1100 cm^{-1}.

^1H NMR (300 MHz) : δ 7.04 (d, J = 8.6 Hz, 4 H, ArH), 6.74 (d, J = 8.6 Hz, 4 H, ArH), 3.89-3.86 (m, 2 H, >C<u>H</u>OCH_3), 3.69 (s, 6 H, -OCH_3), 3.03 (s, 6 H, -OCH_3), 1.62-1.60 (m, 4 H, -CH_2-).

^{13}C NMR (75.5 MHz) : δ 159.28, 134.53, 128.12, 128.05, 113.99, 113.95, 83.83, 56.59, 55.47, 34.83.

GC-MS *m/z* : 298 (M^+-OCH_3-1, 5), 266 (4), 227 (5), 166 (25), 151 (100), 135 (15).

Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93.

Found : C, 72.64; H, 8.15.

1,4-Bis(4'-methoxyphenyl)-4-methoxy-butan-1-one (36)

IR (KBr) ν_{max} : 2954, 1676, 1604, 1258 cm^{-1}.

^1H NMR (300 MHz) : δ 7.85-7.82 (m, 2 H, ArH), 7.18-7.14 (m, 2 H, ArH), 6.85-6.79 (m, 4 H, ArH), 4.10 (dd, J = 7.7, 5.5 Hz, 1 H, >C<u>H</u>OCH_3), 3.79(s, 3 H, -OCH_3), 3.74 (s, 3 H, -OCH_3), 3.12 (s, 3 H, -OCH_3), 2.89 (t, J = 7.2 Hz, 2 H, -CH_2-), 2.10-2.01 (m, 2 H, -CH_2-).

^{13}C NMR (75.5 MHz) : δ 198.83, 163.60, 159.39, 134.14, 130.52, 130.47, 128.06, 114.09, 113.89, 82.74, 56.68, 55.66, 55.49, 34.55, 32.82.

3.4. References

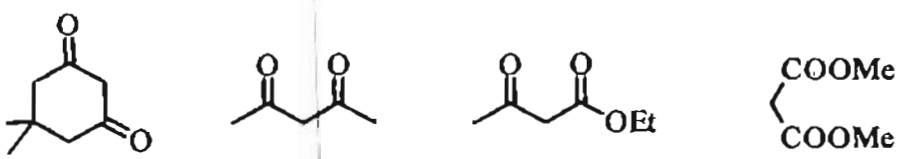
1. Baciocchi, E.; Ruzziconi, R.; Aira, D. D. *Tetrahedron Lett.* **1986**, *27*, 2763.
2. Weinstock, L. M.; Corley, E.; Abramson, N. L.; King, A. O.; Karady, S. *Heterocycles* **1988**, *27*, 2627.
3. Citterio, A.; Sebastiano, R.; Marion, A. *J. Org. Chem.* **1991**, *56*, 5328.
4. Citterio, A.; Sebastiano, R.; Carvayal, M. C. *J. Org. Chem.* **1991**, *56*, 5335.
5. Citterio, A.; Sebastiano, R.; Maronati, A.; Santi, R.; Bergamini, F., *J. Chem. Soc., Chem. Commun.* **1994**, 1517.
6. Baciocchi, E.; Giese, B.; Farshchi, H.; Ruzziconi, R. *J. Org. Chem.* **1990**, *55*, 5688.
7. Schepp, N. P.; Johnston, L. J. *J. Am. Chem. Soc.* **1994**, *116*, 6895.
8. Hussain, S. A. M. T.; Ollis, W. D.; Smith, C.; Stoddart, J. F. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1480.

CHAPTER 4

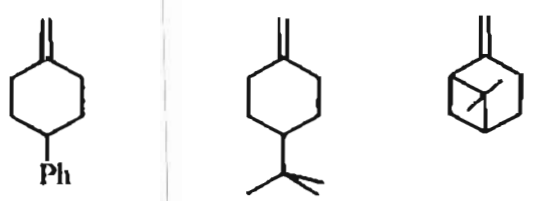
CERIUM(IV) AMMONIUM NITRATE MEDIATED ADDITION OF 1,3-DICARBONYL COMPOUNDS TO EXOCYCLIC ALKENES AND SOME MISCELLANEOUS REACTIONS

4.1. Introduction

The current interest in the synthesis of furanoid derivatives[1,2] as well as the prospect of a seemingly facile entry into the more important oxygen spirocycles offered by the CAN mediated oxidative addition of 1,3-dicarbonyl compounds to exocyclic alkenes inspired us to carry out some investigations in this area. Such a synthesis of spirocyclic compounds using $Mn(OAc)_3$ has recently been reported[3-5]. The dicarbonyl compounds **1-4** and the alkenes **5-7** were selected for our study and the results are described in the Section 4.2.1.



1 **2** **3** **4**



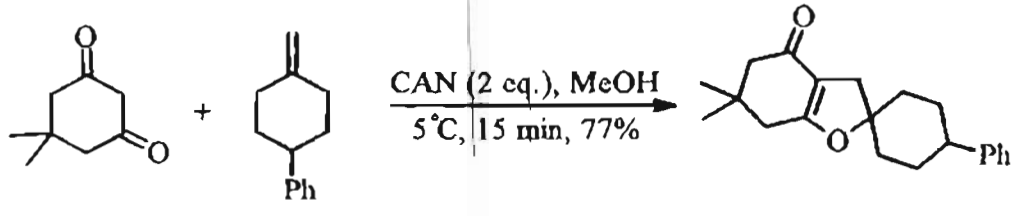
5 **6** **7**

The Section 4.2.2 deals with some miscellaneous reactions mediated by CAN. These include the oxidative addition reactions of the dicarbonyl compounds 1-4 with dienes and acetylenes and our attempts to carry out intramolecular radical cyclizations. Attempted oxidative addition reactions of 2-acetylcyclohexanone and 2-carboethoxycyclohexanone are also discussed.

4.2. Results and Discussion

4.2.1. CAN Mediated Synthesis of Spirodihydrofurans

The oxidative addition of 1,3-dicarbonyl compounds to exomethylene systems occurs smoothly in presence of CAN to afford spiroannulated dihydrofurans in moderate to good yields. The following example is illustrative.



1 **5** **8**

As in the previous cases, two equivalents of CAN are required for the completion of the reaction. The assignment of the structure of product **8** rests on its IR and NMR spectral data. The IR spectrum exhibited carbonyl absorption at 1637 cm^{-1}. In the ^1H NMR spectrum, aromatic protons resonated as a multiplet centred at δ 7.30. The methylene protons of the dihydrofuran moiety appeared as a broad singlet at δ 2.75 (2 H). The ^1H NMR spectrum also contained a singlet at δ 1.15 due to the methyl protons. The ^{13}C NMR spectrum displayed the carbonyl carbon at δ 195.5 and the signals at δ 175.9, 110.6 and 91.2 confirmed the

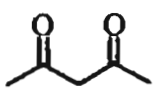
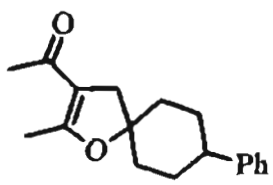
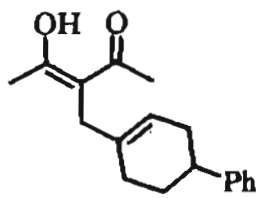
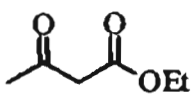
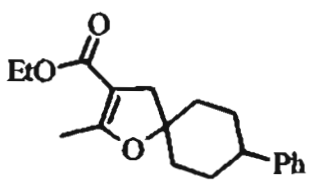
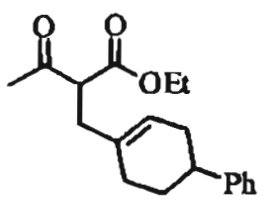
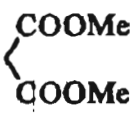
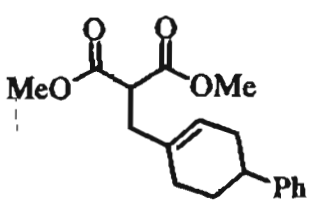
presence of the dihydrofuran moiety. The mass spectrum showed molecular ion peak at *m/z* 310 and this also was in agreement with the proposed structure.

The reactions of acetylacetone and ethyl acetoacetate with the alkene **5** furnished uncyclized compounds **10** and **12** in addition to the spirodihydrofurans **9** and **11**. The structure of **10** was assigned with the help of its IR and NMR spectral data. The IR spectrum displayed carbonyl absorption at 1723 cm^{-1}, along with a hydroxyl absorption at 3446 cm^{-1} which indicated the enolization of the carbonyl group. The enolic hydroxyl proton resonated at δ 16.40 in the ^1H NMR spectrum. The aromatic protons were visible at δ 7.15 and the broad signal at δ 5.33 was attributed to the olefinic proton. The side chain methylene protons appeared at δ 2.75. The carbon resonances in the ^{13}C NMR spectrum at δ 191.77, 146.77, 120.75 and 107.34 were highly characteristic and offered crucial support to the assigned structure **10**.

