NOVEL CYCLOADDITIONS OF *o*-QUINONES AND THE CHEMISTRY OF 1,2-DIONES

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

DAVIS MALIAKAL

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

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DEDICATED TO MY PARENTS

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of the investigations carried out by me in the Organic Chemistry Division of the Regional Research Laboratory, Thiruvananthapuram, under the supervision of ***Dr. G. VIJAY NAIR*** *and the same has not been submitted elsewhere for a degree.*

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CERTIFICATE

*Certified that the work described in this thesis entitled "**NOVEL CYCLOADDITIONS OF o-QUINONES AND THE CHEMISTRY OF 1,2-DIONES**" has been carried out by **Mr. DAVIS MALIAKAL**, under my supervision and the same has not been submitted elsewhere for a degree.*

G. Vijay Nair

G. VIJAY NAIR

THESIS SUPERVISOR

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Thiruvananthapuram ***DAVIS MALIAKAL***

July 1999.

PREFACE

Molecules possessing quinonoid structure constitute a large and important class of organic compounds. They are used as versatile intermediates in organic synthesis and in dye industry; many of them are important therapeutic agents. Chemical reactions of quinonoid systems constitute a vast and complex field in chemistry. In recent years there has been a great deal of interest in the synthesis of quinonoid natural and unnatural products.

o-Benzoquinones undergo facile cycloaddition with styrenes, phenylacetylenes etc. leading to the formation of bicyclo[2.2.2]octenediones. Owing to the presence of two strained carbonyl groups, these compounds appeared interesting from the point of view of their potential transformations to a variety of structurally fascinating and potentially valuable compounds. A systematic investigation of the synthesis and chemistry of bicyclo[2.2.2]octenediones has been carried out and the results obtained are presented in the thesis entitled "**NOVEL CYCLOADDITIONS OF *o*-QUINONES AND THE CHEMISTRY OF 1,2-DIONES**". The thesis is divided into four chapters. Relevant references are given at the end of each chapter.

A general introduction to the cycloaddition chemistry of *o*-benzoquinones and some synthetic applications of bicyclo[2.2.2]octenediones are presented in chapter 1. A definition of the present research problem has also been incorporated.

The second chapter is divided into two sections. The first section deals with the cycloaddition reactions of *o*-benzoquinones with styrenes and the

second section describes the influence of Lewis acid catalysts on these reactions. General information on experimental procedure is given in this chapter.

The third chapter is divided into three sections. The first section deals with the photolysis of the bicyclo[2.2.2]octenediones, derived by the cycloaddition reactions of *o*-benzoquinones with various styrenes, to afford substituted biphenyls. The second section describes the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones to form bicyclo[3.2.1]octenediones. The third section comprises the ring opening reactions of the latter by methanolic KOH leading to cycloheptenones.

The fourth chapter is divided into three sections. The first section deals with the cycloadditions of *o*-benzoquinones with various phenylacetylenes to afford regioisomeric mixture of bicyclo[2.2.2]octenediones. The second section describes the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones to form bicyclo[3.2.1]octenediones. The last section is concerned with the photolytic rearrangement of bicyclo[3.2.1]octenediones to form bicyclo[3.3.0]oct-3,7-diene-2,6-diones.

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

CONTENTS

CHAPTER 1

AN INTRODUCTION TO THE CYCLOADDITION REACTIONS OF *o*-QUINONES AND CHEMISTRY OF BICYCLO[2.2.2]OCTENEDIONES

1.1 General

The focal themes of the thesis are the cycloaddition reactions of *o*-quinones to styrenes and the chemistry of the cycloadducts. Therefore, to put things in perspective, a brief overview of the chemistry of *o*-quinones, their cycloaddition reactions and the transformations of bicyclo[2.2.2]octenediones are given in the following sections. Of necessity, the literature coverage is selective and not intended to be comprehensive.

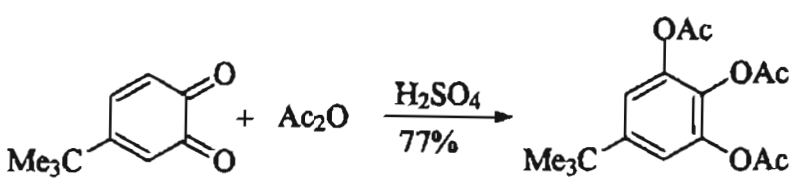
It may be noted that a number of elaborate reviews on the chemistry of *o*-quinones are available.[1-3]

1.2 Synthesis of *o*-quinones

o-Quinones can be prepared from phenols by oxidation with cerium(IV) sulfate in dilute acids,[4] Fremy's salt,[5] benzene seleninic anhydride,[6] iodosobenzene or iodoxybenzene.[7] The most commonly used method for the preparation of *o*-quinones, involves oxidation of the corresponding catechols with appropriate oxidising agents such as Ag_2O, Ag_2CO_3, $FeCl_3$, $NaIO_4$,[8] MnO_2 or sodium hypochlorite in the presence of phase transfer catalyst.[9]

1.3 General reactions of *o*-quinones

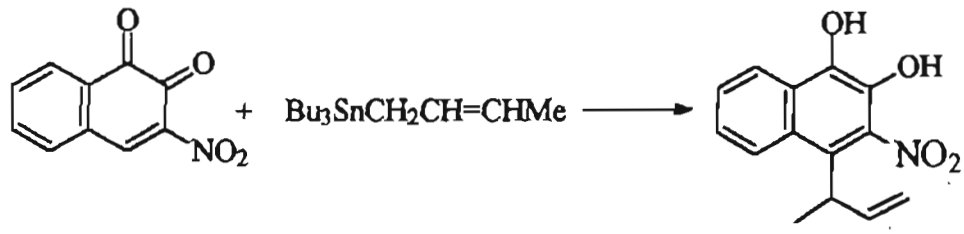
The Thiele-Winter acetoxylation is one of the general and important reactions of *o*-quinones. Reaction of 4-*tert*-butyl-*o*-benzoquinone leading to the triacetoxy derivative is illustrative (Scheme 1).[10]



1 **2**

Scheme 1

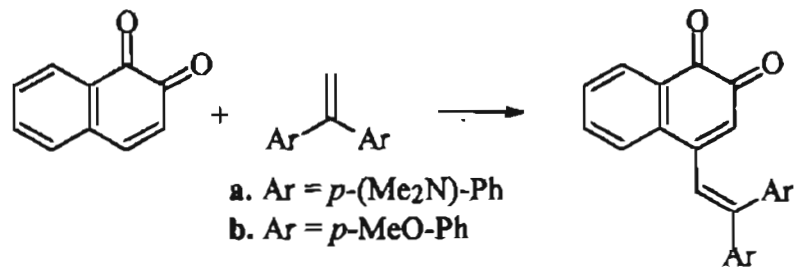
Another important reaction is the alkylation of quinones using organo tin, nickel or silicon reagents. An example is given in scheme 2.[11]



3 **4** **5**

Scheme 2

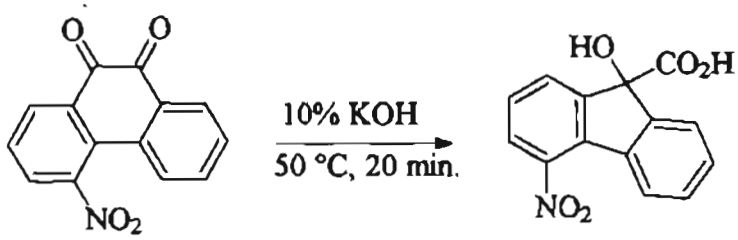
The conjugate addition of highly polarized compounds to 1,2-naphthoquinone is known from the work of Gates (Scheme 3).[12]



6 **7a,b** **8**

Scheme 3

A common reaction of 1,2-dicarbonyl compounds is the benzilic acid rearrangement, which results in ring contraction. The synthetically useful transformation of phenanthrenequinone to 9-hydroxyfluorene carboxylic acid is illustrative (Scheme 4).[13]



9 **10**

Scheme 4

1.4 Cycloaddition reactions of *o*-quinones

Cycloaddition reactions in general and Diels-Alder reactions in particular are among the most important reactions of *o*-quinones. In recent years, Diels-Alder reaction has been widely exploited for the facile synthesis of a number of quinonoid natural products.[14-16] A particularly useful extension of cycloaddition is the Lewis acid catalyzed reaction described by Yates and Eaton.[17] Use of high pressure, aqueous medium, chiral catalysis, various salts etc. to facilitate the reaction represent other advances in this area.[18] Not surprisingly, much of the cycloaddition chemistry of *o*-quinones has involved the readily available and stable *o*-chloranil and *o*-bromanil.

The unique structural features of *o*-benzoquinones predispose them to exhibit multiple cycloaddition profiles; they can participate as carbodienes, heterodienes, dienophiles or heterodienophiles as highlighted in figure 1.

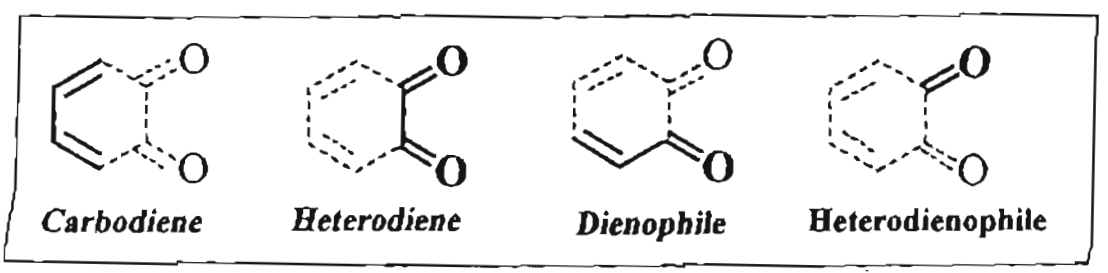


Figure 1

The electronic and steric features of the substituents on the quinone play an important role in the cycloaddition reactions of *o*-benzoquinones. In 1971, Ansell reported that in the reaction of *o*-quinone with acyclic diene the addition occurs preferentially to the more electron deficient carbon-carbon double bond and here quinone acts as a dienophile.[19]

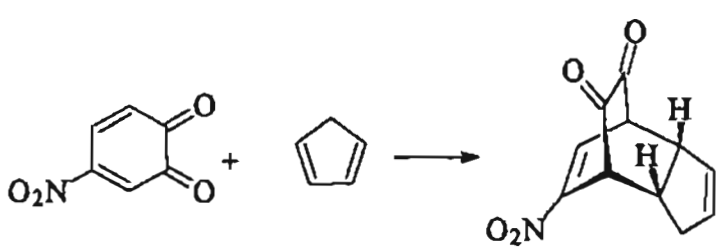
o-Benzoquinone participates as a carbodiene with carbocyclic dienes and it functions as a heterodiene in reactions with heterocyclic dienes such as pyrroles[20] and furans.[21]

Investigations in our laboratory have unraveled novel reactivity patterns of *o*-quinones.[3] We have also shown that in dipolar cycloaddition reactions, *o*-quinones participate as C=C and C=O dipolarophiles.[22]

The different types of reactivity shown by *o*-benzoquinones in [4+2] cycloaddition reactions are discussed in the following sections.

1.4.1 *o*-Quinone as carbodiene

o-Benzoquinones undergo facile Diels-Alder reactions with dienes such as cyclopentadiene and cyclohexadiene to afford bicyclo-1,5-dienes which are shown to undergo Cope rearrangement at high temperatures (Scheme 5).[3,19,23]



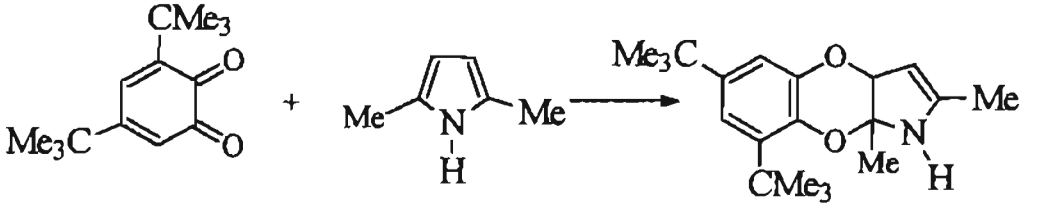
11 **12** **13**

Scheme 5

1.4.2 *o*-Quinone as heterodiene

o-Benzoquinones possess a highly activated heterodiene part and they participate as 4π component in cycloaddition reactions with heterocyclic

dienes,[20,21] enamines[24-26] and substituted indoles[27] leading to the formation of benzodioxin derivatives (Scheme 6). It is noteworthy that benzodioxin moiety is present in a number of natural and synthetic derivatives which often exhibit interesting pharmacological activity.[28]

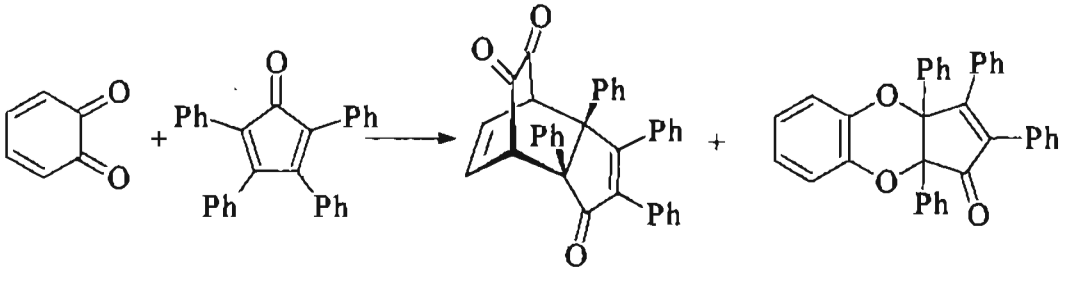


14 **15** **16**

Scheme 6

1.4.3 *o*-Quinone as both carbodiene and heterodiene

In certain cycloaddition reactions, *o*-benzoquinones participate both as a carbodiene and a heterodiene resulting in the formation of bicyclo[2.2.2]octenediones and benzodioxin derivatives respectively. For example the reaction of *o*-benzoquinone with tetracyclone afforded **19** and **20** (Scheme 7).[21]

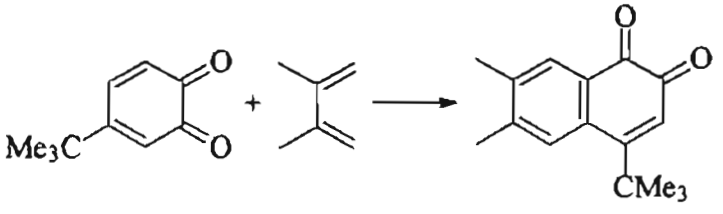


17 **18** **19** **20**

Scheme 7

1.4.4 *o*-Quinone as dienophile

Cycloaddition reactions of *o*-benzoquinones with electron rich dienes such as 2,3-dimethylbutadiene, acetoxybutadiene etc. proceeded smoothly, with the enone moiety of *o*-benzoquinone participating as a powerful dienophile, leading to naphthoquinones, presumably by the aromatization of the primary adducts (Scheme 8).[3]

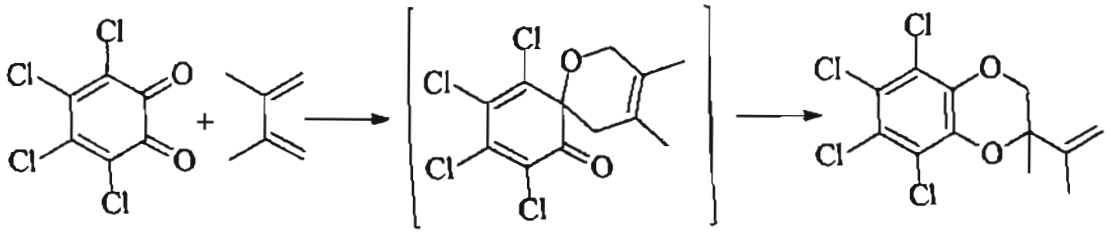


1 **21** **22**

Scheme 8

1.4.5 *o*-Quinone as heterodienophile

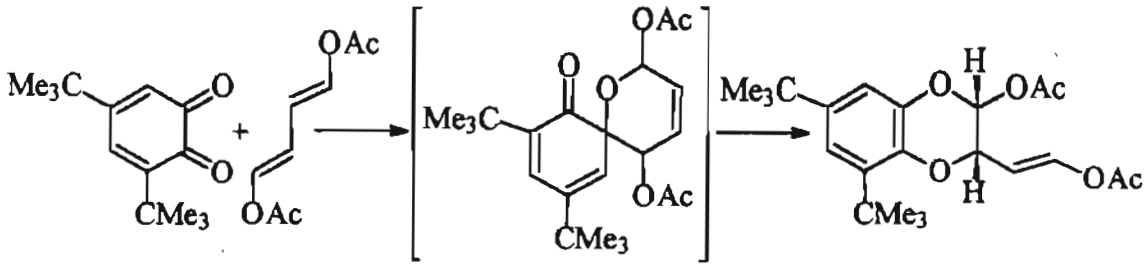
o-Benzoquinones can serve as heterodienophiles in cycloaddition reactions due to the presence of two activated carbonyl groups. *o*-Chloranil is found to react with 2,3-dimethylbutadiene to give a spiro derivative which undergoes a facile [3,3] sigmatropic rearrangement at higher temperatures yielding novel benzodioxin derivatives (Scheme 9).[29]



23 **21** **24** **25**

Scheme 9

Similar reactivity was observed with *o*-quinones in the reaction of electron rich dienes like diacetoxybutadiene (Scheme 10).[30]



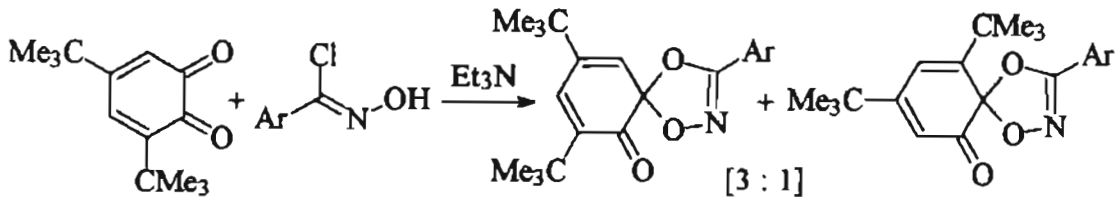
14 **26** **27** **28**

Scheme 10

1.4.6 *o*-Quinone as dipolarophile

The presence of two potential dipolarophilic functionalities *ie*. C=C and C=O, renders *o*-benzoquinones very interesting from the vantage-point of dipolar cycloaddition. Dipolar cycloaddition reactions of *o*-benzoquinone lead to a number of novel heterocyclic compounds.[2,31]

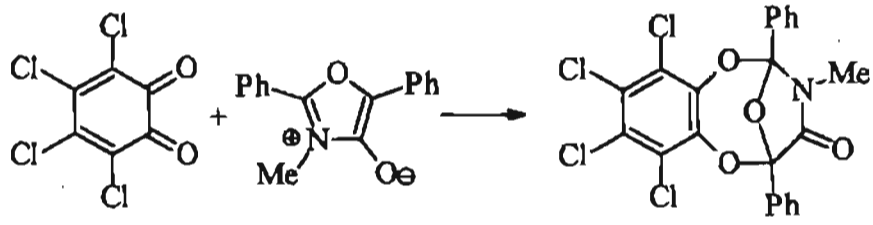
The reaction of *o*-benzoquinones with nitrile oxides revealed that the reactivity of the former depends on the substitution pattern and nature of the substituents on the benzoquinone moiety. With aryl nitrile oxide, 3,5-di-*tert*-butyl-1,2-benzoquinone participates as a heterodipolarophile (Scheme 11).[22]



14 **29** **30** **31**

Scheme 11

Mesoionic compounds such as münchnones and isomünchnones have been shown to react with *o*-chloranil leading to novel heterocyclic systems. The following reaction is illustrative (Scheme 12).[22,32,33]

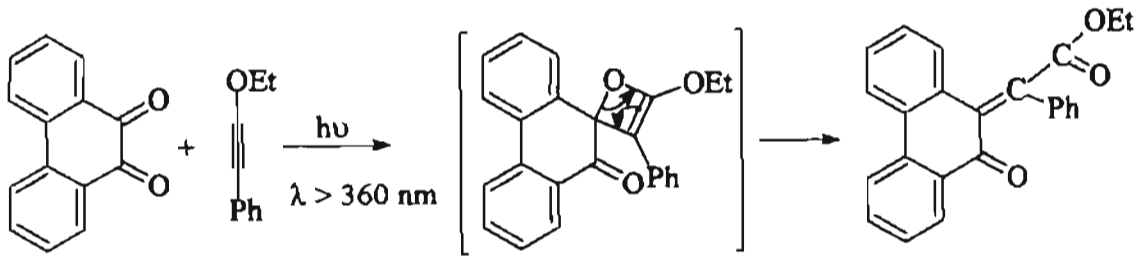


23 **32** **33**

Scheme 12

1.4.7 Photocycloadditions

The photolysis of phenanthrenequinone **34** with 1-ethoxy-2-phenylacetylene **35** initially yielded a [2+2] adduct which underwent electrocyclic reaction to afford γ-oxo-α,β-unsaturated esters **37** (E and Z) having quinonemethide structure (Scheme 13).[34]



34 **35** **36** **37 (E and Z)**

Scheme 13

1.5 Theoretical calculations

In order to gain some insight into the mechanism of cycloaddition reactions, Woodward-Hoffmann rules can be used.[35-37] Indeed, most [4+2] cycloaddition reactions are best described in terms of symmetry allowed one step mechanism. The difference in reactivity of dienes and dienophiles towards Diels-Alder reactions can be explained by the principle of conservation of orbital symmetry.

The rate of a Diels-Alder reaction is determined largely by the degree of interaction between the HOMO of one component and the LUMO of the other; smaller the energy separation between the orbitals more readily the reaction proceeds. In normal Diels-Alder reactions, HOMO of diene interacts with LUMO of dienophile. But in some other cases the LUMO of the diene interacts with HOMO of the dienophile and these reactions are termed as Inverse Electron Demand Diels-Alder reactions.[37]

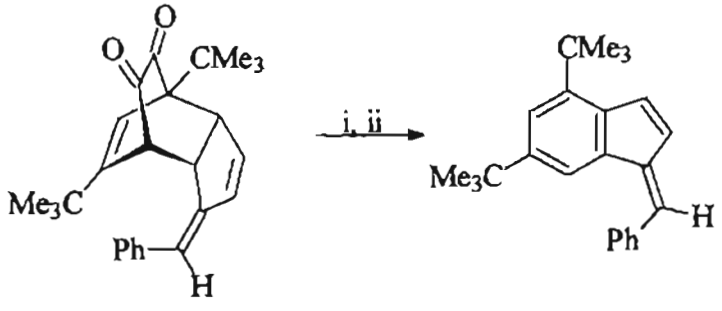
Diels-Alder reactions have high regio- and stereoselectivity. The regioselectivity can be explained by considering the coefficients of the frontier orbitals. The interaction between two orbitals is allowed only when the sign of the overlapping lobes are the same as well as the orbital coefficients have comparable size. Stereoselectivity of Diels-Alder reaction depends mainly on the secondary orbital overlap in the transition state. The secondary orbital overlap stabilizes the *endo* transition state of [4+2] addition and favors the formation of kinetically favored *endo* isomer.

Semiempirical molecular orbital calculations are used to gain better understanding of the reactivity pattern of *o*-quinones in cycloaddition reactions. Thus MNDO and AM1 calculations using MOPAC (version 5.01)

1.6 General reactions of bicyclo[2.2.2]octenediones

Apart from the novel chemistry involved in the cycloadditions of *o*-benzoquinones, attention may be drawn to the fact that the products of the cycloaddition themselves are potentially amenable to a number of interesting and possibly useful transformations.

Bicyclo[2.2.2]octenediones, resulting from the cycloaddition of *o*-quinones, undergo facile double decarbonylation reaction on photolysis providing an efficient route to the synthesis of highly substituted indenes and benzene derivatives (Scheme14).[38]

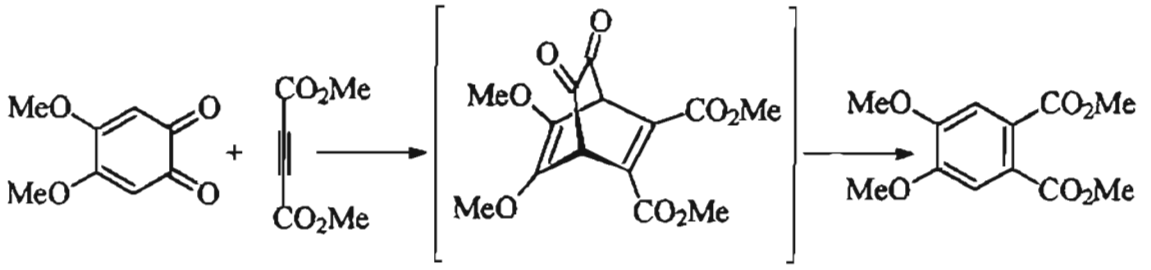


38 **39**

i. hυ, Pyrex, Cyclohexane, 1 h, 79% ii. DDQ, Benzene, Reflux 14 h, 75%

Scheme 14

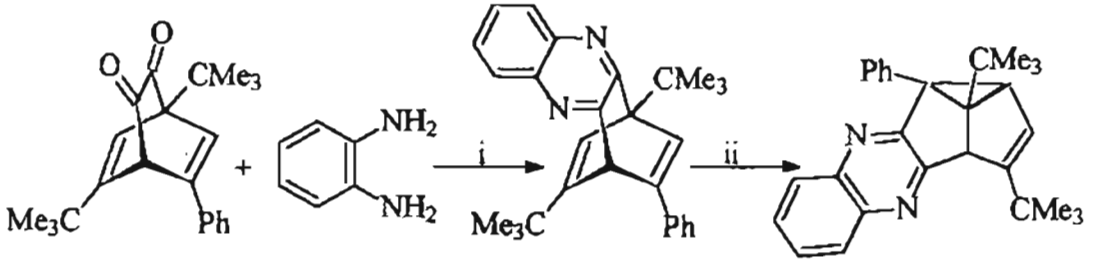
In certain cases, the initial adduct decomposes under the reaction conditions to yield the doubly decarbonylated product (Scheme 15).[39]



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

Scheme 15

The bicyclo[2.2.2]octenediones serve as excellent precursors to pyrazinobarrelenes and the latter undergo facile di-π-methane rearrangement (Scheme 16).[40]



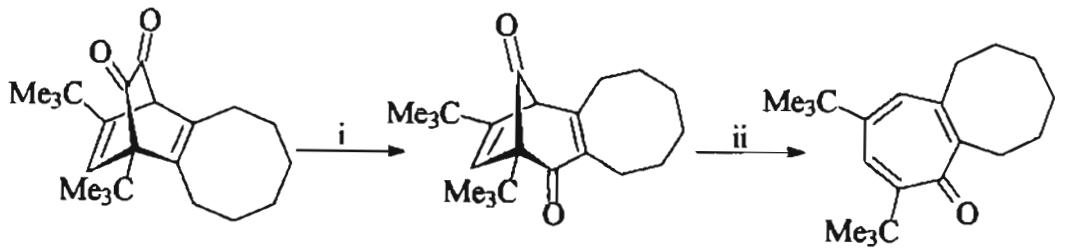
44 **45** **46** **47**

i. EtOH, reflux, 28 h, 67% ii. hυ, cyclohexane, pyrex, 45 min., 94%

Scheme 16

The bicyclo[2.2.2]octenediones can be converted to biphenylglyoxylic acids by treating with a base. Details of this ring opening reactions are explained in the section 3.3 (Chapter 3).

The BF_3-OEt_2 catalyzed conversion of a bicyclo[2.2.2]octenedione to bicyclo[3.2.1]octenediones has been reported (Scheme 17).[41]



48 **49** **50**

i. BF_3-OEt_2 ii. 240 °C

Scheme 17

1.7 Definition of the problem

During the course of our investigations on the cycloaddition reactions of *o*-benzoquinones, somewhat surprisingly, we became aware that there has been very little information available on the cycloaddition reactions of *o*-benzoquinones with aryl alkenes like styrenes. In this context, it was of interest to investigate the reactivity profile of *o*-quinones with styrenes.

The chemical and photochemical transformations of bicyclo[2.2.2]octenediones, resulting from the cycloaddition reactions of *o*-benzoquinones with styrenes, were considered appropriate in the second phase of our studies. Ring opening reactions of the bicyclo[3.2.1]octenediones derived from the BF_3-etherate induced rearrangement of bicyclo[2.2.2]octenediones also formed the subject of investigation.

The last phase of the work explores a novel photolytic method for the synthesis of bicyclo[3.3.0]octenediones from bicyclo[3.2.1]octene diones; the latter in turn were formed by the BF_3-etherate induced rearrangement of bicyclo[2.2.2]octenediones resulting from the cycloaddition reactions of *o*-benzoquinones with phenylacetylenes.

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CHAPTER 2

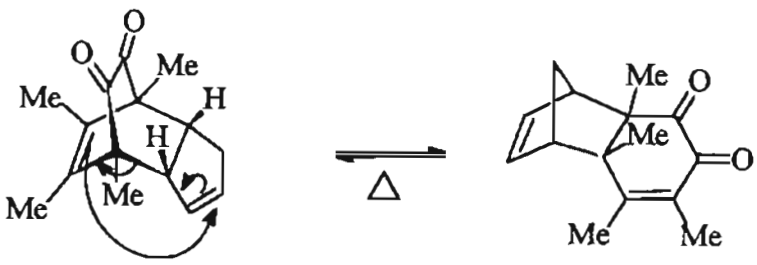
CYCLOADDITION REACTIONS OF *o*-BENZOQUINONES WITH STYRENES

This chapter is divided into two sections. The first section deals with the cycloaddition of *o*-benzoquinones with styrenes and the second section describes the influence of Lewis acid catalysts on these reactions.

2.1 Cycloaddition reaction reactions of *o*-benzoquinones with styrenes

2.1.1 Introduction

[4+2] Cycloaddition reactions of *o*-quinones are important since they offer a convenient route to bicyclo[2.2.2]octenediones or benzodioxin systems, in a highly regio- and stereospecific fashion. In the first report on the cycloaddition reaction of *o*-benzoquinones, Smith and Hac[1] described the reaction of cyclopentadiene with tetramethyl-*o*-benzoquinone leading to a product for which structure **1** was assigned. However, this adduct was shown by Horner and Spietschka[2] to have the oxalylindene structure **2** resulting from the quinone functioning as the carbodiene and cyclopentadiene as the dienophile. The relationship between the adducts **1** and **2** was clearly established by Ansell[3] and co-workers who pointed out that they are both hexa-1,5-dienes and are interconvertable by a Cope rearrangement as shown in scheme 1.

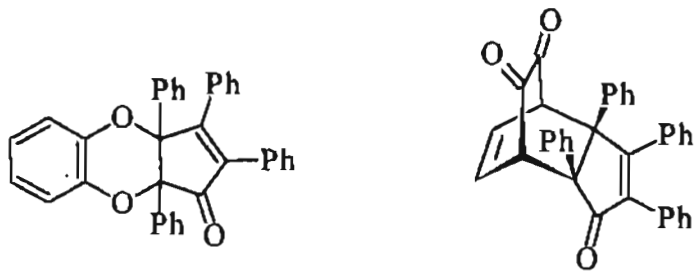


1 2

Scheme 1

The equilibrium for this Cope rearrangement lies entirely on the side of the oxalylindene **2**, presumably due to steric factors favoring the bicyclo[2.2.2]octenedione system **1** rather than bicyclo[2.2.1]heptene system **2**. Diels-Alder reaction between a number of *o*-benzoquinones carrying electron withdrawing groups at 4-position and cyclopentadiene have been reported.[4] At room temperature these reactions gave thermally stable oxalylindene adducts.

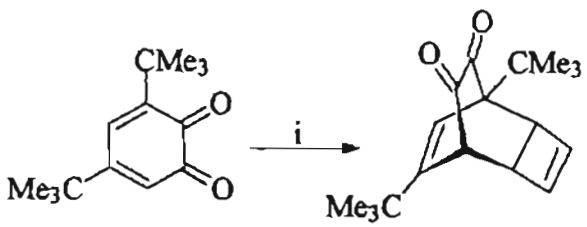
In 1969, Horspool and co-workers reported that the cycloaddition of *o*-benzoquinone with tetracyclone afforded a mixture of benzodioxin **3** and bicyclo[2.2.2] adduct **4** (Figure 1).[5]



3 4

Figure 1

Paquette has studied the cycloaddition reactions of 3,5-di-*tert*-butyl-1,2-benzoquinone **5** with cyclobutadiene. The latter generated *in situ* from the iron tricarbonyl complex by CAN oxidation has been trapped with the quinone as a [4+2] adduct **6** (Scheme 2).[6]

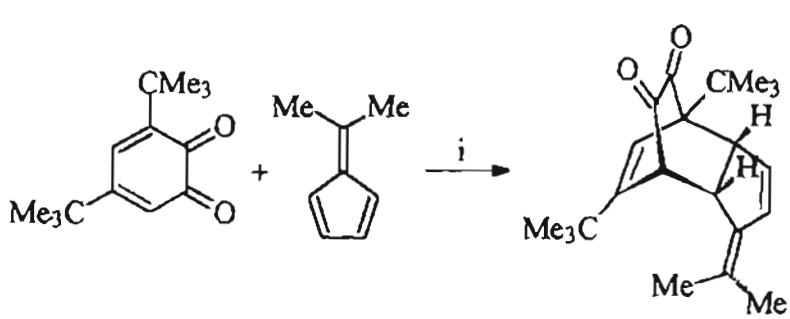


5 **6**

i.  **Fe(CO)3, CAN**

Scheme 2

Fulvenes undergo facile cycloaddition to *o*-quinones resulting in the formation of bicyclo[2.2.2]dione systems. For example 6,6-dimethylfulvene **7**, one of the simplest members of the fulvene family, on refluxing with 3,5-di-*tert*-butyl-1,2-benzoquinone **5** in benzene afforded the adduct **8** in 80% yield (Scheme 3).[7]

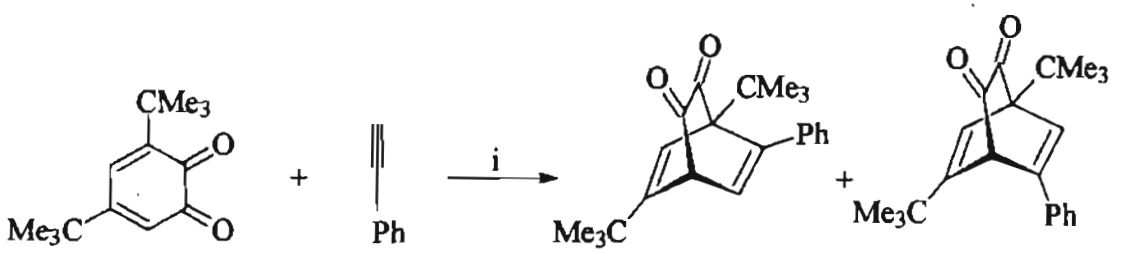


5 **7** **8**

i. Benzene, reflux, 8 h, 80%

Scheme 3

3,5-Di-*tert*-butyl-1,2-benzoquinone, on heating with phenylacetylene in a sealed tube neat at 120 °C afforded two isomeric products **10** and **11**, which were separated by fractional crystallization (Scheme 4).[8]

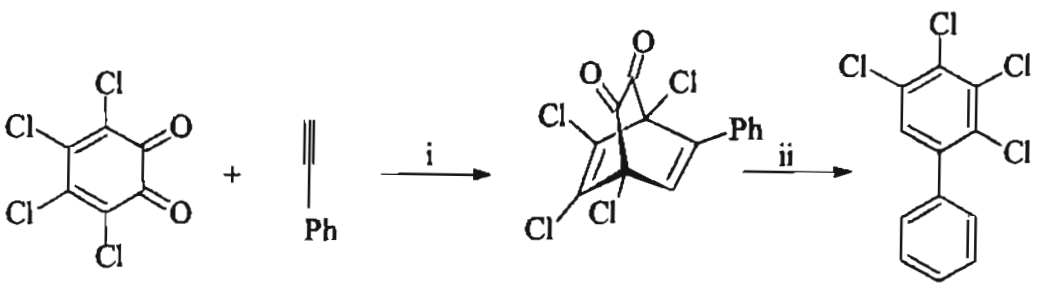


5 **9** **10** **11**

i. Neat, Sealed tube, 120 °C, 36 h, 78%

Scheme 4

Unsymmetrical chlorobiphenyls required for toxicological studies have been prepared from the adducts of *o*-chloranil and appropriate arylacetylene (Scheme 5).[9]

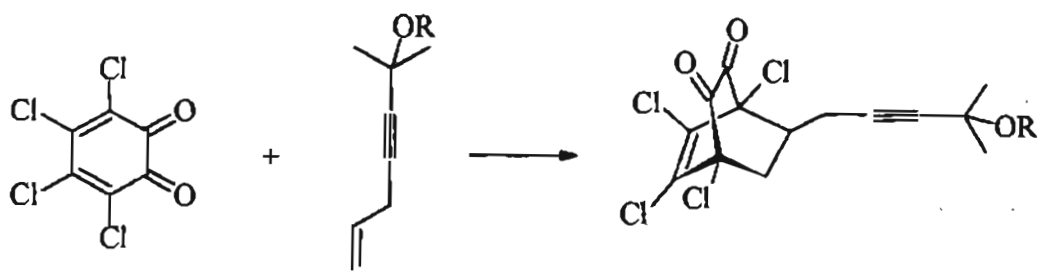


12 **9** **13** **14**

i. Benzene, reflux, 12 h, 70-80%, ii. hυ

Scheme 5

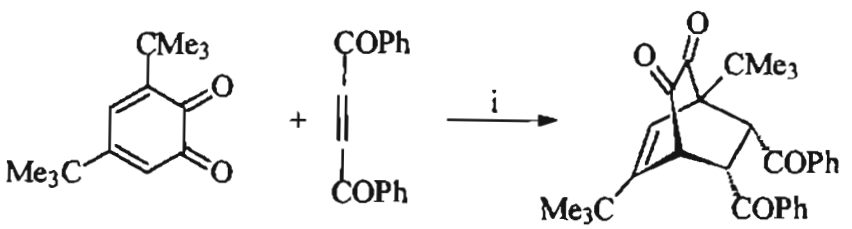
There is an isolated report indicating preferential addition of alkenes to *o*-quinones forming the bicyclo[2.2.2]octenedione system (Scheme 6).[10]



12 **15 (a, b)** **16 (a, b)**

Scheme 6

Dibenzoylethylene **17** underwent cycloaddition to **5** when heated without any solvent in a sealed tube at 120 °C for 22 h (Scheme 7).[8]

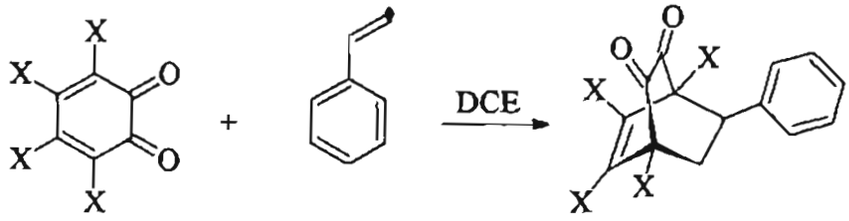


5 **17** **18**

i. Neat, Sealed tube, 120 °C, 22 h, 47%

Scheme 7

From a survey of the literature presented above, we became aware that in spite of the substantial investigations on the cycloadditions of *o*-quinones to a variety of dienophiles, there has been very little work on their reactions with aryl alkenes like styrenes. The meagre information available in this area is derived from the reaction of chloranil and bromanil with styrene (Scheme 8).[11]



X= Cl, Br

12, 19 **20** **21, 22**

Scheme 8

It may also be noted that, very recently, a report on the enzymatic oxidation of catechols to *o*-quinones and the Diels-Alder reaction of the latter to styrenes to give highly functionalized bicyclic 1,2-diketones has appeared.[12]

2.1.2 Results and discussion

It was evident from the literature survey that only scant information is available on the cycloadditions of *o*-benzoquinones with styrenes. We have therefore undertaken, detailed investigations in this area with a view to determine the scope and limitations of the cycloadditions of styrenes to *o*-quinones.

