NOVEL REACTIONS OF *o*-QUINONES AND RELATED CHEMISTRY

THESIS SUBMITTED TO THE UNIVERSITY OF KERALA
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FOR THE DEGREE OF
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IN CHEMISTRY UNDER THE FACULTY OF SCIENCE

BY

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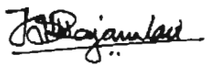
NOVEMBER 1998

Dedicated to my Father

STATEMENT

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



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Dr. G.Vijay Nair
Director

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G. Vijay Nair

G. VIJAY NAIR
THESIS SUPERVISOR

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J. SOMARAJAN NAIR

Thiruvananthapuram

November 1998.

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PREFACE

Quinones are versatile organic compounds endowed with rich and fascinating chemistry. They serve as intermediates in organic synthesis and in dye industry and many are important therapeutic agents.

o-Quinones undergo facile cycloaddition reactions with various dienes, dienophiles and dipolarophiles leading to a variety of interesting products. In view of the confirmed interest in the chemistry of *o*-quinones, a detailed investigation into the reactivity of *o*-quinones has been carried out and the results obtained are presented in this thesis entitled ***"NOVEL REACTIONS OF o-QUINONES AND RELATED CHEMISTRY."***

The thesis is divided into four chapters and relevant references are given at the end of each chapter. A general introduction covering the synthesis and reactivity profile of *o*-quinones is given in the first chapter.

The second chapter is divided into two parts. The first part (*2.1*) deals with the addition of a zwitterionic intermediate, generated by the reaction of triphenylphosphine and dimethyl acetylenedicarboxylate, to *o*-quinones leading to the formation of γ,δ-unsaturated spirolactones and the second part (*2.2*) describes the addition of the zwitterionic intermediate to *p*-quinones to form similar spirolactones.

Chapter -3 describes the isomerization of 6,6-tetramethylene fulvene to the isomerized fulvene, 1-cyclopentenylcyclopentadiene, and its cycloaddition reactions. The isomerised fulvene being unstable, undergoes rapid dimerization. Both the isomerized fulvene and the dimer

Chapter 4 describes some miscellaneous reactions of *o*-quinones and it is divided into two parts. In the first part (4.1), alkylation of catechols with benzhydrols and other alcohols leading to the formation of substituted catechols which are precursors for novel *o*-benzoquinones is presented. The second part (4.2), describes some preliminary experiments directed towards the synthesis of a model for the tea pigment theaflavin from substituted pyrogallol and substituted *o*-quinone.

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

List of Abbreviations

o-	: ortho
p-	: para
HOMO	: Highest Occupied Molecular Orbital
LUMO	: Lowest Unoccupied Molecular Orbital
NCS	: N-Chlorosuccinimide
NBS	: N-Bromosuccinimide
NIS	: N-Iodosuccinimide
EWG	: Electron withdrawing group
s	: singlet
d	: doublet
t	: triplet
dd	: doublet of doublet
brs	: broad singlet
m	: multiplet
R.T.	: room temperature
DMAD	: Dimethyl acetylenedicarboxylate
DME	: Dimethoxyethane

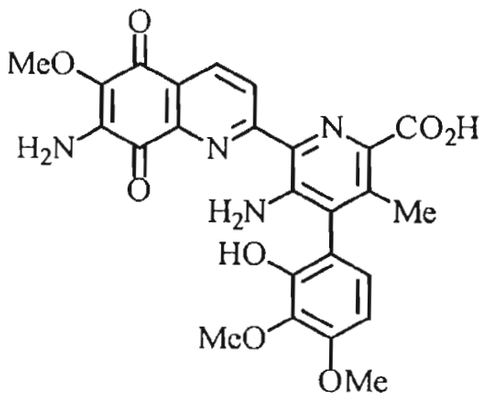
CHAPTER 1

AN INTRODUCTION TO THE CHEMISTRY OF *o*-QUINONES

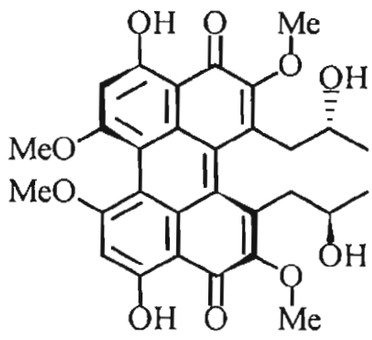
1.1 GENERAL

Compounds with quinonoid skeleton are endowed with rich and fascinating chemistry. They are used as versatile intermediates in organic synthesis and in dye industry. Quinonoid compounds play important roles in electron transport in the respiratory and photosynthetic elements of biological systems as well as a number of redox processes in Nature.