The IR and NMR spectral data revealed that the product **12** obtained from the reaction of ethyl acetoacetate with 4-phenylmethylenecyclohexane has not been enolized. Its IR spectrum did not show any absorption due to -OH group whereas it showed strong absorptions at 1743 and 1720 cm^{-1} (>C=O). The ^1H NMR spectrum contained a broad signal at δ 5.46 due to the olefinic proton. The methine proton appeared as a triplet at δ 3.50 (1 H) and the doublet at δ 2.43 (2 H) was attributed to the side chain methylene protons. The ^{13}C NMR spectrum exhibited carbonyl resonances at δ 202.99 and 169.62. Thus all the spectral data were in agreement with the proposed structure **12**.

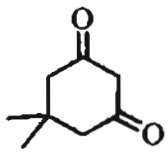
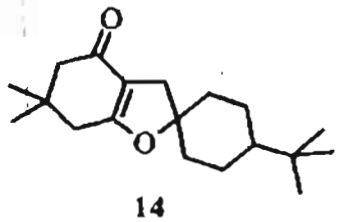
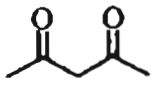
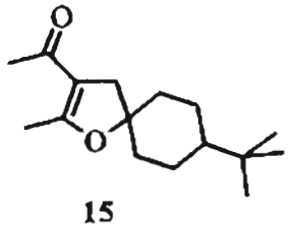
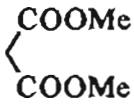
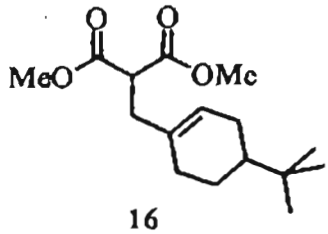
Dimethyl malonate (**4**) on reaction with 4-phenylmethylenecyclohexane furnished **13** in 22% yield along with some polymeric products which were not characterized. These reactions are summarized in Table 1.

Table 1. CAN Mediated Addition of Dicarbonyl Compounds to 4-Phenylmethylenecyclohexane

Entry	Dicarbonyl Compound	Product (yield)	
1		 **9** (41%)	 **10** (27%)
2		 **11** (14%)	 **12** (27%)
3		 **13** (22%)	

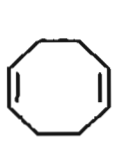
The radical reactions of dimedone and acetylacetone with the exocyclic alkene **6** afforded isomeric mixture of spirodihydrofurans **14** and **15** respectively in 63% and 35% yields. Ethyl acetoacetate furnished a complex and inseparable mixture of products. The corresponding reaction with dimethyl malonate led to the uncyclized product **16**. These results are given in Table 2.

Table 2. CAN Mediated Addition of Dicarbonyl Compounds to 4-*tert*-Butylmethylenecyclohexane

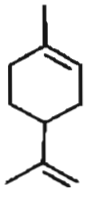
Entry	Dicarbonyl Compound	Product	Yield (%)
1		 **14**	63
2		 **15**	35
3		 **16**	22

The reaction of dimedone with β-pinene afforded an isomeric mixture of spirodihydrofuran **17**. From the reaction of dimethyl malonate and β-pinene, **18** could be separated and characterized while the corresponding reaction with acetylacetone furnished an inseparable mixture of **19** and **20**. The structure of **18** was assigned on the basis of its IR and NMR spectral data. Thus, the IR spectrum contained carbonyl absorptions at 1760 and 1743 cm^{-1}. The signal at δ 5.47 in the ^1H NMR spectrum was attributed to the olefinic proton (1 H). Two sets of methoxy protons resonated as singlets at δ 3.79 ($-COOCH_3$, 6 H) and 3.17 ($-OCH_3$, 3 H). The protons of the two methyl groups appeared at δ 1.09 and 1.07.

reaction of ethyl acetoacetate with 1,3-butadiene[6] there has been no work in this area. Therefore we decided to study the oxidative addition reactions of dicarbonyl compounds **1-4** with non-conjugated dienes **21** and **22**, the conjugated cyclohexadiene (**23**) and acetylenes **30-33**.



21



22

23

PhC≡CH **30**

PhC≡CPh **31**

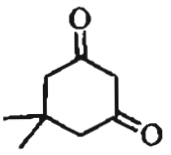
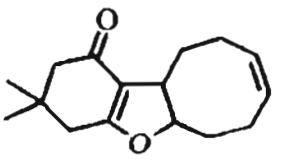
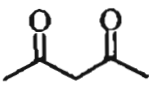
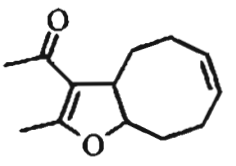
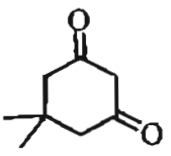
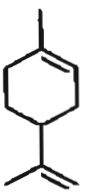
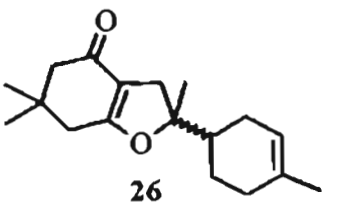
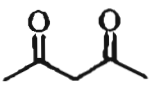
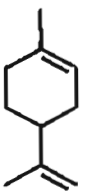
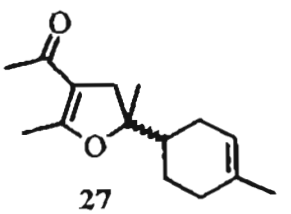
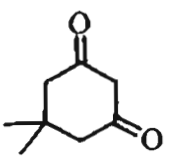
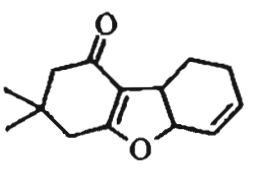
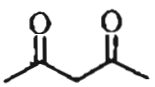
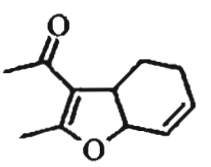
$Me_3SiC{\equiv}CSiMe_3$ **32**

$HC{\equiv}CCH_2OH$ **33**

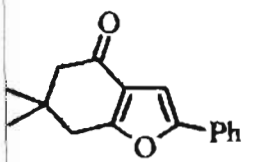
We selected 1,5-cyclooctadiene (**21**) expecting that a transannular radical cyclization would occur and would thus provide a useful entry into fused bicyclic systems. Limonene (**22**), on the other hand, was expected to undergo tandem radical additions to the two double bonds. Contrary to our expectations, the reaction of dimedone and acetylacetone with 1,5-cyclooctadiene and limonene afforded only the dihydrofurans **24- 27** in which one of the double bonds remained unaffected (see Section 4.3 for spectral data). When ethyl acetoacetate and dimethyl malonate were reacted with **21** and **22**, under the same conditions, no well-defined products could be isolated.

The best results with dienes were obtained in the reactions of dimedone and acetylacetone with 1,3-cyclohexadiene (**23**) (entry 5 and 6, Table 4).

Table 4. CAN Mediated Addition of Dicarbonyl Compounds to Dienes

Entry	Dicarbonyl Compound	Diene	Product	Yield (%)
1			 **24**	20
2			 **25**	30
3			 **26**	48
4			 **27**	46
5			 **28**	55
6			 **29**	57

Subsequently, we explored the CAN mediated additions to acetylenes. The addition of dimedone to phenylacetylene (**30**) provided the furan derivative **34**. Our next choice was diphenylacetylene (**31**). In this case, there was no reaction with dimedone, 90% of **31** was recovered. A complex and inseparable mixture of products resulted from the addition of dimedone to **32** and **33**. Same was the case when acetylacetone was reacted with phenylacetylene in presence of CAN. With the failure of these experiments, further studies in this direction with compounds **3** and **4** were not pursued.

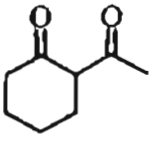


34

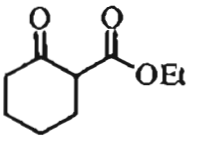
The structural identity of **34** was confirmed by its spectral data. The carbonyl absorption was observed in the IR spectrum at 1668 cm^{-1}. In the ^1H NMR spectrum, the aromatic protons resonated as a multiplet centred at δ 7.33 (5 H) and a singlet at δ 6.70 (1 H). ^{13}C NMR spectrum displayed a signal at δ 193.3 due to the carbonyl carbon. The phenyl and furan ring carbons were seen in the range δ 165.4-100.5. The two methyl carbons appeared as a single signal at δ 28.8.