The styrenes required were prepared from the corresponding substituted benzaldehydes by Wittig reaction. The *o*-benzoquinones selected were 3,5-di-*tert*-butyl-1,2-benzoquinone **5**, 3,5-bis(diphenylmethyl)-1,2-benzoquinone **23** and 4-*tert*-butyl-1,2-benzoquinone **24** (Figure 2). These

were readily obtained from the corresponding catechols by routine oxidation with $NaIO_4$.

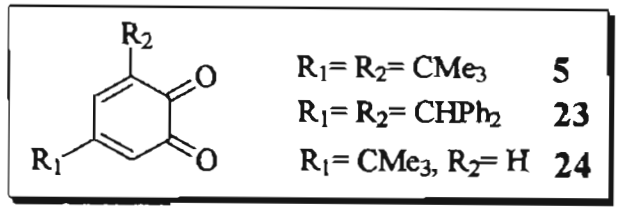
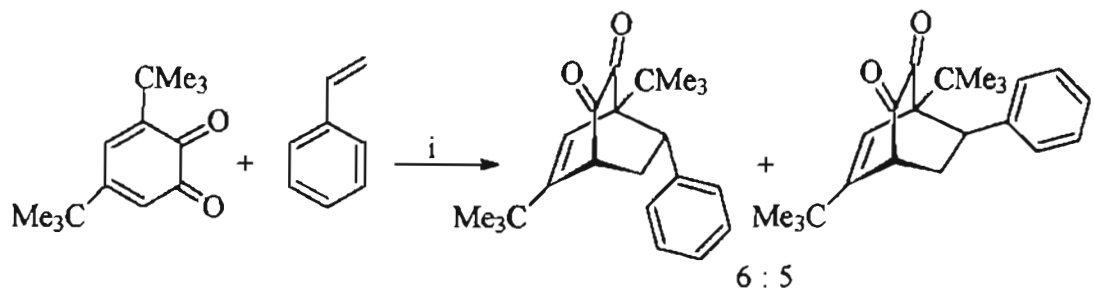


Figure 2

Our studies were initiated with the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **5** with styrene **20**. It was found that these two undergo facile cycloaddition when heated neat in a sealed tube at 110 °C affording bicyclo[2.2.2]octenediones **25** and **26** in the ratio 6:5 (Scheme 9). Attempted reactions of **5** and **20** in solution, *e.g.* with benzene, toluene and dichloroethane were unsuccessful even when the reaction was conducted under sealed tube conditions.



5 **20** **25** **26**

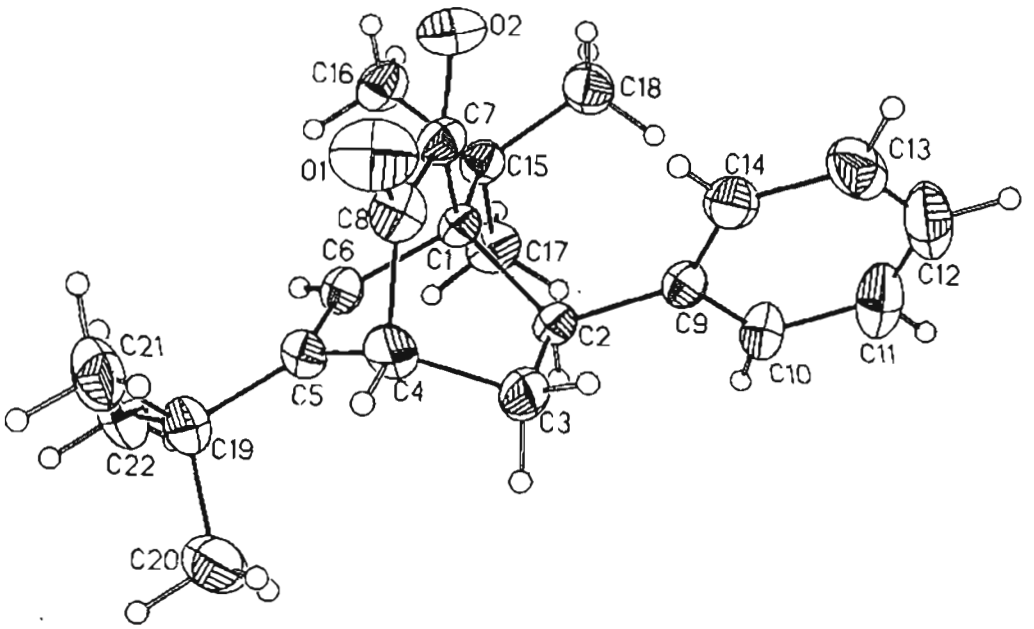
i. Neat, Sealed tube, 110 °C, 11 h, 96%

Scheme 9

The structure of the products was assigned on the basis of spectral and analytical data. The IR spectrum of **25** showed a strong absorption at

1735 cm^{-1} indicating the presence of an α-dione. In the ^1H NMR spectrum, the phenyl protons appeared as a multiplet between δ 7.27-7.12. The olefinic proton resonated as a doublet at δ 6.10 (d, J= 2 Hz) due to allylic coupling. The bridgehead proton appeared as a multiplet between δ 3.65-3.55. The benzylic proton resonated as a double doublet at δ 3.41 (dd, J= 10.04, 6.22 Hz). The methylene protons appeared as separate multiplets between δ 2.70-2.38 and 2.12-1.88, integrating for one proton each. The singlets at δ 1.55 and 0.89 are due to the two *tert*-butyl groups. In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 191.56 and 190.96 and the two bridgehead carbons appeared at δ 63.48 and 48.00. All other signals were in agreement with the assigned structure. The structure was further confirmed by satisfactory elemental analysis.

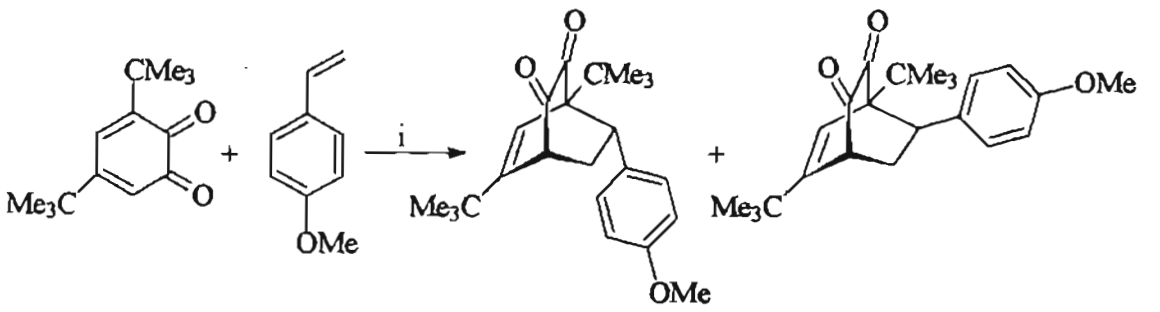
The IR spectrum of **26** showed characteristic carbonyl absorption at 1732 cm^{-1}. In the ^1H NMR spectrum, the bridgehead proton appeared as a multiplet at δ 3.67-3.57 while the benzylic proton resonated as a double doublet at δ 3.50 (dd, J= 12.00, 6.2 Hz). In the ^{13}C NMR spectrum, the two carbonyls resonated at δ 190.94 and 190.40 and the bridgehead carbons appeared at δ 63.45 and 47.97. The structure was further supported by high resolution mass spectrum. All other signals were in agreement with the assigned structure. The structure **26** was confirmed unequivocally by single crystal X-ray structure determination.



X-ray crystal structure of 26

The reactions of **5** with other substituted styrenes, proceeded in a similar fashion, yielding bicyclo[2.2.2]octenediones in high yields. These results are discussed below.

3,5-Di-*tert*-butyl-1,2-benzoquinone **5** on heating with 4-methoxy-styrene **27** in a sealed tube neat at 110 °C for 10 h, afforded two isomeric products **28** and **29** in 92% yield (Scheme 10).



5 **27** **28** **29**

i. Neat, Sealed tube, 110 °C, 10 h, 92%

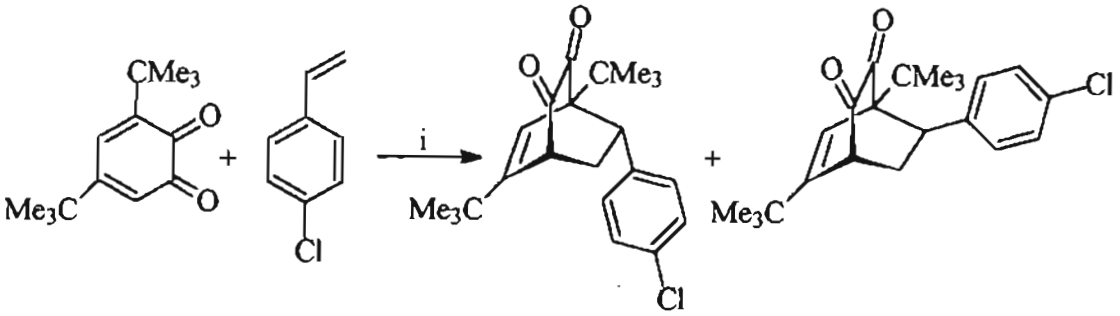
Scheme 10

The structure of the products was ascertained from the spectral and analytical data. The IR spectrum of **28** showed strong absorption at 1738 cm^{-1} which is diagnostic for an α-dione moiety. In the ^1H NMR spectrum, the bridgehead proton appeared as a multiplet between δ 3.67-3.60 while the benzylic proton resonated as a double doublet at δ 3.38 (dd, J= 10.25, 6.5 Hz). The methoxy protons appeared as a singlet at δ 3.78. In the ^{13}C NMR spectrum, the two carbonyls resonated at δ 191.39 and *191.15. The methoxy* and the bridgehead carbons resonated at δ 55.39, 61.79 *and 48.80 respectively. The analytical data also supported the structure.*

The IR spectrum of **29** showed characteristic carbonyl *absorption at* 1735 cm^{-1}. In the ^1H NMR spectrum, the benzylic proton exhibited a double doublet at δ 3.27 (dd, J= 12.5, 6.5 Hz) while the methoxy protons appeared as a singlet at δ 3.75. In the ^{13}C NMR spectrum, the two carbonyls were

visible at δ 192.00 and 191.37, whereas the bridgehead carbons and the methoxy carbon resonated at δ 63.73, 48.26 and 55.39 respectively. The structure assigned was further supported by satisfactory analytical data.

Similarly, 3,5-di-*tert*-butyl-1,2-benzoquinone **5** undergoes facile cycloaddition reaction with 4-chlorostyrene **30** affording the bicyclo[2.2.2]octenediones **31** and **32** in 90% yield (Scheme 11).



5 : 4

5 **30** **31** **32**

i. Neat, Sealed tube, 120 °C, 14 h, 90%

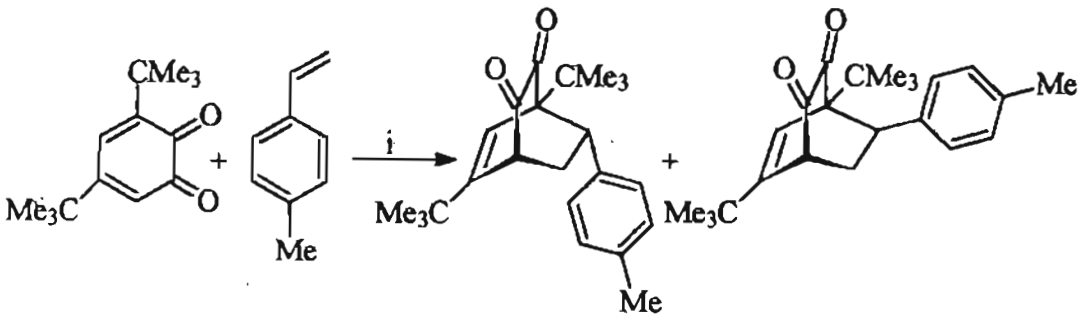
Scheme 11

The structure of the products was established on the basis of spectral and analytical data. The IR spectrum of **31** showed a strong absorption at 1731 cm^{-1}, due to an α-dione moiety. In the ^1H NMR spectrum, the benzylic proton appeared as a double doublet at δ 3.50 (dd, J= 10.08, 6.13 Hz) and the bridgehead proton exhibited a multiplet between δ 3.68-3.65. In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 190.73 and 190.37 and the bridgehead carbons appeared at δ 61.60 and 48.53. Elemental analysis also supported the proposed structure.

The IR spectrum of **32** showed a strong absorption at 1729 cm^{-1} characteristic of an α-dione moiety. In the ^1H NMR spectrum, the benzylic

proton appeared as a double doublet at δ 3.33 (dd, J= 11.97, 6.15 Hz) and the bridgehead proton appeared as a multiplet between δ 3.60-3.49. In the ^{13}C NMR spectrum, the carbonyl groups appeared at δ 191.64 and 190.87 and the bridgehead carbons resonated at δ 63.56 and 48.05. Elemental analysis also supported the assigned structure.

The reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **5** with 4-methylstyrene **33** in a sealed tube neat at 120 °C afforded the products **34** and **35** in 95% yield (Scheme 12).



5 **33** **34** **35**

i. Neat, Sealed tube, 120 °C, 14 h, 95%

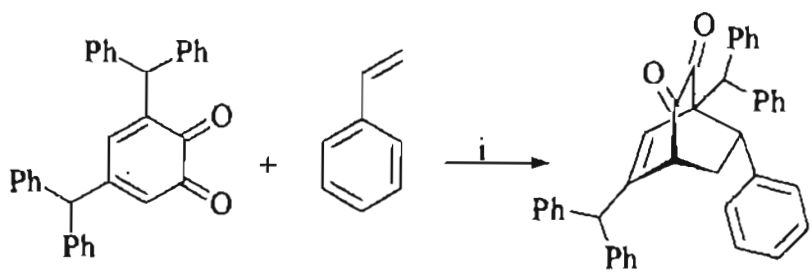
Scheme 12

As usual, the structure of the products was ascertained by spectral and analytical data. The IR spectrum of **34** showed a strong absorption at 1742 cm^{-1} due to 1,2-dione moiety. In the ^{1}H NMR spectrum, the benzylic proton appeared as a double doublet at δ 3.39 (dd, J= 10.01, 6.30 Hz) and the bridgehead proton exhibited a multiplet between δ 3.66-3.63. In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 191.20 and 190.94 and the bridgehead carbons resonated at δ 61.67 and 48.68. Analytical data also supported the structure.

The IR spectrum of **35** showed a characteristic absorption at 1742 cm^{-1} due to the α-diketone moiety. In the ^1H NMR spectrum, the benzylic proton appeared as a double doublet at δ 3.29 (dd, J= 11.95, 6.20 Hz) and the bridgehead proton exhibited a multiplet between δ 3.65-3.58. In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 191.76 and 191.21 while the bridgehead carbons resonated at δ 63.54 and 48.10. All other signals were in agreement with the assigned structure. Analytical data also supported this structure.

After having studied the cycloaddition reactions of 3,5-di-*tert*-butyl-1,2-benzoquinone with various styrenes, we turned our attention to 3,5-bis(diphenylmethyl)-1,2-benzoquinone **23**, readily prepared by the sodium periodate oxidation of the corresponding catechol. The latter was obtained in 100% yield by the reaction of catechol with diphenyl methanol under acid catalysis.[13]

3,5-Bis(diphenylmethyl)-1,2-benzoquinone **23** undergoes cycloaddition with styrene to give the bicyclo[2.2.2]octenedione **36** (Scheme 13).



23 **20** **36**

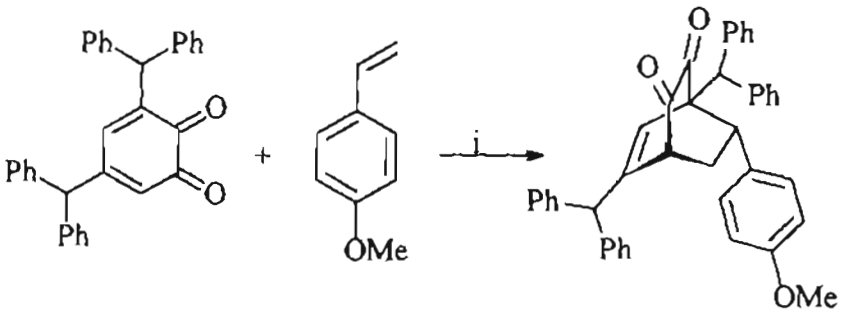
i. Neat, Sealed tube, 120 °C, 16 h, 64%

Scheme 13

The product was characterized on the basis of spectral data. The IR spectrum of **36** showed characteristic carbonyl absorption at δ 1735 cm^{-1}. In the ^{1}H NMR spectrum, the phenyl protons and the olefinic proton appeared as a multiplet between δ 7.39-6.61 integrating for twenty six protons. The two benzylic protons of the diphenylmethyl group were discernible at δ 5.71 as a singlet. The bridgehead proton resonated as a multiplet between δ 3.53-3.52 and the benzylic proton on the bicyclic framework resonated as a doublet at δ 3.45 (d, J= 2.50 Hz). The methylene protons appeared as two separate multiplets between δ 2.31-2.21 and 2.08-2.01 integrating for one proton each. In the ^{13}C NMR spectrum, the carbonyls were visible at δ 190.96 and 190.16 while the bridgehead carbons appeared at δ 58.92 and 51.61. All other signals were in agreement with the assigned structure. High resolution mass spectrum also supported the proposed structure.

The stereochemistry of the adduct **36** (Orange crystals, mp. 199 °C) was indirectly supported by its transformation to the isomer (Yellow crystals, mp. 192 °C), presumably, the thermodynamically more stable *exo* product.

In a similar way, 3,5-bis(diphenylmethyl)-1,2-benzoquinone underwent cycloaddition with 4-methoxystyrene to afford the bicyclo[2.2.2]octenedione **37** (Scheme 14).



23 **27** **37**

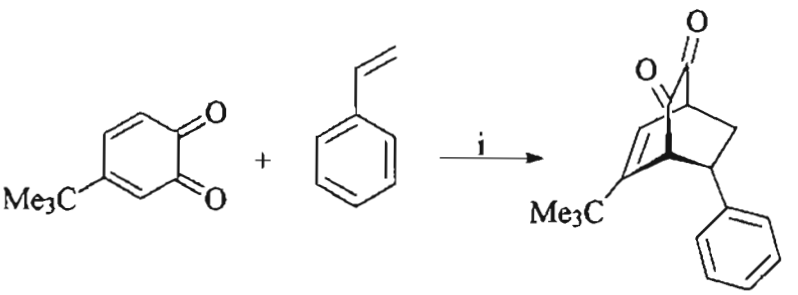
i. Neat, Sealed tube, 120 °C, 16 h, 62%

Scheme 14

The IR spectrum of **37** showed characteristic carbonyl absorption at 1748 cm^{-1}. In the ^{1}H NMR spectrum, the bridgehead proton appeared as a multiplet between δ 3.51-3.49 and the benzylic proton in the bicyclic framework exhibited a doublet at δ 3.40 (d, J= 2.26 Hz). In the ^{13}C NMR spectrum, the carbonyls were visible at δ 191.32 and 190.49. The two bridgehead and the methoxy carbons resonated at δ 59.21, 51.55 and 55.07 respectively. All other signals were in agreement with the assigned structure. High resolution mass spectrum also supported the structure.

Subsequent to the above investigations, we studied some cycloadditions involving 4-*tert*-butyl-1,2-benzoquinone **24**, easily obtainable from the corresponding catechol by routine oxidation with $NaIO_4$.

4-*tert*-Butyl-1,2-benzoquinone **24,** on heating with styrene in a sealed tube neat at 60 °C afforded the bicyclo[2.2.2]octenedione in 72% yield (Scheme 15).



24 **20** **38**

i. Neat, Sealed tube, 60 °C, 2.5 h, 72%

Scheme 15

The structure of the product was assigned on the basis of spectral data. IR spectrum of **38** showed a strong absorption at 1740 cm^{-1} due to the α-dione moiety. The regio- and stereochemical assignments of **38** were derived from extensive NMR analysis. The proton connectivity was established by 2D COSY experiments. 2D ^1H NMR spectroscopy was utilized to distinguish between the two possible regioisomers and to assign the signals in the 1D ^1H NMR spectrum and is explained in figures 3a and 3b.

^1H-^1H relayed COSY of **38** showed the through bond connectivities between the two different sets of hydrogen atoms. The hydrogen at δ 3.67 (m, bridgehead) is connected to the one at δ 6.25 (olefinic) and the methylene moieties at δ 2.56-2.46 (m) and 2.32-2.33 (m). All the ^1H-^{13}C connections were also identified. Of these, the most diagnostic were the connections between δ 38.82, 46.90, 58.53 and 120.77 (^{13}C) and δ 3.67, 3.55, 3.62 and 6.25 (^1H) respectively. In the ^1H NMR spectrum, the olefinic proton appeared as a double doublet at δ 6.27 (dd, J= 6.78, 1.23 Hz). The bridgehead proton vicinal to the phenyl group resonated as a double doublet

at δ 3.62 (dd, J= 6.0, 1.23 Hz) while the other bridgehead proton exhibited a multiplet at δ 3.67. The benzylic proton resonated as a multiplet at δ 3.55. In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 190.68 and 190.44 and the bridgehead carbons resonated at δ 58.53 and 46.90. All other signals were in agreement with the assigned structure.

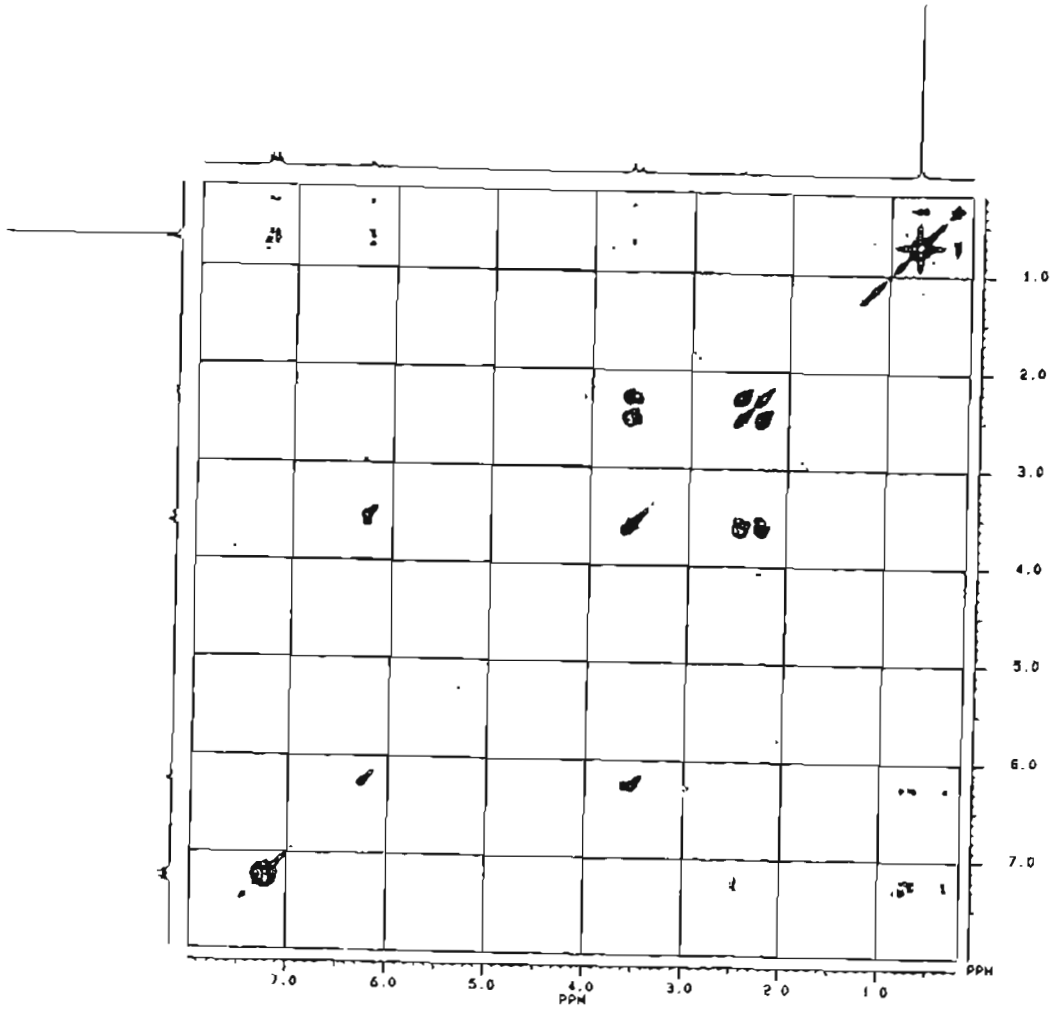


Figure 3a ^{1}H-^{1}H COSY spectrum of **38**

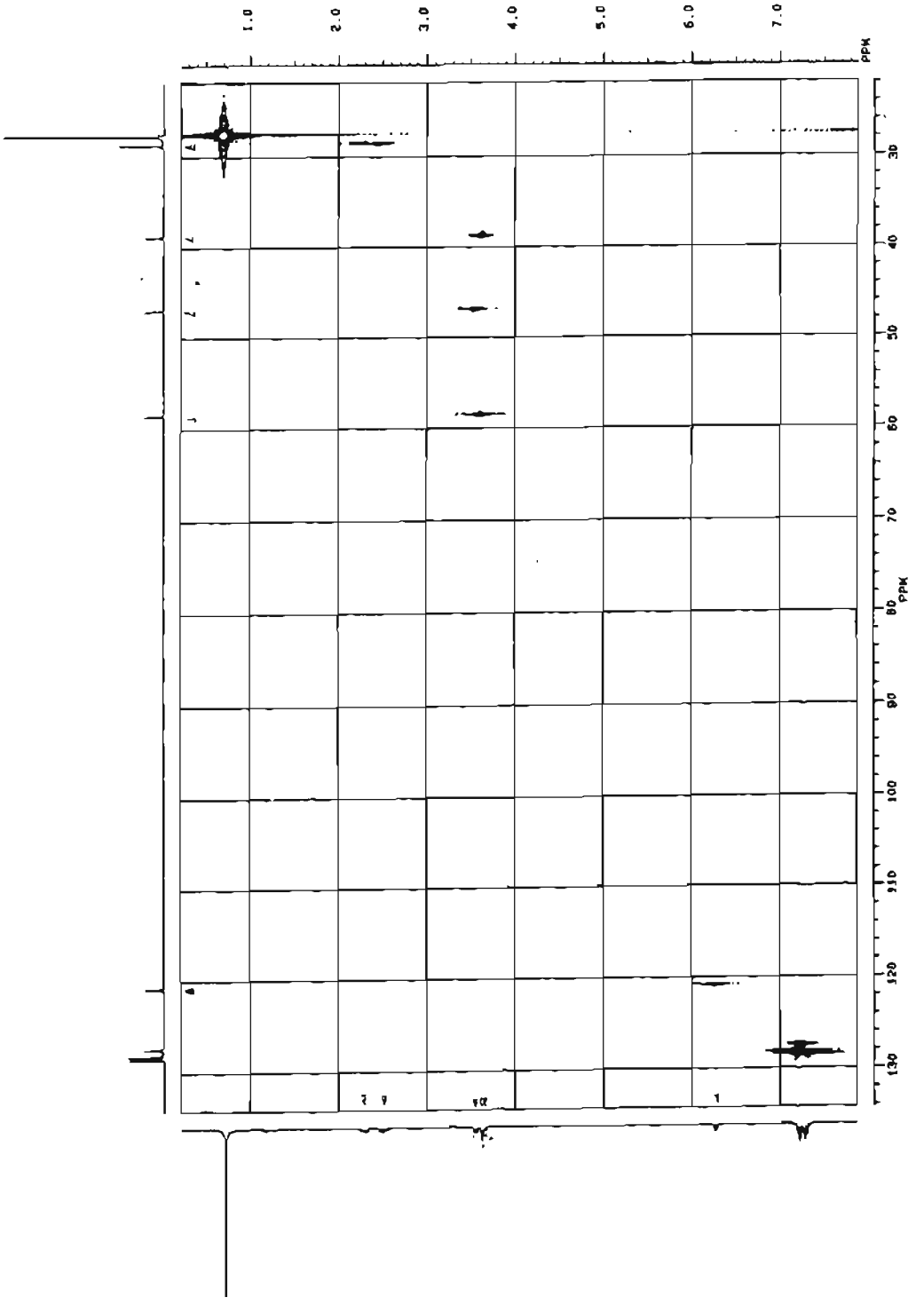
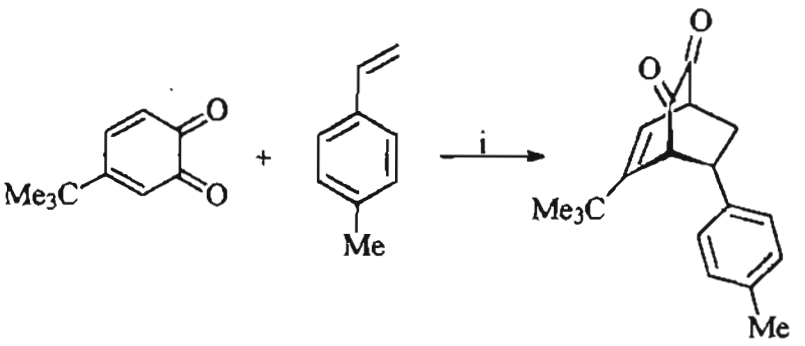


Figure 3b ^{13}C-^{1}H COSY spectrum of **38**

In a similar fashion, 4-*tert*-butyl-1,2-benzoquinone **24,** on reaction with 4-methylstyrene in a sealed tube at 60 °C, afforded bicyclo[2.2.2]octenedione in 43% yield (Scheme 16).



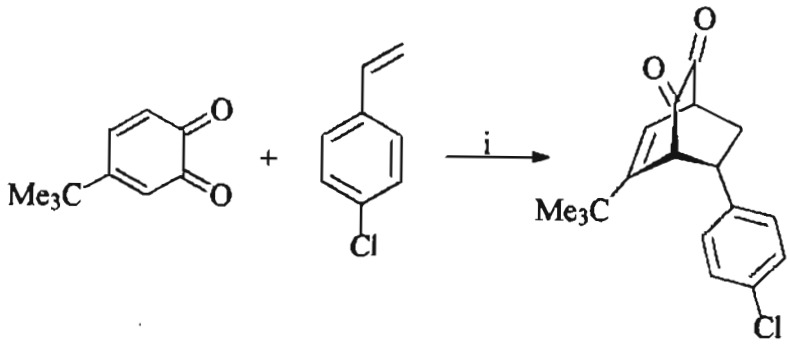
24 **33** **39**

i. Neat, Sealed tube, 60 °C, 5 h, 43%

Scheme 16

The structure of the product was established by spectral analysis. In the IR spectrum of **39,** the strong absorption at 1742 cm^{-1} is due to a 1,2-diketone moiety. In the ^{1}H NMR spectrum, the olefinic proton appeared as a double doublet at δ 6.26 (dd, J= 6.63, 1.44 Hz) and both the bridgehead protons resonated as a multiplet between δ 3.59-3.56. The signal due to the methyl group was discernible at δ 2.31 as a singlet. In the ^{13}C NMR spectrum, both the carbonyls were visible at δ 190.89 and 190.63 and the bridgehead carbon appeared at δ 58.55 and 46.95, whereas the methyl carbon appeared at δ 20.96. Elemental analysis also supported the assigned structure.

4-*tert*-Butyl-1,2-benzoquinone underwent Diels-Alder reaction with 4-chlorostyrene also to afford the bicyclo[2.2.2]octenedione **40** (Scheme 17).



24 **30** **40**

i. Neat, Sealed tube, 70 °C, 1 h, 45%

Scheme 17

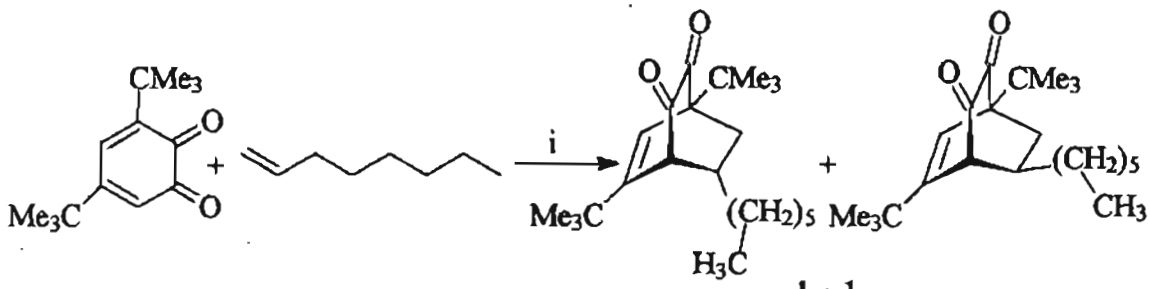
As usual, the structure of the product was ascertained from spectral and analytical data. The IR spectrum of **40** showed a strong absorption at 1735 cm^{-1} due to an α-dione moiety. In the ^1H NMR spectrum, the olefinic proton appeared as a double doublet at δ 6.19 (dd, J= 6.85, 1.98 Hz). The bridgehead proton vicinal to phenyl group resonated as double doublet at δ 3.50 (dd, J= 6.82, 1.98 Hz), while the other bridgehead proton was visible as a multiplet between δ 3.36-3.30. The ^{13}C NMR spectrum displayed the characteristic carbonyl resonances at δ 190.95 and 190.54 and the bridgehead carbons appeared at δ 55.13 and 49.41.