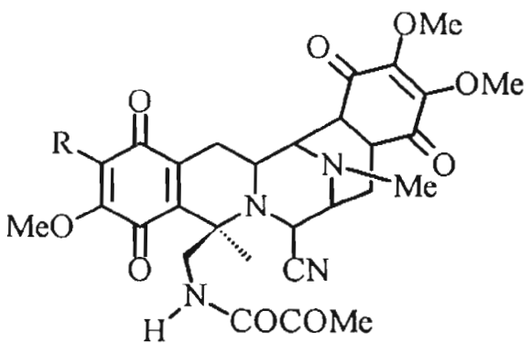
A large number of natural products with quinonoid skeleton have been isolated and many are found to be biologically active.[1,2] A few of these are listed in figure **1.1a** and **1.1b**.



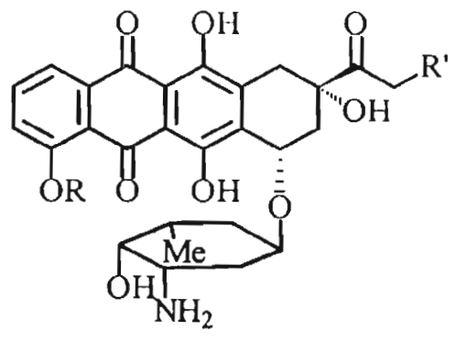
Streptonigrin



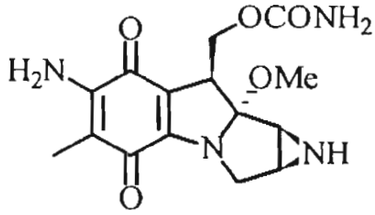
Calphostin D



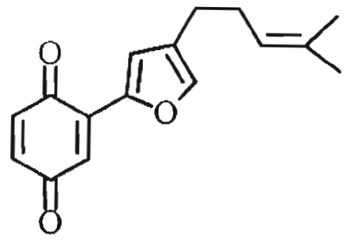
R=Me; Saframycin
R=OMe; Saframycin A



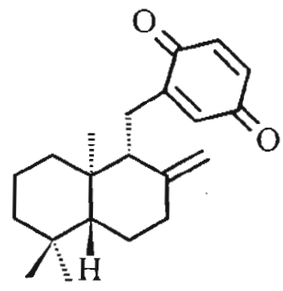
R=Me, R'=OH; Adriamycin
R=Me, R'=H; Daunomycin
R=R'=H; Carminomycin



Mitomycin C

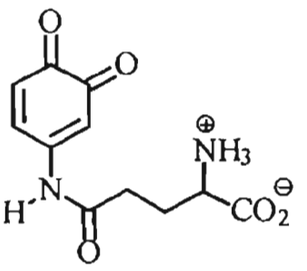


Echinofuran

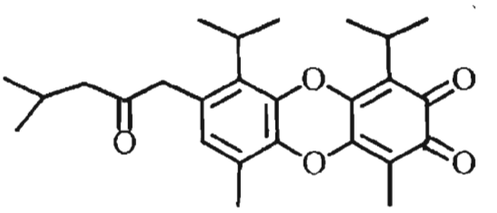


Zonarone

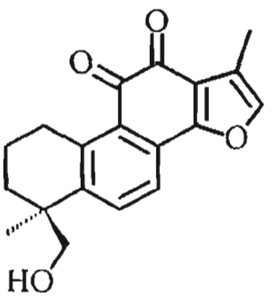
Fig. 1.1a



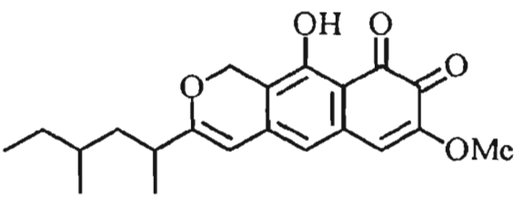
Glutaminyl quinone



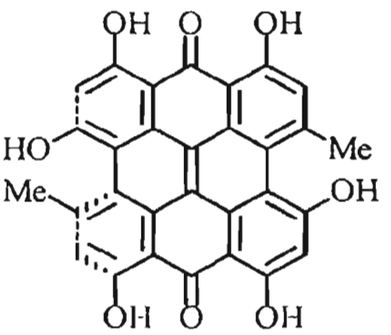
Echlonoquinone



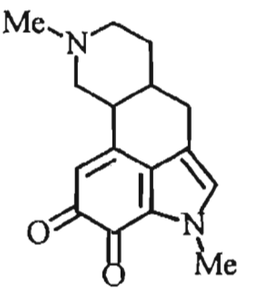
Tanshidiol



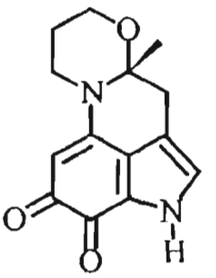
Obionin



Hypericine



Damirone



Haematopodin

Fig. 1.1b

The chemistry of *p*-quinones, especially their cycloaddition reactions, has been extensively investigated. In contrast, the chemistry of *o*-quinones has received only limited attention.