Encouraged by the results of the addition of **1-4** to various types of alkenes described earlier, we turned our attention to the more interesting dicarbonyl compounds, 2-acetylcyclohexanone (**35**) and 2-carboethoxycyclohexanone (**36**). But the results were quite discouraging. The reaction of **35** with 1-phenyl-1-cyclohexene did not afford any addition product. The failure of the reaction may be attributed to steric factors and therefore we repeated the experiment using the

acyclic alkene 2-methyl-2-pentene, instead of 1-phenyl-1-cyclohexene. Again, n addition product could be isolated.



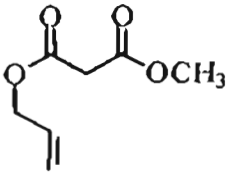
35



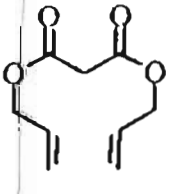
36

Even though the experiments with 2-acetylcyclohexanone failed, we attempted some reactions with 2-carboethoxycyclohexanone (**36**). Two reactions, one using cinnamyl methyl ether and the other using 1-phenyl-1-cyclohexene as the alkene were carried out in the presence of **36** and CAN. Unfortunately, apart from the starting alkenes, no well-defined products were isolable.

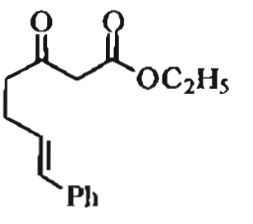
Our attempts to carry out intramolecular radical cyclizations form the last part of the CAN mediated investigations described in this thesis. $Mn(OAc)_3$ mediated intramolecular radical cyclizations reported by Snider[7-9] and others[10-12] have contributed significantly to the synthesis of complex natural products. However, as far as we know, there is just one report on the application of CAN in intramolecular cycloadditions[13]. The superiority of CAN compared to $Mn(OAc)_3$ in intermolecular reactions[14] (Section 2.2.2), was another factor which prompted us to undertake some investigations in this area. The starting materials **37-42** were readily prepared following the literature procedure[15,16].



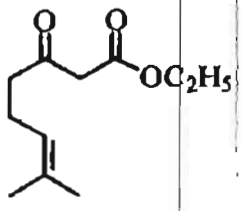
37



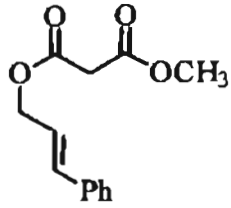
38



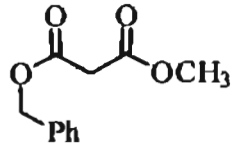
39



40

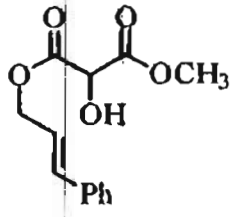


41

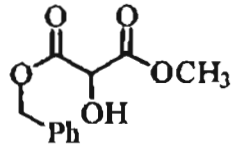


42

The substrates **37-40** were treated with CAN in methanol under the usual conditions. Contrary to expectations, TLC analysis, after the decolourisation of CAN, showed intractable mixture of products in all cases. In the reactions of **41** and **42** also no intramolecular addition occurred, instead hydroxylated products **43** and **44** were isolated in 62% and 82% yields respectively.



43



44

The IR and NMR spectra revealed the structure of **43** and **44**. The IR spectrum of **43** contained hydroxyl absorption at 3432 cm^{-1} and carbonyl absorptions at 1760 and 1739 cm^{-1}. In the ^1H NMR spectrum, the olefinic protons were visible as a multiplet centred at δ 6.45. This indicated that no addition to the double bond has occurred. Another interesting feature of the NMR spectrum was that it was devoid of the signal due to the active methylene protons at δ 3.20 which was present in **41** (see Section 4.3). The ^{13}C NMR spectrum with the signals at δ 168.5 and 167.9 due to the ester groups and at δ 90.7 due to the carbon bearing the -OH group also supports the assigned structure **43**.

4.3. Experimental

A general write-up on the instrumentation and experimental techniques are given in Chapter 2 (Section 2.3).

β-Pinene, 1,3-cyclohexadiene, limonene, phenylacetylene, diphenylacetylene, bis(trimethylsilyl)acetylene and propargyl alcohol purchased from Aldrich were used as such. 4-Phenylmethylenecyclohexane and 4-*tert*-butylmethylenecyclohexane were prepared from the corresponding ketones by Wittig reaction.

Preparation of Spirodihydrofurans: General Procedure

A solution of CAN (3.15 g, 5.75 mmol) in methanol (25 mL) was added dropwise to an ice-cooled, stirred mixture of the dicarbonyl compound (2.5 mmol) and the exocyclic alkene (3.0 mmol) in methanol (10 mL). After the disappearance of the colour of CAN (15-45 min), the reaction mixture was worked up. The residue obtained on silica gel column chromatography using petroleum ether-ethyl acetate mixture (in the ratio 9:1 unless otherwise specified) as eluent furnished the spirodihydrofuran.

Spiro[6,6-dimethyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one-2,1'-(4'-phenylcyclohexane)] (8)

A mixture of 4-phenylmethylenecyclohexane (0.30 g, 1.75 mmol) and dimedone (0.294 g, 2.1 mmol) was treated with CAN (2.20 g, 4.02 mmol) as described in the general procedure. The residue obtained on column chromatography afforded **8** (0.421 g, 77%) as a colourless solid. Crystallization from petroleum ether-ethyl acetate mixture furnished fine platelets of **8** having mp 124-126°C.

IR (KBr) ν_{max} : 2934, 1637, 1401, 1241 cm^{-1}.

^1H NMR (90 MHz) : δ 7.45-7.16 (m, 5 H, ArH), 2.75 (brs, 2 H), 2.65-2.55 (m, 1 H), 2.31 (brs, 2 H), 2.25 (brs, 2 H), 2.10-1.65 (m, 8 H, $-CH_2-$), 1.15 (s, 6 H, $-CH_3$).

^{13}C NMR (22.4 MHz) : δ 195.5, 175.9, 146.2, 128.1, 126.3, 125.9, 110.6, 91.2, 50.1, 42.5, 38.0, 37.5, 33.8, 29.8, 28.5.

GC-MS *m/z* : 310 (M^+, 55), 295 (5), 281 (4), 254 (4), 219 (10), 191 (22), 178 (20), 157 (60), 153 (48), 122 (100), 104 (50).

Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44

Found : C, 80.85; H, 8.40.

Oxidative Addition of Acetylacetone to 4-Phenylmethylenecyclohexane

The reaction of acetylacetone (0.250 g, 2.5 mmol) and 4-phenylmethylene-cyclohexane (0.516 g, 3.0 mmol) with CAN (3.15 g, 5.75 mmol) according to the general procedure afforded **10** (elution with 5% ethyl acetate in petroleum ether, 0.182 g, 27%) and **9** (elution with 10% ethyl acetate in petroleum ether, 0.275 g, 41%) as colourless viscous liquids.

Spiro[4-acetyl-5-methyl-2,3-dihydrofuran-2,1'-(4'-phenylcyclohexane)] (9)

IR (CH_2Cl_2) ν_{max} : 2931, 1669, 1598, 1389 cm^{-1}.

^1H NMR (60 MHz) : δ 7.15 (s, 5 H, ArH), 2.83-2.59 (m, 2 H), 2.12-1.90 (m, 6 H, $-CH_3$), 1.80-1.55 (m, 9 H).

^{13}C NMR (22.4 MHz) : δ 195.1, 166.5, 146.5, 129.2, 127.1, 126.3, 110.7, 88.5, 42.5, 42.3, 37.1, 36.5, 30.5, 29.5, 29.2, 15.1.

GC-MS *m/z* : 270 (M^+, 48), 252 (6), 237 (16), 224 (5), 209 (58), 193 (5), 181 (6), 148 (32), 123 (20), 105 (100).

4-Hydroxy-3-methyl(4'-phenylcyclohex-1'-enyl)-pent-3-en-2-one (10)

IR (CH_2Cl_2) ν_{max} : 3446, 2920, 1723, 1715, 1605, 1434 cm^{-1}.

^1H NMR (60 MHz) : δ 16.40 (s, 1 H, >C=COH), 7.15 (s, 5 H, ArH), 5.33 (s, 1 H, >C=CH-), 2.75 (brs, 2 H), 2.15-1.50 (m, 13 H).

^{13}C NMR (100.4 MHz) : δ 191.77, 146.77, 135.19, 128.41, 128.22, 126.86, 126.71, 125.99, 120.75, 107.34, 40.12, 34.67, 33.27, 29.95, 29.54, 22.99.

EI-MS *m/z* : 270 (M^+, 32), 252 (91), 227 (93), 209 (100), 199 (45), 171 (53), 155 (50), 124 (61).