Reactions of 3-methoxy-1,2-benzoquinone as well as 4-methyl-1,2-benzoquinone with various styrenes were tried under a variety of conditions. These reactions, however, produced complex mixtures from which isolation of pure compounds was not possible. Reactions of 3,5-di-*tert*-butyl-1,2-benzoquinone with β-methyl as well as β-methoxystyrenes resulted in intractable mixture of products.

2.1.3 Cycloaddition reactions with alkenes

In view of the facility with which styrenes underwent cycloaddition to *o*-quinones, it was of interest to probe the reactivity of alkenes towards the latter. Some experiments were performed in this context and the results are presented in this section.

3,5-Di-*tert*-butyl-1,2-benzoquinone **5**, on treatment with 1-octene **41** in a sealed tube at 120 °C underwent cycloaddition to afford bicyclo[2.2.2]octenediones **42** and **43** in low yields as a 1:1 mixture of *endo/exo* isomers (Scheme 18).



5 **41** **42** **43**

i. Neat, Sealed tube, 120 °C, 18 h, 30%

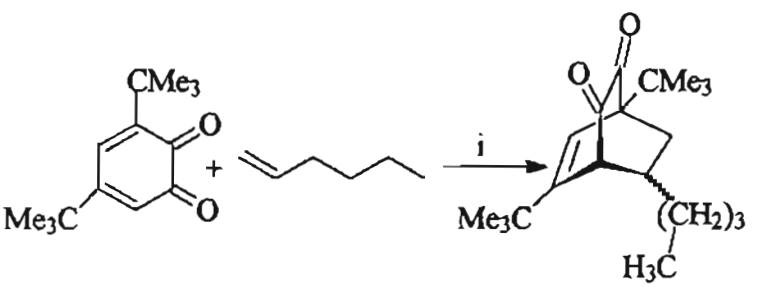
Scheme 18

The structures of the products were tentatively assigned on the basis of spectral and analytical data. The products were separated by Chromatotron® using 1% ethylacetate in hexane which afforded an orange colored liquid **42** and a yellow liquid **43**. IR spectrum of **42** showed a strong absorption at 1742 cm^{-1} due to an α-dione moiety. In the ^1H NMR spectrum, the bridgehead proton appeared as a singlet at δ 3.43. The methine proton appeared as a multiplet at δ 2.09 and the olefinic proton resonated at

δ 5.92 as a singlet. All the methylene protons were visible between δ 2.07-0.84 as a series of multiplets along with the two *tert*-butyl groups as singlets at δ 1.19 and 1.67. In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 192.15 and 190.53 and the bridgehead carbons appeared at δ 61.50 and 48.19. All other signals were in agreement with the assigned structure.

The IR spectrum of **43** showed characteristic absorption at 1742 cm^{-1} indicating an α-dione moiety. In the ^{1}H NMR spectrum, the bridgehead proton appeared as a singlet at δ 3.43 while the methine proton resonated as a double doublet at δ 2.11 (dd, J= 11.26 Hz, 13.41 Hz). In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 192.00 and 190.77 while the bridgehead carbons resonated at δ 57.33 and 53.88.

3,5-Di-*tert*-butyl-1,2-benzoquinone **5**, also underwent cycloaddition to 1-hexene to afford bicyclo[2.2.2]octenediones (Scheme 19).



5 **44** **45, 46**

i. Neat, Sealed tube, 110 °C, 12 h, 37%, (1:1)

Scheme 19

The product (a yellow liquid) was isolated as a mixture of stereoisomers. The structure of the products was tentatively assigned on the basis of spectral and analytical data.

Attempted reactions of 4-*tert*-butyl-1,2-quinones with alkenes resulted in the formation of dimer of the quinone, instead of the expected bicyclo adduct.

2.1.4 Theoretical Calculations

Frontier molecular orbitals (FMO)[14] and the equivalent approaches based on orbital correlation diagrams are widely recognized as being useful for the understanding of organic reactivity. The energies, relative atomic orbital coefficients and nodel characteristics of FMOs can be used to rationalize the rates as well as chemo-, regio- and stereoselectivities of various pericyclic reactions. Among the various mathematical approaches available for molecular energy calculations, we opted for the AM1 procedure which belongs to semiempirical molecular orbital method.[15] The energies corresponding to HOMO and LUMO of molecules concerned were obtained from eigen vectors. Molecular coefficients at the reacting centres are discerned from the magnitude of these vectors in XYZ directions. The major advantage of semiempirical procedure is that equilibrium geometries, heat of formation, reasonable wave function and bonding descriptions can be routinely calculated for even complex organic molecules.

In order to explain the observed reactivity and periselectivity in the above reactions, we have carried out some theoretical calculations using PC SPARTAN Graphical Interface Package for Molecular Mechanics and Molecular Orbital Models.[16] The correlation diagram for the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **5** with styrene **20** is provided as an illustrative example in figure 4.

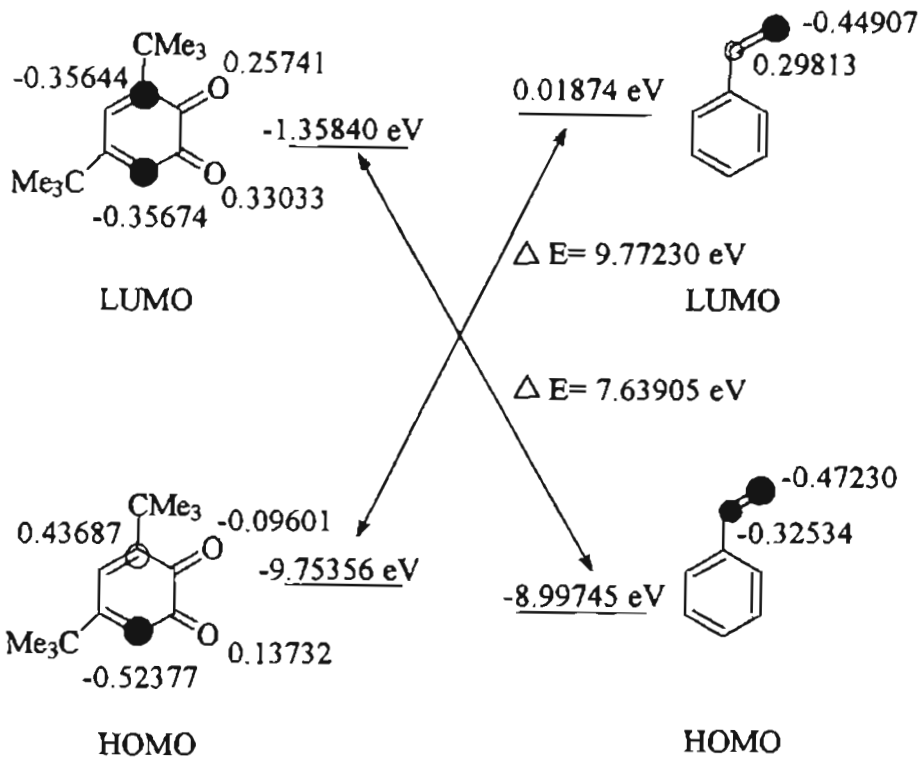


Figure 4. Molecular orbital correlation diagrams of 3,5-di-*tert*-butyl-1,2-benzoquinone with styrene

From the correlation diagram in figure 4, it is evident that the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone with styrene **20** follows inverse electron demand Diels-Alder pathway *i.e.* controlled by LUMO of diene (**5**). The size and sign of the orbital coefficients of the reacting carbon centres show that HOMO (**5**) - LUMO (**20**) interaction is unimportant due to large energy gap while HOMO (**20**) - LUMO (**5**) interaction is favorable.

In conclusion, our investigations have revealed that the [4+2] cycloaddition reaction of *o*-benzoquinones with styrenes is a very efficient process for the high yield synthesis of bicyclo[2.2.2]octenediones.

2.1.5 Experimental Details

All reactions were carried out in oven dried glassware under an atmosphere of argon. Melting points were recorded on a Büchi-530 melting point apparatus and were uncorrected. The IR spectra were recorded on a Perkin-Elmer model 882 infrared spectrophotometer and Nicolet Impact 400D infrared spectrophotometer, using potassium bromide pellets. NMR spectra were recorded on Jeol EX-90, Bruker-300 and Varian Unity-500 spectrometers using chloroform-d as solvent. The chemical shifts are given in the δ scale with tetramethylsilane as internal standard. Abbreviations used in ^{1}H NMR data are s: singlet, brs: broad singlet, d: doublet, t: triplet, q: quartet, dd: double doublet, m: multiplet and brm: broad multiplet. Elemental analyses were done using a Perkin-Elmer 2400 CHN analyzer. High-resolution mass spectra were obtained using Finnigan MAT model 8430 and the EIMS mass spectra from GCMS-MD 800 instrument. Ratio of the products was determined on the basis of HPLC analysis, which was performed on a Shimadzu LC-10AS instrument. Solvents used for experiments were dried and distilled according to literature procedure.

Analytical thin layer chromatography was performed on glass plates coated with silica gel (E. Merck) containing 13% calcium sulfate as the binder. Purification by gravity column chromatography was carried out using silica gel (100-200 mesh). Mixtures of ethylacetate and petroleum ether (60-80 °C) or hexane were used as eluents. The solvents were removed using a Büchi-EL rotary evaporator.

Diels-Alder adducts 25 and 26: 3,5-Di-*tert*-butyl-*o*-benzoquinone **5** (440 mg, 2 mmol) and styrene **20** (312 mg, 3 mmol) were heated in a Schlenk glass tube at 110 °C for 11 h. Chromatography of the reaction mixture on silica gel (100-200 mesh) using 2% ethyl acetate in hexane afforded **25** and **26** (622 mg, 96%). These adducts were recrystallised from dichloromethane/ hexane solvent system.

6-Phenyl-1,3-bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*endo* 25) Orange crystals (mp. 191-193 °C).

IR (KBr) : 2969, 2874, 1735, 1627, 1458, 1364, 1236, 1142 cm^{-1}.

^1H NMR : δ 7.27-7.12 (m, 5H), 6.10 (d, J= 2 Hz, 1H), 3.65-3.55 (m, 1H), 3.41 (dd, J= 10.04, 6.22 Hz, 1H), 2.70-2.38 (m, 1H), 2.12-1.88 (m, 1H), 1.55 (s, 9H), 0.89 (s, 9H).

^{13}C NMR : δ 191.56, 190.96, 152.90, 144.00, 129.68, 129.27, 128.40, 127.03, 126.76, 124.55, 63.48, 48.00, 46.30, 36.84, 35.61, 34.24, 27.53.

Anal. Calcd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70. Found: C, 81.39; H, 8.58.

6-Phenyl-1,3-bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*exo* 26) Yellow crystals (mp.177-179 °C).

IR (KBr) : 2956, 2877, 1732, 1617, 1466, 1365, 1242, 1156 cm^{-1}.

^1H NMR : δ 7.28-7.12 (m, 5H), 6.16 (d, J= 2, 1H), 3.67-3.57 (m, 1H), 3.50 (dd, J= 12.00, 6.2 Hz, 1H), 2.90-2.60 (m, 1H), 2.04-1.80 (m, 1H), 1.22 (s, 9H), 0.71 (s, 9H).

^{13}C NMR : δ 190.94, 190.40, 152.87, 144.00, 129.65, 128.31, 128.01, 127.21, 126.73, 124.52, 63.45, 47.97, 46.27, 36.81, 35.20, 34.21, 27.50.

HRMS Calcd for $C_{22}H_{28}O_2$: 324.20892. Found: 324.20836.

Crystal data of **26:** $C_{22}H_{28}O_2$. Fw 324.44. Crystal size 0.40 x 0.38 x 0.36 mm. Monoclinic. Space group $P2_1/c$. Unit cell dimensions a= 8.4436(1) Å, α= 90°; b= 19.033 Å, β= 103.183(1)°; c= 12.4493(1) Å, γ= 90°. R indices (all data) R1= 0.0769, wR2= 0.1459. Volume Z= 1947.92(3) $Å^3$, 4. D calc= 1.106 Mg/m^3. F (000)= 704. Absorption Coefficient= 0.069 mm^{-1}. Reflections collected= 37186. λ= 0.71073A°. (Sheldrick, G. M., Siemens, Analytical X-ray Division, Madison, WI, 1995).

Diels-Alder adducts 28 and **29**: 3,5-Di-*tert*-butyl-*o*-benzoquinone **5** (440 mg, 2 mmol) and 4-methoxystyrene **27** (348 mg, 2.6 mmol) were heated in a Schlenk glass tube at 120 °C for 10 h. The reaction mixture was subjected to chromatography on a silica gel column using 2% ethylacetate in hexane afforded **28** and **29** (326 mg, 92%) and were recrystallised from dichloromethane/ hexane solvent system.

6-(4-Methoxyphenyl)-1,3-bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*endo* 28) Orange crystals (mp.187-189 °C).

IR (KBr) : 2975, 2875, 1738, 1615, 1515, 1480, 1370, 1250, 1195, 1145, 1040 cm^{-1}.

^{1}H NMR : δ 7.12-6.73 (m, 4H), 6.12 (d, J= 2 Hz, 1H), 3.78 (s, 3H), 3.67-3.60 (m, 1H), 3.38 (dd, J= 10.25, 6.5 Hz, 1H), 2.75-2.69 (m, 1H), 1.89-1.84 (m, 1H), 1.22 (s, 18H).

^{13}C NMR : δ 191.39, 191.15, 158.79, 152.07, 137.58, 131.39, 129.64, 121.73, 115.34, 112.66, 61.79, 55.39, 48.80, 42.69, 37.39, 36.16, 34.47, 27.88.

Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.96; H, 8.47. Found: C, 77.65; H, 8.35.

6-(4-Methoxyphenyl)-1,3-bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*exo* 29) Yellow crystals (mp. 184-186 °C).

IR (KBr) : 2975, 2881, 1735, 1613, 1512, 1472, 1364, 1256, 1189, 1135, 1040 cm^{-1}.

^{1}H NMR : δ 7.06-6.63 (m, 4H), 6.07 (d, J= 1.5 Hz, 1H), 3.75 (s, 3H), 3.59-3.56 (m, 1H), 3.27 (dd, J= 12.5, 6.5 Hz, 1H), 2.53-2.47 (m, 1H), 1.98-1.94 (m, 1H), 1.11 (s, 18H).

^{13}C NMR : δ 192.00, 191.37, 158.59, 152.99, 136.04, 130.88, 128.21, 124.87, 115.37, 113.58, 63.73, 55.39, 48.26, 45.78, 37.07, 35.94, 34.48, 27.83.

Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.96; H, 8.47. Found: C, 77.72; H, 8.62.

Diels-Alder adducts 31 and 32: 3,5-Di-*tert*-butyl-*o*-benzoquinone **5** (440 mg, 2 mmol) and 4-chlorostyrene **30** (308 mg, 2.6 mmol) were heated in a Schlenk glass tube at 120 °C for 14 h. The cycloadducts **31** and **32** (304 mg, 90%) were isolated by column chromatography using 2% ethylacetate in hexane. These adducts were recrystallised from dichloromethane/ hexane solvent system.

6-(4-Chlorophenyl)-1,3-bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*endo* 31) Yellow crystals (mp. 174-176 °C).

IR (KBr) : 2971, 2913, 1731, 1615, 1495, 1400, 1368, 1236, 1196, 1145, 1095, 1017 cm^{-1}.

^1H NMR : δ 7.27-7.12 (m, 4H), 6.15 (d, J= 2 Hz, 1H), 3.68-3.65 (m, 1H), 3.50 (dd, J= 10.08, 6.13 Hz, 1H), 2.88-2.60 (m, 1H), 1.95-1.70 (m, 1H), 1.21 (s, 18H).

^{13}C NMR : δ 190.73, 190.37, 152.33, 144.15, 132.85, 131.50, 129.86, 129.12, 128.13, 121.33, 61.60, 48.53, 42.66, 37.17, 35.97, 34.30, 27.59.

Anal. Calcd for $C_{22}H_{27}O_2Cl$: C, 73.53; H, 7.52. Found: C, 73.44; H, 7.62.

6-(4-Chlorophenyl)-1,3bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*exo* 32) Yellow crystals (mp. 211-213 °C).

IR (KBr) : 2973, 2879, 1729, 1610, 1497, 1466, 1369, 1247, 1092, 1014 cm^{-1}

^1H NMR : δ 7.23-7.00 (m, 4H), 6.04 (d, J= 1.99 Hz, 1H), 3.60-3.49 (m, 1H), 3.33 (dd, J= 11.97, 6.15 Hz, 1H), 2.62-2.30 (m, 1H), 2.00-1.72 (m, 1H), 1.1 (s, 9H), 0.82 (s, 9H).

^{13}C NMR : δ 191.64, 190.87, 153.24, 142.77, 132.78, 131.14, 129.68, 128.72, 128.48, 124.57, 63.56, 48.05, 45.84, 36.89, 35.81, 34.41, 27.67.

Anal. Calcd for $C_{22}H_{27}O_2Cl$: C, 73.53; H, 7.52. Found: C, 73.82; H, 7.65.

Diels-Alder adducts 34 and **35**: 3,5-Di-*tert*-butyl-*o*-benzoquinone **5** (440 mg, 2 mmol) and 4-methylstyrene **33** (355 mg, 3 mmol) were heated in

a Schlenk glass tube at 120 °C for 14 h. The cycloadducts **34** and **35** (321mg, 95%) were isolated by column chromatography using 2% ethylacetete in hexane. These adducts were recrystallised from dichloromethane/ hexane solvent system.

6-(4-methylphenyl)-1,3-bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*endo* 34) Orange crystals (mp. 174-176 °C).

IR (KBr) : 2969, 2870, 1742, 1634, 1465, 1371, 1249, 1202, 1148, 1020, 939 cm^{-1}.

^1H NMR : δ 7.26-7.01 (m, 4H), 6.13 (d, J= 2 Hz, 1H), 3.66-3.63 (m, 1H), 3.39 (dd, J= 10.01, 6.30 Hz, 1H), 2.76-2.68 (m, 1H), 2.31 (s, 3H), 1.92-1.85 (m, 1H), 1.22 (s, 18H).

^{13}C NMR : δ 191.20, 190.94, 151.88, 142.55, 136.79, 130.29, 129.76, 128.61, 128.51, 121.65, 61.67, 48.68, 42.95, 37.29, 35.98, 34.34, 27.68, 20.99.

Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.36; H, 8.92.

6-(4-Methylphenyl)-1,3-bis(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*exo* 35) Yellow crystals (mp. 179-181 °C).

IR (KBr) : 2962, 2867, 1742, 1634, 1519, 1465, 1371, 1249, 1135, 1034, 936, 825 cm^{-1}.

^1H NMR : δ 7.26-7.01 (m, 4H), 6.08 (d, J= 2 Hz, 1H), 3.65-3.58 (m, 1H), 3.29 (dd, J= 11.95, 6.20 Hz, 1H), 2.55-2.46 (m, 1H), 2.31 (s, 3H), 2.01-1.95 (m, 1H), 1.12 (s, 18H).

^{13}C NMR : δ 191.76, 191.21, 152.88, 140.97, 136.53, 130.21, 129.67, 129.05, 126.97, 124.70, 63.54, 48.10, 46.01, 36.94, 35.73, 34.33, 27.64, 20.98.

Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.60; H, 8.93.

Diels-Alder adduct 36: 3,5-Bis(diphenylmethyl)-*o*-benzoquinone **23** (440 mg, 1 mmol) and styrene **20** (135 mg, 1.3 mmol) were heated in a Schlenk glass tube at 120 °C for 16 h. The cycloadduct **36** (348 mg, 64%) was isolated by column chromatography using 10% ethylacetate in hexane and recrystallised from dichloromethane/ hexane solvent system.

6-Phenyl-3,5-bis(diphenylmethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (36)

Orange crystals (mp. 197-199 °C).

IR (KBr) : 3022, 2955, 1735, 1593, 1485, 1445, 1222, 1088, 717 cm^{-1}.

^{1}H NMR : δ 7.39-6.61 (m, 26H), 5.71 (s, 2H), 3.53-3.52 (m, 1H), 3.45 (d, J= 2.50 Hz, 1H), 2.31-2.21 (m, 1H), 2.08-2.01 (m, 1H).

^{13}C NMR : δ 190.96, 190.16, 157.91, 141.11, 140.81, 140.66, 139.80, 139.44, 129.15, 128.79, 128.58, 127.27, 127.06, 58.92, 51.61, 50.95, 49.46, 43.94, 30.63.

HRMS Calcd for $C_{40}H_{32}O_2$: 544.24023. Found: 544.24012.

Diels-Alder adduct 37: 3,5-Bis(diphenylmethyl)-*o*-benzoquinone **23** (440 mg, 1 mmol) and 4-methoxystyrene **27** (174.2 mg, 1.3 mmol) were heated in a Schlenk glass tube at 120 °C for 16 h. The cycloadduct **37** (335 mg, 62%) was isolated by column chromatography using 10% ethylacetate in hexane and recrystallised from dichloromethane/ hexane solvent system.

6-(4-Methoxyphenyl)-3,5-bis(diphenylmethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (37) Orange crystals (mp. 218-220 °C).

IR (KBr) : 3016, 2962, 1748, 1600, 1499, 1452, 1263, 1189, 1094, 1040 cm^{-1}.

^1H NMR : δ 7.39-6.54 (m, 25H), 5.70 (s 2H), 3.69 (s, 3H), 3.51-3.49 (m, 1H), 3.40 (d, J= 2.26 Hz, 1H), 2.29-2.19 (m, 1H), 2.04-1.96 (m, 1H).

^{13}C NMR : δ 191.32, 190.49, 158.41, 140.69, 139.80, 139.44, 139.38, 133.00, 129.06, 128.88, 128.70, 128.52, 128.01, 127.21, 127.03, 114.14, 59.21, 55.07, 51.55, 50.89, 43.07, 30.54, 29.11.

HRMS Calcd for $C_{41}H_{34}O_3$: 574.25079. Found: 574.25001.

Diels-Alder adduct 38: 4-*tert*-Butyl-*o*-benzoquinone **24** (328 mg, 2 mmol) and styrene **20** (270 mg, 2.6 mmol) were heated in a Schlenk glass tube at 60 °C for 2.5 h. The cycloadduct **38** (386 mg, 72%) was isolated by column chromatography using 5% ethylacetate in hexane and recrystallised from dichloromethane/ hexane solvent system.

5-Phenyl-3-(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (38) Golden yellow crystals (mp. 175-177 °C).

IR (KBr) : 2970, 2876, 1740, 1610, 1473, 1367, 1265, 1244, 1207, 1144, 1098 cm^{-1}.

^1H NMR : δ 7.32-7.16 (m, 5H), 6.25 (dd, J= 6.78, 1.23 Hz, 1H), 3.67 (m, 1H), 3.62 (dd, J= 6.0, 1.23 Hz, 1H), 3.55 (m, 1H), 2.56-2.46 (m, 1H), 2.32-2.23 (m, 1H), 0.71 (s, 9H).

^{13}C NMR : δ 190.68, 190.44, 152.31, 141.97, 128.47, 128.17, 127.39, 120.77, 58.53, 46.90, 38.82, 35.19, 28.60, 27.61.

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.59; H, 7.46. Found: C, 80.11; H, 7.52.

Diels-Alder adduct 39: 4-*tert*-Butyl-*o*-benzoquinone **24** (328 mg, 2 mmol) and 4-methylstyrene **33** (355 mg, 3 mmol) were heated in a Schlenk glass tube at 60 °C for 5 h. The cycloadduct **39** (243 mg, 43%) was isolated using Chromatotron® by elution with 2% ethylacetate in hexane and recrystallised from hexane.

5-(4-Methylphenyl)-3-(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (39) Pale yellow solid (mp. 124-126 °C).

IR (KBr) : 2969, 2874, 1742, 1610, 1526, 1472, 1378, 1263, 1202, 1142, 1101 cm^{-1}.

^{1}H NMR : δ 7.08 (m, 4H), 6.26 (dd, J= 6.63, 1.44 Hz, 1H), 3.59-3.56 (m, 2H), 3.55-3.50 (m, 1H), 2.52-2.43 (m, 1H), 2.31 (s, 3H), 2.28-2.20 (m, 1H), 0.73 (s, 9H).

^{13}C NMR : δ 190.89, 190.63, 152.38, 138.90, 137.03, 129.13, 128.04, 120.74, 58.55, 46.95, 38.45, 35.21, 28.82, 27.70, 20.96.

Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.80; H, 7.86.

Diels-Alder adduct 40: 4-*tert*-Butyl-*o*-benzoquinone **24** (328 mg, 2 mmol) and 4-chlorostyrene **30** (308 mg, 2.6 mmol) were heated in a Schlenk glass tube at 70 °C for 1 h. The cycloadduct **40** (127 mg, 45%) was isolated using Chromatotron® by elution with 2% ethylacetate in hexane and recrystallised from dichloromethane/ hexane solvent system.

5-(4-Chlorophenyl)-3-(1,1-dimethylethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (40) Pale yellow solid (mp. 153-155 °C).

IR (KBr) : 2962, 2867, 1735, 1607, 1499, 1357, 1270, 1094, 1020 cm^{-1}.

^1H NMR : δ 7.26-6.97 (m, 4H), 6.19 (dd, J= 6.85, 1.98 Hz, 1H), 3.73-3.70 (m, 1H), 3.50 (dd, J= 6.82, 1.98 Hz, 1H), 3.36-3.30 (m, 1H), 2.46-2.36 (m, 1H), 2.20-2.13 (m 1H), 1.15 (s, 9H).

^{13}C NMR : δ 190.95, 190.54, 154.60, 140.44, 133.00, 129.14, 128.62, 120.95, 55.13, 49.41, 42.16, 35.75, 30.55, 27.59.

Anal. Calcd for $C_{18}H_{19}O_2Cl$: C, 71.28; H, 6.27. Found : C, 70.03; H, 6.38.

Diels-Alder adducts 42 and **43**: 3,5-Di-*tert*-butyl-*o*-benzoquinone **5** (330 mg, 1.5 mmol) and 1-octene **41** (220 mg, 0.3 mL, 2.25 mmol) were heated in a Schlenk glass tube at 120 °C for 14 h. The cycloadducts **42** and **43** (144 mg, 30%) were isolated in a ratio of 1:1 using Chromatotron® by elution with 2% ethylacetate in hexane.

Data for **42**: Orange liquid.

IR (neat) : 2962, 2867, 1742, 1485, 1378, 1243 cm^{-1}

^1H NMR : δ 5.92 (s, 1H), 3.43 (s, 1H), 2.07-1.07 (brm, 31H), 0.86 (t, J= 6.48 Hz, 3H).

^{13}C NMR : δ 192.15, 190.53, 153.63, 124.23, 61.50, 48.19, 37.62, 34.66, 31.71, 29.31, 27.94, 27.60, 22.57, 14.02.

Data for **43:** Yellow liquid.

IR (neat) : 2969, 2867, 1742, 1479, 1378, 1236 cm^{-1}

^{1}H NMR : δ 5.92 (s, 1H), 3.43 (s, 1H), 2.12-1.08 (brm, 31H), 0.08 (t, J= 6.31 Hz, 3H)

^{13}C NMR : δ 192.00, 190.77, 154.07, 122.21, 57.33, 53.88, 37.52, 35.77, 31.67, 31.37, 29.13, 27.71, 22.58, 14.04.

Diels-Alder adducts 45 and **46**: 3,5-Di-*tert*-butyl-*o*-benzoquinone **5** (330 mg, 1.5 mmol) and 1-hexene **44** (189 mg, 0.28 mL, 2.25 mmol) were heated in a Schlenk glass tube at 120 °C for 14 h. The cycloadducts **45** and **46** (168 mg, 37%) were isolated as a mixture using Chromatotron® by elution with 2% ethylacetete in hexane.

Data for **45** and **46**: Yellow liquid.

IR (neat) : 2962, 2874, 1732, 1482, 1362, 1233 cm^{-1}

^{1}H NMR : δ 6.15 (s, 2H), 4.48 (s, 2H), 1.56-0.85 (brm, 60H)

^{13}C NMR : δ 192.11, 190.50, 153.60, 124.20, 123.36, 61.47, 53.10, 48.15, 37.56, 35.58, 34.60, 34.33, 34.12, 31.48, 30.65, 29.56, 28.16, 27.90, 27.57, 22.68, 13.95.

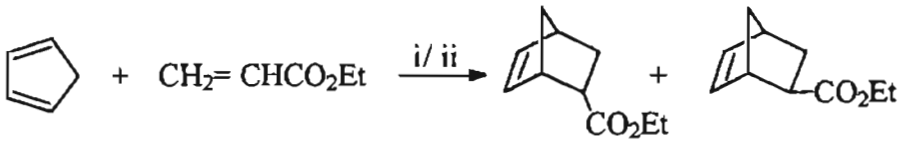
2.2 Cycloaddition reactions of *o*-benzoquinones with styrenes in presence of catalysts

2.2.1 Introduction

Many reactions can be influenced in a variety of ways by the solvent employed. A case to the contrary is the Diels-Alder reaction, which remains largely unaffected by the surrounding organic medium. In the mid-eighties, however, Breslow[17] as well as Grieco[18] demonstrated that Diels-Alder reactions proceed with rate enhancement and improved *endo-exo* selectivity when they are carried out in aqueous medium instead of organic solvents. In the case of conventional organic solvents, the rate enhancement and improved stereoselectivities were observed under ultra high pressure.[19] The effect is also enhanced by salts such as lithium chloride (salting-in effect), whereas the addition of guanidium chloride has the opposite effect (salting-out effect). The use of water as solvent for such cycloadditions had

already been described by Alder[20] and later by Koch[21]. The rate enhancement is attributed to a suitable aggregation induced by hydrophobic interactions between the reaction partners (hydrophobic effect). Conceivably, this phenomenon exercises an internal pressure on the reactants encapsulated in solvent cavities comparable to a high external pressure, especially in the case of Diels-Alder reactions.[22]

Grieco[23] has postulated that solvents that possess internal solvent pressure equal to or greater than that of water should provide comparable rate accelerations for intermolecular cycloaddition processes and described a solvent system, namely 5M solution of lithium perchlorate in diethyl ether (LPDE),[24] which has a comparable, if not greater accelerating effect on Diels-Alder reactions. He has observed that ethyl acrylate dissolved in a 5M solution of LPDE when treated with cyclopentadiene yielded the cycloadducts in high yield (Scheme 20).



47 **48** **49** **50**

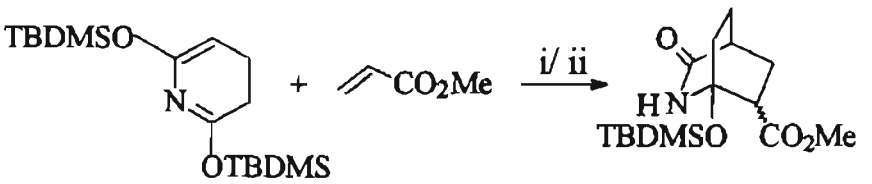
i. 5M $LiClO_4$, Et_2O, 5 h, 93%, *endo : exo* (8:1)

ii. H_2O, 5 h, 73%, *endo : exo* (4:1)

Scheme 20

Vast majority of organic compounds is insoluble in water and many others are water sensitive, thus precluding the use of water as a reaction medium. The 5M LPDE solvent system is devoid of such limitations and is effective in enhancing reaction rates as well as *endo* selectivity.

The rate acceleration effect of this reagent has been clearly demonstrated in the reaction of azadiene **51** with methyl acrylate **52**. The reaction occurs at room temperature in the presence of lithium salt to give the desired cycloadduct **53** in 80% yield in 5 h, whereas the same reaction in benzene afforded **53** in 75% yield only after 72 h at 60 °C (Scheme 21).[25]



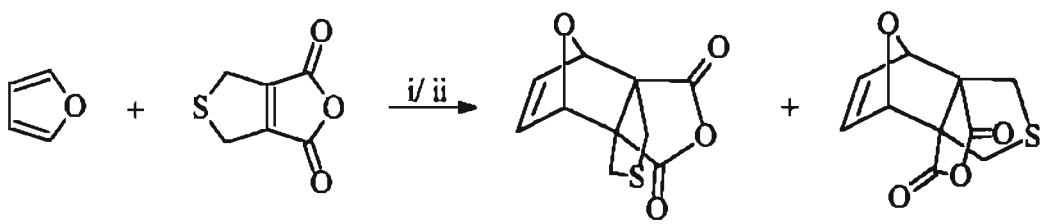
51 **52** **53**

i. 5M $LiClO_4$, Et_2O, 5 h, 80%, *endo* : *exo* (2.9:1)

ii. Benzene, 72 h, 60 °C, 75%, *endo* : *exo* (1 : 11.5)

Scheme 21

Another example illustrating the advantage of LPDE is the cycloaddition of furan **54** with the anhydride **55**.[26] This reaction in dichloromethane required 6 h under 15 Kbar of pressure in order to realize an 85:15 mixture of cycloadducts **56** and **57**. However, with 5M LPDE, the reaction proceeded at ambient temperature and pressure giving rise to the cycloadducts **56** and **57** (70%) in the same ratio after 9.5 h.[23]



54 **55** **56** **57**

i. CH_2Cl_2, 6 h, 15 Kbar, 100%, 56:57 (85:15)

ii. 5M $LiClO_4$, OEt_2, 9.5 h, 70%, 56:57 (85:15)

Scheme 22

A number of applications of the use of LPDE as a mild Lewis acid for cycloaddition reactions,[27] conjugate additions,[28] ring opening of epoxides,[29] ring expansion of cyclopropanes,[30] 1,3-sigmatropic rearrangements,[31] allylation of quinones with allyl silanes[32] etc. are known.

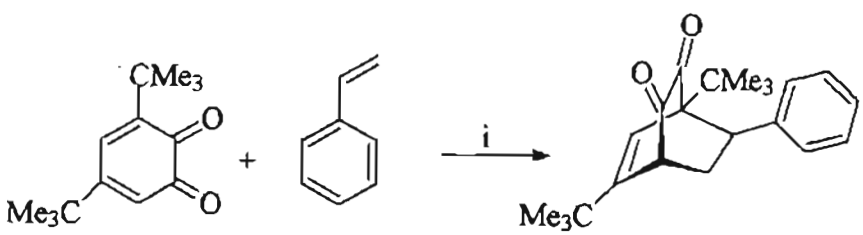
Several explanations of the acceleration effect of reactions in LPDE medium have been offered. We have already discussed the rate acceleration due to internal pressure in the LPDE medium.[23] Another explanation invokes catalysis by the Li^+ cation as a Lewis acid.[33-35] Forman and Dailey[33] have showed that the rate acceleration observed in LPDE medium is consistent with Li^+ catalysis of the Diels-Alder reaction. In addition, the accelerating effect of LPDE is not universal, suggesting that if a Diels-Alder reaction cannot be catalyzed by a Lewis acid, then LPDE may be of no value. Righetti[34] has shown that the rate increases as the salt concentration increases. This supports the view that catalysis promoted by a Li^+ acting as a Lewis acid is operating. Another explanation is the solvophobic interaction of the reagents just as observed in going from usual organic solvents to water or to salting-out water-salt solutions.[36] Kiselev has shown that the rate acceleration of cycloaddition reactions in presence of such Lewis acids as Aluminium, Gallium or Boron halides is due to the sharp increase of π acceptor properties of dienophiles and therefore increasing energy of orbital interaction, whereas LPDE medium demonstrates strong stabilization of static and/or dynamic polar forms and favors reaction with charge control.[36]

2.2.2 Results and Discussion

2.2.2.1 Cycloaddition reactions under the influence of Lithium trifluoromethane sulfonate (Lithium triflate)

With the expectation that coordination of the quinone carbonyls by Li^+ ions would alter the reactivity of the quinone and therefore the product distribution, it was of interest to investigate the cycloaddition of *o*-quinones with styrenes in the presence of a suitable lithium salt. Current literature describes a number of examples indicating facile cycloaddition in lithium perchlorate-diethyl ether medium (see introduction). With the latter, under mild conditions, high yields of products were obtained. Lithium perchlorate, however, has been responsible for several accidents, sometimes lethal.[37] The preparation of anhydrous lithium perchlorate from the commercially available (Aldrich) sample is also a tedious process.[23] In contrast, lithium triflate does not pose such problems and it was of interest to examine its effect on the rate acceleration and stereocontrol.