1.2 SYNTHESIS OF *o*-QUINONES

o-Quinones are generally prepared from phenols and catechols by oxidation with cerium(IV) sulfate in dilute acids.[3] *o*-Quinones in small scale can be prepared by oxidation of the corresponding phenols with Fremy's salt.[4] Benzeneselenenic anhydride,[5] iodosobenzene, iodoxybenzene, etc. also have been effectively used for the oxidation of phenols to corresponding quinones.[6,7]

The most commonly used method for the preparation of *o*-quinones is the oxidation of the corresponding catechols with appropriate oxidising agents such as Ag_2O, Ag_2CO_3, $FeCl_3$, $NaIO_4$,[8] MnO_2, etc. Stable quinones with high reduction potential such as *o*- and *p*-chloranil, DDQ, etc. are useful reagents for the oxidation of catechols to *o*-quinones.

1.3 GENERAL REACTIVITY PROFILE OF *o*-QUINONES

o-Quinones can exhibit multiple reactivity profiles, especially in cycloaddition reactions, as they can participate as carbodiene, heterodiene, dienophile or dipolarophile. The potential for such multiple modes of cycloaddition is implicit in the following representations of *o*-quinones.

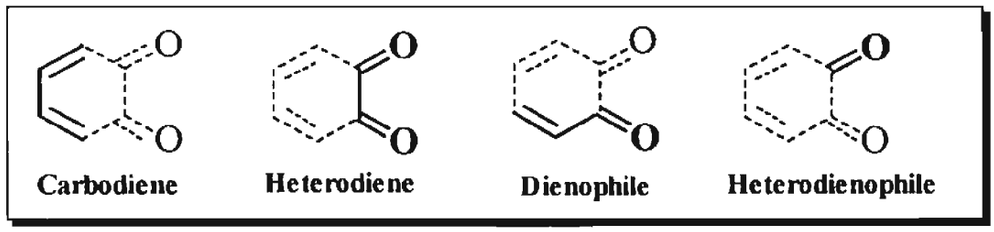
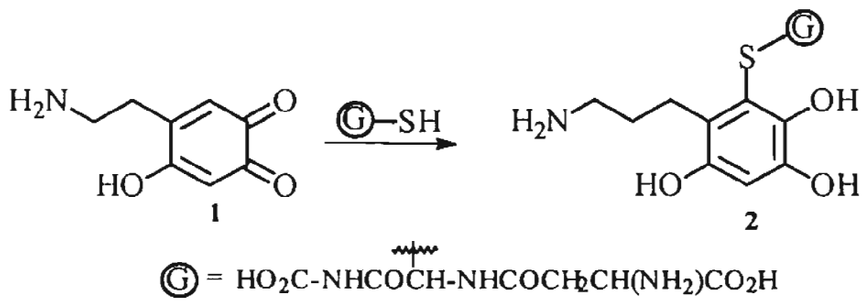


Fig. 1.2

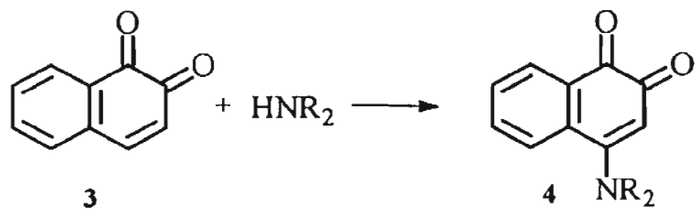
An overview of the chemistry of *o*-quinones is presented in the following sections.

Addition of sulfur and nitrogen nucleophiles to *o*-quinones has been shown to yield ring substituted derivatives. For example the addition of glutathione to 6-hydroxydopaminoquinone gave **2** (Scheme 1.1).[9]



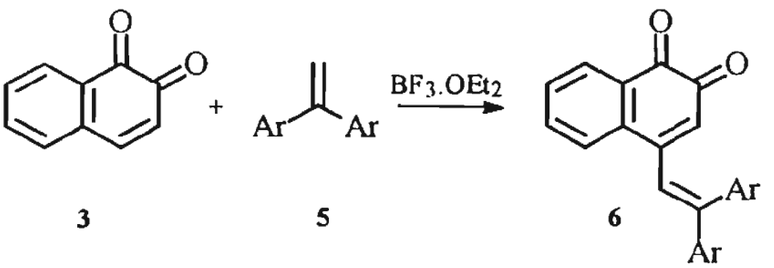
Scheme 1.1

Amines are reported to add to 1,2-naphthoquinone to give 4-substituted naphthoquinones after oxidation of the initial adduct (Scheme 1.2).[10]