Oxidative Addition of Ethyl Acetoacetate to 4-Phenylmethylenecyclohexane

A mixture of ethyl acetoacetate (0.325 g, 2.5 mmol) and 4-phenyl-methylenecyclohexane (0.520 g, 3.0 mmol) was treated with CAN (3.15 g, 5.75 mmol) according to the general procedure. The residue obtained was subjected to column chromatography. Elution with 5% ethyl acetate in petroleum ether furnished **11** (0.105 g, 14%) and **12** (0.206 g, 27%) as pale yellow viscous liquids.

Spiro[5-methyl-2,3-dihydrofuran-4-carboxylic acid ethyl ester-2,1'-(4'-phenyl-cyclohexane)] (11)

IR (neat) ν_{max} : 2934, 1707, 1653, 1384, 1230 cm^{-1}.

^1H NMR (60 MHz) : δ 7.10 (s, 5 H, ArH), 4.15 (q, J = 7.2 Hz, 2 H, $-OCH_2-$), 2.70-2.52 (m, 2 H), 2.11 (s, 3 H, $-CH_3$),

1.80-1.65 (m, 9 H), 1.25 (t, J = 7.2 Hz, 3 H, $-CH_2C\underline{H}_3$).

^{13}C NMR (22.4 MHz) : δ 167.0, 146.9, 146.1, 128.8, 127.1, 126.3, 101.4, 88.2, 59.3, 43.6, 37.5, 37.1, 30.8, 30.2, 14.2.

2-Methyl(4'-phenylcyclohex-1'-enyl)-3-oxo-butanoic acid ethyl ester (12)

IR (CH_2Cl_2) ν_{max} : 2928, 2863, 1743, 1720, 1246 cm^{-1}.

^1H NMR (60 MHz) : δ 7.08 (s, 5 H, ArH), 5.46 (brs, 1 H, olefinic), 4.18 (q, J = 7.1 Hz, 2 H, $-OCH_2-$), 3.50 (t, J = 8.0 Hz, 1 H), 2.43 (d, J = 8.0 Hz, 2 H), 2.12 (s, 3 H, $-CH_3$), 2.06-1.59 (m, 7 H), 1.26 (t, J = 7.1 Hz, 3 H, $-CH_2C\underline{H}_3$).

^{13}C NMR (100.4 MHz) : δ 202.99, 169.62, 146.73, 133.74, 128.44, 128.38, 128.32, 126.78, 125.99, 123.28, 61.34, 58.29, 58.19, 39.78, 35.88, 33.36, 29.80, 28.89, 14.11.

GC-MS *m/z* : 300 (M^+, 30), 280 (100), 250 (26), 230 (60), 205 (85), 187 (80), 159 (62).

2-Methyl(4'-phenylcyclohex-1'-enyl)propanedioic acid dimethyl ester (13)

The reaction of dimethyl malonate (0.330 g, 2.5 mmol) and 4-phenyl-methylenecyclohexane (0.520 g, 3.0 mmol) with CAN (3.15 g, 5.75 mmol) was carried out as described in the general procedure. The product **13** (elution with 5% ethyl acetate in petroleum ether, 0.211 g, 22%) was obtained as a colourless oil.

IR (neat) ν_{max} : 2958, 1742, 1438, 1238, 1155 cm^{-1}.

^{1}H NMR (400 MHz) : δ 7.42-7.20 (m, 5 H, ArH), 5.57 (brs, 1 H, olefinic), 3.80 (s, 6 H, -$COOCH_3$), 3.41 (t, J = 7.9 Hz, 1 H), 2.76-2.65 (m, 1 H), 2.60 (d, J = 7.9 Hz, 2 H), 2.11-1.75 (m, 6 H).

^{13}C NMR (100.4 MHz) : δ 169.65, 146.79, 133.59, 128.34, 126.82, 126.77, 125.99, 123.43, 52.52, 50.42, 39.77, 36.55, 33.36, 29.84, 28.56.

GC-MS *m/z* : 302 (M^+, 8), 284 (4), 270 (6), 239 (9), 210 (7), 198 (5), 170 (30), 155 (10), 133 (14), 115 (10), 104 (100).

Spiro[6,6-dimethyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one-2,1'-(4'-*tert*-butylcyclohexane)] (14)

A mixture of dimedone (0.350 g, 2.5 mmol) and 4-*tert*-butylmethylene-cyclohexane (0.456 g, 3.0 mmol) was subjected to dropwise treatment with a solution of CAN (3.15 g, 5.75 mmol) in methanol according to the general procedure. After chromatography **14** was obtained as a colourless oil in 63% yield (0.456 g).

IR (CH_2Cl_2) ν_{max} : 2932, 1647, 1470, 1372 cm^{-1}.

^{1}H NMR (200 MHz) : δ 2.49 (s, 2 H), 2.24 (s, 2 H), 2.18 (s, 2 H), 2.09-1.92 (m, 3 H), 1.68-1.21 (m, 6 H), 1.06 (s, 6 H, -CH_3), 0.84 (s, 9 H, -CH_3).

^{13}C NMR (50 MHz) : δ 195.01, 175.36, 110.93, 91.68, 50.88, 46.95, 38.26, 37.97, 34.03, 32.37, 28.72, 27.54, 27.27, 23.19.

GC-MS *m/z* : 290 (M^+, 40), 275 (15), 257 (15), 233 (100), 219 (5), 215 (6), 191 (12), 153 (80), 137 (20), 122 (20).

Spiro[4-acetyl-5-methyl-2,3-dihydrofuran-2,1'-(4'-*tert*-butylcyclohexane)] (15)

The reaction of a mixture of acetylacetone (0.250 g, 2.5 mmol) and 4-*tert*-butylmethylenecyclohexane (0.456 g, 3.0 mmol) with CAN (3.15 g, 5.75 mmol) according to the general procedure afforded **15** (0.216 g, 35%) as a colourless oil.

This product is a mixture of isomers.

IR (neat) ν_{max} : 2956, 1675, 1601, 1367, 1236 cm^{-1}.

^1H NMR (400 MHz) : δ 2.71-2.62 (m, 2 H), 2.21 (s, 3 H, $-CH_3$), 2.17 (s, 3 H, $-CH_3$), 2.02-1.05 (m, 9 H), 0.88 (s, 9 H, $-CH_3$).

^{13}C NMR (100.4 MHz) : δ 195.02, 194.93, 167.19, 167.01, 113.51, 112.83, 89.18, 86.94, 47.02, 46.81, 42.95, 39.57, 37.88, 37.13, 34.56, 32.37, 32.24, 29.28, 27.53, 27.49, 23.99, 23.07, 15.57, 15.49.

GC-MS *m/z* : 250 (M^+, 60), 235 (12), 217 (30), 189 (40), 175 (100), 157 (30), 133 (18), 113 (80).

2-Methyl(4'-*tert*-butylcyclohex-1'-enyl)propanedioic acid dimethyl ester (16)

A mixture of dimethyl malonate (0.330 g, 2.5 mmol) and 4-*tert*-butylmethylenecyclohexane (0.456 g, 3.0 mmol) was treated with CAN (3.15 g, 5.75 mmol) as described in the general procedure. It was worked up after 2.5 h and the residue was subjected to column chromatography to obtain **16** (0.116 g, 22%) as a colourless oil.

IR (neat) ν_{max} : 2959, 1758, 1745, 1438, 1235 cm^{-1}.

^1H NMR (60 MHz) : δ 5.50 (brs, 1 H, olefinic), 3.85 (s, 6 H, $-COOCH_3$), 3.36-3.13 (m, 1 H), 2.56-2.23 (m, 2 H), 2.03-1.63 (m, 5 H), 1.30-1.06 (m, 2 H), 0.83 (s, 9 H, $-CH_3$).

^{13}C NMR (100.4 MHz) : δ 169.91, 149.49, 124.27, 52.61, 50.78, 44.11, 36.73, 34.44, 32.64, 27.21, 24.36, 22.48.

GC-MS *m/z* : 282 ($M^{+\cdot}$ 10), 264 (5), 251 (8), 219 (12), 190 (8), 165 (20), 145 (61), 133 (77), 105 (30), 94 (100).

Oxidative Addition of Ethyl Acetoacetate to 4-*tert*-Butylmethylenecyclohexane

A mixture of ethyl acetoacetate (0.325 g, 2.5 mmol) and 4-*tert*-butylmethylenecyclohexane (0.456 g, 3.0 mmol) was treated with CAN (3.15 g, 5.75 mmol) as described in the general procedure. TLC analysis of the solution revealed an intractable mixture of products. Therefore purification was not attempted.

Oxidative Addition of Dimedone to β-Pinene

The reaction of dimedone (0.350 g, 2.5 mmol) and β-pinene (0.408 g, 3.0 mmol) with CAN (3.15 g, 5.75 mmol) according to the general procedure gave **17** (0.453 g, 66%) as a pale yellow viscous liquid.

This product is a mixture of isomers.