With the above objective 3,5-di-*tert*-butyl-1,2-benzoquinone **5** and styrene **20** were heated with 5M lithium triflate in acetonitrile and it was found that this reaction afforded only the *exo* isomer in high yield (Scheme 23).

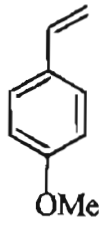
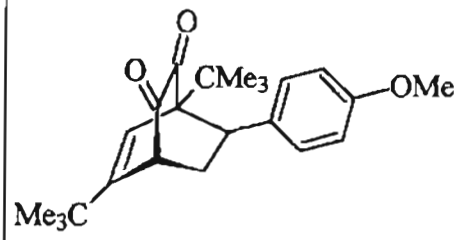
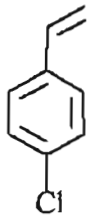
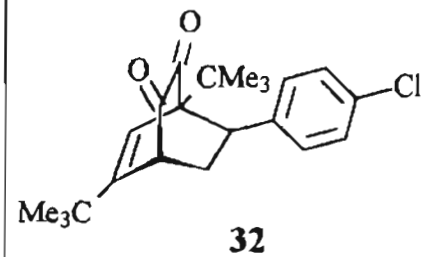
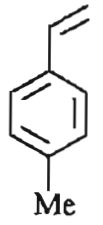
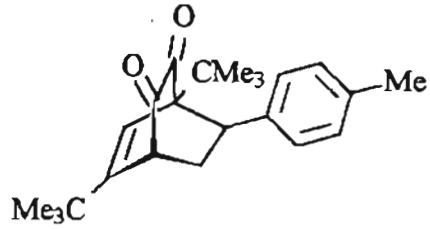


5 **20** **26**

i. 5M LiOTf/ CH_3CN, Reflux, 16 h, 92%

Scheme 23

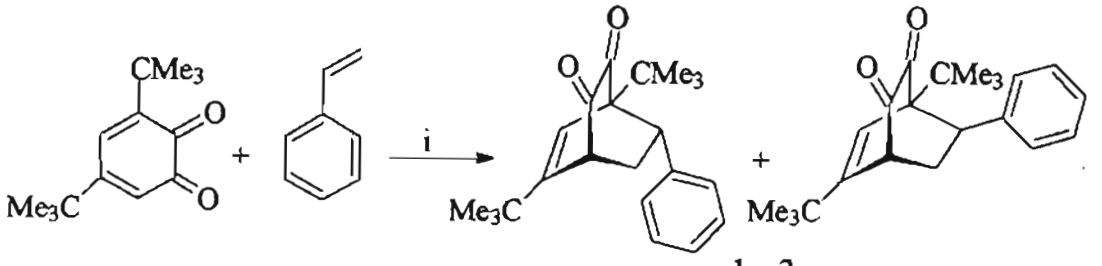
The reactions of **5** with substituted styrenes also proceeded in a similar fashion yielding only the *exo* isomer of bicyclo[2.2.2]octenediones in good yields. The results are summarized in Table 1.

Entry	Styrene	Reaction Conditions[1]	Product	Yield (%)[2]
1	 **27**	15 h	 **29**	95
2	 **30**	20 h	 **32**	85
3	 **33**	17 h	 **35**	91

1. Reflux, CH_3CN 2. Isolated yield

Table 1. Cycloaddition reactions of 3,5-di-*tert*-butyl-1,2-benzoquinone with styrenes in 5M LiOTf/ CH_3CN

For the sake of comparison, we have carried out the reaction of 3,5-di-*tert*-butyl-*o*-benzoquinone **5** with styrene **20** in 5M solution of lithium perchlorate in acetonitrile. In this case we obtained 98% of the adducts in the ratio 1:3 (*endo:exo*).



5 **20** **25** **26**

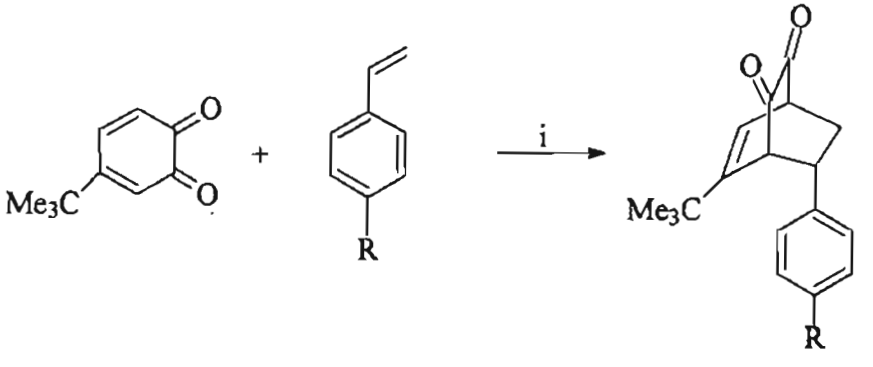
i. 5M $LiClO_4$/ CH_3CN, Reflux, 16 h, 98%

Scheme 24

From the above experiments it appears that lithium triflate may be a suitable substitute for the hazardous lithium perchlorate.

Interestingly, as expected the *endo* adduct **25** undergoes transformation to **26** on refluxing in acetonitrile containing 5M lithium triflate for 20 h, whereas **26** is stable.

Rate acceleration of the reaction of 4-*tert*-butyl-1,2-benzoquinone with styrene and 4-methylstyrene was also observed in presence of 5M lithium triflate yielding bicyclo[2.2.2]octenediones in high yields. The results are summarized in scheme 25.



24 **R= H, 20** **R= H, 38 (79%)**

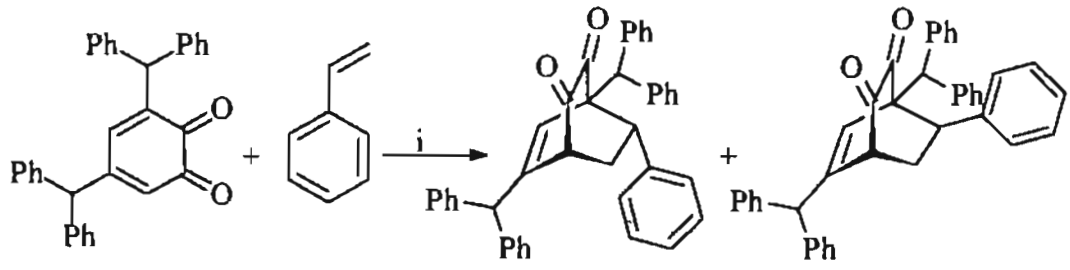
R= Me, 33 **R= Me, 39 (67%)**

i. 5M LiOTf/ CH_3CN, Reflux, 1 h

Scheme 25

It is noteworthy that the cycloaddition involving **24** and **20,** when carried out in the absence of lithium triflate in refluxing acetonitrile yielded only 30% of **38** even after 24 h, thus confirming the rate acceleration effect of lithium triflate.

In continuation of the above studies, we have investigated the reaction of 3,5-bis(diphenylmethyl)-1,2-benzoquinone **23** with styrene in presence of 5M lithium triflate in acetonitrile (Scheme 26).



23 **20** **36** **58**

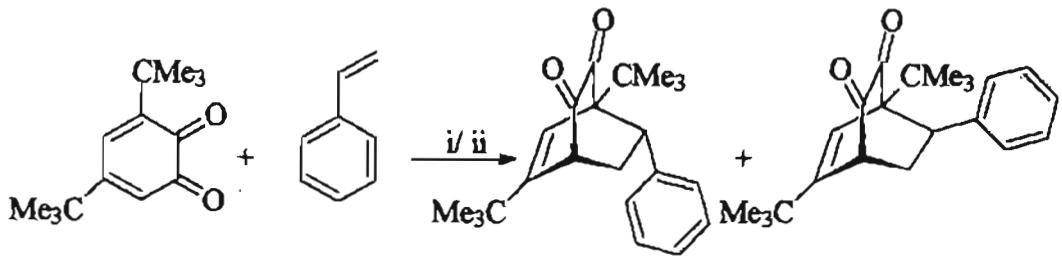
i. 5M LiOTf/ CH_3CN, Reflux, 24 h, 90%, *endo:exo* (2.5:1)

Scheme 26

In this case, for reasons that are not clear, both the products were obtained as a mixture of *exo* and *endo* adducts. These adducts were separated by fractional crystallization.

It was discerned from the literature that lithium ion concentration has an effect on the rate of the reaction. Therefore, in the course of our detailed investigation of cycloaddition reactions of *o*-benzoquinones with styrenes in lithium triflate/ acetonitrile system, we carried out a number of experiments with varying concentration of lithium ions. 3,5-Di-*tert*-butyl-1,2-benzoquinone **5** underwent facile cycloaddition reaction with styrene when treated with 3M lithium triflate in acetonitrile. Interestingly, under these

conditions, both the isomers are formed in the ratio 1.3:1 (*exo:endo*) and at 1M concentration the ratio is 1:1 (*exo:endo*).



5 **20** **25** **26**

i. 3M LiOTf/ CH_3CN, Reflux, 16 h, 60%, *endo:exo* (1:1.3)

ii. 1M LiOTf/ CH_3CN, Reflux, 16 h, 47%, *endo:exo* (1:1)

Scheme 27

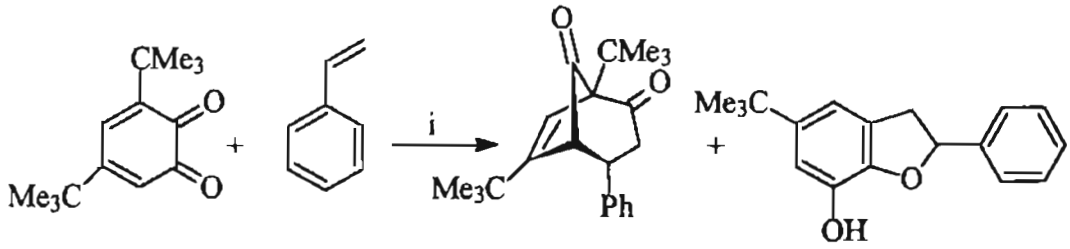
It is evident from the results that the stereochemistry of this reaction is affected by the lithium ion concentration in the reacting system. The exact reason for this is unknown.

In conclusion, an impressive rate acceleration of Diels-Alder reactions of *o*-benzoquinones with styrenes was achieved by using 5M lithium triflate in acetonitrile. Increasing the concentration of lithium ions in the system, increases the rate of the reaction as well as the formation of the thermodynamically stable *exo* product.

2.2.2.2 Reactions mediated by other Lewis acids

It has been known from the pioneering work of Yates and Eaton that Diels-Alder reactions are accelerated by the use of Lewis acids.[38,39] Lewis acids coordinate with the carbonyl of the quinone and thereby decrease the energy gap between the HOMO-LUMO interacting orbitals and

consequently enhance the rate of the cycloaddition reaction. In the light of this, we have carried out the cycloaddition reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **5** with styrene in presence of Lewis acids. 3,5-Di-*tert*-butyl-1,2-benzoquinone **5** on treatment with styrene **20** in presence of BF_3-etherate, afforded two products **59** (55%) and **60** (37%) in 92% yield (Scheme 28).



5 **20** **59** **60**

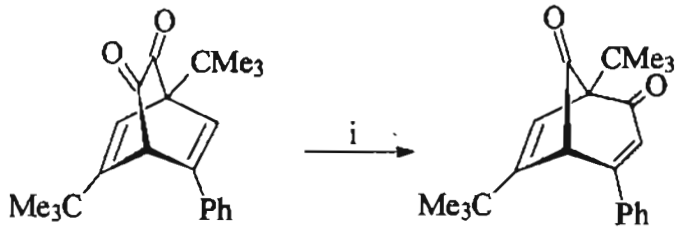
i. BF_3-OEt_2, $CHCl_3$, -10 °C, 2 h, 92%

Scheme 28

The structures of the products were assigned on the basis of spectral and analytical data. The IR spectrum of **59** showed two strong absorptions at 1763 and 1701 cm^{-1} due to the presence of two different carbonyl moieties. In the ^1H NMR spectrum, the phenyl protons appeared as a multiplet between δ 7.35-7.18. The olefinic proton resonated as a singlet at δ 6.03. The bridgehead proton appeared as a singlet at δ 3.60. The benzylic proton and one of the methylene protons appeared together as a multiplet at δ 3.30, whereas the other methylene proton resonated as a doublet at δ 2.52 (d, J= 10.2 Hz). The *tert*-butyl protons were visible as singlets at δ 1.15 and 0.71 integrating for nine protons each. In the ^{13}C NMR spectrum, the carbonyls were visible at δ 207.00 and 201.97 while the bridgehead carbons

resonated at δ 78.56 and 60.87. All other signals were in agreement with the assigned structure. Elemental analysis also supported this structure.

It can be surmised that **59** arises by an acid catalyzed rearrangement of the corresponding bicyclo[2.2.2]octenedione which is most likely the product of cycloaddition of styrene to 3,5-Di-*tert*-butyl-1,2-benzoquinone. Such rearrangements are well precedented and reminiscent of an earlier observation in our laboratory (Scheme 29).[40] For a detailed discussion of such reactions see section 3.2.



11 **61**

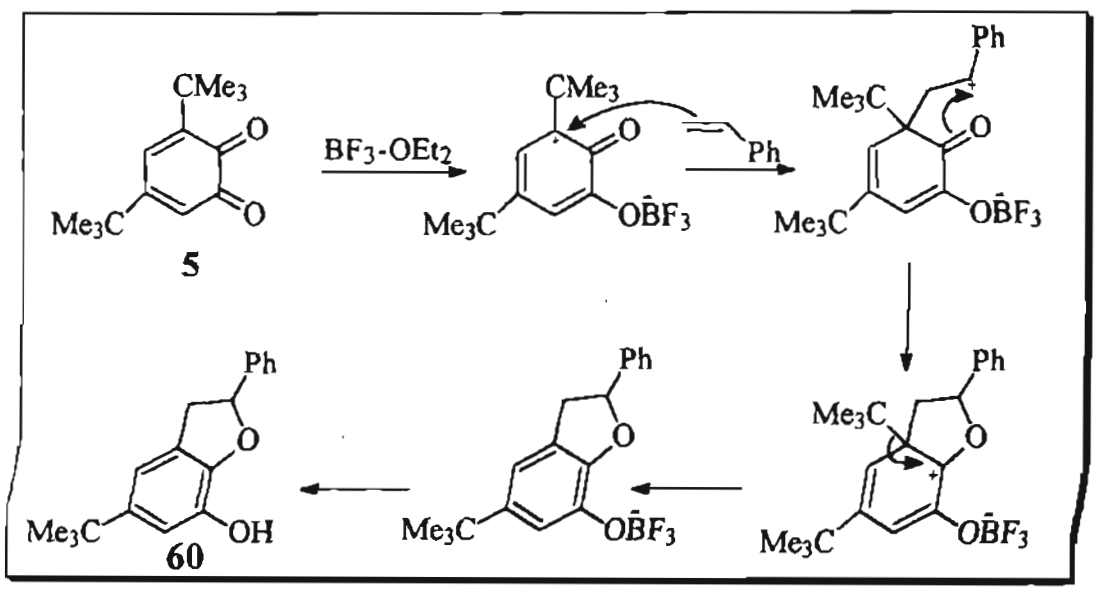
i. BF_3-OEt_2, $CHCl_3$, Reflux, 2 h, 92%

Scheme 29

The structure of the product **60** was assigned on the basis of spectral and analytical data. The IR spectrum of **60** was devoid of any carbonyl absorption. The absorption at 3481 cm^{-1} can be attributed to the presence of a hydroxyl group. In the ^1H NMR spectrum, the protons of the phenyl group appeared as a multiplet between δ 7.33-7.28 while the two protons in the benzene ring resonated as singlets at δ 6.78 and 6.72. The methine proton appeared as a triplet at δ 5.70 (t, J= 8.88 Hz). The methylene protons appeared as separate double doublets at δ 3.55 (dd, J= 15.30, 8.88 Hz) and at δ 3.20 (dd, J= 8.88, 15.30 Hz). The hydroxyl proton was visible as a singlet at δ 5.23, which was further confirmed by D_2O exchange study of **60**. The

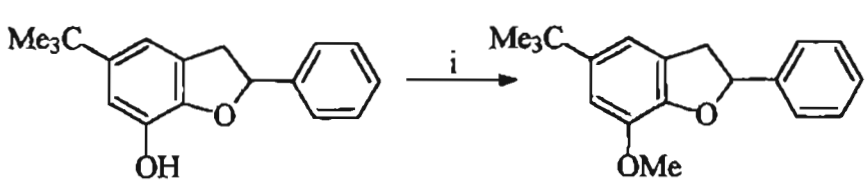
tert-butyl group resonated as a singlet at δ 1.27 integrating for nine protons. In the ^{13}C NMR spectrum, the benzylic carbon was visible at δ 85.07 and the methylenic carbon resonated at δ 39.30. All other peaks are in agreement with the assigned structure. Analytical data also supported this structure.

Regarding the mechanism of formation of **60** a rationalization as outlined in scheme 30 may be invoked.



Scheme 30

The compound **60** on treatment with methyl iodide in the presence of K_2CO_3 afforded the methyl ether **62** thus confirming the presence of a hydroxyl group in **60** (Scheme 31).



60 **62**

i. K_2CO_3, CH_3I, CH_3CN, 2 h, 86%

Scheme 31

The IR spectrum of **62** was devoid of hydroxyl absorption. In the ^{1}H NMR spectrum, the methoxy protons were visible at δ 3.89 as a singlet. In the ^{13}C NMR spectrum, the methoxy carbon appeared at δ 56.29. All other signals were in agreement with the assigned structure.

Reactions of 3,5-di-*tert*-butyl-*o*-benzoquinone with styrene as well as phenylacetylene were tried under a variety of conditions in the presence of various Lewis acids such as $ZnCl_2$, $AlCl_3$ and $TiCl_4$. These reactions were unsuccessful.

2.2.3 Experimental Details

General information about the experiments is given in 2.1.3.

Typical experimental procedure for lithium triflate reaction: To a 5M solution of lithium triflate in dry acetonitrile (4 mL), 3,5-di-*tert*-butyl-*o*-benbzoquinone **5** (440 mg, 2 mmol) and styrene **20** (312 mg, 3 mmol) were added and the mixture was refluxed under argon atmosphere for 16 h. The reaction mixture was diluted with water (20 mL), extracted with dichloromethane (2 x 20 mL) and the organic layer was dried over Na_2SO_4. The solvent was evaporated off and the residue on chromatography using 2% ethyl acetate in hexane afforded **26** (596 mg, 92%) as a yellow crystalline solid (mp. 177-179 °C).

Diels-Alder adduct 36 and 58

To a 5M solution of lithium triflate in dry acetonitrile (4 mL), 3,5-bis(diphenylmethyl)-*o*-benzoquinone **23** (440 mg, 1 mmol) and styrene **20** (135 mg, 1.3 mmol) were added and the mixture was refluxed under argon atmosphere for 24 h. The usual work up followed by chromatographic purification on a silica gel column using 10% ethyl acetate in hexane as eluent afforded the products **36** and **58** (489 mg, 90%) and were separated by fractional crystallization using dichloromethane/ hexane as solvent system.

6-Phenyl-3,5-bis(diphenylmethyl)bicyclo[2.2.2]oct-2-ene-7,8-dione (*exo* 58) Yellow crystals (mp. 191-193 °C).

IR (KBr) : 3024, 2930, 1732, 1595, 1495, 1445, 1270, 1083, 1026 cm^{-1}.

^1H NMR : δ 7.36-6.43 (m, 26H), 5.70 (s, 1H), 5.24 (s, 1H), 3.51-3.49 (m, 1H), 3.38-3.33 (m, 1H), 2.29-2.20 (m, 1H), 1.92-1.90 (m, 1H).

^{13}C NMR : δ 190.96, 189.88, 141.84, 141.00, 140.58, 139.35, 139.42, 139.35, 138.28, 129.12, 129.07, 128.73, 128.50, 127.71, 127.42, 127.00, 126.78, 59.16, 53.67, 51.55, 50.49, 40.03, 29.20.

BF_3-OEt_2 induced rearranged products 59 and 60

To a solution of 3,5-di-*tert*-butyl-*o*-benzoquinone **5** (220 mg, 1 mmol) and styrene **20** (124 mg, 1.2 mmol) in dry chloroform, BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) was added and the mixture stirred for 2 h at -10 °C. On completion of the reaction, the mixture was stirred with a few drops of water and extracted with dichloromethane (4 x 15 mL). The extract

was dried over anhydrous sodium sulfate and concentrated. The crude product was then purified by chromatography on silica gel column using 2% ethylacetate in hexane as eluent to afford the products **59** (178 mg, 55%) and **60** (99 mg, 37%).

Data for 59 Colorless crystals (mp. 179-181 °C).

IR (KBr) : 2956, 2868, 1763, 1701, 1495, 1457, 1357, 1076 cm^{-1}.

^1H NMR : δ 7.35-7.18 (m, 5H), 6.03 (s, 1H), 3.60 (s, 1H), 3.30 (m, 2H), 2.52 (d, J= 10.2 Hz, 1H), 1.15 (s, 9H), 0.71 (s, 9H).

^{13}C NMR : δ 207.00, 201.97, 153.83, 139.07, 128.65, 127.19, 127.05, 126.84, 78.56, 60.87, 39.75, 36.90, 33.26, 32.50, 29.19.

EIMS *m/z* : 324 (M^+, 29), 309 (10), 268 (24), 240 (10), 131 (100), 91 (9).

Data for 60 Greenish yellow liquid

IR (neat) : 3481, 2969, 2867, 1620, 1506, 1324, 1196 , 1061 cm^{-1}.

^1H NMR : δ 7.33-7.28 (m, 5H), 6.78 (s, 1H), 6.72 (s, 1H), 5.70 (t, J= 8.88 Hz, 1H), 5.23 (s, 1H), 3.55 (dd, J = 15.30, 8.88 Hz, 1H), 3.20 (dd, J = 15.30, 8.88 Hz, 1H), 1.27 (s, 9H).

^{13}C NMR : δ 145.32, 143.87, 141.51, 139.16, 128.53, 128.03, 126.60, 125.79, 113.24, 112.55, 85.07, 39.30, 34.36, 31.68.

EIMS *m/z* : 268 (M^+, 48), 253 (100), 165 (4), 91 (8).

Data for 62

To a solution of **60** (268 mg, 1 mmol) in dry acetonitrile (10 mL) was added methyl iodide (212 mg, 2 mmol) followed by potassium carbonate (166 mg, 1.2 mmol) and stirred it for 2 h. The usual work up followed by

chromatographic purification on a silica gel column using 1% ethyl acetate in hexane as eluent afforded the product **62** (242 mg, 86%) as a liquid.

IR (neat) : 2956, 2868, 1601, 1489, 1457, 1320, 1195, 1108, 1083 cm^{-1}.

^1H NMR : δ 7.39-7.21 (m, 5H), 6.82 (s, 1H), 6.80 (s, 1H), 5.75 (t, J= 8.66 Hz, 1H), 3.89 (s, 3H), 3.59 (dd, J= 15.34, 8.66 Hz, 1H), 3.22 (dd, J = 15.34, 8.66 Hz, 1H), 1.30 (s, 9H).

^{13}C NMR : δ 145.82, 144.90, 143.50, 141.88, 128.48, 127.89, 127.24, 125.98, 113.93, 109.68, 84.84, 56.29, 39.12, 34.60, 31.77.

EIMS *m/z* : 282 (M^+, 45), 267 (100), 165 (7), 91 (11).

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CHAPTER 3

SYNTHETIC APPLICATIONS OF BICYCLO[2.2.2]OCTENEDIONES

This chapter is divided into three sections. The first section deals with the photolysis of the bicyclo[2.2.2]octenediones derived from the cycloaddition reactions of *o*-benzoquinones with various styrenes. The second section describes the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones to form bicyclo[3.2.1]octenediones. The third section comprises the ring opening reactions of the latter by methanolic KOH.

3.1 Photolysis of bicyclo[2.2.2]octenediones

3.1.1 Introduction

Bicyclo[2.2.2]octenediones readily obtainable from *o*-benzoquinones (see chapter 2) appeared to be interesting from the point of view of a number of interesting and possibly useful synthetic transformations. Initially we focused our attention on the photolytic decarbonylation of these adducts and the results of our investigations are presented in this section.

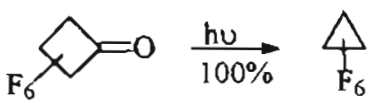
Photochemistry is concerned with chemical change that occurs through the electronically excited state of molecules. By far the most widely used method of generating such excited states is through the absorption by a molecule of one photon of visible or ultraviolet light. In this section we deal with photoextrusion of molecules, which is a Norrish type I cleavage.

Photoextrusion can be envisaged as a formal ring contraction due to the removal of small molecules like N_2, CO_2, CO, SO_2 etc. This is an interesting process because in many cases it leads to a structural framework that is inaccessible by conventional synthesis.[1]

Photoextrusion of carbon monoxide from cyclic ketones is one of the earliest extrusion reactions known. It has been the subject of numerous mechanistic studies and has found some synthetic applications.[2-8] The reaction proceeds *via* a homolytic fragmentation of the n, π^* singlet or sometimes a triplet, followed by the extrusion of carbon monoxide through a second homolytic step. It is generally accepted that the process takes place in two steps involving sequential homolysis of the ring bonds leading to the

intermediate diradical. The initial homolysis product, the acyl radical, undergoes a second homolysis in competition with other free radical processes like disproportionation, recombination etc.[6]

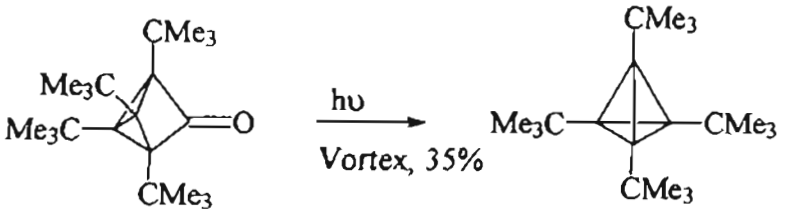
Photoextrusion reaction has been successfully employed for the construction of small strained molecules. England has reported that hexafluorocyclobutanone **1** on photolysis yielded cyclopropane derivative **2** quantitatively (Scheme 1).[7]



1 **2**

Scheme 1

Another example is the synthesis of tetra-*tert*-butyltetrahedrane **4** (Scheme 2).[9]



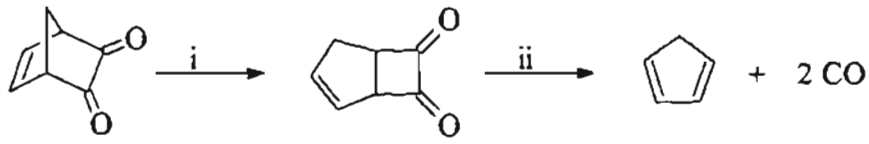
3 **4**

Scheme 2

Photolysis of cyclic aliphatic ketones yield not only the decarbonylated product but other products also; several of these have important synthetic utility. The particular reaction that occurs depend on the size of the ring, the substitution pattern and the conditions under which photolysis is carried out. In the case of cyclopropanes, the major process is

the decarbonylation that gives rise to carbon monoxide and a simple alkene. Cyclobutanones undergo three types of photoreactions.[10] The unusual photochemistry of cyclobutanones has been explained on the basis of ring strain and symmetry considerations.[3] Moreover, the stability of the decarbonylated radical and the availability of a β-H atom for ketene or aldehyde formation also play an important role in the formation of the product. The larger and medium sized ketones show little propensity towards decarbonylation while the bicyclic ketones with carbonyl on the bridgehead undergo decarbonylation efficiently due to the release of ring strain.[11]

Diketones undergo double decarbonylation under photolytic conditions giving the corresponding alkenes. In some cases a rearrangement takes place at first, followed by decarbonylation as illustrated in scheme 3.[12]

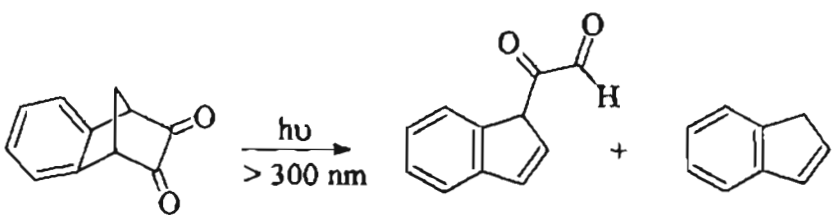


5 **6** **7**

i. hυ, 404 nm. ii. hυ, 436 nm.

Scheme 3

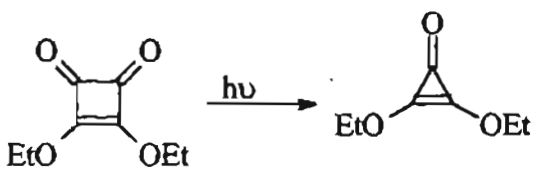
In the benzo series, hydrogen abstraction competes with decarbonylation affording glyoxals.[12] Here the product formation is wavelength dependent and at shorter wavelengths, decarbonylation is the major reaction (Scheme 4).



8 **9** **10**

Scheme 4

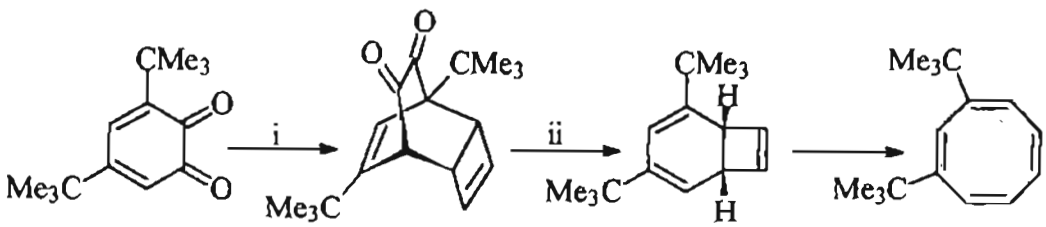
West has accomplished the conversion of diethylsquarate **11** to diethyldeltate **12** by photoextrusion of carbon monoxide (Scheme 5).[13]



11 **12**

Scheme 5

Paquette has used the photolytic double decarbonylation methodology in the synthesis of cyclooctatetraenes. The cyclobutadiene generated *in situ* from the iron tricarbonyl complex by CAN oxidation has been trapped with the quinone as a [4+2] adduct **14**. The latter under photolytic conditions eliminates two molecules of carbon monoxide and the resulting triene **15** undergoes electrocyclic ring opening to afford the cyclooctatetraene (Scheme 6).[14,15]



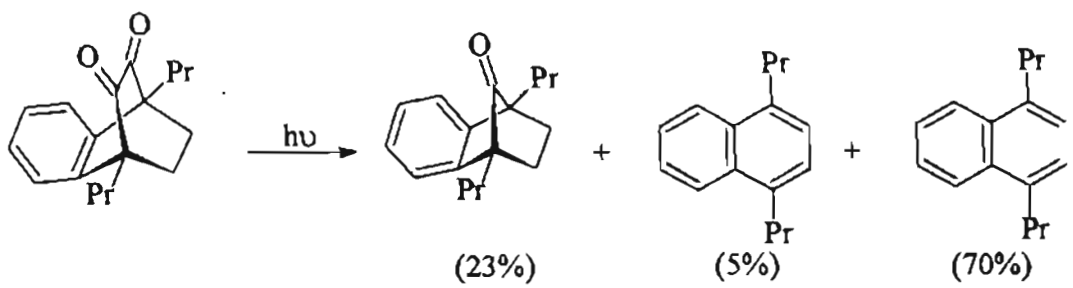
13 14 15 16

i. Fe(CO)3, CAN ii. hυ

Scheme 6

There is an isolated report of photodecarbonylation of certain bicyclic α-diones leading to phthalic acid derivatives.[16] In a limited investigation, Friedrichsen has reported a few examples of photodecarbonylation of Diels-Alder adducts obtained from methyl-*o*-benzoquinones and symmetrical diaryl fulvenes.[17]

Liao and Ueng have reported that the photolysis of the benzobicyclo[2.2.2]octenedione **17** afforded the monodecarbonylated product **18** along with **19** and **20**. Detailed mechanistic postulates have been proposed by these authors to account for the different products (Scheme 7).[18]

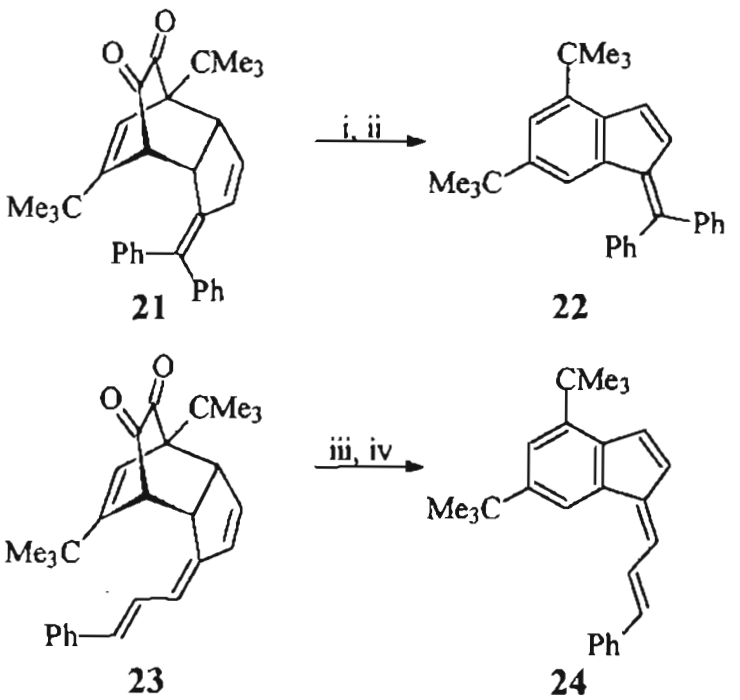


(23%) (5%) (70%)

17 **18** **19** **20**

Scheme 7

It is evident from the literature survey that there are only limited investigations on the photodecarbonylation of α-diones. Reports from our laboratory have explored the generality and synthetic utility of such reactions with certain bicyclo[2.2.2]octenediones (Scheme 8).[19,20]



i. hυ, Pyrex, Cyclohexane, 1 h, 92% ii. DDQ, Benzene, Reflux, 5 h, 80%

iii. hυ, Pyrex, Cyclohexane, 2 h, 72% iv. DDQ, Benzene, Reflux, 1 h, 34%

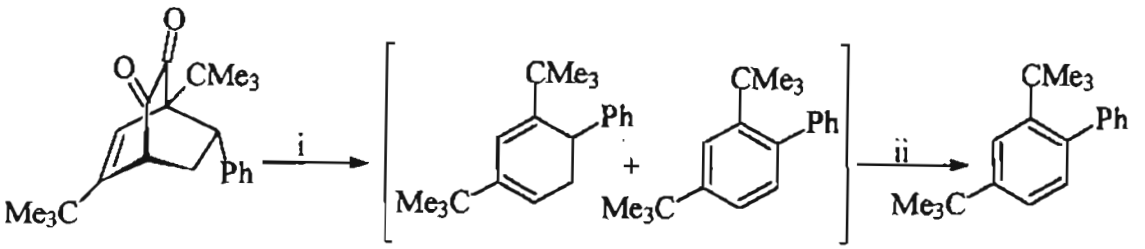
Scheme 8

Our present studies are concerned with the decarbonylation reactions of bicyclo[2.2.2]octenediones derived from the cycloaddition reactions of *o*-benzoquinones with styrenes.

3.1.2 Results and discussion

The substrates used for the investigations were synthesized by the cycloaddition reactions of *o*-benzoquinones with styrenes as described in chapter 2.

Initially we investigated the decarbonylation of the Diels-Alder adduct **27** obtained by the cycloaddition of 3,5-di-*tert*-butyl-1,2-benzoquinone and styrene (Scheme 9).