Scheme 1.2

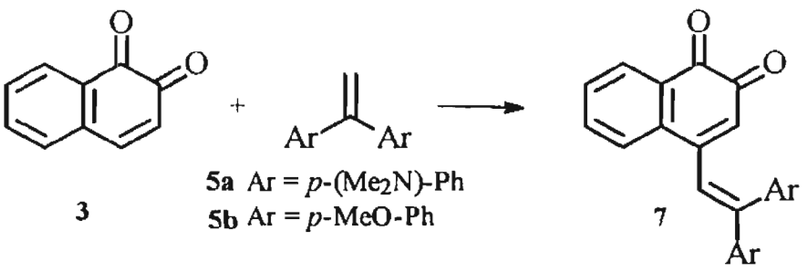
Similar products have been isolated in the reaction of 1,2-naphthoquinone with electron rich ethylenes in presence of Lewis acids (Scheme 1.3).[11]



3 5 6

Scheme 1.3

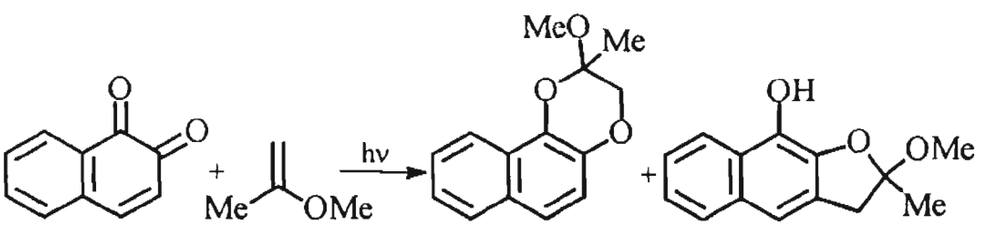
The conjugate addition of highly polarized 1,1-bis-[*p*-(dimethylamino)phenyl]ethylene to 1,2-naphthoquinone is known from the work of Gates (Scheme 1.4).[12]



3 7

Scheme 1.4

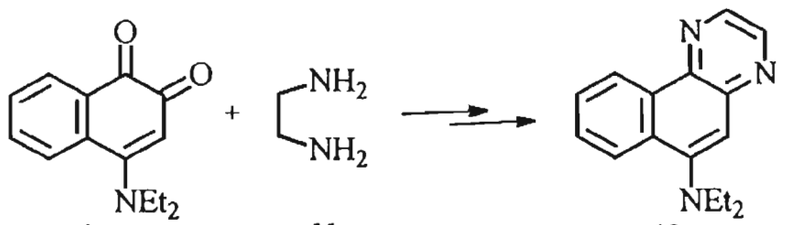
Photoinduced cycloaddition of electron rich olefins with 1,2-naphthoquinone afforded benzodioxin and dihydrofuran derivatives as illustrated in scheme 1.5.[13]



3 8 9 10

Scheme 1.5

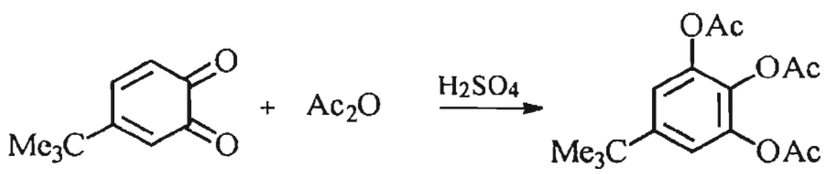
Quinoxaline derivatives, which are known to be excellent dyes, are obtained by the condensation of ethylene diamine with 1,2-naphthoquinone derivative **4** (Scheme 1.6).[10]



4 **11** **12**

Scheme 1.6

The Thiele-Winter acetoxylation is one of the general and important reactions of quinones. Reaction of 4-*tert*-butyl-1,2-benzoquinone leading to the triacetoxy derivative is illustrative (Scheme 1.7).[14]



13 **14**

Scheme 1.7

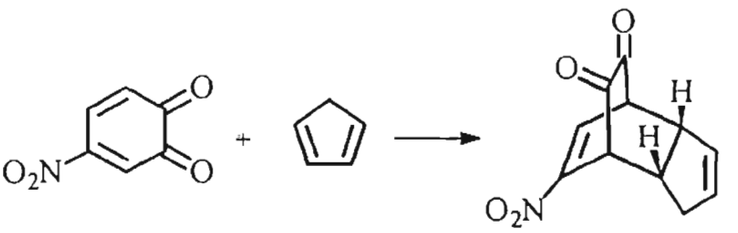
1.4 CYCLOADDITION REACTIONS OF *o*-QUINONES