IR (CH_2Cl_2) ν_{max} : 2959, 1640, 1405, 1243 cm^{-1}.

^1H NMR (300 MHz) : δ 2.68-2.64 (m, 2 H), 2.22-2.14 (m, 6 H), 1.99-1.89 (m, 6 H), 1.18 (s, 3 H, $-CH_3$), 1.02 (s, 6 H, $-CH_3$), 0.86 (s, 3 H, $-CH_3$).

^{13}C NMR (75.5 MHz) : δ 195.20, 175.02, 111.34, 110.46, 98.72, 98.48, 51.97, 51.01, 41.74, 40.96, 40.25, 38.55, 38.30, 34.27, 32.13, 31.88, 29.05, 28.97, 28.91, 27.27, 27.07, 26.79, 24.47, 24.39, 23.33, 23.11.

GC-MS *m/z* : 274 (M^+, 20), 259 (9), 231 (30), 153 (70), 121 (30), 97(100).

Oxidative Addition of Ethyl Acetoacetate to β-Pinene

A mixture of ethyl acetoacetate (0.325 g, 2.5 mmol) and β-pinene (0.408 g, 3.0 mmol) was treated with CAN (3.15 g, 5.75 mmol) as described in the general procedure. TLC analysis showed an intractable mixture of products and no attempt was made to isolate them.

Oxidative Addition of Dimethyl Malonate to β-Pinene

The reaction of a mixture of dimethyl malonate (0.330 g, 2.5 mmol) and β-pinene (0.408 g, 3.0 mmol) with CAN (3.15 g, 5.75 mmol) as described in the general procedure for 2.5 h furnished **18** (0.146 g, 22%) as a colourless oil.

IR (neat) ν_{max} : 2959, 1760, 1743, 1439 cm^{-1}.

^{1}H NMR (400 MHz) : δ 5.47 (brs, 1 H, olefinic), 3.79 (s, 6 H, $-COOCH_3$), 3.57 (t, J = 9.7 Hz, 1 H), 3.17 (s, 3 H, $-OCH_3$), 2.6 (d, J = 9.7 Hz, 2 H, $-CH_2-$), 1.91-1.55 (m, 7 H), 1.09 (s, 3 H, $-CH_3$), 1.07 (s, 3 H, $-CH_3$), .

^{13}C NMR (100.4 MHz) : δ 169.64, 169.59, 133.51, 123.52, 76.47, 52.43, 52.39, 50.41, 48.69, 41.53, 36.43, 28.94, 26.78, 23.71, 22.14, 21.73.

GC-MS *m/z* : 266 (M^+-OCH_3-1, 5), 235 (6), 191 (8), 159 (12).

Oxidative Addition of Acetylacetone to β-Pinene

The reaction of acetylacetone (0.250 g, 2.5 mmol) with β-pinene (0.408 g, 3.0 mmol) in presence of CAN (3.15 g, 5.75 mmol) as described in the general procedure afforded an inseparable mixture of **19** and **20** (0.295 g, 50%) as a yellow viscous liquid.

IR (neat) ν_{max} : 2924, 1723, 1629, 1602, 1386, 1243 cm^{-1}.

^1H NMR (90 MHz) : δ 5.25 (brs, olefinic), 3.15 (s, -OCH_3), 2.76 (s, -CH_2-), 2.08 (s, -$COCH_3$), 1.82 (s, -CH_3), 1.80-1.65 (m, -CH_2-), 1.20-0.94 (m, -CH_3), 0.86 (s, -CH_3).

^{13}C NMR (22.4 MHz) : δ 194.2, 191.4, 165.9, 120.7, 111.6, 93.2, 93.0, 51.4, 51.1, 48.5, 45.9, 45.2, 42.0, 39.9, 39.8, 37.8, 34.4, 32.0, 31.6, 29.0, 28.9, 27.1, 26.8, 26.7, 26.4, 26.2, 23.9, 23.6, 22.9, 22.7, 21.9, 21.6, 15.3, 15.1.

Oxidative Addition of Dimedone to 1,5-Cyclooctadiene

To an ice-cooled mixture of 1,5-cyclooctadiene (0.270 g, 2.5 mmol) and dimedone (0.420 g, 3.0 mmol) in methanol (10 mL) was added a solution of CAN (3.15 g, 5.75 mmol) in methanol (25 mL) and stirred for 15 min. Worked up by the usual procedure and the residue was subjected to column chromatography. On elution with 5% ethyl acetate in petroleum ether, **24** (0.123 g, 20%) was obtained as a pale yellow oil.

IR (CH_2Cl_2) ν_{max} : 2958, 1629, 1405, 1228 cm^{-1}.

^{1}H NMR (60 MHz) : δ 5.35-5.27 (m, 2 H, olefinic), 4.65-4.21 (m, 1 H, >CHO-), 3.30-2.95 (m, 1 H), 2.31-1.95 (m, 12 H), 1.15 (s, 3 H, -CH_3), 0.97 (s, 3 H, -CH_3).

^{13}C NMR (22.4 MHz) : δ 194.5, 175.3, 130.1, 128.2, 114.0, 92.2, 51.2, 44.9, 37.8, 33.6, 31.5, 28.7, 28.5, 28.2, 24.3, 22.1.

Oxidative Addition of Acetylacetone to 1,5-Cyclooctadiene

A mixture of 1,5-cyclooctadiene (0.270 g, 2.5 mmol) and acetylacetone (0.30 g, 3.0 mmol) was reacted with CAN (3.15 g, 5.75 mmol) as described in the preparation of **24**. The product **25** (0.154 g, 30%) was obtained as a colourless oil.

IR (CH_2Cl_2) ν_{max} : 2928, 1641, 1601, 1420, 1260 cm^{-1}.

^{1}H NMR (60 MHz) : δ 5.58-5.28 (m, 2 H, olefinic), 4.48-4.01 (m, 1 H), 3.30-2.85 (m, 1 H), 2.35-1.85 (m, 14 H).

EI-MS *m/z* : 206 (M^+, 10), 191 (5), 178 (16), 163 (8), 151 (17), 137 (22).

Oxidative Addition of Ethyl Acetoacetate to 1,5-Cyclooctadiene

A mixture of 1,5-cyclooctadiene (0.270 g, 2.5 mmol) and ethyl aceto-acetate (0.390 g, 3.0 mmol) was treated with CAN (3.15 g, 5.75 mmol) as described for the preparation of **24**. TLC analysis of the solution after the disappearance of the colour (45 min), revealed a complex mixture of products. Therefore attempts were not made to separate the products.

Oxidative Addition of Dimethyl Malonate to 1,5-Cyclooctadiene

A mixture of 1,5-cyclooctadiene (0.270 g, 2.5 mmol) and dimethyl

malonate (0.396 g, 3.0 mmol) was treated with CAN (3.15 g, 5.75 mmol) as described for the preparation of **24**. The reaction mixture decolourised after stirring for 2 h. TLC analysis showed an intractable mixture of products and no attempts were made to isolate them.

Oxidative Addition of Dimedone to Limonene

Limonene (0.272 g, 2.0 mmol) and dimedone (0.336 g, 2.4 mmol) were dissolved in methanol (10 mL) and cooled in an ice-bath. This was subjected to dropwise treatment with CAN (2.52 g, 4.6 mmol) dissolved in methanol (20 mL). Work-up and column chromatography of the residue using 10% ethyl acetate in petroleum ether as eluent furnished an isomeric mixture of **26** (0.262 g, 48%) as a colourless oil.

IR (CH_2Cl_2) ν_{max} : 2934, 1638, 1405, 1243 cm^{-1}.

^1H NMR (60 MHz) : δ 5.25 (brs, 1 H, olefinic), 2.55-2.32 (m, 2 H, $-CH_2-$), 2.20 (s, 3 H), 2.11 (s, 2 H), 1.95-1.66 (brs, 6 H, $-CH_2-$), 1.55 (s, 3 H, $-CH_3$), 1.31 (s, 3 H, $-CH_3$), 1.05 (s, 6 H, $-CH_3$).

^{13}C NMR (22.4 MHz) : δ 194.2, 174.9, 135.5, 119.9, 110.9, 95.1, 94.9, 50.5, 42.7, 42.5, 37.5, 34.8, 34.0, 33.5, 29.9, 28.3, 28.1, 25.9, 25.5, 24.4, 24.2, 22.6.

Oxidative Addition of Acetylacetone to Limonene

Limonene (0.272 g, 2.0 mmol) and acetylacetone (0.240 g, 2.4 mmol) dissolved in methanol (10 mL) were treated with a solution of CAN (2.52 g, 4.6 mmol) in methanol (20 mL). The reaction mixture was worked up after 15 min

and the residue purified by column chromatography to obtain **27** (elution with 10% ethyl acetate in petroleum ether, 0.215 g, 46%) as a colourless oil.

This product is a mixture of isomers.