25 **26** **27** **27**

i. hυ, Pyrex, Cyclohexane, 2 h, 70% ii. DDQ, Xylene, Reflux, 24 h, 60%

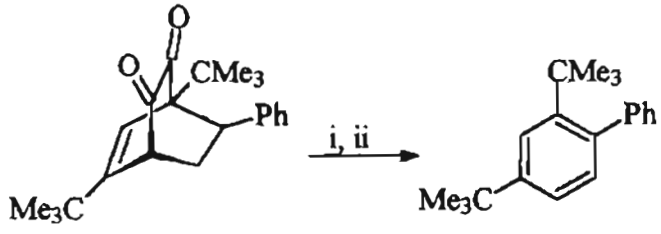
Scheme 9

A cyclohexane solution of the α-dione **25** on irradiation, using a medium pressure mercury vapor lamp, afforded the double decarbonylated product **26** along with its dehydrogenated product **27** (identified by GC analysis). The products **26** and **27** could not be separated by column chromatography due to their highly nonpolar nature. The mixture on filtration through a silica gel column, using petroleum ether as eluent followed by DDQ oxidation in xylene, under reflux conditions, afforded the substituted biphenyl **27** exclusively.

The product was characterized by spectral analysis. The IR spectrum of **27** was devoid of any carbonyl absorption. The two *tert*-butyl groups

resonated at δ 1.44 and 1.28 as two singlets integrating for nine protons each. The proton ortho to the phenyl group appeared at δ 7.01 as a doublet (d, J= 8.60 Hz). The rest of the protons appeared together as multiplet. The mass spectrum displayed a molecular ion peak at *m/z* 266. All other signals were in agreement with the assigned structure.

The cycloadduct **28**, the stereoisomer of **25**, under similar conditions furnished the biphenyl derivative **27** in high yield (Scheme 10).



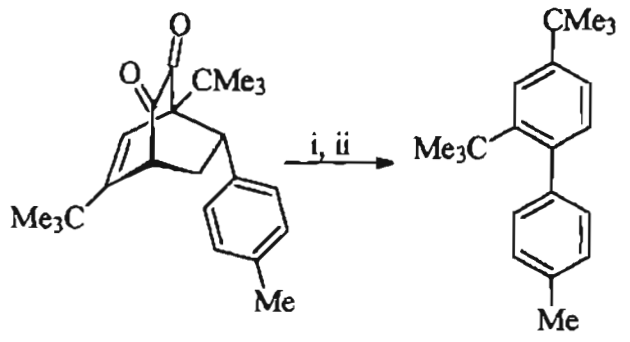
28 **27**

i. hυ, Pyrex, Cyclohexane, 2 h, 90% ii. DDQ, Xylene, Reflux, 24 h, 83%

Scheme 10

The product was characterized on the basis of spectral and analytical data. All the signals were in agreement with the assigned structure.

The cycloadduct **29** on irradiation followed by DDQ oxidation afforded the substituted biphenyl **30** (Scheme 11).



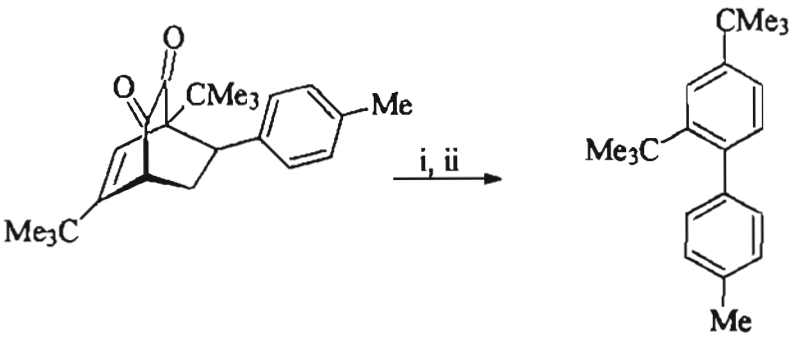
29 **30**

i. hυ, Pyrex, Cyclohexane, 2 h, 76% ii. DDQ, Toluene, Reflux, 3 days, 59%

Scheme 11

The structure of the product was ascertained on the basis of spectral and analytical data. The IR spectrum of **30** showed no carbonyl absorption. In ^{1}H NMR spectrum, the two *tert*-butyl groups resonated at δ 1.35 and 1.19 as two singlets integrating for nine protons each. The proton *ortho* to the 4-methyl phenyl group appeared at δ 6.92 as a doublet (J= 7.83 Hz). Rest of the aromatic protons resonated as multiplet. The methyl protons were visible at δ 2.38 as a singlet. In the ^{13}C NMR spectrum, the methyl carbon was discernible at δ 21.17. All other signals were in good agreement with the assigned structure. The molecular ion peak at *m/z* 280 also supported this structure.

In a similar manner, the dione **31**, stereoisomer of **29,** on photolysis in cyclohexane solution afforded the substituted biphenyl **30** (Scheme 12).



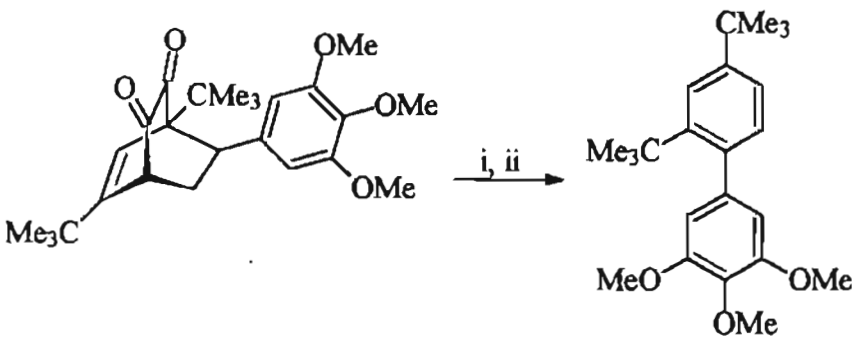
31 **30**

i. hυ, Pyrex, Cyclohexane, 2 h, 70% ii. DDQ, Toluene, Reflux, 3 days, 50%

Scheme 12

The structure of the compound **30** was assigned on the basis of spectral and analytical data as described previously.

The bicyclic dione **32** obtained by the Diels-Alder reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone and 3,4,5-trimethoxy styrene, was subjected to irradiation followed by DDQ oxidation to afford the biphenyl derivative **33** (Scheme 13).



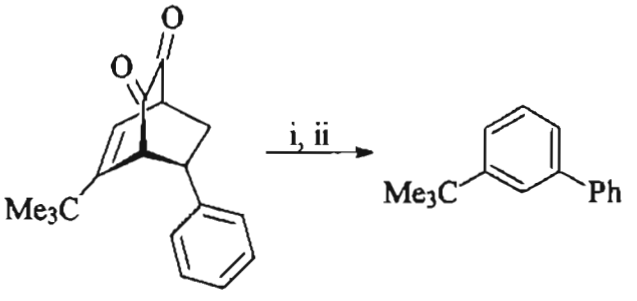
32 **33**

i. hυ, Pyrex, Cyclohexane, 1.5 h, 60% ii. DDQ, Benzene, Reflux, 5 h, 41%

Scheme 13

The product **33** was characterized by spectral analysis. The IR spectrum of **33** was devoid of carbonyl absorption. In the ^{1}H NMR spectrum, the three methoxy groups appeared as singlets at δ 3.81, 3.80 and 3.79. In the ^{13}C NMR spectrum, the methoxy carbons resonated at δ 60.85, 55.95 and 55.84. All other signals were in agreement with the assigned structure. The molecular ion peak at *m/z* 356 also supported this structure.

Similarly, irradiation of **34** followed by DDQ oxidation afforded the biphenyl derivative **35** (Scheme 14).



34 **35**

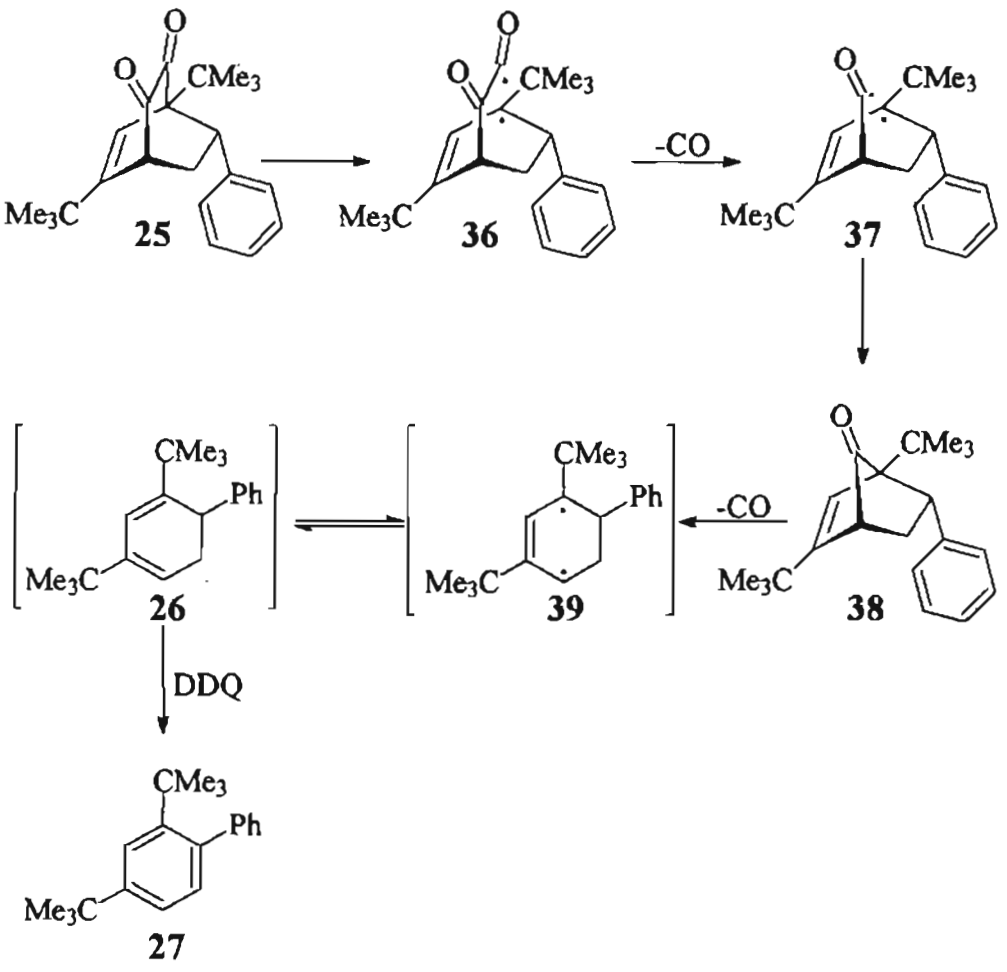
i. hυ, Pyrex, Cyclohexane, 2 h, 70% ii. DDQ, Xylene, Reflux, 24 h, 35%

Scheme 14

The structure of the product **35** was established on the basis of spectral data. The IR spectrum of **35** showed no carbonyl absorption. In the ^{1}H NMR spectrum, the *tert*-butyl group resonated at δ 1.50 as a singlet and the aromatic protons appeared as a multiplet between δ 7.63-7.25. All other signals were in agreement with the assigned structure. The molecular ion peak at *m/z* 210 in the mass spectrum also supported this structure.

In order to unravel the mechanism of these reactions, the photolysis was done for 30 minutes. The reaction mixture was subjected to rapid chromatographic purification, a new product was isolated and it was

tentatively characterized as **38**, along with **26** and **27**. The new product **38** may be considered as an intermediate and based on this observation a tentative rationalization along the following lines was invoked to explain the formation of the final product (Scheme 15).



Scheme 15

A Norrish type I cleavage of **25** in the excited state generates the diradical **36** which then loses a molecule of CO, producing a second diradical **37**. The diradical **37** on ring closure produces **38** which further eliminates a second molecule of CO to produce **26** and the latter on DDQ oxidation affords the substituted biphenyl **27**.

The structure of the product **38** was assigned on the basis of spectral and analytical data. IR spectrum of **38** showed a strong absorption at 1768 cm^{-1} due to bridgehead carbonyl. In the ^{1}H NMR spectrum, the phenyl protons were visible as a multiplet between δ 7.28-7.16. The olefinic proton appeared as a singlet at δ 6.05. The bridgehead proton resonated as a multiplet at δ 3.63. The benzylic proton resonated as a double doublet at δ 3.46 (J= 9.39 Hz, 14.97 Hz). The methylene protons resonated as separate multiplets between δ 2.27-2.18 and 2.02-1.92. The *tert*-butyl groups were visible at δ 1.07 and 0.98 integrating for nine protons each. In the ^{13}C NMR spectrum, the carbonyl group was visible at δ 207.32. All other signals were in agreement with the assigned structure. The presence of a molecular ion peak at *m/z* 296 further supported this structure.

In conclusion, we have developed a facile route to the synthesis of substituted biphenyls by photodecarbonylation of bicyclo[2.2.2]octenediones followed by DDQ oxidation.

3.1.3 Experimental Details

General information about the experiments is given in the section 2.15 (chapter 2). Distilled cyclohexane was used as solvent for photolysis. Irradiation was carried out in a 300 mL Photochemical Vessel of Ace Glass Incorporated, USA using a Hanovia 450W medium pressure mercury vapour lamp.

Typical procedure for the photolytic double decarbonylation of bicyclic α-diones

The adduct **25** (298 mg, 0.91 mmol) was dissolved in cyclohexane (300 mL) and the solution was purged with argon for 30 minutes with stirring. It was then irradiated for 2 h using a 450W mercury vapour lamp and a pyrex filter. The solvent was evaporated under reduced pressure and the residue was charged on a short length silica gel column. Elution with petroleum ether afforded a mixture (187 mg, 70%) of diene **26** and the substituted biphenyl **27** as a viscous liquid.

Typical procedure for DDQ oxidation

To a stirred solution of the mixture (187 mg) of **26** and **27** in dry xylene, DDQ (313 mg, 1.38 mmol) was added and the mixture was gently refluxed with stirring for 24 h. Most of the solvent was evaporated under reduced pressure and the residue was charged on a silica gel column. Elution with petroleum ether afforded the biphenyl derivative **27** (111 mg, 60%) as colorless crystalline solid, recrystallised from cold hexane (mp. 60-61 °C).

IR (KBr) : 2967, 2877, 1485 cm^{-1}.

^1H NMR : δ 7.65 (brs, 1H), 7.42-7.14 (m, 6H), 7.01 (d, J= 8.60 Hz, 1H), 1.44 (s, 9H), 1.28 (s, 9H).

^{13}C NMR : δ 149.41, 146.96, 145.50, 139.12, 132.22, 130.23, 127.15, 126.35, 123.57, 121.72, 36.81, 34.72, 32.84, 31.59.

EIMS *m/z* : 266 (M^+, 28), 251 (55), 195 (17), 57 (100).

Decarbonylation of 28

The diketone **28** (298 mg, 0.91 mmol) was irradiated for 2 h as in the case of **25**. Processing of the reaction mixture followed by chromatographic separation on silica gel using hexane as eluent afforded the product (221 mg; 90%) as a mixture of diene and biphenyl derivative. This mixture was then subjected to oxidation using DDQ (374 mg, 1.64 mmol) in refluxing xylene (10 mL) for 24 h. Purification of the reaction mixture by chromatography on silica gel using hexane as eluent yielded **27** (182 mg, 83%) as a crystalline solid, recrystallised from cold hexane (mp. 60-61 °C).

Decarbonylation of 29

A solution of diketone **29** (265 mg, 0.78 mmol) in cyclohexane (300 mL) was irradiated for 2 h. The reaction mixture was then processed as usual and purification on silica gel column using hexane as eluent afforded the product as a mixture of diene and biphenyl derivative. This mixture was then treated with DDQ (270 mg, 1.19 mmol) in refluxing toluene for 3 days to obtain the product **30** (98 mg, 59%) as a slight yellow crystalline solid (mp. 99-101 °C).

IR (KBr) : 2956, 2862, 1476, 1389, 1357, 1239 cm^{-1}.

^1H NMR : δ 7.52 (s, 1H), 7.21-7.12 (m, 5H), 6.92 (d, J= 7.83 Hz, 1H), 2.38 (s, 3H), 1.35 (s, 9H), 1.19 (s, 9H).

^{13}C NMR : δ 149.34, 147.14, 142.46, 139.03, 135.78, 132.29, 130.06, 127.79, 123.57, 121.64, 36.74, 34.69, 32.68, 31.47, 21.17.

EIMS *m/z* : 280 (M^+, 10), 265 (19), 209 (13), 193 (14), 178 (9), 57 (100).

Decarbonylation of 31

A solution of the diketone **31** (233 mg, 0.68 mmol) in cyclohexane (300 mL) was irradiated for 2 h. Processing of the reaction mixture followed by purification by column chromatography on silica gel using hexane afforded the mixture of substituted biphenyl and its dihydro product which on DDQ (219 mg, 0.96 mmol) oxidation in refluxing toluene for 3 days afforded **30** (67 mg, 50%) as a pale yellow crystalline solid (mp. 99-101 °C).

Decarbonylation of 32

A solution of the diketone **32** (300 mg, 0.72 mmol) in cyclohexane (300 mL) was irradiated for 1.5 h. Processing of the reaction mixture followed by purification by column chromatography on silica gel using hexane afforded the mixture of substituted biphenyl and its dihydro product which on DDQ (196 mg, 0.86 mmol) oxidation in refluxing benzene for 5 h afforded **33** (63 mg, 41%) as a semisolid.

IR (neat) : 2956, 2862, 2825, 1581, 1505, 1463, 1237, 1128 cm^{-1}.

^1H NMR :δ 7.53 (s, 1H), 7.25-6.95 (m, 3H), 6.43 (d, J= 9.89 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 1.38 (s, 9H), 0.95 (s, 9H).

^{13}C NMR : δ 140.65, 138.75, 133.41, 131.96, 130.58, 123.63, 121.65, 119.96, 107.80, 104.81, 60.85, 55.95, 55.84, 34.04, 32.72, 31.43, 31.31.

EIMS *m/z* : 356 (M^+, 22), 341 (12), 325 (10), 201 (15), 156 (18), 141 (28), 57 (100).

Decarbonylation of 34

A solution of the diketone **34** (298, 1.11 mmol) in cyclohexane (300 mL) was irradiated for 2 h. Processing of the reaction mixture followed by purification by column chromatography on silica gel using hexane afforded the mixture of substituted biphenyl and its dihydro product which on DDQ (353 mg, 1.55 mmol) oxidation in refluxing xylene for 24 h afforded **35** (108 mg, 35%) as a semisolid.

IR (neat) : 2930, 2850, 1545, 1507, 1451 cm^{-1}.

^1H NMR : δ 7.63-7.25 (m, 9H), 1.50 (s, 9H).

^{13}C NMR : δ 149.41, 146.96, 145.50, 139.12, 128.61, 128.50, 127.32, 127.13, 126.35, 123.57, 34.78, 31.48.

EIMS *m/z* : 210 (M^+, 33), 195 (100), 180 (19), 165 (35), 152 (26), 115 (13), 83 (15), 41 (17).

Procedure for the isolation of the intermediate 38

The adduct **25** (298 mg, 0.91 mmol) was dissolved in cyclohexane (300 mL) and the solution was purged with argon for 30 minutes with stirring. It was then irradiated for 30 min. using a 450W mercury vapour lamp and a pyrex filter. The solvent was evaporated under reduced pressure and the residue on rapid chromatographic purification using petroleum ether as eluent afforded **38** (10 mg, 4%) along with the diene **26** and the substituted biphenyl **27** (167 mg, 67%).

IR (neat) : 2964, 2869, 1768, 1543, 1451, 1366 cm^{-1}.

^1H NMR : δ 7.28-7.16 (m, 5H), 6.05 (s, 1H), 3.63 (m, 1H). 3.46 (dd, J= 9.39, 14.97 Hz, 1H), 2.27-2.18 (m, 1H), 2.02-1.92 (m, 1H), 1.07 (s, 9H), 0.98 (s, 9H).

^{13}C NMR : δ 207.32, 154.06, 142.66, 128.66, 128.37, 127.97, 126.23, 50.70, 48.14, 42.26, 38.01, 32.01, 30.24, 26.80.

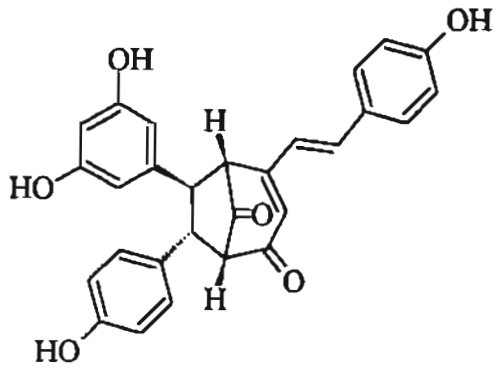
EIMS *m/z* : 296 (M^+, 3), 284 (3), 208 (19), 196 (6), 155 (7), 104 (100), 91 (9), 57 (17).

3.2 Rearrangement of bicyclo[2.2.2]octenediones to bicyclo[3.2.1]octenediones induced by BF_3-etherate

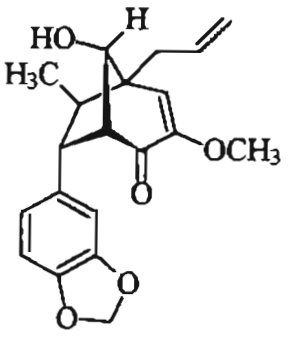
3.2.1 Introduction

As already stated the bicyclo[2.2.2]octenediones, readily obtainable from the Diels-Alder reaction of *o*-benzoquinones and styrenes, appeared interesting from the vantage point of synthetically useful transformations. On the basis of our experience in a related series, it was reasonable to assume that the BF_3-etherate induced rearrangement of bicyclo[2.2.2]octenediones would lead to an efficient synthesis of bicyclo[3.2.1]octenediones.[21]

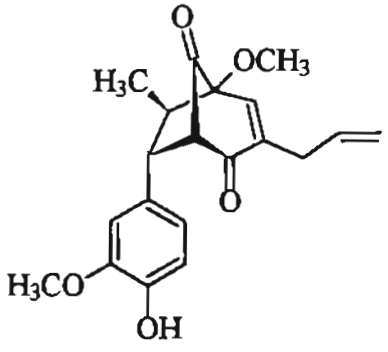
It is noteworthy that bicyclo[3.2.1]octane skeleton constitutes the framework of a number of natural products as illustrated by the following examples (Figure 1).



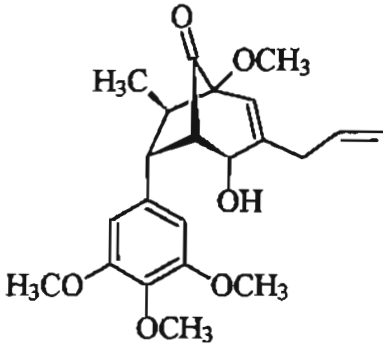
Gnetin A[22]



Guianin[23]



Liliflodione[24]

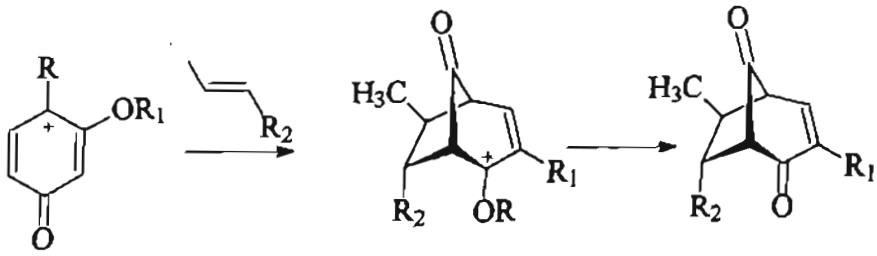


Macrophyllin B[25]

Figure 1

The bicyclo[3.2.1]octane skeleton was constructed in the past by the controlled opening of cyclopropyl ketones,[26] the transannular cyclization of cycloocta-1,5-diene,[27] the thermal rearrangement of bicyclo[4.2.0]octenediones[28] and the Pummerer rearrangement of some alkyl sulfoxides.[29] In 1981 Wender[30,31] has elegantly demonstrated the formation of bicyclo[3.2.1]octane system *via* arene-alkene photocycloaddition in the synthesis of a complex molecule like (±) Cedrene. Tricyclic compounds containing bicyclo[3.2.1]octane skeleton can be prepared by a Cope rearrangement of substrates possessing a 1,2-divinylcyclopropane moiety.[32]

Various 3-alkoxy-4-alkylcyclohexa-2,5-diene-1-one-4-yl cations **40**, generated *in situ* by different methods[33,34] react with alkenes affording the bicyclo[3.2.1]octenyl cations **41**, probably *via* a concerted [5+2] cycloaddition,[35] and the latter on dealkylation[36] and oxidation yield the bicyclic diones **42** (Scheme 16).

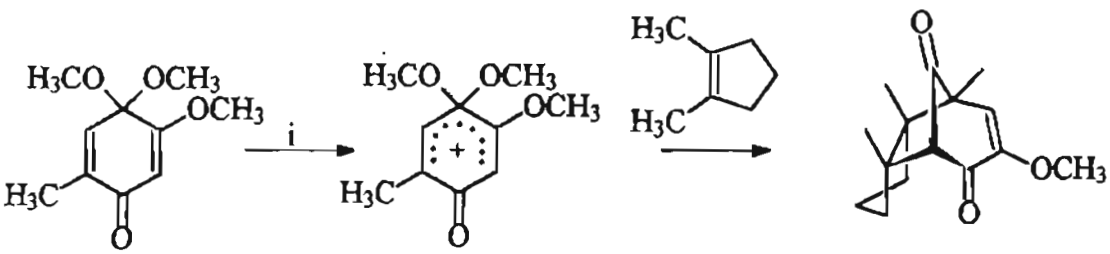


40 ***41*** ***42***

Scheme 16

Engler has shown that the Lewis acid promoted reaction of (E) propenyl benzenes with 2-alkoxy and 2-alkoxy-6-alkyl-1,4-benzoquinone produces bicyclo[3.2.1]octene-2,8-diones in small amounts along with other products.[37]

The adduct **45**, an intermediate in a sesquiterpene synthesis, was formed in the reaction of 1,2-dimethylcyclopentene with the hemi-ketal **43** in the presence of tin(IV) chloride (Scheme 17).[38]

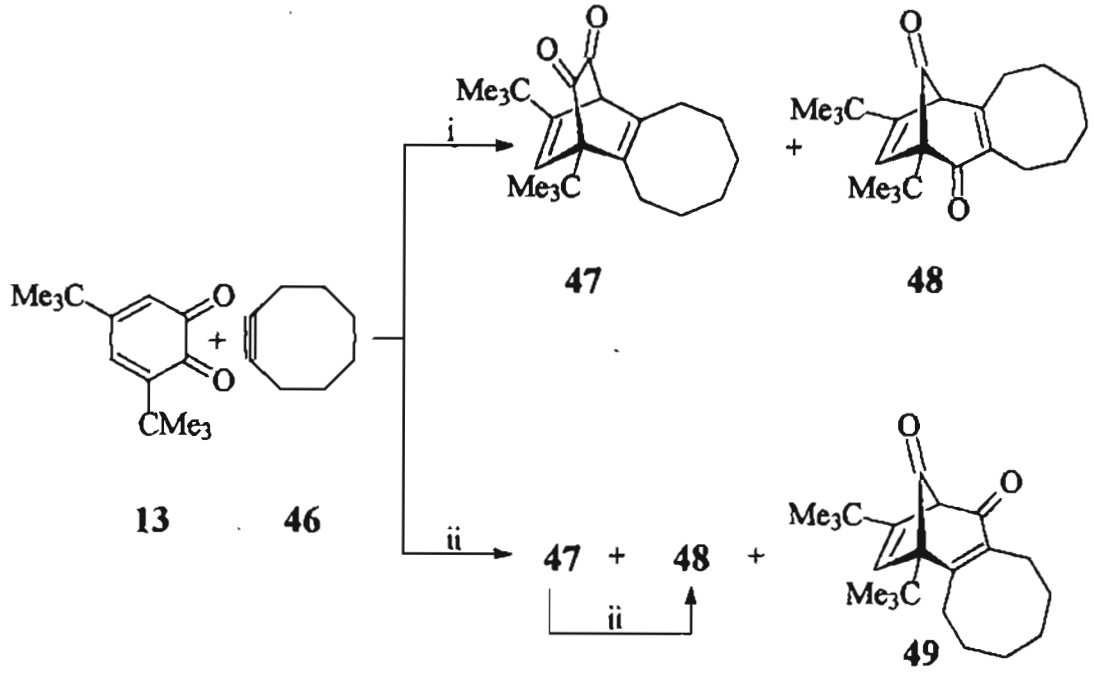


43 **44** **45**

i. $SnCl_4$, CH_3NO_2-CH_2Cl_2, -20 °C

Scheme 17

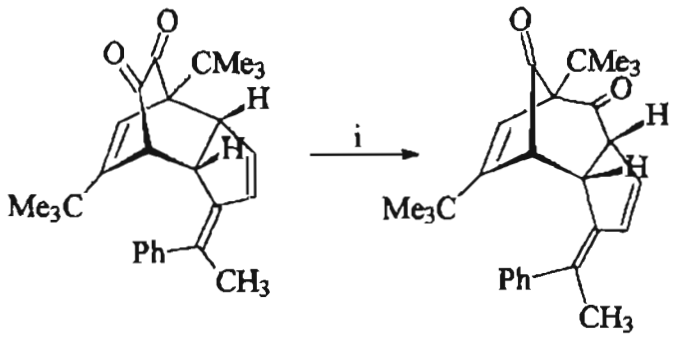
Cycloaddition reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **13** with a strained dienophile cyclooctyne **46**, has been reported to afford the cycloadduct **47** and the rearranged product **48**. Under the influence of the Lewis acid BF_3-OEt_2, the reaction leads in addition to **48** the isomeric derivative **49** (Scheme 18).[39]



i. $CHCl_3$, RT, 4.5 h ii. BF_3-OEt_2, RT

Scheme 18

Against the background presented and in the light of some work carried out earlier in our laboratory (Scheme 19),[21] we have now undertaken a study of the BF_3-etherate induced rearrangement of bicyclo[2.2.2]octenediones obtained by the Diels-Alder reaction of *o*-benzoquinones with styrenes.



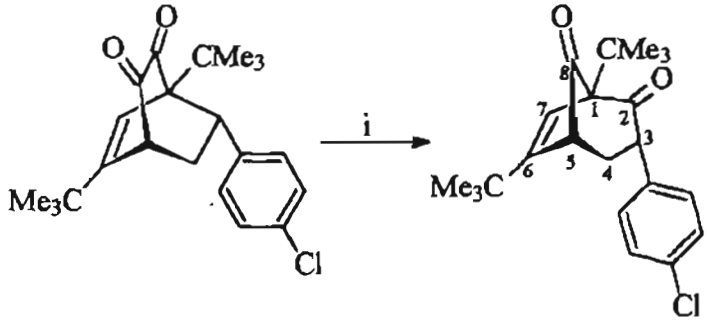
50 **51**

i. BF_3-OEt_2, $CHCl_3$, Reflux, 4 h, 70%

Scheme 19

3.2.2 Results and discussion

The dione **52** readily obtained by the cycloaddition reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone and styrene (see chapter 2) was selected for our initial studies. A solution of dione **52** in chloroform on treatment with BF_3-OEt_2 at room temperature afforded the bicyclo[3.2.1]octene-2,8-dione in 82% yield (Scheme 20).



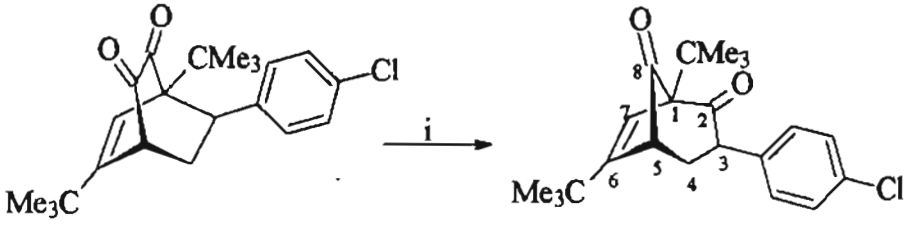
52 **53**

i. BF_3-OEt_2, $CHCl_3$, RT, 2 h, 82%

Scheme 20

The structure of the product was assigned on the basis of spectral data. The IR spectrum of **53** showed absorptions at 1769 and 1701 cm^{-1} indicating the presence of bridgehead carbonyl and the C-2 carbonyl moieties respectively. In the ^1H NMR spectrum, the phenyl protons appeared as a multiplet between δ 7.32-6.96. The olefinic proton resonated as a singlet at δ 5.88. The benzylic proton was visible as a triplet at δ 3.65 (t, J= 8.9 Hz). The bridgehead proton exhibited a doublet at δ 3.17 (d, J= 6.53 Hz). The methylene protons appeared as separate multiplets between δ 2.70-2.61 and 2.02-1.94 integrating for one proton each. In the ^{13}C NMR spectrum, the carbonyl carbons were visible at δ 210.37 and 200.38 and the bridgehead carbons appeared at δ 75.21 and 55.85. The analytical data also supports this structure. Ultimately the structure was confirmed unequivocally by single crystal X-ray analysis.

The dione **54** also rearranged smoothly on treating with BF_3-etherate to afford the bicyclo[3.2.1]octenedione **55** in high yield (Scheme 21).



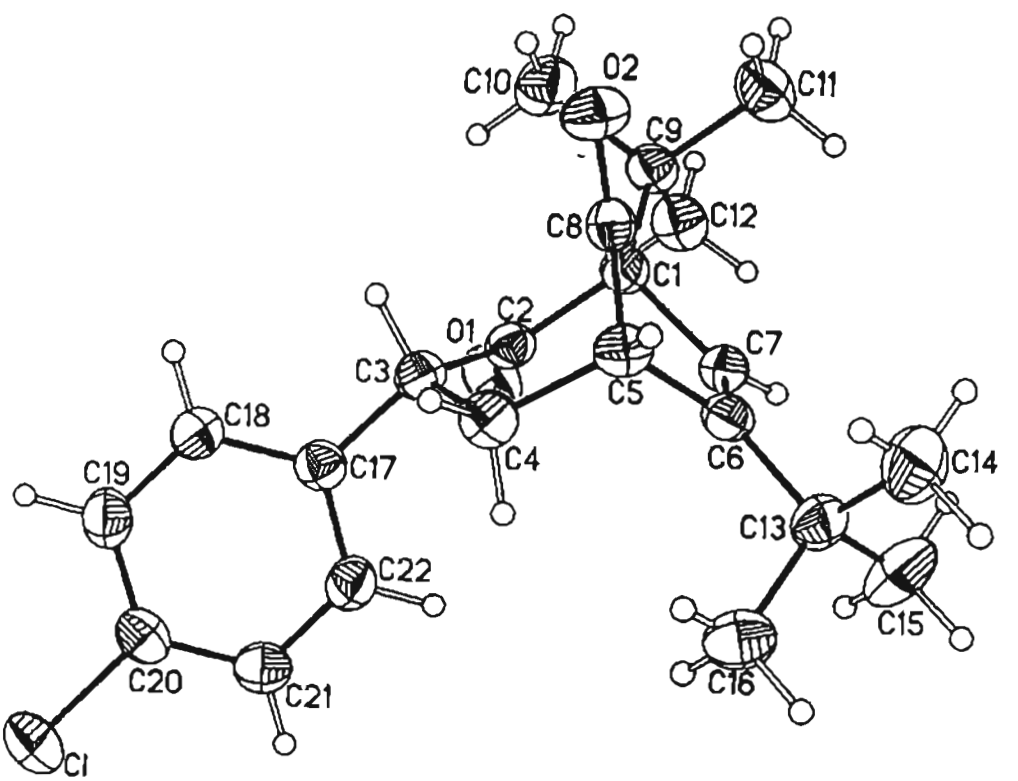
54 **55**

i. BF_3-OEt_2, $CHCl_3$, RT, 2 h, 90%

Scheme 21

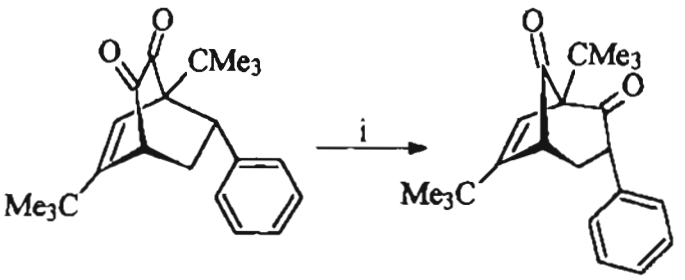
*The structure of the product was determined on the basis of spectral data. The IR spectrum of **55** showed two strong absorptions at 1769 and*

1708 cm^{-1} due to the bridgehead carbonyl and the C-2 carbonyl respectively. In the ^{1}H NMR spectrum, the bridgehead proton appeared as a multiplet between δ 3.36 and the benzylic proton resonated as a double doublet at δ 3.98 (dd, J= 8.86, 11.89 Hz). In ^{13}C NMR spectrum, the two carbonyls resonated at δ 207.62 and 202.38. All other signals were in agreement with the assigned structure. The analytical data also supported this structure.