As mentioned earlier, *o*-quinones can participate as 4π or 2π components in cycloaddition reactions. The reactivity of *o*-benzoquinones is influenced by the electronic and steric factors imparted by the substituents on the quinonoid skeleton. Ansell in 1971 reported that the electron deficient enone moiety of *o*-quinone acts as a dienophile in cycloaddition reactions.[15] The reactions of *o*-benzoquinones in general and cycloadditions in particular, have been the subject of investigation in our laboratory.[16] As already mentioned, the versatility of *o*-quinones as

carbodiene, heterodiene, dienophile and dipolarophile has been reported. *o*-Quinones participate as both carbodiene and heterodiene in their reactions. They participate as a typical carbodiene with carbocyclic dienes. Multiple reactivity profiles are encountered in the reaction of quinones with acyclic dienes. *o*-Quinones afford benzodioxin derivatives with heterocyclic dienes such as pyrroles and furans with the latter participating as dienophiles and the quinones as heterodienes. Reports from our laboratory have shown that in dipolar cycloadditions, *o*-quinones participate as C=C and C=O dipolarophiles.[17] A summary of the reactivity pattern exhibited by *o*-quinones in cycloaddition reactions is given below.

1.4.1 *o*-Quinone as carbodiene

o-Quinone offers a highly electron deficient carbodiene system in cycloaddition reactions with dienes such as cyclopentadiene, cyclohexadiene etc. to afford bicyclo-1,5-dienes which are shown to undergo Cope rearrangement at high temperatures (Scheme 1.8).[15,18]

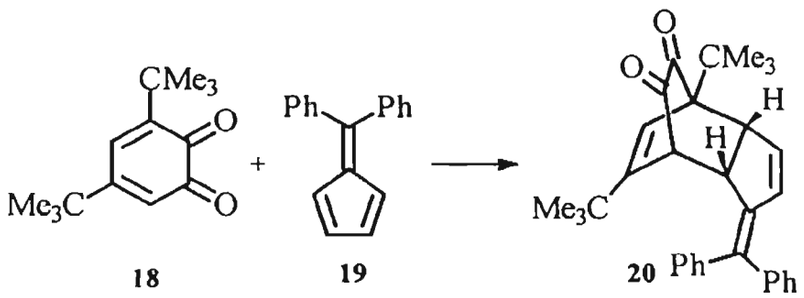


15 **16** **17**

Scheme 1.8

The formation of bicyclooctenediones with phenyl acetylene[19] and pentafulvenes,[16,20] including vinyl fulvenes,[21] also illustrates the reactivity of *o*-quinones as carbodiene (Scheme 1.9). It is noteworthy that the

resulting bicyclooctenediones undergo a number of interesting and useful transformations.[22]

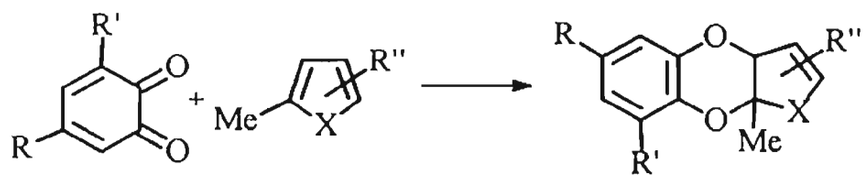


18 19 20

Scheme 1.9

1.4.2 *o*-Quinone as heterodiene

o-Quinones undergo cycloaddition reaction with heterocycles such as furans[23] and pyrroles[24] yielding benzodioxin derivatives (Scheme1.10a). Indoles[25] and enamines[26,27] also show similar reactivity pattern in which *o*-quinones function as heterodienes (Scheme 1.10b).