IR (CH_2Cl_2) ν_{max} : 2927, 1673, 1601, 1385, 1270 cm^{-1}.

^1H NMR (60 MHz) : δ 5.25 (brs, 1 H, olefinic), 2.94-2.32 (m, 3 H), 2.15 (s, 6 H, $-CH_3$), 1.92-1.70 (m, 6 H, $-CH_2-$), 1.55 (s, 3 H, $-CH_3$), 1.20 (s, 3 H, $-CH_3$).

^{13}C NMR (22.4 MHz) : δ 194.4, 166.3, 133.5, 119.9, 111.7, 91.1, 90.9, 42.9, 42.6, 39.2, 38.8, 30.2, 30.0, 29.1, 26.2, 25.7, 24.1, 23.8, 23.1, 14.9.

3,3-Dimethyl-1,2,3,4,5a,8,9,9a-octahydrodibenzofuran-1-one (28)

A solution of CAN (3.15 g, 5.75 mmol) in methanol (30 mL) was added dropwise to an ice-cooled mixture of 1,3-cyclohexadiene (0.20 g, 2.5 mmol) and dimedone (0.420 g, 3.0 mmol) in methanol (15 mL). Worked up after decolourisation of the reaction mixture (20 min) and the residue was purified by column chromatography (petroleum ether : ethyl acetate, 9:1). Pure product **28** was obtained as a colourless oil (0.278 g, 55%).

IR (neat) ν_{max} : 2964, 1627, 1404, 1221 cm^{-1}.

^1H NMR (90 MHz) : δ 6.22-5.68 (m, 2 H, olefinic), 4.91-4.70 (m, 1 H, >CHO-), 3.22-2.88 (m, 1 H), 2.20 (s, 2 H, $-CH_2-$), 2.10 (s, 2 H, $-CH_2-$), 1.95-1.76 (m, 4 H, $-CH_2-$), 1.10 (s, 3 H, $-CH_3$), 0.95 (s, 3 H, $-CH_3$).

^{13}C NMR (22.4 MHz) : δ 194.1, 175.8, 134.8, 123.1, 116.0, 80.2, 50.9, 38.1, 36.9, 33.5, 29.1, 27.9, 23.3, 22.2.

3-Acetyl-2-methyl-3a,4,5,7a-tetrahydrobenzofuran (29)

1,3-Cyclohexadiene (0.240 g, 3.0 mmol) and acetylacetone (0.360 g, 3.6 mmol) were taken in methanol (30 mL) and cooled in an ice-bath. A solution of CAN (3.78 g, 6.9 mmol) in methanol (50 mL) was added dropwise and the reaction mixture was worked up after decolourisation (20 min). Column chromatography of the residue using petroleum ether-ethyl acetate mixture in the ratio 9:1 as the eluent furnished **29** (0.303 g, 57%) as a colourless oil.

IR (neat) ν_{max} : 2939, 1663, 1618, 1389, 1225 cm^{-1}.

^1H NMR (90 MHz) : δ 6.35-5.85 (m, 2 H, olefinic), 4.82-4.64 (m, 1 H), 3.16-2.87 (m, 1 H), 2.25 (s, 3 H, $-CH_3$), 2.21 (s, 3 H, $-CH_3$), 2.12-1.85 (m, 4 H, $-CH_2-$).

^{13}C NMR (22.4 MHz) : δ 193.1, 167.1, 133.4, 121.8, 117.7, 77.0, 39.5, 27.9, 23.9, 22.1, 14.4.

GC-MS *m/z* : 178 (M^+, 70), 163 (22), 159 (30), 145 (18), 135 (20), 121 (17), 117 (85).

6,6-Dimethyl-2-phenyl-4,5,6,7-tetrahydro-1-benzofuran-4-one (34)

Phenylacetylene (0.255 g, 2.5 mmol) and dimedone (0.420 g, 3.0 mmol) were dissolved in methanol (10 mL) and cooled in an ice-bath. CAN (3.15 g, 5.75 mmol) dissolved in methanol (25 mL) was added dropwise and stirred until the colour of CAN disappeared. Work-up and column chromatography of the residue using 10% ethyl acetate in petroleum ether as eluent furnished **34** (0.450 g, 41%) as a pale yellow viscous liquid.

IR (CH_2Cl_2) ν_{max} : 2967, 1668, 1437, 1219 cm^{-1}.

^{1}H NMR (60 MHz) : δ 7.62-7.05 (m, 5 H, ArH), 6.70 (s, 1 H), 2.65 (s, 2 H, $-CH_2-$), 2.22 (s, 2 H, $-CH_2-$), 1.41 (s, 6 H, $-CH_3$)

^{13}C NMR (22.4 MHz) : δ 193.3, 165.4, 154.2, 129.5, 128.5, 127.7, 123.6, 121.4, 100.5, 50.6, 37.1, 34.8, 28.8.

Oxidative Addition of Dimedone to Diphenylacetylene

A mixture of dimedone (0.252 g, 1.8 mmol) and diphenylacetylene (0.267 g, 1.5 mmol) in methanol (10 mL) was treated with CAN (1.89 g, 3.45 mmol) in methanol (20 mL) at 5°C. The colour of the reaction mixture disappeared after 15 min. Worked up as usual and the residue was subjected to column chromatography. No product was obtained, instead the starting material diphenylacetylene was recovered (0.25 g, 90%).

Oxidative Addition of Dimedone to Propargyl Alcohol

A solution of CAN (3.78 g, 6.9 mmol) in methanol (25 mL) was added to an ice-cooled mixture of propargyl alcohol (0.168 g, 3.0 mmol) and dimedone (0.504 g, 3.6 mmol) and stirred until the colour of CAN disappeared. The reaction mixture was analysed by TLC. A highly complex TLC pattern was observed. No attempts were made to separate and identify the individual components.

Oxidative Addition of Dimedone to Bis(trimethylsilyl)acetylene

Bis(trimethylsilyl)acetylene (0.340 g, 2.0 mmol) and dimedone (0.336 g, 2.4 mmol) were dissolved in methanol (10 mL) and cooled (5°C). A solution of CAN (2.52 g, 4.6 mmol) in methanol (20 mL) was added dropwise to the above

mixture. After 40 min, the solution decolourised. TLC analysis showed a complex mixture of products. Therefore, no attempts were made to separate and analyse the products.

Oxidative Addition of Acetylacetone to Phenylacetylene

A solution of CAN (3.15 g, 5.75 mmol) in methanol (20 mL) was added to an ice-cooled mixture of phenylacetylene (0.255 g, 2.5 mmol) and acetylacetone (0.30 g, 3.0 mmol) and stirred. TLC analysis showed an intractable mixture of products. Attempts were not made to separate them.

2-Acetylcyclohexanone (35)

Cyclohexanone (10.0 g, 100 mmol) and morpholine (8.71 g, 101 mmol) were dissolved in benzene (50 mL). *p*-Toluenesulphonic acid (1.92 g, 10.1 mmol) was added and refluxed for 12 h using a Dean and Stark apparatus. The mixture was cooled, acetyl chloride (15.70 g, 200 mmol) was added and again stirred for 12 h. Dil. H_2SO_4 (50 mL) was added to it, stirred well and extracted with diethyl ether (3 x 150 mL) after diluting with water (200 mL). The combined organic extracts were washed with $NaHCO_3$ solution, then with water, dried and evaporated. The crude product obtained was purified by distillation under reduced pressure to obtain **35** (4.12 g, 32%) as a colourless oil.

^{1}H NMR (60 MHz) : δ 15.64 (s, 1 H), 2.43-2.22 (m, 4 H), 1.97 (s, 3 H, $-COCH_3$), 1.75-1.48 (m, 4 H).

2-Carboethoxycyclohexanone (36)

Diethyl carbonate (8.85 g, 75.0 mmol) was added to a suspension of

NaH (3.75 g, *ca.* 93.0 mmol) in dry THF (40 mL) and refluxed for 1 h. Cyclohexanone (2.94 g, 30.0 mmol) dissolved in dry THF (25 mL) was added dropwise and again refluxed for 2 h. After cooling the reaction mixture, dil. HOAc (50 mL) was added and stirred well. The contents of the flask were poured into aqueous NaCl (150 mL) and extracted with CH_2Cl_2 (3 x 70 mL). The combined organic extracts were washed with $NaHCO_3$ solution, then with water, dried and evaporated. The residue was purified by column chromatography using 5% ethyl acetate in petroleum ether as the eluent. Pure product **36** (2.20 g, 43%) was obtained as a colourless oil.

^{1}H NMR (60 MHz) : δ 11.8 (s, 1 H), 4.1 (q, J = 7.0 Hz, 2 H, -OCH_2-), 2.31-2.05 (m, 3 H), 1.75-1.47 (m, 5 H), 1.25 (t, J = 7.0 Hz, 3 H, -$CH_2C\underline{H}_3$).