X-ray structure of **53**

In a similar fashion the bicyclic dione **25** afforded the rearranged product **56** in 80% yield on treating with BF_3-etherate in $CHCl_3$ at room temperature for 2 h (Scheme 22).



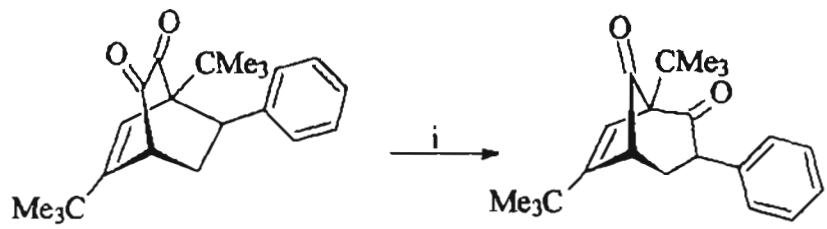
25 **56**

i. BF_3-OEt_2, $CHCl_3$, RT, 2 h, 80%

Scheme 22

The structure of the product **56** was ascertained from the spectral data. The two absorptions at 1769 and 1708 cm^{-1} in the IR spectrum are diagnostic for the presence of bridgehead and other carbonyl group respectively. In the ^1H NMR spectrum, the bridgehead hydrogen appeared as a doublet at δ 3.17 (d, J= 6.77 Hz) and the benzylic proton appeared as a triplet at δ 3.66 (t, J= 9.34 Hz). In the ^{13}C NMR spectrum, the two signals at δ 210.77 and 200.82 were assigned to two carbonyl groups. All other signals were in agreement with the assigned structure. The structure of the product was further supported by satisfactory elemental analysis.

The dione **28**, *exo* isomer of **25** also underwent similar rearrangement when treated with BF_3-OEt_2 in chloroform to yield the bicyclo[3.2.1]octenedione **57** in 90% yield (Scheme 23).



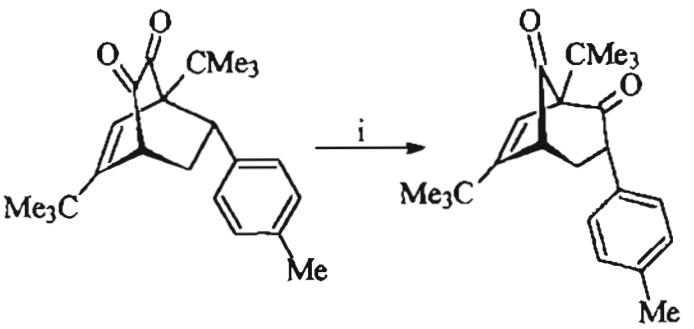
28 **57**

i. BF_3-OEt_2, $CHCl_3$, RT, 2 h, 90%

Scheme 23

The structure of the product was established from its spectral data. The IR spectrum of **57** showed strong absorptions at 1762 and 1708 cm^{-1} characteristic of bridgehead carbonyl and the other carbonyl respectively. In the ^1H NMR spectrum, the bridgehead proton appeared as a multiplet at δ 3.37 and the benzylic proton was visible as a double doublet at δ 4.00 (dd, J= 11.97, 8.97 Hz). In the ^{13}C NMR spectrum, the two carbonyls were discernible at δ 208.47 and 202.68. All other signals were in agreement with the assigned structure. Elemental analysis also supported this structure.

The dione **29** obtained by the Diels-Alder reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone and 4-methylstyrene, also rearranged smoothly on treatment with BF_3-etherate in chloroform (Scheme 24).



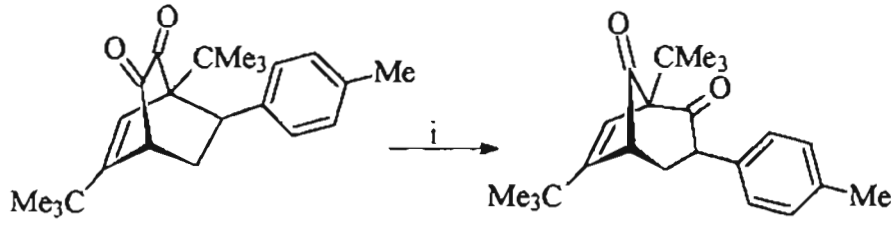
29 **58**

i. BF_3-OEt_2, $CHCl_3$, RT, 2 h, 100%

Scheme 24

As usual, the structure of the product was ascertained from its spectral data. IR spectrum of **58** showed two strong absorptions at 1769 and 1715 cm^{-1} due to a bridgehead carbonyl and the other carbonyl respectively. In the ^1H NMR spectrum, the bridgehead proton appeared as a doublet at δ 3.13 (d, J= 6.75 Hz) and the benzylic proton exhibited a triplet at δ 3.60 (t, J= 9.39 Hz). The ^{13}C NMR spectrum showed two signals at δ 210.36 and 200.55 corresponding to the two carbonyl groups. All other signals were in agreement with the assigned structure. The structure of the product was further supported by satisfactory elemental analysis.

The dione **31**, the *exo* isomer of **29** also underwent similar rearrangement to afford the rearranged product **59** in 95% yield (Scheme 25).



31 **59**

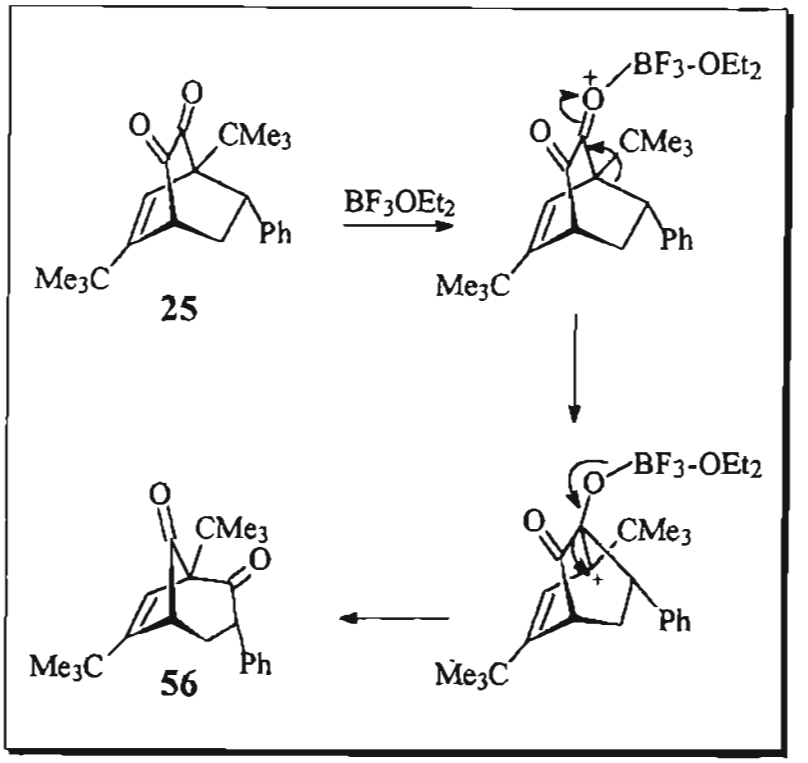
i. BF_3-OEt_2, $CHCl_3$, RT, 2 h, 95%

Scheme 25

The structure of the product was determined on the basis of spectral and analytical data. In the IR spectrum of **59**, the bridgehead carbonyl and the other carbonyl absorbed at 1764 and 1708 cm^{-1} respectively. In the ^1H NMR spectrum, the benzylic proton appeared as a double doublet at δ 3.95 (dd, J= 8.93, 11.79 Hz) and the bridgehead proton resonated as a multiplet at δ 3.35. In the ^{13}C NMR spectrum, the two carbonyls were visible at δ 207.90 and 202.82. All other signals were in agreement with the assigned structure. Further support for the structure was obtained from satisfactory elemental analysis.

The dione **34** obtained by the cycloaddition reaction of 4-*tert*-butyl-1,2-benzoquinone and styrene failed to undergo this rearrangement.

Although the mechanistic details of the BF_3-etherate induced rearrangement are not known, a rationalization along the following lines may be invoked to account for the formation of the product (Scheme 26).



Scheme 26

In conclusion, we have developed a facile method for the synthesis of bicyclo[3.2.1]octenediones in high yields by the BF_3-etherate induced rearrangement of bicyclo[2.2.2]octene diones.

3.2.3 Experimental Details

BF_3-etherate was purchased from Aldrich Co., U.S.A. and was used as such using syringe-septum technique. Chloroform was dried over P_2O_5 prior to use. All the products were recrystallised from dichloromethane/ hexane solvent system.

1,6-Bis(1,1-dimethylethyl)-3-(4-chlorophenyl)bicyclo[3.2.1]oct-6-ene-2,8-dione (*endo* **53**):

A solution of **52** (358 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 2 h. The progress of the reaction was monitored by TLC. On completion of the reaction, the mixture was stirred with a few drops of water and extracted with dichloromethane (4 x 15 mL). The extract was dried over anhydrous sodium sulfate and concentrated. The crude product was then purified by chromatography on silica gel column using 2% ethyl acetate in hexane as eluent to afford the product **53** (294 mg, 82%) as colorless crystals (mp. 132-135 °C).

IR (KBr) : 2969, 2881, 1769, 1701, 1472, 1243, 1081 cm^{-1}.

^1H NMR : δ 7.32-6.96 (m, 4H), 5.88 (s, 1H), 3.65 (t, J= 8.9 Hz, 1H), 3.17 (d, J= 6.53 Hz, 1H), 2.70-2.61 (m, 1H), 2.02-1.94 (m, 1H), 1.17 (s, 9H), 1.14 (s, 9H).

^{13}C NMR : δ 210.37, 200.38, 159.28, 138.19, 132.97, 130.15, 128.82, 121.19, 75.21, 55.85, 49.53, 35.60, 34.53, 33.07, 28.94, 26.58.

Anal. Calcd for $C_{22}H_{27}O_2Cl$: C, 73.62; H, 7.58; Cl, 9.88. Found: C, 73.42; H,7.35; Cl, 9.98.

1,6-Bis(1,1-dimethylethyl)-3-(4-chlorophenyl)bicyclo[3.2.1]oct-6-ene-2,8-dione (*exo* **55**):

A solution of **54** (358 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 2 h. The usual work up followed by chromatographic purification of the

product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **55** (323 mg, 90%) as colorless crystals (mp. 167-169 °C).

IR (KBr) : 2962, 2881, 1769, 1708, 1485, 1357, 1249, 1094 cm^{-1}.

^1H NMR : δ 7.29-6.92 (m, 4H), 6.01 (s, 1H), 3.98 (dd, J= 8.86, 11.89 Hz, 1H), 3.36 (m, 1H), 2.34-2.25 (m, 1H), 1.93-1.84 (m, 1H), 1.19 (s, 18H).

^{13}C NMR : δ 207.62, 202.38, 153.88, 136.40, 133.18, 130.60, 128.72, 124.55, 79.99, 52.81, 50.75, 34.36, 32.94, 31.21, 28.40.

Anal. Calcd for $C_{22}H_{27}O_2Cl$: C, 73.62; H, 7.58; Cl, 9.88. Found: C, 73.41; H, 7.59; Cl, 9.71.

1,6-Bis(1,1-dimethylethyl)-3-phenylbicyclo[3.2.1]oct-6-ene-2,8-dione (*endo* **56**):

A solution of **25** (324 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 2 h. The usual work up followed by chromatographic purification of the product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **56** (260 mg, 80%) as colorless crystals (mp. 147-149 °C).

IR (KBr) : 2962, 2874, 1769, 1708, 1472, 1364, 1243 cm^{-1}.

^1H NMR : δ 7.33-7.02 (m, 5H, Ar), 5.88 (s, 1H), 3.66 (t, J= 9.34 Hz, 1H), 3.17 (d, J= 6.77 Hz, 1H), 2.70-2.60 (m, 1H), 2.08-2.01 (m, 1H), 1.18 (s, 9H), 1.13 (s, 9H).

^{13}C NMR : δ 210.77, 200.82, 159.08, 139.73, 128.66, 128.56, 127.07, 121.22, 75.21, 56.53, 49.66, 35.61, 34.50, 33.06, 28.94, 26.59.

Anal. Calcd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70. Found: C, 80.92; H, 8.78.

1,6-Bis(1,1-dimethylethyl)-3-phenylbicyclo[3.2.1]oct-6-ene-2,8-dione (*exo* **57**):

A solution of **28** (324 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 2 h. The usual work up followed by chromatographic purification of the product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **57** (292 mg, 90%) as colorless crystals (mp. 157-159 °C).

IR (KBr) : 2969, 2867, 1762, 1708, 1458, 1357, 1236, 1047 cm^{-1}.

^1H NMR : δ 7.31-6.99 (m, 5H), 6.02 (s, 1H), 4.00 (dd, J= 11.97, 8.97 Hz, 1H), 3.37 (m, 1H), 2.37-2.28 (m, 1H), 1.99-1.90 (m, 1H), 1.20 (s, 18H).

^{13}C NMR : δ 208.47, 202.68, 154.00, 138.09, 129.38, 128.69, 127.39, 124.66, 78.50, 61.07, 53.08, 40.01, 35.00, 31.28, 29.34, 28.49.

Anal. Calcd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70. Found: C, 81.44; H, 8.67.

1,6-Bis(1,1-dimethylethyl)-3-(4-methylphenyl)bicyclo[3.2.1]oct-6-ene-2,8-dione (*endo* **58**):

A solution of **29** (338 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 2 h. The usual work up followed by chromatographic purification of the product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **58** quantitatively as colorless crystals (mp. 57-59 °C).

IR (KBr) : 2962, 2874, 1769, 1715, 1472, 1371, 1256, 1088 cm^{-1}.

^1H NMR : δ 7.12-6.88 (m, 4H), 5.86 (s, 1H), 3.60 (t, J= 9.39 Hz, 1H), 3.13 (d, J= 6.75 Hz, 1H), 2.66-2.56 (m, 1H), 2.30 (s, 3H), 2.04-1.97 (m, 1H), 1.17 (s, 9H), 1.13 (s, 9H).

^{13}C NMR : δ 210.36, 200.55, 158.94, 136.75, 136.49, 129.29, 128.61, 121.25, 75.11, 56.15, 49.64, 35.63, 34.46, 33.03, 28.98, 26.63, 21.05.

Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.52; H, 8.98.

1,6-Bis(1,1-dimethylethyl)-3-(4-methylphenyl)bicyclo[3.2.1]oct-6-ene-2,8-dione (*exo* **59**):

A solution of **31** (338 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 2 h. The usual work up followed by chromatographic purification of the product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **59** (321 mg, 95%) as colorless crystals (mp. 114-116 °C).

IR (KBr) : 2963, 2876, 1764, 1708, 1471, 1366, 1245, 1049 cm^{-1}.

^{1}H NMR : δ 7.11-6.87 (m, 4H), 6.01 (s, 1H), 3.95 (dd, J= 8.93, 11.79 Hz, 1H), 3.35 (m, 1H), 2.34-2.25 (m, 4H), 1.96-1.87 (m, 1H), 1.19 (s, 18H).

^{13}C NMR : δ 207.90, 202.82, 153.69, 136.62, 134.79, 129.15, 129.01, 124.42, 79.82, 52.84, 50.84, 34.23, 32.80, 31.15, 28.32, 21.00.

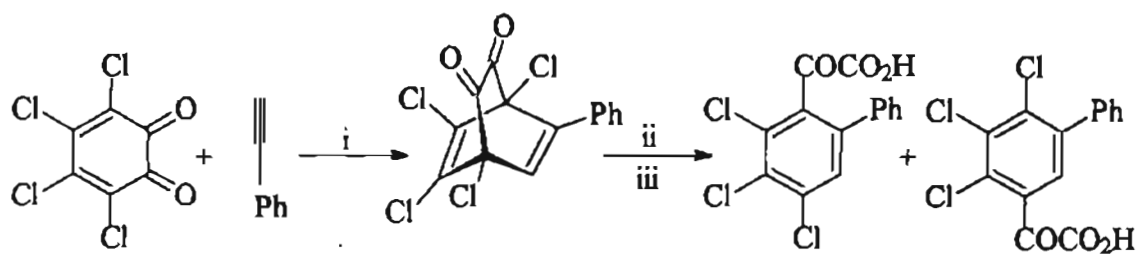
Anal. Calcd. for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.57; H, 8.96.

3.3 KOH/ MeOH assisted ring opening reaction of bicyclo[3.2.1]octenediones

3.3.1 Introduction

It was of interest to investigate the ring opening of bicyclo[3.2.1]octenediones (readily obtainable from bicyclo[2.2.2]octenediones by BF_3-etherate induced rearrangement, as described in the previous section) from the point of view of their conversion to cycloheptanone derivatives. Experiments conducted with this objective and the results obtained are presented here.

The ring opening reaction of 1,2-diones under the influence of NaOH has been known. Pyle has shown that the Diels-Alder adduct obtained in the reaction of *o*-chloranil with phenylacetylene on basic hydrolysis afforded a nearly quantitative yield of two isomeric biphenyl glyoxylic acids (Scheme 27).[40,41]

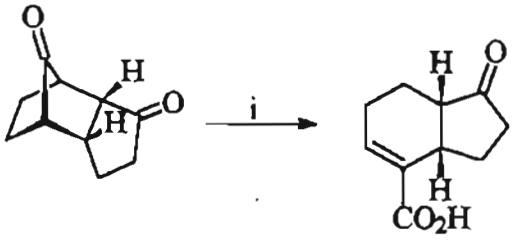


60 **61** **62** **63** **64**

i. Benzene, reflux, 24 h ii. H_2O/ NaOH iii. HCl

Scheme 27

Mehta[42] has shown that the tricyclodione **65** undergoes ring opening by the cleavage of bridgehead carbonyl, by hydroxide ions. Such reactions can be considered as hydroxide mediated Haller-Bauer type cleavage of non enolisable ketones (Scheme 28).



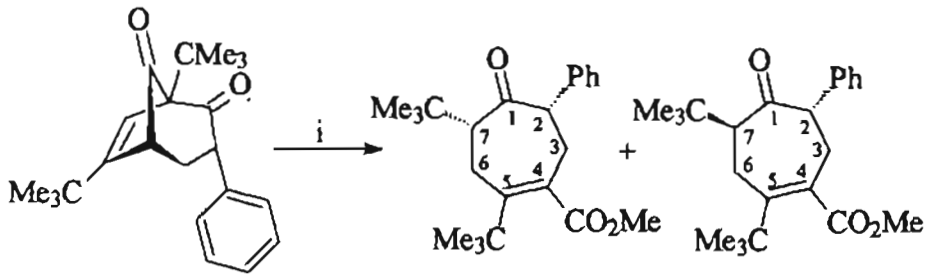
65 **66**

i. 30% aq. NaOH, benzene, heat, 2-3 h. 60-70%

Scheme 28

3.3.2 Results and discussion

The 1,3-dione **56** derived from bicyclo[2.2.2]octenedione (see section 3.2) was selected for our initial studies. The dione **56** on treatment with 2% solution of KOH in methanol afforded the products **67** and **68** in 40% yield (Scheme 29).



7 : 3

56 **67** **68**

i. 2% KOH/ MeOH, RT, 24 h, 40%

Scheme 29

The products were separated by Chromatotron® and their structures were tentatively ascertained on the basis of spectral and analytical data.

IR spectrum of **67** showed strong absorptions at 1742 and 1694 cm^{-1} characteristic of ester and carbonyl groups respectively. In the ^{1}H NMR spectrum, the phenyl protons were visible as a multiplet between δ 7.31-7.19. The methyl protons in the ester group resonated as a singlet at δ 3.58. The C-2 proton appeared as a triplet at δ 4.14 (t, J= 7.83 Hz). The C-3 protons resonated as separate double doublets at δ 3.10 (dd, J= 7.83, 13.78 Hz) and at δ 2.80 (dd, J= 7.83, 13.78 Hz). The C-7 proton appeared as a double doublet at δ 2.01 (dd, J= 2.25, 6.69 Hz). The C-6 protons were visible as separate double doublets, one at δ 2.55 (dd, J= 6.69, 18.63 Hz) and the other at δ 2.32 (dd, J= 18.63, 2.25 Hz). In the ^{13}C NMR spectrum, the carbonyl group was visible at δ 211.01 and the ester carbonyl appeared at δ 178.72. All other signals were in accordance with the assigned structure. The structure was further supported by the satisfactory elemental analysis.

The IR spectrum of **68** showed strong absorptions at 1748 and 1701 cm^{-1} due to the presence of ester and carbonyl functionalities. In the ^{1}H NMR spectrum, the C-2 proton appeared as a triplet at δ 4.08 (t, J= 7.49 Hz). The ester group protons resonated as a singlet at δ 3.62. The C-3 protons appeared as separate double doublets at δ 3.07 (dd, J= 14.01, 7.49 Hz) and at δ 2.82 (dd, J= 14.01, 7.49 Hz). The C-7 proton was visible as a double doublet at δ 2.01 (dd, J= 2.64, 6.81 Hz). The C-6 protons appeared as separate double doublets at δ 2.54 (dd, J= 17.95, 6.81, Hz) and at δ 2.30 (dd, J= 2.64, 17.95 Hz). In the ^{13}C NMR spectrum, the carbonyl group resonated at δ 210.96 and the ester carbonyl was visible at δ 178.72. All other signals

were also in accordance with the assigned structure. The structure was further supported by the mass spectrum having molecular ion peak at *m/z* 356.

The structure of the product was established on the basis of extensive NMR analysis. From the DEPT-135 spectrum, the presence of two methylene moieties and seven quaternary carbons was easily discernible (Figure 2a). The proton connectivity was established by 2D COSY experiments. The ^{1}H-^{1}H relayed COSY of **68** showed the through bond connectivities between two different sets of hydrogen atoms. The hydrogen at δ 4.08 (t) is connected to the one at δ 3.07 (dd) and another at δ 2.82 (dd). The hydrogen at δ 2.01 (dd) is connected to the one at δ 2.30 (dd) and another at δ 2.54 (dd) (Figure 2b).

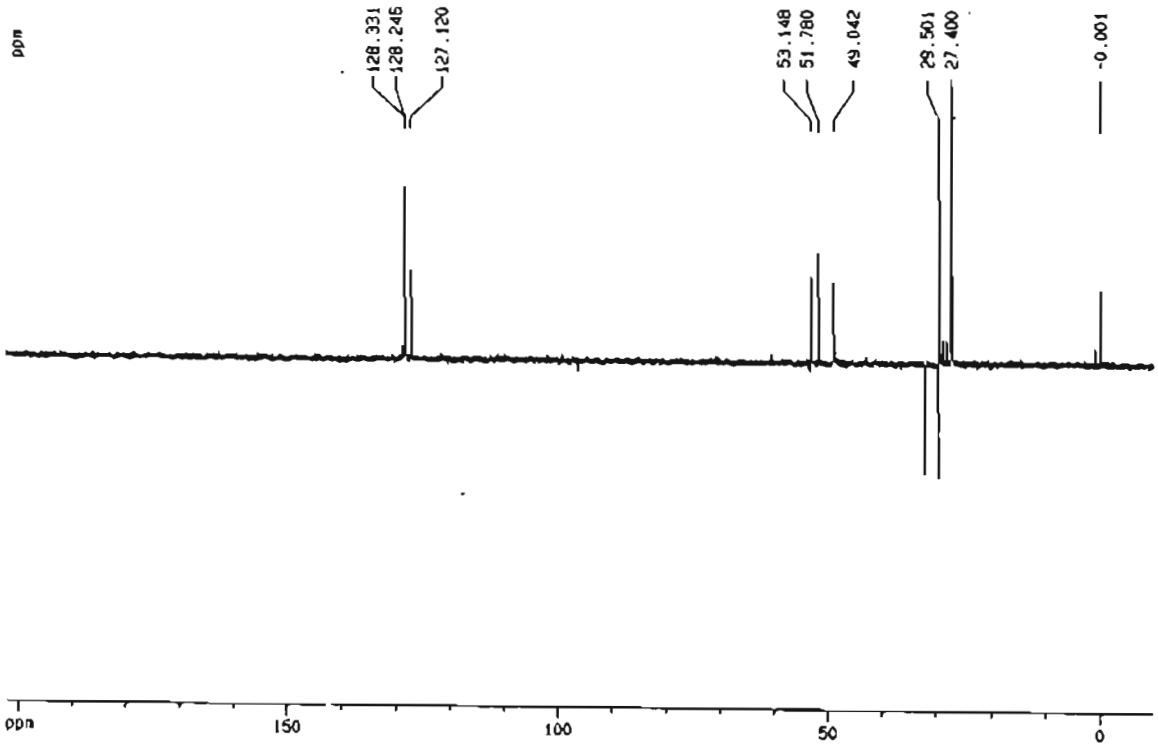


Figure 2a DEPT-135 spectrum of **68**

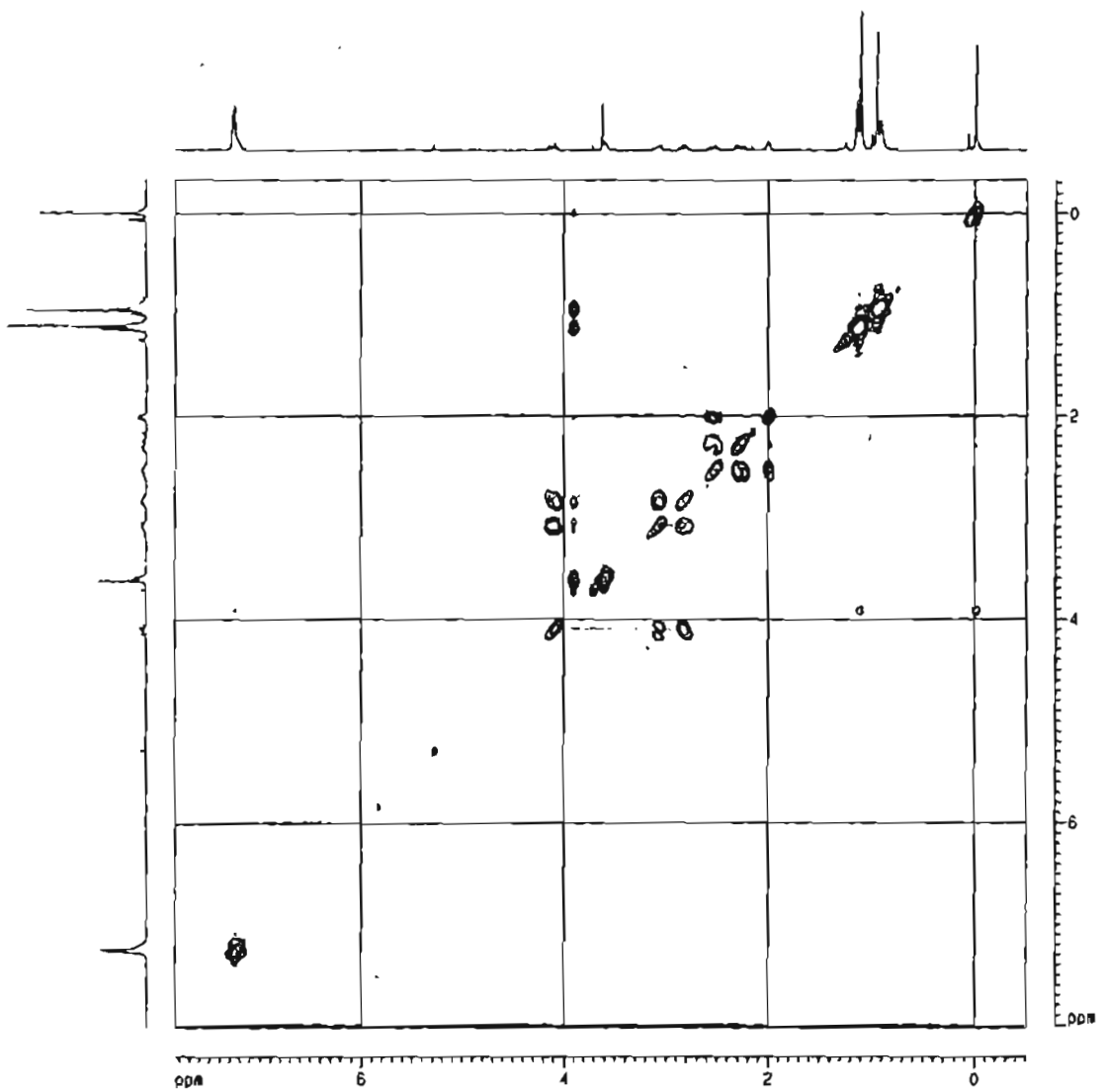
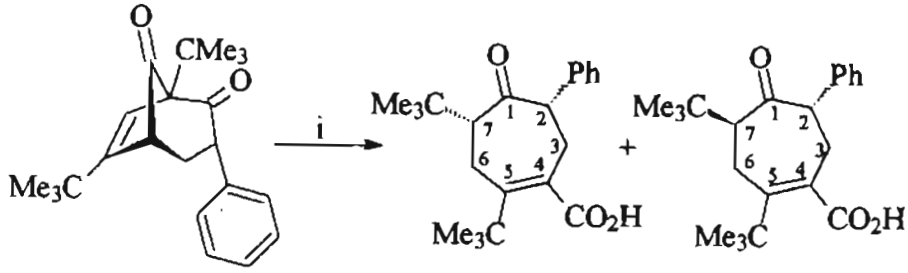


Figure 2b ^{1}H-^{1}H COSY spectrum of **68**

Since the ring opening was sluggish with 2% KOH in methanol, it was decided to increase the concentration of base with a view to obtain better results. Accordingly when the 1,3-dione **56** was treated with 10% KOH in methanol at room temperature for 5 h the products **69** and **70** were obtained in 72% yield (Scheme 30).



56 **69** **70**

i. 10% KOH/ MeOH, RT, 5 h, 72% (1:1)

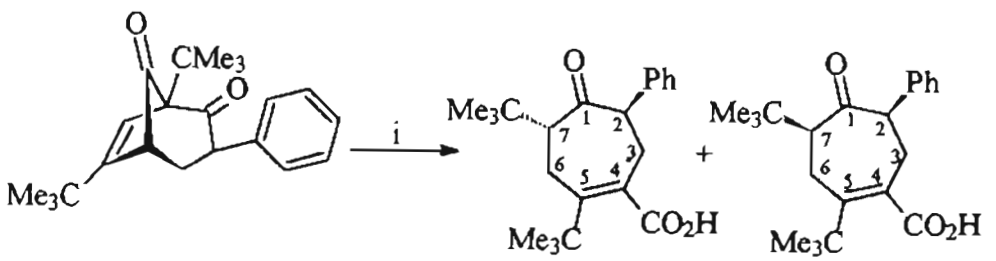
Scheme 30

The products were separated by Chromatotron®. The structure of the products was tentatively assigned on the basis of spectral and analytical data.

The IR spectrum of **69** showed a broad band at 3211 cm^{-1} due to the acid group and a strong band at 1713 cm^{-1} corresponding to carbonyl group. In the ^{1}H NMR spectrum, the C-7 protons exhibited a doublet at δ 1.99 (d, J= 6.66 Hz) and C-6 protons were visible as separate signals; one appeared as a double doublet at δ 2.49 (dd, J= 6.66, 18.24 Hz) and the other resonated as a doublet at δ 2.31 (d, J= 18.24 Hz). In the ^{13}C NMR spectrum, the carboxyl group was discernible at δ 179.18 and the carbonyl group appeared at δ 211.12. All other signals were in agreement with the assigned structure. The molecular ion peak at *m/z* 342 also supported this structure.

The IR spectrum of **70** showed a broad band at 3200 cm^{-1} and a strong band at 1707 cm^{-1} characteristic of acid and keto group respectively. In the ^1H NMR spectrum, the C-7 proton resonated as a double doublet at δ 2.02 (dd, J= 6.64, 2.48 Hz). All other signals were in agreement with the assigned structure.

The 1,3-dione **57**, stereoisomer of **56**, also underwent facile ring opening reaction when treated with 10% KOH in methanol to afford **71** and **72** (Scheme 31).



57 **71** **72**

i. 10% KOH/ MeOH, RT, 5 h, 72% (1:1)

Scheme 31

As usual the products were separated by Chromatotron®. The structures of the products were tentatively assigned on the basis of spectral data.

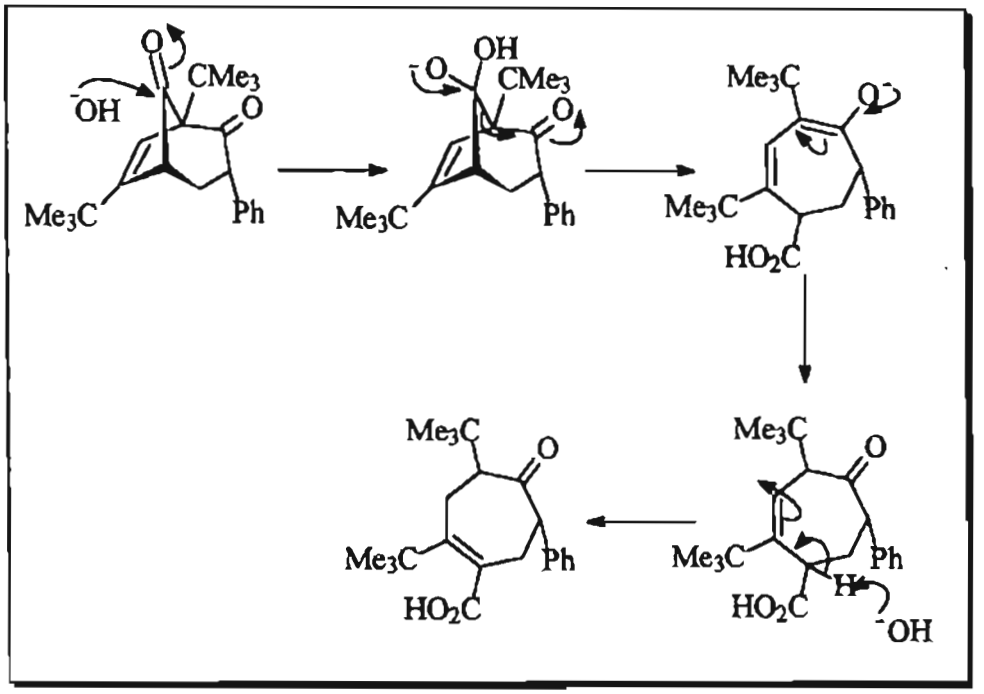
IR spectrum of **71** showed the characteristic absorptions at 3211 and 1708 cm^{-1} due to the carboxylic acid and carbonyl moieties respectively. In the ^1H NMR spectrum, the C-2 proton appeared as triplet at δ 4.13 (t, J= 7.51 Hz) and the C-3 protons resonated as separate double doublets at δ 3.06 (dd, J= 7.51, 13.71 Hz) and δ 2.83 (dd, J= 7.51, 13.71 Hz). The C-7 proton appeared as doublet at δ 2.00 (d, J= 6.61 Hz). The C-6 protons were

visible as separate signals, one as a double doublet at δ 2.53 (dd, J= 6.61, 18.25 Hz) and the other as a doublet at δ 2.31 (d, J= 18.25 Hz). In the ^{13}C NMR spectrum, the carbonyl group was visible at δ 211.21 and the carboxylic acid group resonated at δ 179.05. All other signals were in agreement with the assigned structure. The EIMS showed a peak at *m/z* 298 due to $[M^{+}-CO_2]$.