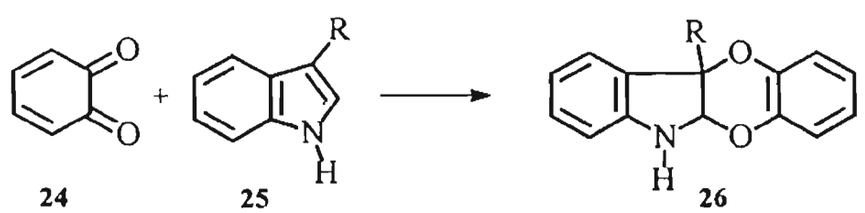


R=R'=CMe_3
R=Alkyl; R'=H
21

X=O, NH
R''=Me or H
22

23

Scheme 1.10a

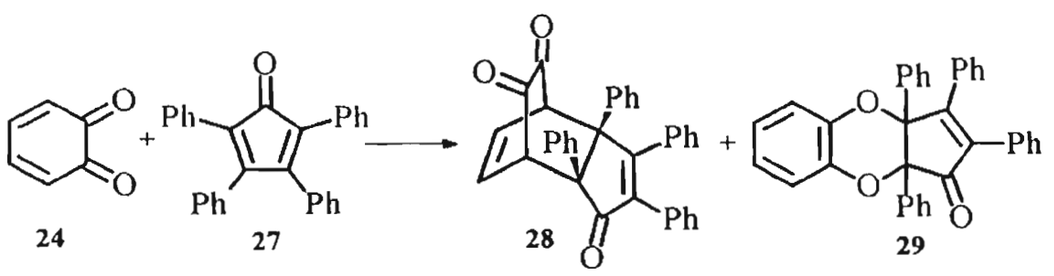


24 **25** **26**

Scheme 1.10b

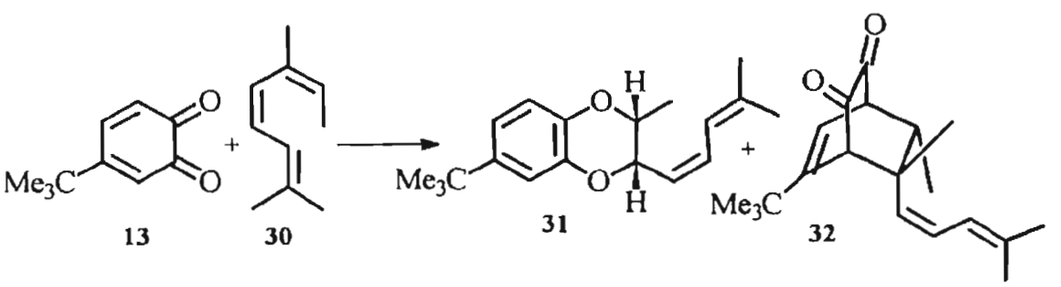
1.4.3 *o*-Quinone as both carbodiene and heterodiene

o-Quinone can exhibit dual reactivity in cycloaddition reactions with certain substrates. The reaction of *o*-benzoquinone with tetracyclone afforded the adducts **28** and **29** with the quinone participating as carbodiene and heterodiene respectively (Scheme 1.11).[23]



Scheme 1.11

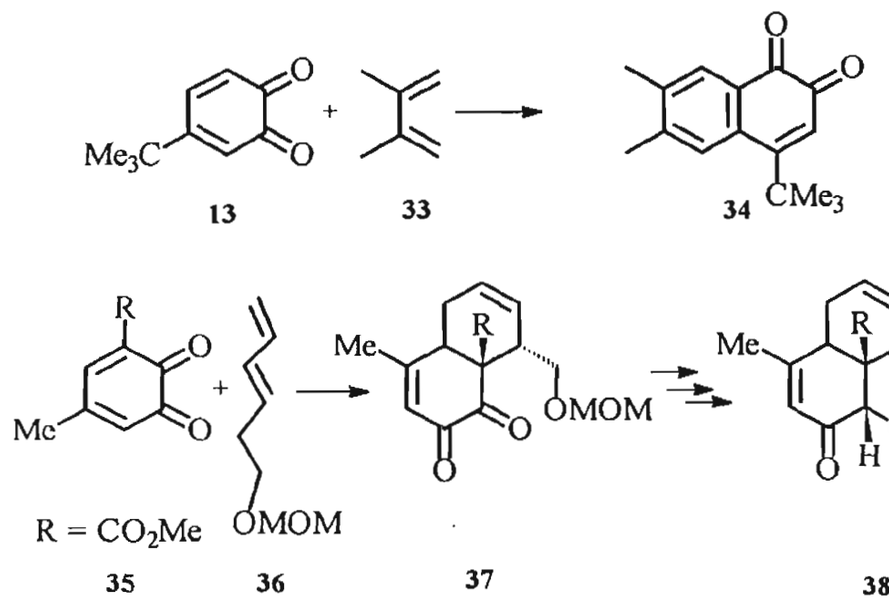
Similar reactivity was observed with conjugated trienes such as alloocimine (Scheme 1.12).[28]



Scheme 1.12

1.4.4 *o*-Quinone as dienophile

The enone moiety of *o*-quinones has been used as a powerful dienophile in cycloaddition reactions with electron rich dienes such as 2,3-dimethylbutadiene[28,29,16] and acetoxybutadiene. This strategy has been employed in synthetic approaches to quassinoids (Scheme 1.13).[30]