Oxidative Addition of 2-Acetylcyclohexanone to 1-Phenyl-1-cyclohexene

A solution of CAN (2.52 g, 4.6 mmol) in methanol (20 mL) was added to to an ice-cooled mixture of 1-phenyl-1-cyclohexene (0.316 g, 32 mmol) and 2-acetylcyclohexanone (**35**, 0.364 g, 2.6 mmol) and stirred. After the decolourisation of the reaction mixture (20 min), it was worked up by the usual procedure and the residue was subjected to column chromatography. 1-Phenyl-1-cyclohexene (0.20 g, 63%) was recovered. No well-defined products could be isolated.

Oxidative Addition of 2-Acetylcyclohexanone to 2-Methyl-2-pentene

A mixture of 2-methyl-2-pentene (0.168 g, 2.0 mmol) and 2-acetylcyclohexanone (0.336 g, 2.4 mmol) was treated with CAN (2.52 g, 4.6 mmol) as

described above. Only polymeric products were obtained and these were not characterized.

Oxidative Addition of 2-Carboethoxycyclohexanone to 1-Phenyl-1-cyclohexene

A mixture of 1-phenyl-1-cyclohexene (0.138 g, 0.87 mmol) and 2-carboethoxycyclohexanone (0.178 g, 1.04 mmol) in ethanol (5 mL) was treated with a solution of CAN (1.10 g, 2.0 mmol) in ethanol (20 mL) as described previously. 1-Phenyl-1-cyclohexene (0.091 g, 66%) was recovered along with some polymeric products which were not analysed.

Oxidative Addition of 2-Carboethoxycyclohexanone to Cinnamyl Methyl Ether

Cinnamyl methyl ether (0.148 g, 1.0 mmol) and 2-carboethoxycyclohexanone (0.204 g, 1.2 mmol) were dissolved in ethanol (5 mL) and treated with CAN as described above. Except the recovered cinnamyl methyl ether (0.110 g, 74%), no other well-defined product was isolated.

Preparation[14] of Allyl Methyl Malonate (37), Cinnamyl Methyl Malonate (41) and Benzyl Methyl Malonate (42)

Mono potassium salt of dimethyl malonate (10.0 mmol) was dissolved in water (15 mL). The bromo compound (allyl bromide, cinnamyl bromide or benzyl bromide, 12.0 mmol) and tetrabutylammonium bromide (1.0 mmol) dissolved in CH_2Cl_2 (20 mL) were added and stirred at RT for 48 h. The reaction mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic extracts were washed, dried and evaporated. The residue was purified by column chromatography.

^{1}H NMR (60 MHz) of **37** : δ 6.16-5.49 (m, 1 H, =CH-), 5.36-4.95 (m, 2 H, $=CH_2$), 4.48 (d, J = 4.9 Hz, 2 H, $-OCH_2-$), 3.62 (s, 3 H, $-COOCH_3$), 3.22 (s, 2 H, $-CH_2-$).

^{1}H NMR (60 MHz) of **41** : δ 7.06 (s, 5 H, ArH), 6.35-5.75 (m, 2 H, olefinic), 4.59 (d, J = 5.0 Hz, 2 H, $-OCH_2-$), 3.56 (s, 3 H, $-COOCH_3$), 3.20 (s, 2 H, $-CH_2-$).

^{1}H NMR (60 MHz) of **42** : δ 7.15 (s, 5 H, ArH), 4.95 (s, 2 H, $-OCH_2-$), 3.52 (s, 3 H, $-COOCH_3$), 3.22 (s, 2 H, $-CH_2-$).

Preparation of Diallyl Malonate (38)

Malonic acid (10.41 g, 10.0 mmol) was dissolved in CH_2Cl_2 (50 mL). Allyl alcohol (1.45 g, 25.0 mmol) was added followed by four drops of con. H_2SO_4 and stirred for 24 h. It was worked up and the residue was subjected to chromatography over silica gel column. Elution with 5% ethyl acetate in petroleum ether furnished **38** (8.20 g, 44%), as a colourless oil.

^{1}H NMR (90 MHz) : δ 6.16-5.68 (m, 2 H, olefinic), 5.47-5.17 (m, 4 H, $=CH_2$), 4.77-4.51 (m, 4 H, $-OCH_2-$), 3.45 (s, 2 H, $-CH_2-$).

Preparation of the esters 39 and 40

To a stirred suspension of NaH (*ca.* 11.0 mmol) in dry THF (25 mL) at 0°C under nitrogen atmosphere was added ethyl acetoacetate (10.0 mmol). After 15 min, 6.6 mL of 1.6 M n-BuLi was added and again stirred (15 min). This was followed by the addition of the bromo compound (11.0 mmol) and the mixture was warmed to RT and stirred for 15 min. The reaction mixture was

quenched with a mixture of con. HCl (2 mL), water (5 mL) and diethyl ether (15 mL), diluted with water (50 mL) and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic extracts were washed with $NaHCO_3$ solution, then with water, dried and evaporated. The residue was purified by column chromatography.

^{1}H NMR (60 MHz) of **39** : δ 7.09 (s, 5 H, ArH), 6.56-5.69 (m, 2 H, olefinic), 4.06 (q, J = 7.0 Hz, 2 H, -OCH_2-), 3.23 (s, 2 H), 2.71-2.37 (m, 4 H, -CH_2-), 1.16 (t, J = 7.0 Hz, 3 H, -$CH_2C\underline{H}_3$).

^{1}H NMR (60 MHz) of **40** : δ 5.21-4.80 (m, 1 H, olefinic), 4.12 (q, J = 7.0 Hz, 2 H, -OCH_2-), 3.25 (s, 2 H, -CH_2-), 2.65-2.12 (m, 4 H, -CH_2-), 1.65 (s, 6 H, -CH_3), 1.22 (t, J = 7.0 Hz, 3 H, -$CH_2C\underline{H}_3$).

Reaction of Allyl Methyl Malonate (37) with CAN

Allyl methyl malonate (0.60 g, 3.79 mmol) was dissolved in methanol (20 mL) and cooled in an ice-bath. A solution of CAN (4.78 g, 8.72 mmol) in methanol (50 mL) was added to it dropwise and stirred. TLC analysis showed a highly complex mixture of products. Therefore purification was not attempted.

Reaction of Diallyl Malonate (38) with CAN

A solution of CAN (3.75 g, 6.9 mmol) in methanol (30 mL) was added to an ice-cooled solution of diallyl malonate (0.550 g, 3.0 mmol) in methanol (20 mL). The reaction mixture was warmed to RT after 1 h and stirred until the colour of CAN disappeared (6 h). TLC analysis showed complex mixture of products. Attempts to separate the products were not successful.

Reaction of the Ester 39 with CAN

A solution of CAN (2.52 g, 4.6 mmol) in methanol (40 mL) was added to an ice-cold solution of the ester **39** (0.492 g, 2.0 mmol) in methanol (20 mL). Stirred at this temperature for 1 h and at RT for 3 h. TLC analysis showed intractable mixture of products and attempts were not made to separate them.

Reaction of the Ester 40 with CAN

The ester **40** (0.550 g, 2.8 mmol) was dissolved in methanol (30 mL) and stirred in an ice-bath. A solution of CAN (3.53 g, 6.44 mmol) in methanol (50 mL) was added dropwise and stirred until the colour of CAN disappeared (2 h). TLC analysis, after work-up, showed a complex mixture of products. Attempts to separate the products were not successful.

Reaction of the Ester 41 with CAN

A solution of the ester (**41**, 0.470 g, 2.0 mmol) in methanol (30 mL) was treated with CAN (2.52 g, 6.9 mmol) in methanol (50 mL) for 6 h (5°C→RT). The reaction mixture was worked up after removing the methanol *in vacuo* and the residue was purified by column chromatography. Elution with 30% ethyl acetate in petroleum ether furnished **43** (0.311 g, 62%) as a colourless viscous liquid.

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

^1H NMR (90 MHz) : δ 7.55-7.25 (m, 5 H, ArH), 6.81-6.10 (m, 2 H, olefinic), 5.12-4.50 (m, 4 H), 3.86 (s, 3 H, $-COOCH_3$).

^{13}C NMR (22.4 MHz) : δ 168.5, 167.9, 135.6, 135.1, 128.4, 128.1, 126.5, 121.3, 90.7, 67.3, 53.6.

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

Reaction of the Ester 42 with CAN

The ester **42** (0.521 g, 2.5 mmol) was dissolved in methanol (30 mL) and reacted with CAN (3.15 g, 5.75 mmol) in methanol (40 mL) for 6 h. Work-up and purification by column chromatography (petroleum ether : ethyl acetate, 7:3) afforded **44** (0.493 g, 82%) as a colourless viscous liquid.

IR (neat) ν_{max} : 3459, 1749, 1455, 1234, 1112 cm^{-1}.