The IR spectrum of **72** showed the characteristic carbonyl and acid absorptions at 1707 and 3180 cm^{-1} respectively. In the ^{1}H NMR spectrum, the C-2 proton exhibited a triplet at δ 4.13 (t, J= 7.76 Hz). The C-3 protons were visible as separate double doublets at δ 3.08 (dd, J= 7.76, 13.63 Hz) and at δ 2.83 (dd, J= 7.76, 13.63 Hz). The C-7 proton appeared as double doublet at δ 2.03 (dd, J= 8.26, 3.48 Hz). The C-6 protons were visible as separate double doublets at δ 2.55 (dd, J= 3.48, 17.50 Hz) and at δ 2.27 (dd, J= 17.50, 8.26, Hz). In the ^{13}C NMR spectrum, the carbonyl and acid groups were visible at δ 211.43 and 179.43 respectively. All other signals were in agreement with the assigned structure.

Tentative assignments of the stereochemistry of all the compounds were made on the basis of spectral data.

A mechanistic rationalization of the ring opening may be presented as shown (Scheme 32).



Scheme 32

In conclusion, we have developed a facile method for the synthesis of cycloheptenones by the ring opening reaction of bicyclo[3.2.1]octenediones.

3.3.3 Experimental Details

To a 2% solution of KOH in methanol (10 mL) bicyclo[3.2.1]octenedione **56** (324 mg, 1 mmol) was added and stirred for 24 h at room temperature. The reaction mixture was diluted with water (40 mL), extracted with dichloromethane (4 x 20 mL) and the organic layer was dried over Na_2SO_4. The solvent was evaporated off and the residue on purification by Chromatotron® using hexane as the eluent, afforded **67** (100 mg, 28%) and **68** (43 mg, 12%) as colorless liquids.

Data for 67

IR (neat) : 2962, 1742, 1694, 1472, 1216, 1169 cm^{-1}.

^1H NMR : δ 7.31-7.19 (m, 5H), 4.14 (t, J= 7.83 Hz, 1H), 3.58 (s, 3H), 3.10 (dd, J= 7.83, 13.78 Hz, 1H), 2.80 (dd, J= 7.83, 13.78 Hz, 1H), 2.55 (dd, J= 6.69, 18.63, Hz, 1H), 2.32 (dd, J= 2.25, 18.63 Hz, 1H), 2.01 (dd, J= 2.25, 6.69 Hz, 1H), 1.50 (s, 9H), 0.91 (s, 9H).

^{13}C NMR : δ 211.01, 178.72, 174.02, 138.89, 136.17, 128.21, 128.14, 127.11, 53.14, 51.62, 48.83, 36.19, 33.24, 29.51, 28.82, 28.13, 27.23.

EIMS *m/z* : 356 (M^+, 22), 324 (30), 296 (100), 239 (43), 91 (35), 57 (88).

Anal. Calcd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.52; H, 9.09.

Data for 68

IR (KBr) : 2955, 1748, 1701, 1627, 1472, 1209, 1162 cm^{-1}.

^1H NMR : δ 7.26-7.19 (m, 5H), 4.08 (t, J= 7.49 Hz, 1H), 3.62 (s, 3H), 3.07 (dd, J= 14.01, 7.49 Hz, 1H), 2.82 (dd, J= 14.01, 7.49 Hz, 1H), 2.54 (dd, J= 6.81, 17.95 Hz, 1H), 2.30 (dd, J= 2.64, 17.95 Hz, 1H), 2.01 (dd, J= 2.64, 6.81 Hz, 1H), 1.11 (s, 9H), 0.95 (s, 9H).

^{13}C NMR : δ 210.96, 178.72, 174.12, 138.96, 136.27, 128.33, 128.24, 127.12, 53.14, 51.78, 49.04, 36.00, 33.18, 32.11, 29.68, 29.50, 27.40.

EIMS *m/z* : 356 (M^+, 8), 296 (10), 239 (6), 121 (12), 91 (23), 57 (100).

Data for 69 and 70

To a 10% solution of KOH in methanol (10 mL) bicyclo[3.2.1]octenedione **56** (324 mg, 1 mmol) was added and the mixture stirred for 5 h at room temperature. The reaction mixture was neutralized with 2 N HCl, extracted with dichloromethane (4 x 20 mL) and the extract was dried over anhydrous Na_2SO_4. The solvent was evaporated off and the residue was purified by Chromatotron® using 5% ethylacetate in hexane as the eluent, to afford **69** (126 mg, 36%) and **70** (124 mg, 36%) as colorless liquids.

Data for 69

IR (neat) : 3211, 2962, 2874, 1713, 1695, 1463, 1370, 1239 cm^{-1}.

^1H NMR : δ 8.78 (brs, 1H), 7.27-7.22 (m, 5H), 4.13 (t, J= 7.45 Hz, 1H), 3.06 (dd, J= 7.45, 13.72 Hz, 1H), 2.83 (dd, J= 7.45, 13.72 Hz, 1H), 2.49 (dd, J= 6.66, 18.24 Hz, 1H), 2.31 (d, J= 18.24 Hz, 1H), 1.99 (d, J= 6.66 Hz, 1H), 1.12 (s, 9H), 0.88 (s, 9H).

^{13}C NMR : δ 211.12, 179.18, 178.95, 138.26, 136.01, 128.34, 128.30, 127.23, 53.09, 48.91, 36.16, 33.22, 32.10, 29.62, 29.21, 27.22.

EIMS *m/z* : 342 (M^+, 3), 324 (30), 296 (100), 281 (5), 239 (30), 225 (7), 184 (10), 151 (10), 91 (14), 57 (24).

Data for 70

IR (neat) : 3200, 2962, 2868, 1707, 1463, 1364, 1233 cm^{-1}.

^1H NMR : δ 8.76 (brs, 1H), 7.27-7.23 (m, 5H), 4.12 (t, J= 7.41 Hz, 1H), 3.10 (dd, J= 7.41, 13.97 Hz, 1H), 2.85 (dd, J= 7.41, 13.97 Hz, 1H), 2.54 (dd, J= 6.64, 18.28 Hz, 1H), 2.26 (dd, J= 2.48, 18.28

Hz, 1H), 2.02 (dd, J= 6.64, 2.48 Hz, 1H), 1.11 (s, 9H), 0.93 (s, 9H).

^{13}C NMR : δ 211.13, 179.09, 179.00, 138.35, 136.05, 128.90, 128.42, 128.34, 127.27, 53.03, 48.97, 36.11, 33.15, 32.14, 29.63, 29.40, 27.38.

Data for 71 and 72

To a 10% solution of KOH in methanol (10 mL) bicyclo[3.2.1]octenedione **56** (324 mg, 1 mmol) was added and the mixture stirred for 5 h at room temperature. The reaction mixture was neutralized with 2 N HCl, extracted with dichloromethane (4 x 20 mL) and the organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated off and the residue was purified by Chromatotron® using 5% ethylacetate in hexane as the eluent, to afford **71** (130 mg, 36%) and **72** (126 mg, 36%) as colorless liquids.

Data for 71

IR (neat) : 3211, 2956, 2863, 1708, 1690, 1607, 1463, 1364, 1226 cm^{-1}.

^{1}H NMR : δ 8.73 (brs, 1H), 7.27-7.23 (m, 5H), 4.13 (t, J= 7.51 Hz, 1H), 3.06 (dd, J= 7.51, 13.71 Hz, 1H), 2.83 (dd, J= 7.51, 13.71 Hz, 1H), 2.53 (dd, J= 6.61, 18.25 Hz, 1H), 2.31 (d, J= 18.25 Hz, 1H), 2.00 (d, J= 6.61 Hz, 1H), 1.12 (s, 9H), 0.88 (s, 9H).

^{13}C NMR : δ 211.21, 179.05, 138.30, 136.05, 128.56, 128.37, 127.26, 53.15, 48.96, 36.19, 33.25, 32.14, 29.64, 29.51, 27.25.

EIMS *m/z* : 298 ([M^+-CO_2], 100), 193 (13), 165 (66), 77 (12).

Data for 72

IR (neat) : 3180, 2968, 2868, 1707, 1463, 1357, 1233 cm^{-1}.

^{1}H NMR : δ 8.78 (brs, 1H), 7.28-7.22 (m, 5H), 4.13 (t, J= 7.76 Hz, 1H), 3.08 (dd, J= 7.76, 13.63 Hz, 1H), 2.83 (dd, J= 7.76, 13.63 Hz, 1H), 2.55 (dd, J= 3.48, 17.50 Hz, 1H), 2.27 (dd, J= 8.26, 17.50 Hz, 1H), 2.03 (dd, J= 8.26, 3.48 Hz, 1H) 1.14 (s, 9H), 0.99 (s, 9H).

^{13}C NMR : δ 211.43, 179.43, 138.41, 136.20, 128.56, 128.51, 127.44, 53.35, 49.14, 36.36, 33.41, 32.31, 29.67, 29.35, 27.54.

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CHAPTER 4

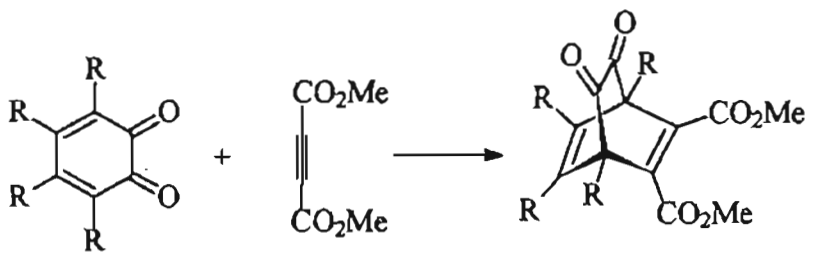
NOVEL SYNTHESIS OF BICYCLO[3.3.0]OCTA-3,7-DIENE-2,6-DIONES

This chapter is divided into three sections. The first section deals with the cycloadditions of *o*-benzoquinones with various phenylacetylenes. The second section describes the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones resulting from the cycloadditions. The last section is concerned with the photolytic rearrangement of bicyclo[3.2.1]octenediones to form bicyclo[3.3.0]octa-3,7-diene-2,6-diones.

4.1 Cycloaddition reactions of *o*-benzoquinones with phenylacetylenes

4.1.1 Introduction

It has been reported that *o*-benzoquinones undergo facile Diels-Alder reactions with DMAD to afford bicyclo[2.2.2]octenediones (Scheme 1).[1]



R= H, Pr, allyl, CH=CHMe

1 2 3

Scheme 1

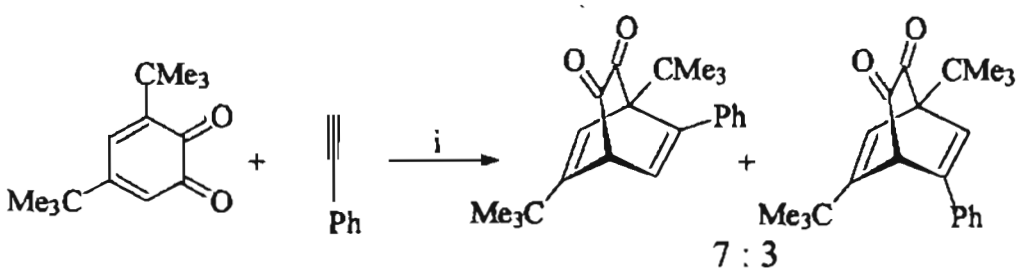
As the follow-up of our investigations on the cycloadditions of *o*-quinones to styrenes, it was of interest to study the reactions with aryl acetylenes.

General introduction to the synthesis of bicyclo[2.2.2]octenediones is given in chapter 2 (Section 2.1).

4.1.2 Results and discussion

We have studied the cycloaddition of a number of *o*-quinones with substituted phenylacetylenes and the results are presented here.

The cycloaddition studies were initiated by the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **4** with phenylacetylene **5**. These on heating in a sealed tube under argon atmosphere afforded two isomeric products **6** and **7** and were separated by Pasteur style physical separation (Scheme 2)*.



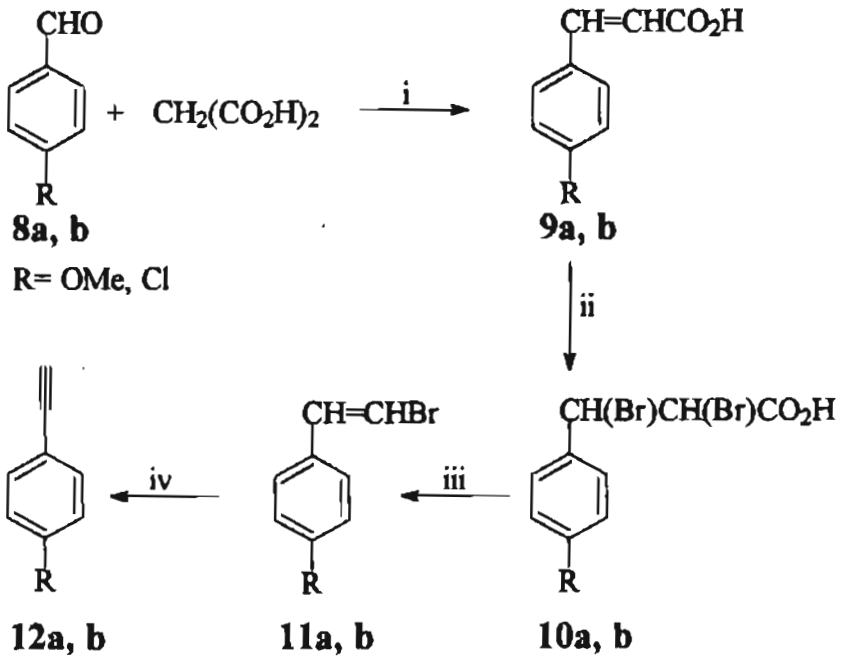
4 **5** **6** **7**

i. Neat, Sealed tube, 120 °C, 36 h, 78%.

Scheme 2

The products were characterized by spectral analysis as reported.[2a,b] In view of the facility with which the cycloaddition occurred, it was decided to extend it to other aryl acetylenes such as 4-methoxyphenylacetylene **12a** and 4-chlorophenylacetylene **12b**. These were prepared by a literature procedure (Scheme 3).[3]

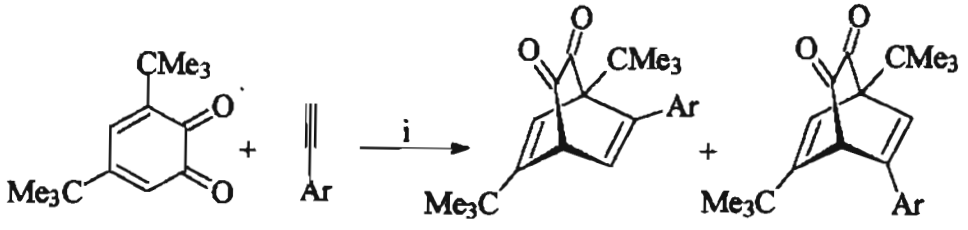
*This reaction has been carried out earlier in our laboratory by Dr. G. Anilkumar.[2]



i. C_5H_5N, $C_5H_{11}N$ ii. Br_2/ $CHCl_3$ iii. aq. Na_2CO_3 iv. KOH, Δ

Scheme 3

The quinone **4** on heating with 4-methoxyphenylacetylene **12a** in a sealed tube, neat at 120 °C under argon atmosphere for 48 h, afforded the products **13** and **14** in 75% yield (Scheme 4). The products were separated by fractional recrystallisation using dichloromethane/ hexane as solvent system.



Ar= 4-methoxyphenyl 5 : 3

4 **12a** **13** **14**

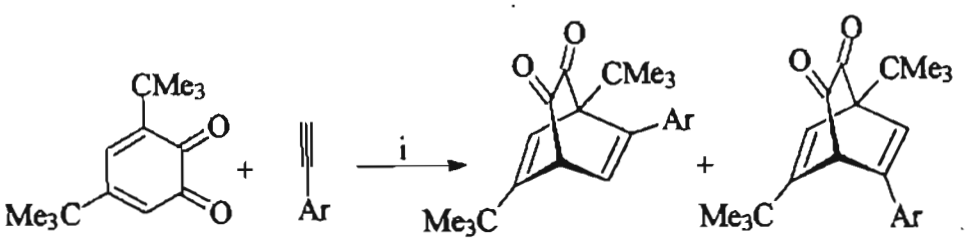
i. Neat, Sealed tube, 120 °C, 48 h, 75%.

Scheme 4

The structure of the products was ascertained from their spectral and analytical data. The IR spectrum of **13** showed a strong absorption at 1742 cm^{-1} indicating the presence of an α-dione. In the ^1H NMR spectrum, the aromatic protons appeared as a multiplet between δ 7.00-6.76. The styrenic proton resonated as a doublet at δ 6.26 (d, J= 6.51 Hz) and the other olefinic proton appeared as a doublet at δ 6.17 (d, J= 2.16 Hz). The bridgehead proton was visible as a double doublet at δ 4.11 (dd, J= 6.51, 2.16 Hz). The methoxy protons were discernible as a singlet at δ 3.80 and the two *tert*-butyl groups appeared as singlets at δ 1.17 and 1.03. In the ^{13}C NMR spectrum, the two carbonyls resonated at δ 182.49 and 181.28. The structure of the product was further supported by satisfactory elemental analysis.

The IR spectrum of **14** showed a strong absorption at 1735 cm^{-1} characteristic of a 1,2-dione moiety. In the ^1H NMR spectrum, the bridgehead proton appeared as a double doublet at δ 4.56 (dd, J= 1.77, 1.55 Hz) and the styrenic proton was visible as a doublet at δ 6.47 (d, J= 1.77 Hz). In the ^{13}C NMR spectrum, the two carbonyls were discernible at δ 182.65 and 181.40. All other peaks were in agreement with the assigned structure. Analytical data also supported this structure.

In a similar experiment, **4** on heating with 4-chlorophenylacetylene **12b** in a sealed tube neat at 120 °C under argon atmosphere for 40 h, afforded the products **15** and **16** in 84% yield (Scheme 5).



Ar= 4-chlorophenyl 6 : 5

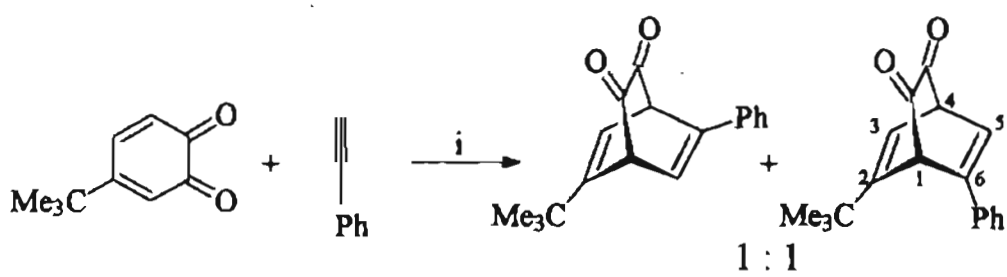
4 **12b** **15** **16**

i. Neat, Sealed tube, 120 °C, 40 h, 84%.

Scheme 5

The products were isolated as an inseparable mixture and the ratio of the adducts was ascertained on the basis of ^{1}H NMR spectrum. In the IR spectrum of the mixture, a strong absorption band at 1744 cm^{-1} indicated the presence of α-dione moiety. In the ^{1}H NMR spectrum, the bridgehead proton of **15** was seen as a double doublet at δ 4.16 (dd, J= 6.53, 2.37 Hz) and that of **16** appeared also as a double doublet at δ 4.54 (dd, J= 1.76, 2.12 Hz). The styrenic proton of **15** was visible as a doublet at δ 6.31 (d, J= 6.53 Hz) while that of **16** resonated as a doublet at δ 6.60 (d, J= 1.76 Hz). In the ^{13}C NMR spectrum, the carbonyls were discernible at δ 182.23, 182.18, 181.19 and 180.92 and the bridgehead carbons appeared at δ 65.97, 62.44, 55.30, and 51.95. All other signals were in agreement with the assigned structure.

4-*tert*-Butyl-*o*-benzoquinone **17** on heating with phenylacetylene **5** in a Schlenk glass tube neat at 80 °C for 10 h, afforded the products **18** and **19** in 67% yield (Scheme 6).



17 **5** **18** **19**

i. Neat, Sealed tube, 80 °C, 10 h, 67%.

Scheme 6

The products were isolated as an inseparable mixture and the ratio was determined to be 1:1 on the basis of ^{1}H NMR spectrum. IR spectrum of the mixture of **18** and **19** displayed a strong absorption band at 1744 cm^{-1} due to α-dione moiety. In the ^{1}H NMR spectrum, the C-1 proton in **19** appeared as a triplet at δ 4.66 (t, J= 2.05 Hz) and the C-4 proton resonated also as a triplet at δ 4.14 (t, J= 6.39 Hz), whereas the bridgehead protons of **18** resonated as double doublets at δ 4.26 (dd, J= 6.50, 2.31 Hz) and δ 4.53 (dd, J= 6.48, 2.35 Hz). In the ^{13}C NMR spectrum, the carbonyls were discernible at δ 182.18, 181.01, 180.92 and 179.82 and the bridgehead carbons resonated at δ 56.44, 53.84, 53.27 and 50.75. All other signals were in agreement with the assigned structure.

4.1.3 Experimental Details

General information about the experiments is given in chapter 2.

Diels-Alder adducts 13 and 14

3,5-Di-*tert*-butyl-*o*-benzoquinone **4** (500 mg, 2.27 mmol) and 4-methoxyphenylacetylene **12a** (356 mg, 2.72 mmol) were heated in a sealed tube neat at 120 °C for 48 h. The crude product on purification by column chromatography on silica gel using 2% ethylacetate in hexane as eluent afforded the product (598 mg, 75%) as a mixture of regioisomers **13** and **14** in the ratio 5:3. The two isomers were separated by fractional crystallization using dichloromethane/ hexane solvent system.

1,5-Bis(1,1-dimethylethyl)-7-(4-methoxyphenyl)bicyclo[2.2.2]oct-5,7-diene-2,3-dione (13) Yellow crystals (mp. 136-138 °C).

IR (KBr) : 2969, 2867, 1742, 1607, 1499, 1472, 1364, 1297, 1243, 1034 cm^{-1}.

^1H NMR : δ 7.00-6.76 (m, 4H), 6.26 (d, J= 6.51 Hz, 1H), 6.17 (d, J= 2.16 Hz, 1H), 4.11 (dd, J= 6.51, 2.16 Hz, 1H), 3.80 (s, 3H), 1.17 (s, 9H), 1.03 (s, 9H).

^{13}C NMR : δ 182.49, 181.28, 159.00, 153.43, 149.16, 132.78, 131.40, 131.09, 123.76, 112.80, 65.91, 55.01, 51.81, 35.09, 33.34, 27.97.

Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.38; H, 8.01. Found: C, 78.77; H, 7.93.

1,5-Bis(1,1-dimethylethyl)-8-(4-methoxyphenyl)bicyclo[2.2.2]oct-5,7-diene-2,3-dione (14) Orange Crystals (mp. 123-125 °C).

IR (KBr) : 2969, 2867, 1735, 1613, 1519, 1256, 1034 cm^{-1}.

^1H NMR : δ 7.43-6.87 (m, 4H), 6.47 (d, J= 1.77 Hz, 1H), 6.09 (d, J= 1.55 Hz, 1H), 4.56 (dd, J= 1.77, 1.55 Hz, 1H), 3.81 (s, 3H), 1.24 (s, 9H), 1.17 (s, 9H).

^{13}C NMR : δ 182.65, 181.40, 160.12, 154.50, 143.16, 127.80, 126.94, 124.94, 122.46, 114.19, 61.95, 55.28, 55.15, 35.47, 31.64, 28.27.

Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.38; H, 8.01. Found: C, 78.67; H, 7.85.

Diels-Alder adducts 15 and 16

3,5-Di-*tert*-butyl-*o*-benzoquinone **4** (330 mg, 1.5 mmol) and 4-chlorophenylacetylene **12b** (265 mg, 1.95 mmol) were heated in a sealed tube at 120 °C without any solvent for 40 h. The crude product, on purification by column chromatography on silica gel using 2% ethylacetate in hexane as eluent afforded the product (451 mg, 84%) as a mixture of regioisomers **15** and **16**.

Data for Diels-Alder adducts 15 and 16 Yellow solid.

IR (KBr) : 2968, 2881, 1744, 1482, 1364, 1089 cm^{-1}.

^1H NMR : δ 7.41-7.02 (m, 8H), 6.60 (d, J= 1.76 Hz, 1H), 6.31 (d, J= 6.53 Hz, 1H), 6.18 (d, J= 2.37 Hz, 1H), 6.11 (d, J= 2.12 Hz, 1H), 4.54 (dd, J= 1.76, 2.12 Hz, 1H), 4.16 (dd, J= 6.53 Hz, 2.37 Hz, 1H), 1.17 (s, 36H).

^{13}C NMR : δ 182.23, 182.18, 181.19, 180.92, 154.67, 153.84, 148.26, 142.65, 137.76, 134.81, 133.94, 133.80, 133.37, 131.74, 129.09, 127.91, 127.69, 126.99, 123.71, 122.46, 65.97, 62.44, 55.30, 51.95, 35.56, 35.19, 33.40, 31.71, 28.27, 27.99.

Anal. calcd for $C_{22}H_{25}O_2Cl$: C, 74.04; H, 7.06; Cl, 9.93. Found: C, 74.49; H, 7.19; Cl, 9.52.

Diels-Alder adducts 18 and 19

4-*tert*-Butyl-*o*-benzoquinone **17** (308 mg, 1.8 mmol) and phenylacetylene **5** (249 mg, 2.44 mmol) were heated in a sealed tube at 80 °C without any solvent for 10 h. The crude product on purification by column chromatography on silica gel using 5% ethylacetate in hexane as eluent afforded the product (250 mg, 50%) as a mixture of regioisomers **18** and **19** in the ratio 1:1.

Data for Diels-Alder adducts 18 and 19 Yellow solid.

IR (KBr) : 2962, 2868, 1744, 1626, 1476, 1357, 1270, 1114 cm^{-1}.

^{1}H NMR : δ 7.48-7.31 (m, 10H), 6.66-6.64 (m, 2H), 6.22-6.18 (m, 2H), 4.66 (t, J= 2.05 Hz, 1H), 4.53 (dd, J= 6.48, 2.35 Hz, 1H), 4.26 (dd, J= 6.50, 2.31 Hz, 1H), 4.14 (t, J= 6.39 Hz, 1H), 1.15 (s, 18H).

^{13}C NMR : δ 182.18, 181.01, 180.92, 179.82, 154.92, 154.49, 143.95, 143.30, 135.07, 134.96, 128.93, 128.84, 128.65, 127.23, 126.92, 125.68, 123.94, 123.18, 119.71, 119.23, 56.44, 53.84, 53.27, 50.75, 35.34, 31.46, 28.27, 27.95.

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.48; H, 6.78.

4.2 Synthesis of bicyclo[3.2.1]octenediones by the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones

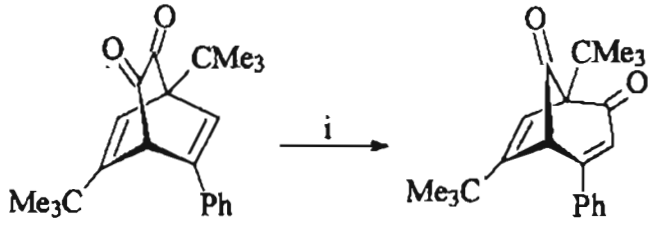
4.2.1 Introduction

A general introduction to the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones leading to bicyclo[3.2.1]octenediones has been presented in section 3.2 (Chapter 3).

4.2.2 Results and discussion

The bicyclo[2.2.2]octenediones described in the previous section (4.1) are interesting from the point of view of their potential for further transformations. Hence it was decided to study some aspects of their chemistry.

The bicyclo[2.2.2]octenedione **7** when refluxed with BF_3-etherate in chloroform yielded the bicyclo[3.2.1]octene-2,8-dione **20** in 92% yield (Scheme 7).



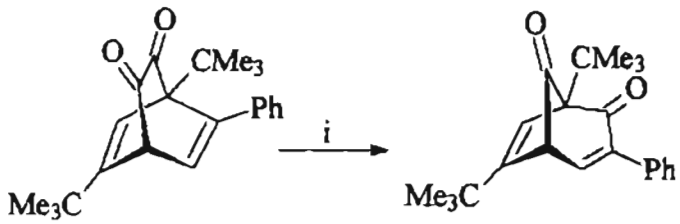
7 **20**

i. BF_3-OEt_2, $CHCl_3$, Reflux, 2h, 92%

Scheme 7

The structure of the product was ascertained on the basis of spectral and analytical data.[2b,2c]

The bicyclic dione **6** also rearranged smoothly on refluxing with BF_3-OEt_2 to afford the bicyclo[3.2.1]octenedione **21** in 89% yield (Scheme 8).



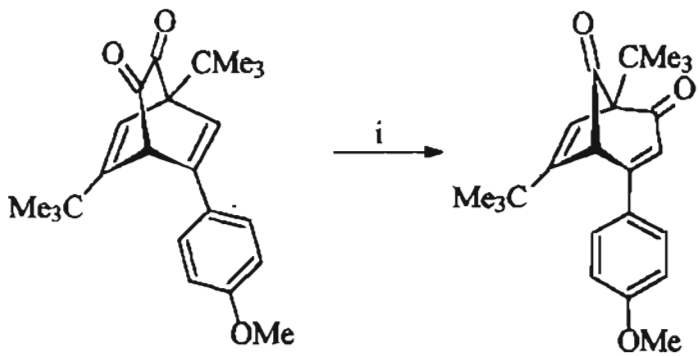
6 **21**

i. BF_3-OEt_2, $CHCl_3$, Reflux, 4 h, 89%

Scheme 8

The structure of the product was ascertained on the basis of spectral and analytical data.[2b,2c]

Similarly, the bicyclo[2.2.2]octenedione **14** when treated with BF_3-etherate in chloroform afforded the bicyclo[3.2.1]octenedione **22** in quantitative yield (Scheme 9).



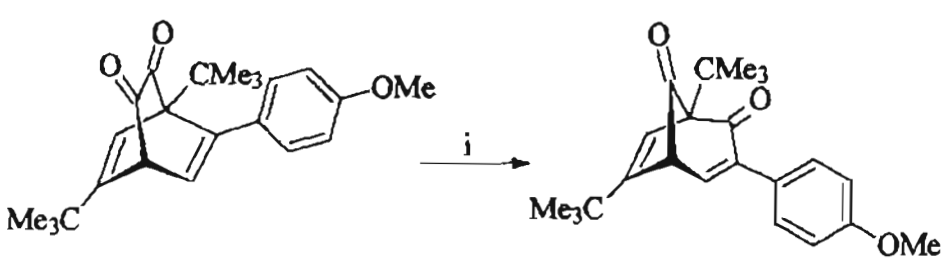
14 **22**

i. BF_3-OEt_2, $CHCl_3$, RT, 1 h, 100%

Scheme 9

The product was characterized by analytical and spectroscopic methods. The IR spectrum of **22** showed two strong absorptions at 1773 and 1666 cm^{-1} indicating the presence of bridgehead carbonyl and enone carbonyl respectively. The ^1H NMR spectrum exhibited two signals at δ 0.98 and 1.23 integrating for nine protons each, corresponding to the two tertiary butyl groups. The singlet at δ 4.25 has been assigned to the bridgehead proton and those at δ 6.19 and 5.91 have been attributed to the styrenic and the other olefinic protons respectively. The methoxy protons were visible as a singlet at δ 3.85. The four aromatic protons appeared as a multiplet at δ 7.53-6.93. In the ^{13}C NMR spectrum, the two carbonyl carbons resonated at δ 200.51 and 192.14. The structure was further supported by analytical data.

The bicyclo[2.2.2]octenedione **13**, the regioisomer of **14** when treated with BF_3-etherate in chloroform afforded the bicyclo[3.2.1]octenedione **23** in high yield (Scheme 10).



13 **23**

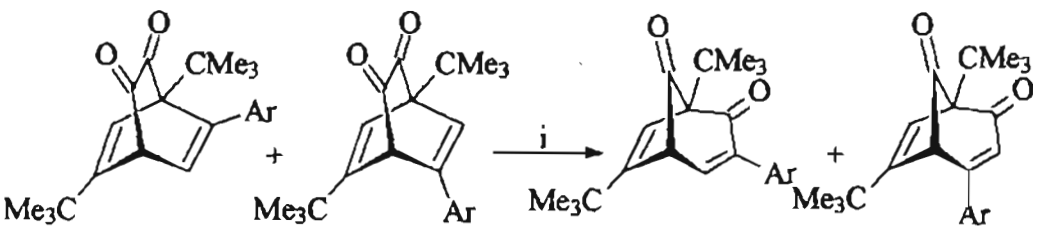
i. BF_3-OEt_2, $CHCl_3$, RT, 1 h, 94%

Scheme 10

The IR spectrum of **23** showed absorptions at 1770 and 1674 cm^{-1} indicating the presence of bridgehead carbonyl and enone carbonyl

respectively. In the ^1H NMR spectrum, the proton β to the enone carbonyl and the phenyl protons appeared together as a multiplet at δ 7.33-6.83. The bridgehead proton and the methoxy protons appeared together as a singlet at δ 3.78 integrating for four protons. The two carbonyl carbons resonated at δ 199.61 and 191.80 in the ^{13}C NMR spectrum. All other signals were in agreement with the assigned structure.

The mixture of the diones **15** and **16** when refluxed with BF_3-etherate in chloroform afforded the bicyclo[3.2.1]octenediones **24** and **25** in 90% yield (Scheme 11).



15 **16** **24** **25**

i. BF_3-OEt_2, $CHCl_3$, Reflux, 3 h, 90%

Scheme 11

The products were isolated as a mixture and were separated by fractional crystallization from hexane to afford **24** as a white spongy solid and **25** as a pale green crystalline solid. As usual, the structures of the products were ascertained from their spectral data. In the IR spectrum of **24**, the two carbonyls absorbed at 1782 and 1681 cm^{-1}. In the ^1H NMR spectrum, the bridgehead proton displayed a doublet at δ 3.84 (d, J= 7.64 Hz). The ^{13}C NMR spectrum showed two peaks at δ 199.04 and

191.10 corresponding to the two carbonyl groups. All other signals were in agreement with the assigned structure.

IR spectrum of **25** showed the carbonyl absorptions at 1775 and 1667 cm^{-1}. The bridgehead proton resonated as a singlet at δ 4.17 in the ^{1}H NMR spectrum. The ^{13}C NMR spectrum showed the presence of two carbonyls at δ 199.92 and 191.74. All other signals were in agreement with the assigned structure.

4.2.3 Experimental Details

General information about the BF_3-etherate induced rearrangement was described in section 3.2.3 (Chapter 3).

1,6-Bis(1,1-dimethylethyl)-4-(4-methoxyphenyl)bicyclo[3.2.1]oct-3,6-diene-2,8-dione (22)

A solution of **14** (352 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 1 h. The usual work up followed by chromatographic purification of the product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **22** quantitatively as a pale yellow crystals (mp. 103-105 °C).

IR (KBr) : 2967, 2878, 1773, 1666, 1367, 1232 cm^{-1}.

^{1}H NMR : δ 7.53-6.93 (m, 4H), 6.19 (s, 1H), 5.91 (s, 1H), 4.25 (s, 1H), 3.85 (s, 3H), 1.23 (s, 9H), 0.98 (s, 9H).

^{13}C NMR : δ 200.51, 192.14, 161.32, 157.62, 128.04, 127.67, 124.14, 122.73, 114.54, 113.96, 77.33, 57.49, 55.21, 34.32, 32.63, 28.40.

Anal. Calcd for $C_{23}H_{28}O_3$: C,78.38; H, 8.01. Found: C, 78.12; H, 8.08.

1,6-Bis(1,1-dimethylethyl)-3-(4-methoxyphenyl)bicyclo[3.2.1]oct-3,6-diene-2,8-dione (23)

A solution of **13** (352 mg, 1 mmol) in dry chloroform (20 mL) was stirred at room temperature with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 1 h. The usual work up followed by chromatographic purification of the product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **23** (317 mg, 90%) as a pale green liquid.

IR (neat) : 2962, 2872, 1770, 1674, 1510, 1463, 1364, 1247, 1178 cm^{-1}.

^1H NMR : δ 7.33-6.83 (m, 5H), 5.83 (s, 1H), 3.78 (s, 4H), 1.12 (s, 18H).

^{13}C NMR : δ 199.61, 191.80, 162.81, 159.58, 143.58, 139.41, 130.02, 127.92, 120.98, 113.48, 79.44, 56.21, 55.14, 33.85, 33.27, 28.16.

Data for 24 and 25.