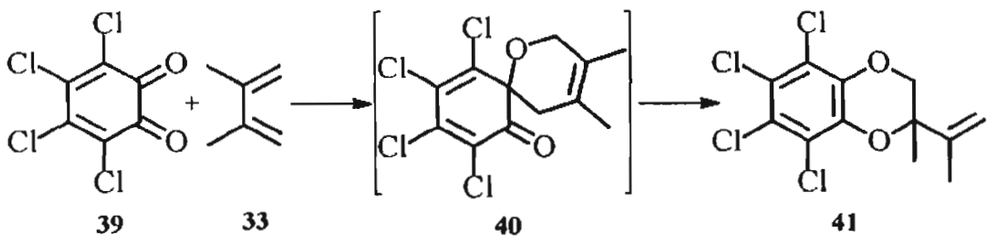


13 **33** **34** **35** **36** **37** **38**

Scheme 1.13

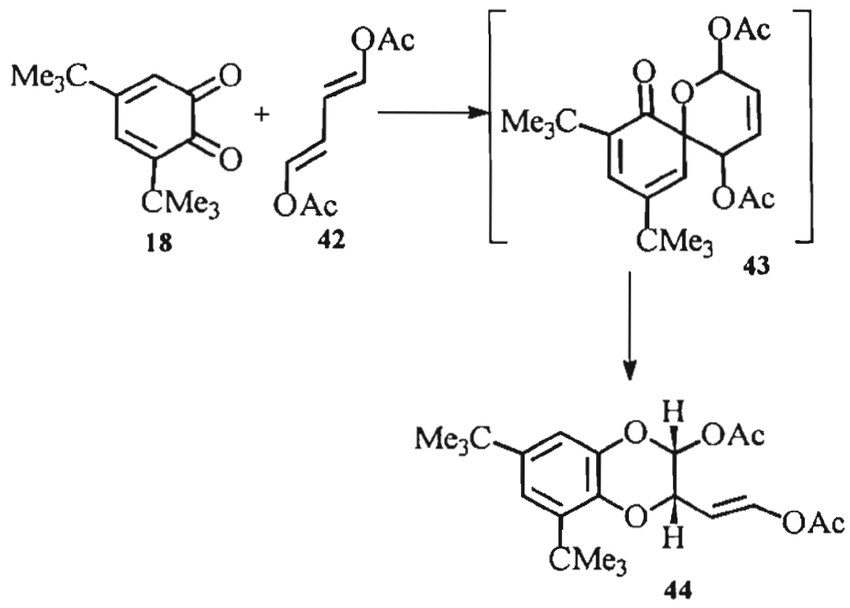
1.4.5 *o*-Quinone as heterodienophile

A number of reactions involving C=O of quinone serving as heterodienophile have been reported. In the reaction of *o*-chloranil with 2,3-dimethylbutadiene, a primary spiroadduct is obtained which undergoes [3.3] sigmatropic rearrangement at high temperature yielding benzodioxin derivative.[31] Similar reactivity is observed in the reaction of 3,5-di-*tert*-butyl-1,2-quinone with 1,4-diacetoxybutadiene (Scheme 1.14a and 1.14b).[32]



39 **33** **40** **41**

Scheme 1.14a

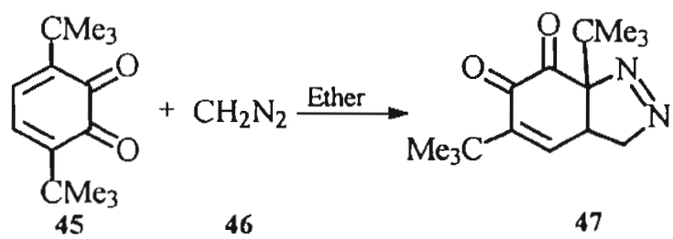


Scheme 1.14b

1.4.6 *o*-Quinone as dipolarophile

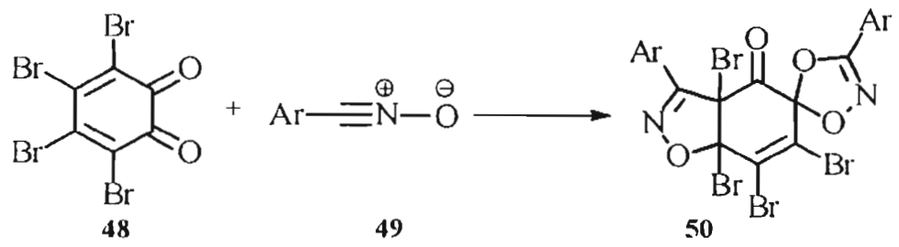
Dipolar cycloaddition reaction provides a powerful method for the synthesis of many nitrogen and oxygen heterocyclic compounds. *o*-Quinones exhibit dual reactivity in dipolar cycloaddition reactions as they can react as either C=C or C=O dipolarophiles.