^{1}H NMR (90 MHz) : δ 7.36 (s, 5 H, ArH), 5.31 (s, 2 H, -OCH_2-), 5.12-4.63 (brs, 2 H, >C<u>H</u>O<u>H</u>), 3.75 (s, 3 H, -$COOCH_3$).

^{13}C NMR (22.4 MHz) : δ 168.3, 167.7, 134.2, 128.1, 127.7, 90.6, 68.1, 53.2.

GC-MS *m/z* : 222 (M^+-2, 5), 119 (2), 105 (6), 91 (100).

4.4. References

1. Donnelly, D. M. X.; Meegan, M. J. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R.; Rees, C. W., Ed.; Pergamon: New York, 1984; Vol. 4, p. 657.
2. Katritzky, A. R.; Li, J.; Gordev, M. F. *J. Org. Chem.* **1993**, *58*, 3038.
3. Mellor, J. M.; Mohammed, S *Tetrahedron Lett.* **1991**, *32*, 7107.
4. Mellor, J. M.; Mohammed, S. *Tetrahedron Lett.* **1991**, *32*, 7111.
5. Mellor, J. M.; Mohammed, S. *Tetrahedron* **1993**, *49*, 7547.
6. Baciocchi, E.; Ruzziconi, R.; Aira, D. D. *J. Org. Chem.* **1986**, *51*, 1645.
7. Snider, B. B.; Zhang, Q.; Dombroski, M. A. *J. Org. Chem.* **1992**, *57*, 4195.
8. Melikyan, G. G. *Synthesis* **1993**, 833.
9. Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.
10. Peterson, J. R.; Egler, R. S.; Horsley, D. B.; Winter, T. J. *Tetrahedron Lett.* **1987**, *28*, 6109.
11. Oumar-Mahamat, H.; Moustrou, C.; Surzur, J. -M.; Bertrand, M. P. *J. Org. Chem.* **1989**, *54*, 5684.
12. Citterio, A.; Fancelli, D.; Finzi, C.; Pesce, L.; *J. Org. Chem.* **1989**, *54*, 2713.
13. Snider, B. B.; Kwon, T. *J. Org. Chem.* **1990**, *55*, 4786.
14. Nair, V.; Mathew, J. *J. Chem. Soc., Perkin Trans. 1* (in Press).
15. Strube, R. E. *Organic Synthesis*; John Wiley: New York, 1963; Coll. Vol. 4, p. 417.
16. Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.

SUMMARY

The thesis entitled "Novel Carbon-Carbon Bond Forming Reactions Mediated by Cerium(IV) Ammonium Nitrate" embodies the results of a comprehensive investigation which was carried out to explore the potential application of CAN in generating carbon centred radicals and their use in C-C bond forming reactions.

A brief account of the developments of radical reactions from the old and erroneous notion of their "uncontrollable nature" to the recent appreciation and widespread acceptance of their application in complex carbocyclic construction has been presented in the first chapter of the thesis. This chapter also surveys the limited literature on the applications of Ce(IV) reagents in C-C bond forming reactions.

Chapter 2 deals with a facile, experimentally simple and efficient procedure for the CAN mediated addition of 1,3-dicarbonyl compounds to alkenes. The dicarbonyl compounds selected for the study are: dimedone (**1**), acetylacetone (**2**), ethyl acetoacetate (**3**) and dimethyl malonate (**4**). The oxidative addition of **1**, **2** and **3** to a variety of cyclic and acyclic alkenes furnished dihydrofuran derivatives in high yields. In the reaction with 2-methyl-2-pentene, acetylacetone and ethyl acetoacetate furnished uncyclized products **21** and **26** in addition to the dihydrofurans **20** and **25**. CAN mediated addition of ethyl acetoacetate to indene afforded two products **31** and **33** along with the dihydrofuran **30**. In all these reactions, the initial step involves the generation of a carbon centred radical by CAN from the dicarbonyl compound. This radical gets trapped by the alkene giving an intermediate radical. The latter undergoes

oxidation by a second equivalent of CAN leading to the cation which then cyclizes to the dihydrofuran derivative. The formation of **21** can be explained by the loss of a proton from the intermediate cation **19**. In the reaction of ethyl acetoacetate with indene, the benzylic radical **29** formed by the oxidation of the radical **28** either gets converted to **31** by methanol addition or cyclizes to the dihydrofuran derivative **30**. Alternatively, radical **28** can be trapped by NO_3^- to form the unstable radical anion **32** which on oxidative fragmentation would lead to the ketone **33**.

Unlike dimedone and acetylacetone, dimethyl malonate reacted differently with most of the alkenes. For example, the addition of **4** to cinnamyl methyl ether led to the lactone **38**. The CAN mediated addition of dimethyl malonate to indene furnished **41** and **42** and the reaction with 2-methyl-2-pentene afforded the uncyclized product **44** and the lactone **47**.

A comparative study of the above reactions mediated by $Mn(OAc)_3$ has also been presented in Chapter 2. This study reveals the superiority of CAN in terms of the mildness of the procedure, experimental simplicity and higher yields of products.

During the course of this work, we came across an unprecedented and interesting reaction between dimethyl malonate and styrene and this forms the subject matter of Chapter 3. In contrast to an earlier report on the exclusive formation of the nitrate **10** and the methoxy compound **11**, when dimethyl malonate was reacted with styrene in presence of CAN, we obtained products **5** and **8** in 42% and 29% yields respectively. The products **10** and **11** were obtained in minor amounts only. A tentative mechanism has been suggested for the formation of these products. The benzylic radical **3** formed by the addition of malonyl radical to styrene gets trapped by NO_3^- to form the radical anion **4**.

The oxidative fragmentation of **4** would lead to the ketone **5** whereas direct fragmentation of **4** followed by protonation of the resulting alkoxide would furnish the carbinol **7**, the precursor for the lactone **8**. The mechanism of formation of the nitrate **10** can involve either the oxidation of **4** or the trapping of the benzylic cation **9** by NO_3^-. Similarly, **9** can be trapped by methanol to afford **11**.

The addition of dimethyl malonate to 4-chloro-, 4-methyl- and 3-methyl substituted styrenes furnished products analogous to those obtained in the reaction with unsubstituted styrene. In the case of 3-chlorostyrene, the corresponding reaction afforded only the ketone **24** and the lactone **25**. 3-Nitrostyrene on the other hand furnished the ketone **26** and the nitrate **27**. The reaction of 4-nitro-styrene led to the ketone **28**. When 4-methoxystyrene was used in this reaction, instead of the addition of malonyl radical to the styrene, the latter underwent oxidative coupling leading to **34** and **36**.

Chapter 4 deals with the synthesis of spirodihydrofurans by the oxidative addition of dicarbonyl compounds to exocyclic alkenes. Dimedone on reaction with 4-phenylmethylenecyclohexane (**5**), 4-*tert*-butylmethylenecyclohexane (**6**) and β-pinene (**7**) furnished spirodihydrofurans in moderate to good yields. In the case of acetylacetone and ethyl acetoacetate the reaction with **5** afforded uncyclized products **10** and **12** respectively in addition to the spirodihydrofurans **9** and **11**.

Subsequent to the oxidative addition of 1,3-dicarbonyl compounds to alkenes, their additions to dienes such as 1,5-cyclooctadiene (**21**), limonene (**22**) and 1,3-cyclohexadiene (**23**) were investigated. The expected transannular radical cyclization in the reaction of dimedone or acetylacetone with 1,5-cycloocta-diene and the tandem radical additions in the case of limonene did not occur.

The dihydrofurans **24-27** in which one of the double bonds remained unaffected were the only products isolated.

Chapter 4 also describes the oxidative addition reactions of dicarbonyl compounds to acetylenes like phenylacetylene (**30**), diphenylacetylene (**31**), bis-(trimethylsilyl)acetylene (**32**) and propargyl alcohol (**33**). Except the addition of dimedone to phenylacetylene which provided the furan derivative **34**, all other reactions led to complex and inseparable mixture of products. We have also carried out some reactions with 2-acetylcyclohexanone (**35**) and 2-carboethoxy-cyclohexanone (**36**) with alkenes in presence of CAN. Again, no addition products could be isolated. Our attempts to carry out intramolecular radical cyclizations form the last part of Chapter 4. The starting materials **37-40** were reacted with CAN in methanol under the usual conditions. Intractable mixture of products resulted in all cases. In the reaction of **41** and **42** also no intra-molecular addition occurred. However, hydroxylated products **43** and **44** were isolated in 62% and 82% yields respectively.

In conclusion, CAN mediated addition of 1,3-dicarbonyl compounds to alkenes provides a facile, efficient and simple method for C-C bond formation and it appears that this method has potential application in the synthesis of a number of natural products containing dihydrofuran moiety. Thus it is anticipated that CAN will find wider use in Organic Synthesis.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