A solution of **15** and **16** (356 mg, 1 mmol) in dry chloroform (20 mL) was refluxed with BF_3-etherate (0.15 mL, 170 mg, 1.2 mmol) for 1 h. The usual work up followed by chromatographic purification of the product on silica gel column using 2% ethyl acetate in hexane as eluent afforded **24** and **25** (320 mg, 90%) as a mixture and were separated by fractional crystallization from hexane to afford **24** as a white spongy solid and **25** as a pale green crystalline solid in the ratio 2.5:1.

1,6-Bis(1,1-dimethylethyl)-3-(4-chlorophenyl)bicyclo[3.2.1]oct-3,6-diene-2,8-dione (24), white spongy solid (mp. 181-183 °C).

IR (KBr) : 2969, 2874, 1782, 1681, 1485, 1101 cm^{-1}.

^{1}H NMR : δ 7.39 (d, J= 7.64 Hz, 1H), 7.31-7.16 (m, 4H), 5.84 (s, 1H), 3.84 (d, J= 7.64 Hz, 1H), 1.26 (s, 9H), 1.14 (s, 9H).

^{13}C NMR : δ 199.04, 191.10, 162.76, 144.84, 138.87, 134.25, 133.79, 130.07, 128.18, 121.02, 79.60, 56.18, 33.83, 33.25, 28.11.

EIMS *m/z* : 356 (M^+, 54), 341 (100), 313 (100), 293 (33), 271 (10), 149 (14).

1,6-Bis(1,1-dimethylethyl)-4-(4-chlorophenyl)bicyclo[3.2.1]oct-3,6-diene-2,8-dione (25), pale green crystalline solid (mp. 140-142 °C).

IR (KBr) : 2962, 2874, 1775, 1667, 1600, 1411 cm^{-1}.

^{1}H NMR : δ 7.44-7.41 (m, 4H), 6.17 (s, 1H), 5.89 (s, 1H), 4.17 (s, 1H), 1.23 (s, 9H), 0.96 (s, 9H).

^{13}C NMR : δ 199.92, 191.74, 161.61, 156.97, 136.44, 134.85, 129.45, 127.27, 126.41, 122.50, 77.74, 57.87, 34.29, 32.71, 28.39.

EIMS *m/z* : 358 (M^++2, 20), 356 (M^+, 57), 341 (97), 313 (100), 293 (33).

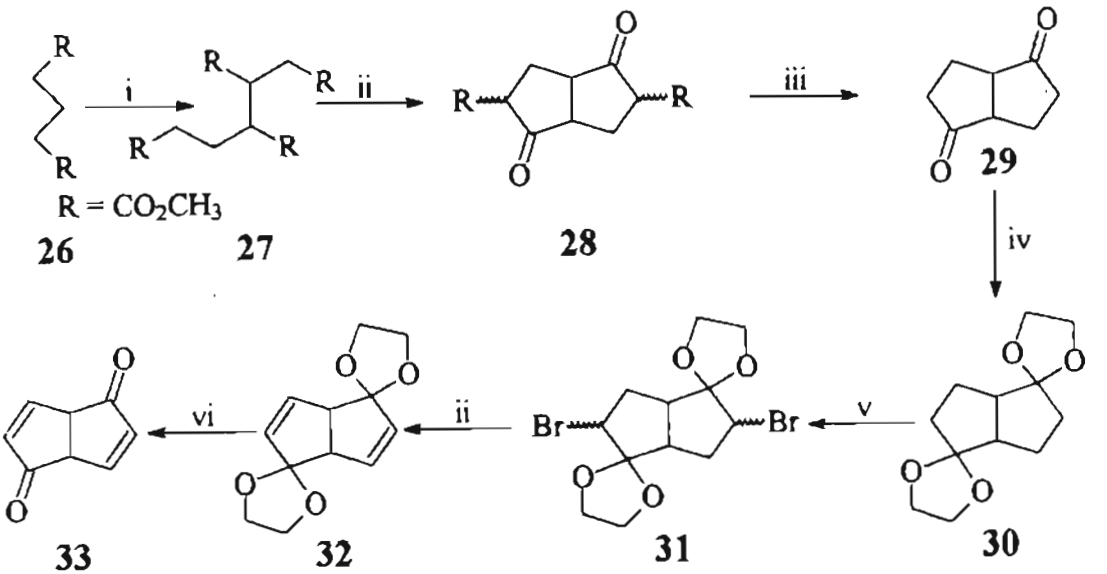
4.3 Synthesis of bicyclo[3.3.0]octa-3,7-diene-2,6-diones by the photolytic rearrangement of bicyclo[3.2.1]octenediones

4.3.1 Introduction

The bicyclo[3.2.1]octenediones resulting from the BF_3-etherate induced rearrangement of the cycloadducts of aryl acetylenes and *o*-quinones, appeared to be interesting substrates for photochemical investigations. It was expected that, on photolysis the bicyclo[3.2.1]octenedione system would lose its ring strain either by a photodecarbonylation of the bridgehead carbonyl group or by a Norrish type-I cleavage involving the other carbonyl group followed by a ring closure. The first pathway would lead to a tropone derivative, whereas a bicyclo[3.3.0]octa-3,7-diene-2,6-dione would result from the second pathway. In the event, the bicyclo[3.2.1]octenediones, on photolysis, underwent facile rearrangement to afford bicyclo[3.3.0]octa-3,7-diene-2,6-dione systems. The results of these studies are presented in this section.

At this point, it is appropriate to briefly review the methods for the construction of this bicyclo[3.3.0]octa-3,7-diene-2,6-dione system.

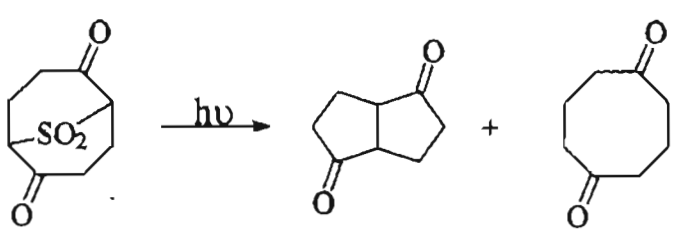
Although these compounds have been known from the work of Ruzicka[4] and Dauben,[5] the original procedures are cumbersome, especially for molar quantity operations. Later Farnum and Hagedorn described a method for the synthesis of these systems on molar scale (Scheme 12).[6]



i. $(CH_3)_3COOC(CH_3)_3$, Δ ii. $NaOCH_3$, $(CH_3)_2SO$ iii. H^+, H_2O iv. $HOCH_2CH_2OH$, H^+, Δ v. $C_5H_6N^+Br_3^-$, THF vi. $(CH_3)_2CO$, H^+, Δ

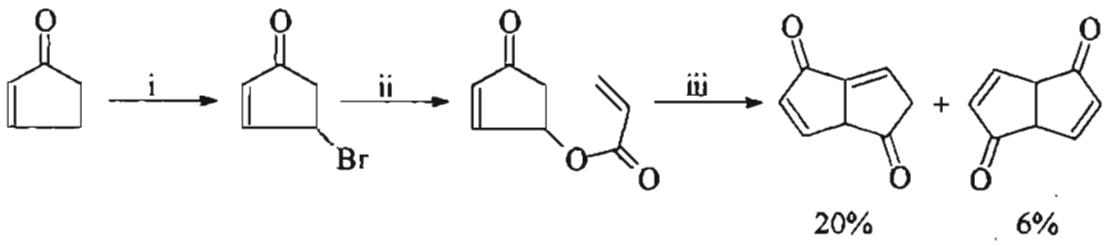
Scheme 12

The compound **29** has also been prepared by a photolytic method. Photolysis of the sulfone **34** in methanol leads to the loss of the bridging SO_2 leading to the formation of **29** and **35** (Scheme 13).[7]



Scheme 13

Gavina has developed a method[8] for the synthesis of bicyclo[3.3.0]octa-1,3,7-triene-2,6-dione as outlined below (Scheme 14).

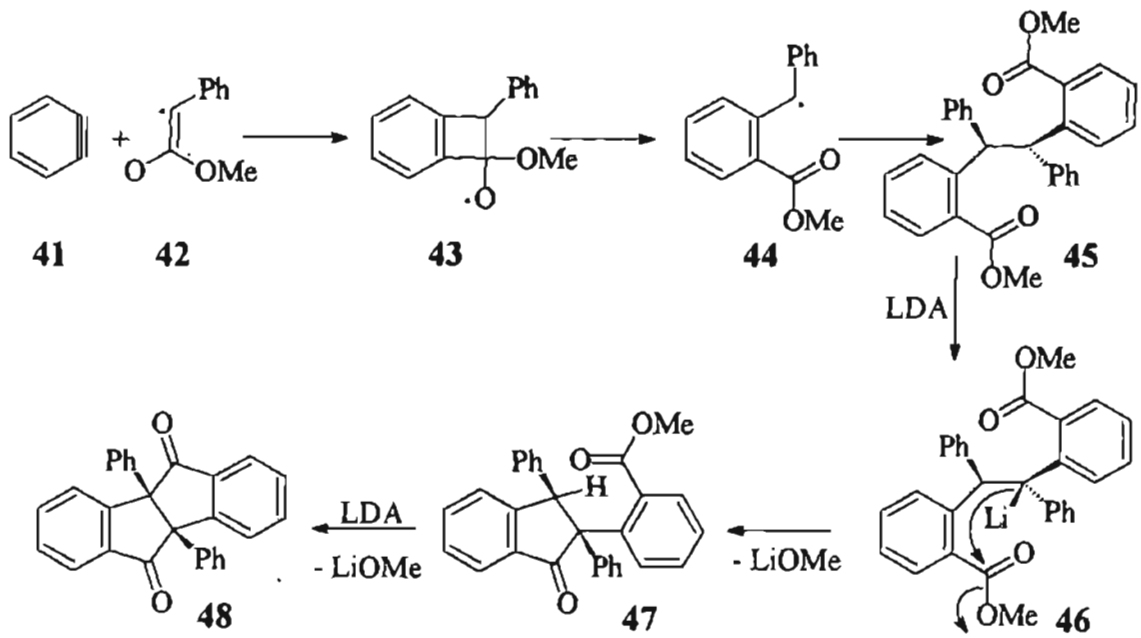


36 **37** **38** **39** **40**

i. NBS, CCl_4, ii. $CH_2 = CHCO_2Ag$, iii. PPA, H_2O

Scheme 14

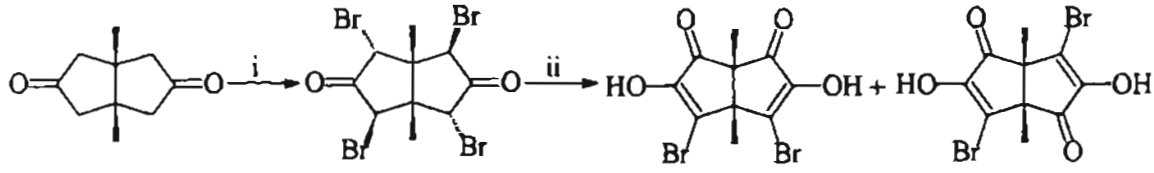
The bicyclo[3.3.0]octa-2,6-dione derivative with fused benzene rings on both sides *eg. cis*-4b,9b-diphenyl-4b,5,9b,10-tetrahydroindeno-2,1,*a*-indene-5,10-dione **48** was prepared starting from benzyne (Scheme 15).[9]



41 **42** **43** **44** **45** **46** **47** **48**

Scheme 15

The bicyclo[3.3.0]octa-3,7-diene-2,6-dione derivative **52** was prepared from bicyclo[3.3.0]octa-3,7-dione by acid treatment of the tetrabromo compound **50** (Scheme 16).[10]



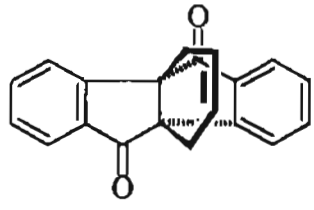
49 **50** **51** **52**

i. Br_2 ii. H_2SO_4

Scheme 16

Bicyclo[3.3.0]octa-3,7-diene-2,6-diones are synthetically valuable compounds. Some derivatives have been used for the synthesis of dodecahedron.[11] These bicyclic systems can be easily be converted to bisazo compounds, used as important ligands in coordination chemistry.[12]

A number of bicyclo[3.3.0]dienedione derivatives have been found to be biologically active. One of the enantiomers of **53** is effective as a non-nucleoside HIV-1 reverse transcriptase inhibitor.[13]

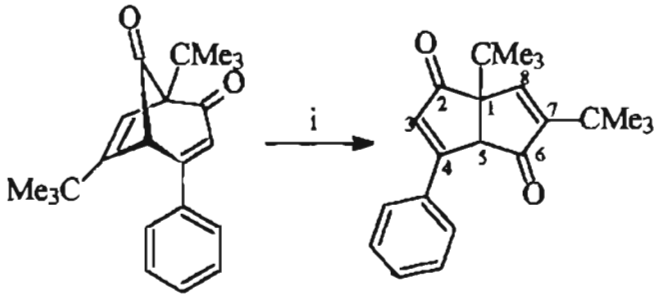


53

It is evident from the literature survey that there has been only a few methods available for the synthesis of this bicyclo[3.3.0]octa-3,7-diene-2,6-dione systems and these are of limited scope. The details of the novel photolytic route to these compounds encountered by us are presented here.

4.3.2 Results and discussion

The bicyclo[3.2.1]octenedione **20**, when subjected to photolysis in acetonitrile in a pyrex vessel at 300 nm, using a Rayonet Photochemical Reactor afforded a compound which was identified as **54** on the basis of its spectral and analytical data (Scheme 17).

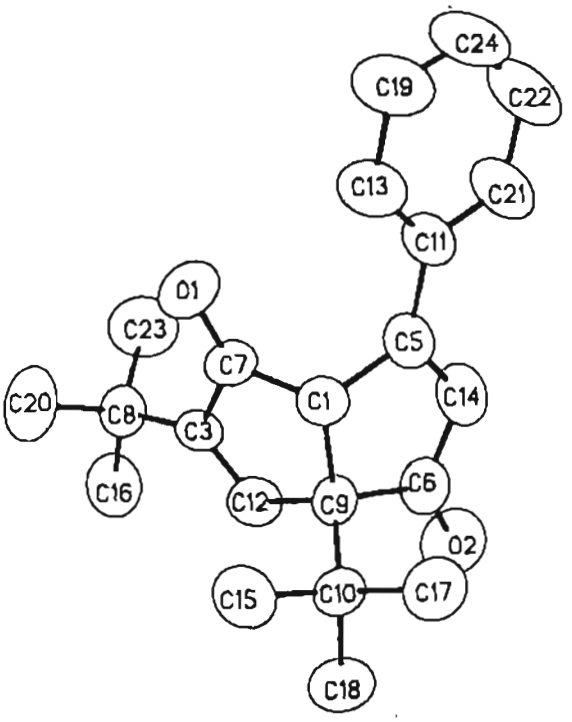


20 **54**

i. hν, Pyrex, 300 nm, 30 min., 52%

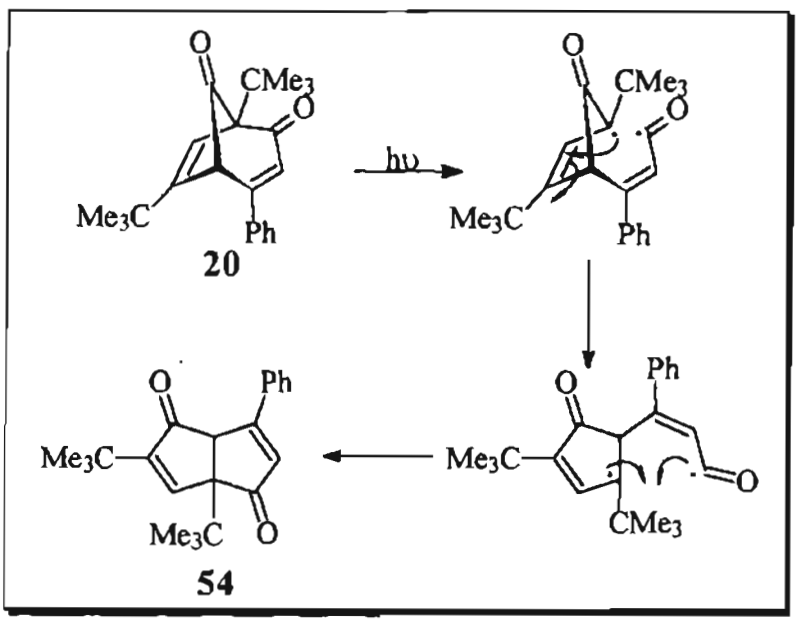
Scheme 17

The IR spectrum of compound **54**, showed strong absorptions at 1682 and 1705 cm^{-1} attributed to the presence of C-2 and C-6 enone carbonyls respectively. In the ^{1}H NMR spectrum, the ring junction proton appeared as a singlet at δ 4.09. The styrenic proton resonated as a singlet at δ 6.31. The other olefinic proton appeared along with the phenyl protons as a multiplet between δ 7.92-7.48 and the *tert*-butyl groups displayed two singlets at δ 1.08 and 1.13 integrating for nine protons each. In the ^{13}C NMR spectrum, the two carbonyls resonated at δ 205.86 and 200.90 and the ring junction carbons appeared at δ 66.20 and 57.56. The analytical data was also in agreement with the assigned structure. The structure was confirmed unequivocally by single crystal X-ray determination.



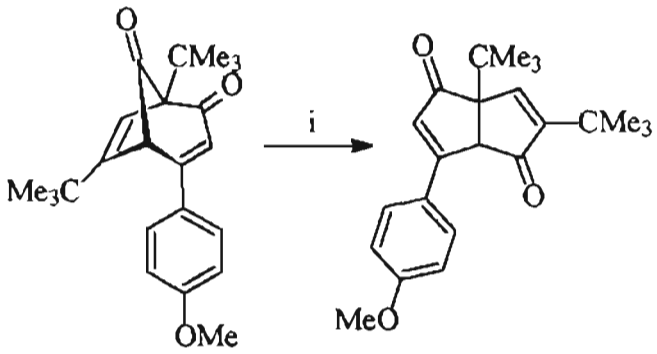
X-Ray crystal structure 54

Regarding the mechanism of the photolytic rearrangement, a rationalization along the following line may be invoked (Scheme 18).



Scheme 18

The bicyclic compound **22** on irradiation under conditions identical to those described earlier afforded **55** in 67% yield (Scheme 19).



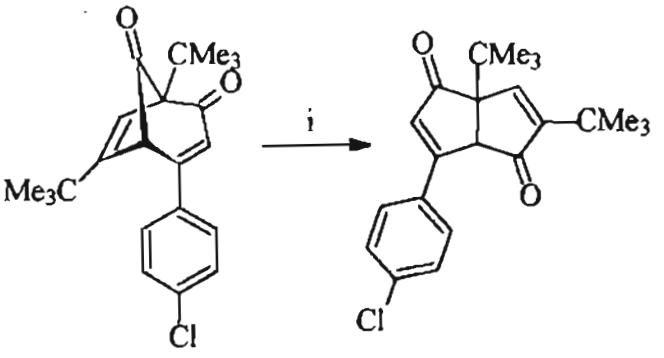
22 **55**

i. hν, Pyrex, 300 nm, 10 min., 67%

Scheme 19

The structure of the product was ascertained by spectral analysis. The IR spectrum showed two enone carbonyls at 1703 and 1679 cm^{-1}. In the ^{1}H NMR spectrum, the methoxy protons exhibited a singlet at δ 3.84 and the ring junction proton resonated as a doublet at δ 3.99 (d, J= 0.88 Hz). In the ^{13}C NMR spectrum, the two carbonyls resonated at δ 205.38 and 201.06. All other signals were in agreement with the assigned structure. The structure was further confirmed by satisfactory elemental analysis.

Similarly, the adduct **25** on irradiation in acetonitrile afforded the product **56** in very high yield (Scheme 20).



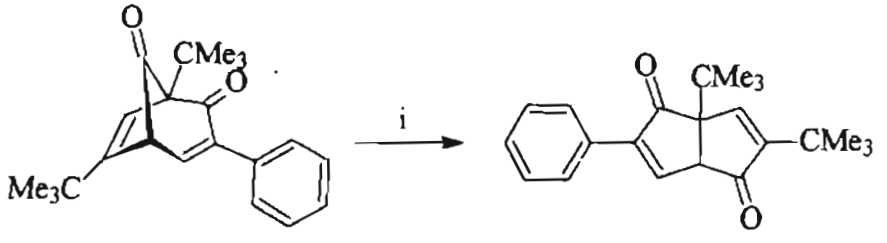
25 **56**

i. hυ, Pyrex, 300 nm, 15 min., 94%

Scheme 20

The IR spectrum of **56** showed two carbonyl absorptions at 1710 and 1686 cm^{-1}. In the ^{1}H NMR spectrum, the ring junction proton appeared as a doublet at δ 4.01 (d, J= 0.96 Hz) and the styrenic proton was discernible as a doublet at δ 6.26 (d, J= 0.96 Hz). In the ^{13}C NMR spectrum, the two carbonyls resonated at δ 205.25 and 200.65 and the two bridgehead carbons appeared at δ 66.19 and 57.45. All other signals were in agreement with the assigned structure.

The product **21** also rearranged smoothly on photolysis in acetonitrile using pyrex vessel at 300 nm in a Rayonet Photochemical Reactor and yielded the compound **57** (Scheme 21).



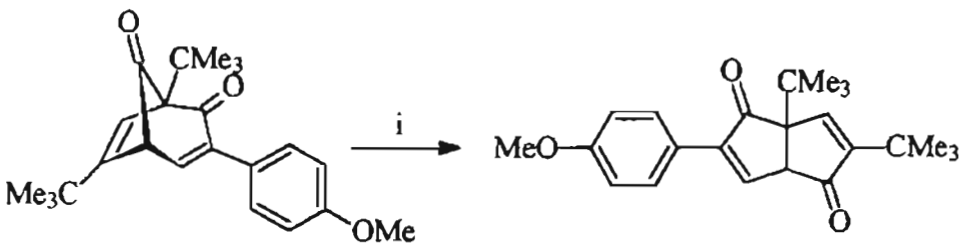
21 **57**

i. hν, Pyrex, 300 nm, 75 min., 45%

Scheme 21

The structure of the product was ascertained on the basis of spectral data. The IR spectrum showed a characteristic enone absorption at 1700 cm^{-1}. In the ^1H NMR spectrum, the ring junction proton appeared as a doublet at δ 3.57 (J= 4.5 Hz). In the ^{13}C NMR spectrum, the carbonyls were visible at δ 204.21 and 202.16. The high resolution mass spectrum also supported the assigned structure.

Similarly, compound **23** when subjected to photolysis in acetonitrile in a pyrex vessel at 300 nm using a Rayonet Photochemical Reactor yielded the dione **58** (Scheme 22).



23 **58**

i. hυ, Pyrex, 300 nm, 30 min., 30%

Scheme 22

The structure of the product was determined on the basis of spectral and analytical data. The IR spectrum of **58** showed absorptions at 1726 and 1701 cm^{-1} corresponding to the two enone carbonyls. In the ^1H NMR spectrum, both the vinylic protons resonated along with the phenyl protons as a multiplet between δ 7.68-6.86. In the ^{13}C NMR spectrum, the two carbonyls resonated at δ 204.52 and 202.19 and the two ring junction carbons were visible at δ 56.58 and 38.72. All other signals were similar to those of **77**. The assigned structure was further supported by the mass spectrum showing the presence of a molecular ion peak at *m/z* 352.

In conclusion, we have developed a simple synthesis of bicyclo[3.3.0]oct-3,7-diene-2,6-diones by photolytic rearrangement of bicyclo[3.2.1]octenediones, the latter being prepared by the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones, obtained by the Diels-Alder reactions of 3,5-di-*tert*-butyl-1,2-benzoquinone with phenylacetylenes.

4.3.3 Experimental Details

Distilled acetonitrile was used as solvent for photolysis. Irradiation was carried out in a 250 mL photochemical pyrex vessel using 300 nm lamp.

1,7-Bis(1,1-dimethylethyl)-4-phenylbicyclo[3.3.0]oct-3,7-diene-2,6-dione (54)

A solution of the dione **20** (100 mg, 0.3 mmol) in acetonitrile (300 mL) was purged with argon for 1 h in a pyrex vessel and irradiated for 30 min. inside a Rayonet Photochemical Reactor using 300 nm lamp. The reaction mixture was then concentrated and purified by a Chromatotron® using 1% ethylacetate in hexane as eluent to afford **54** (52 mg, 52%) as a colorless crystalline solid (mp. 165-167 °C).

IR (KBr) : 2968, 2874, 1705, 1682, 1594, 1570, 1467, 1366, 1184 cm^{-1}.

^1H NMR : δ 7.92-7.48 (m, 5H), 7.29 (s, 1H), 6.31 (s, 1H), 4.09 (s, 1H), 1.13 (s, 9H), 1.08 (s, 9H).

^{13}C NMR : δ 205.86, 200.90, 167.75, 153.96, 152.62, 132.23, 131.63, 128.77, 128.72, 125.34, 66.20, 57.56, 36.10, 32.30, 28.24, 26.08.

Anal. Calcd for $C_{22}H_{26}O_2$: C,81.94; H, 8.13. Found: C, 81.82; H, 8.14.

1,7-Bis(1,1-dimethylethyl)-4-(4-methoxyphenyl)bicyclo[3.3.0]oct-3,7-diene-2,6-dione (55)

A solution of the dione **22** (45 mg, 0.12 mmol) in acetonitrile (300 mL) was purged with argon for 1 h and irradiated for 10 min. The reaction mixture on purification using usual methods afforded **55** (30 mg, 67%) as a colorless crystalline solid (mp. 151-153 °C).

IR (KBr) : 2956, 2862, 1703, 1679, 1590, 1563, 1461, 1263, 1185 cm^{-1}.

^1H NMR : δ 7.87 (d, J= 8.88 Hz, 2H), 7.26 (s, 1H), 6.96 (d, J= 8.88 Hz, 2H), 6.15 (d, J= 0.88 Hz, 1H), 3.99 (d, J= 0.88 Hz, 1H), 3.84 (s, 3H), 1.10 (s, 9H), 1.05 (s, 9H).

^{13}C NMR : δ 205.38, 201.06, 167.08, 162.45, 154.19, 152.41, 130.81, 124.80, 122.95, 114.09, 66.06, 57.46, 55.36, 36.03, 32.30, 28.29, 26.15.

Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.38; H, 8.01. Found: C, 78.67; H, 8.07.

1,7-Bis(1,1-dimethylethyl)-4-(4-chlorophenyl)bicyclo[3.3.0]oct-3,7-diene-2,6-dione (56)

A solution of the dione **25** (50 mg, 0.14 mmol) in acetonitrile (300 mL) was purged with argon for 1 h and irradiated for 15 min. The reaction mixture on purification using usual methods afforded **56** (47 mg, 94%) as a colorless crystalline solid (mp. 181-183 °C).

IR (KBr) : 2930, 2856, 1710, 1686, 1592, 1489, 1464, 1317, 1182 cm^{-1}.

^{1}H NMR : δ 7.87 (d, J= 8.58 Hz, 2H), 7.46 (d, J= 8.58 Hz, 2H), 7.26 (s, 1H), 6.26 (d, J= 0.96 Hz, 1H), 4.01 (d, J= 0.96 Hz, 1H), 1.13 (s, 9H), 1.07 (s, 9H).

^{13}C NMR : δ 205.25, 200.65, 166.09, 153.92, 152.63, 137.89, 130.61, 130.08, 129.03, 125.45, 66.19, 57.45, 36.14, 32.34, 28.27, 26.11.

EIMS *m/z* : 356 (M^+, 10), 300 (100), 244 (39), 57 (11).

1,7-Bis(1,1-dimethylethyl)-3-phenylbicyclo[3.3.0]oct-3,7-diene-2,6-dione (57)

A solution of the dione **21** (200 mg, 0.62 mmol) in acetonitrile (100 mL) was purged with argon for 1 h and irradiated for 75 min. The reaction mixture on purification by usual methods afforded **57** (90 mg, 45%) as colorless needles (mp. 193-194 °C).

IR, (KBr) : 2971, 1700, 1606, 1369 cm^{-1}.

^{1}H NMR : δ 7.77-7.59 (m, 3H), 7.43-7.28 (m, 3H), 7.25 (s, 1H), 3.57 (d, J= 4.5 Hz, 1H), 1.17 (s, 9H), 1.08 (s, 9H).

^{13}C NMR : δ 204.21, 202.16, 153.71, 151.53, 128.85, 128.43, 127.21, 56.80, 36.07, 32.25, 28.16, 26.01.

HRMS Calcd for $C_{22}H_{26}O_2$: 322.19327. Found 322.19288.

1,7-Bis(1,1-dimethylethyl)-3-(4-methoxyphenyl)bicyclo[3.3.0]oct-3,7-diene-2,6-dione (58)

A solution of the dione **23** (45 mg, 0.12 mmol) in acetonitrile (100 mL) was purged with argon for 1 h and irradiated for 30 min. The

reaction mixture on purification using usual methods afforded **58** (14mg, 30%) as a colorless semisolid.

IR (KBr) : 2968, 2862, 1726, 1701, 1507, 1451 cm^{-1}.

^1H NMR : δ 7.68-6.86 (m, 6H), 3.81 (s, 3H), 3.53 (d, J= 3.65 Hz, 1H), 1.15 (s, 9H), 1.07 (s, 9H).

^{13}C NMR : δ 204.52, 202.19, 153.52, 149.28, 130.68, 128.71, 128.49, 113.80, 67.97, 56.58, 38.72, 30.35, 28.89, 28.21, 26.07.

EIMS *m/z* : 352 (M^+, 10), 296 (100), 237 (5), 165 (3), 91 (5), 57 (17).

4.4 References

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SUMMARY

The thesis entitled "**NOVEL CYCLOADDITIONS OF *o*-QUINONES AND THE CHEMISTRY OF 1,2-DIONES**" embodies the results of extensive investigations carried out to gain some insight into the reactivity of *o*-benzoquinones in cycloaddition reactions as well as to uncover the synthetic utility of bicyclo[2.2.2]octenediones resulting from such cycloaddition reactions of *o*-quinones.

A general introduction to the cycloaddition chemistry of *o*-benzoquinones as well as the synthetic utility of bicyclo[2.2.2]octenediones is presented in chapter 1. A definition of the present research problem has also been incorporated.

The second chapter deals with the cycloaddition reactions of various *o*-benzoquinones with different styrenes. 3,5-Di-*tert*-butyl-1,2-benzoquinone **5** underwent facile Diels-Alder reaction with styrene **20** leading to a high yield synthesis of stereoisomers of bicyclo[2.2.2]octenediones **25** and **26**. The stereochemistry of the products was confirmed by single crystal X-ray analysis of **26**. Interestingly, such Diels-alder reactions involving *o*-benzoquinones and aryl alkenes have very little precedence.

In order to explain the observed reactivity and periselectivity in these reactions, we have carried out some theoretical calculations using PC SPARTAN Graphical Interface Package for molecular mechanics and molecular orbital methods. The HOMO-LUMO energies were calculated by this programme and it was found that the reaction can be explained in terms of inverse electron demand Diels-Alder reaction.

It was surmised that co-ordination of the quinone carbonyl by Li^+ ions, would alter the reactivity of quinone and therefore the product distribution. 3,5-Di-*tert*-butyl-1,2-benzoquinone **5** and styrene **20** were heated with 5M LiOTf in acetonitrile and it was found that this reaction afforded only the *exo* isomer **26** in high yield. The same reaction in presence of BF_3-OEt_2 at -10 °C afforded bicyclo[3.2.1]octenedione **59** and a new product **60**. Formation of **59** can be explained by invoking the acid catalyzed rearrangement of the corresponding bicyclo[2.2.2]octanedione which is the most likely product of cycloaddition of styrene to 3,5-di-*tert*-butyl-1,2-benzoquinone **5**, whereas **60** may be considered to arise by the electrophilic substitution of styrene to the quinone followed by elimination of the *tert*-butyl group.

The third chapter describes various synthetically important transformations of bicyclo[2.2.2]octenediones. This chapter is divided into three sections. The first section deals with the photolytic double decarbonylation of bicyclo[2.2.2]octenediones. A brief introduction to photodecarbonylation precedes the presentation of our results. We have found that the dione **25** resulting from the cycloaddition of 3,5-di-*tert*-butyl-1,2-benzoquinone and styrene, on photolysis in cyclohexane solution followed by oxidation with DDQ in refluxing xylene afforded the substituted biphenyl **27**. This reaction is general in scope and it offers a very efficient route for the preparation of substituted biphenyls. A facile synthesis of bicyclo[3.2.1]octenediones by the BF_3-OEt_2 induced rearrangement of bicyclo[2.2.2]octenediones constitutes the subject matter of section 3.2. The transformation of bicyclo[2.2.2]octenedione **52** to bicyclo[3.2.1]octanedione **53** under the influence of BF_3-OEt_2 in chloroform at room temperature is

illustrative. The structure of **53** was confirmed by single crystal X-ray analysis. This reaction unveils a hitherto unexploited method for the generation of bicyclo[3.2.1]octenediones. The third section explains a facile method for the synthesis of cycloheptenones by the ring opening reaction of bicyclo[3.2.1]octenediones.

Chapter four is concerned with novel synthesis of bicyclo[3.3.0]octa-3,7-diene-2,6-diones. This chapter is divided into three sections. The first section deals with the cycloaddition reactions of *o*-benzoquinone with phenylacetylenes. 3,5-Di-*tert*-butyl-1,2-benzoquinone underwent facile Diels-Alder reaction with phenylacetylene leading to a high yield synthesis of, regioisomeric mixture of, bicyclo[2.2.2]octenediones. The second section describes the BF_3-etherate induced rearrangement of the latter to form bicyclo[3.2.1]octenediones. The third section is concerned with the photolysis of bicyclo[3.2.1]octenediones to form bicyclo[3.3.0]octa-3,7-diene-2,6-dione. An example is the photolysis of a solution of **20** in acetonitrile in a pyrex vessel at 300 nm resulting in the bicyclo[3.3.0]octa-3,7-diene-2,6-dione **54**. The structure of **54** was confirmed by single crystal X-ray analysis.

In conclusion, we have encountered some novel chemistry in the cycloadditions of *o*-benzoquinones to styrenes. Rate acceleration of these reactions was achieved by the use of 5M LiOTf in acetonitrile. We have also uncovered some interesting transformations of bicyclo[2.2.2]octenediones. It is especially noteworthy that this work has opened up efficient routes to the synthesis of substituted biphenyls, bicyclo[3.2.1]octenediones, bicyclo[3.3.0]octa-3,7-diene-2,6-diones and cycloheptenones.

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3. Nair, V.; **Maliakal, D.**; Treesa, P. M.; Rath, N. P.; Eigendorf, G. K. **1999**. Lithium triflate induced rate acceleration in the Diels-Alder reaction of *o*-quinones with styrenes (to be communicated to *Synthesis*).
4. Nair, V.; **Maliakal, D.**; Anilkumar, G ; Rath, N. P. **1999**. Boron trifluoride-etherate induced rearrangement of Bicyclo[2.2.2]octene diones: An efficient synthesis of Bicyclo[3.2.1]octene diones (to be communicated to *Tetrahedron*).
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POSTERS PRESENTED AT SYMPOSIUM

1. Nair, J. S.; Radhakrishnan, K. V.; **Maliakal, D.**; Treesa. P. M.; Vinod, A. U; Mathew, B. Sheela, K. C.; Nair, V. *"Novel cycloaddition chemistry of o-Benzoquinones"*. Presented in National Symposium on Emerging Trends in Organic Chemistry held at Trivandrum, Nov. 18-19, 1996, Poster # P 21.

ABBREVIATIONS

AM1	: austin method 1
brm	: broad multiplet
brs	: broad singlet
CAN	:cerium(IV) ammonium nitrate
COSY	: correlation spectroscopy
DCE	: 1,2-dichloroethane
DDQ	: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEPT	: distorsionless enhancement by polarization transfer
DMAD	: dimethyl acetylenedicarboxylate
EIMS	: electron impact mass spectrum
HOMO	: highest occupied molecular orbital
HPLC	: high pressure liquid chromatography
HRMS	: high resolution mass spectrum
LPDE	: lithium perchlorate-diethyl ether
LUMO	: lowest unoccupied molecular orbital
M^+	: molecular ion
MS	: mass spectrum
m/z	: mass charge ratio
NBS	: N-bromosuccinimide
PPA	: polyphosphoric acid
RT	: room temperature
THF	: tetrahydrofuran
TLC	: thin layer chromatography
TMS	: tetramethylsilane