The reaction of diazomethane with 3,6-di-*tert*-butyl-*o*-benzoquinone affords indazole (Scheme 1.15).[33]



Scheme 1.15

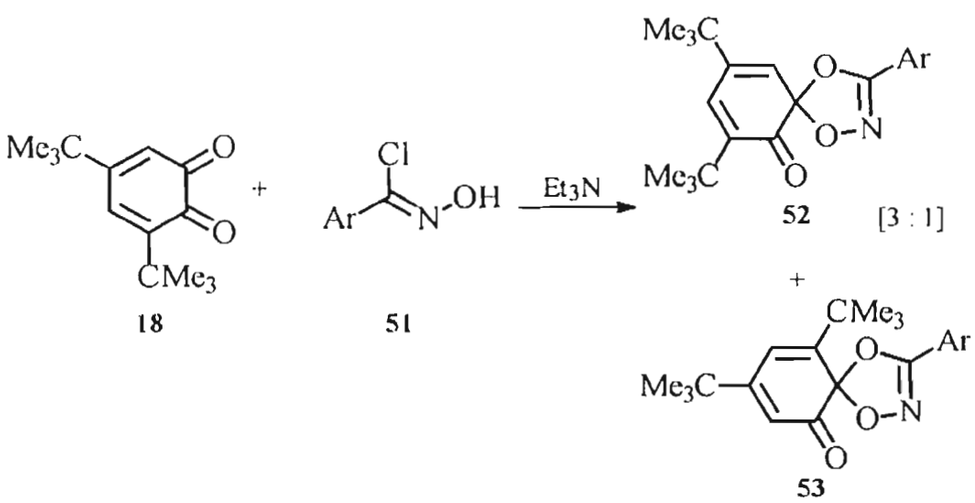
o-Bromanil and 1,2-benzoquinone are known to participate as multiple dipolarophiles in cycloaddition reactions with nitrile oxides leading to bis adduct (Scheme 1.16).[34]



48 49 50

Scheme 1.16

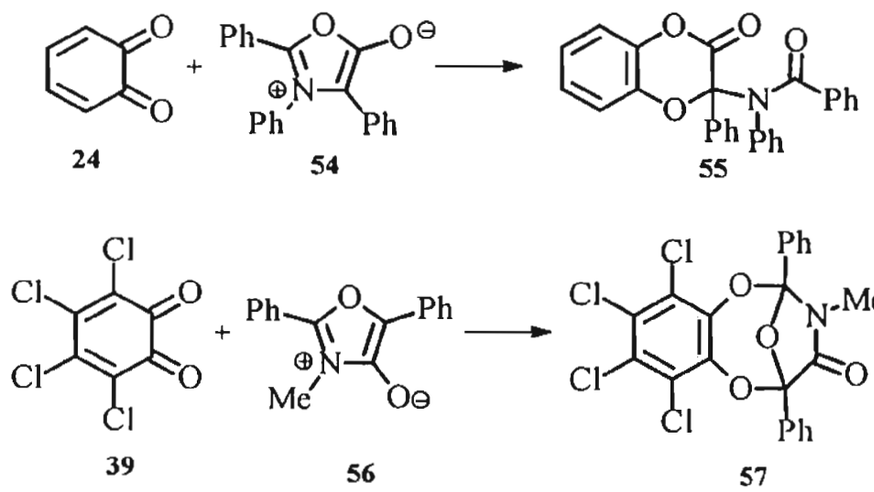
Investigation of the reaction of nitrile oxides with *o*-quinones in our laboratory has revealed that the reactivity profile of the latter depends on the substitution pattern and nature of the substituents. With aryl nitrile oxide as the dipole, 3,5-di-*tert*-butyl-1,2-benzoquinone acts as heterodipolarophile (Scheme 1.17).[35]



18 51

Scheme 1.17

Mesoionic compounds such as münchnones and isomünchnones have been added to *o*-quinones leading to the formation of interesting heterocycles (Scheme 1.18).[36-38]

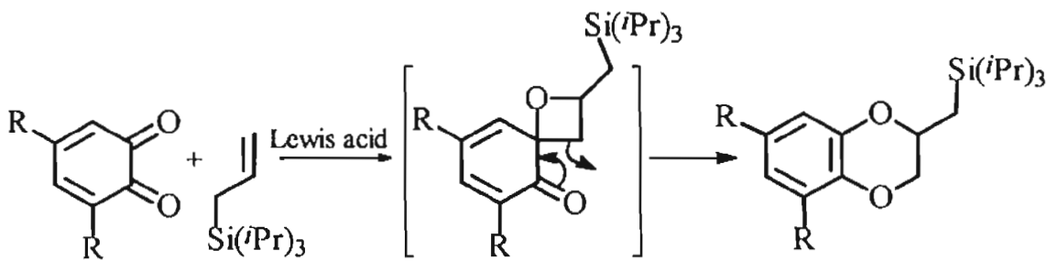


24 54 55

39 56 57

Scheme 1.18

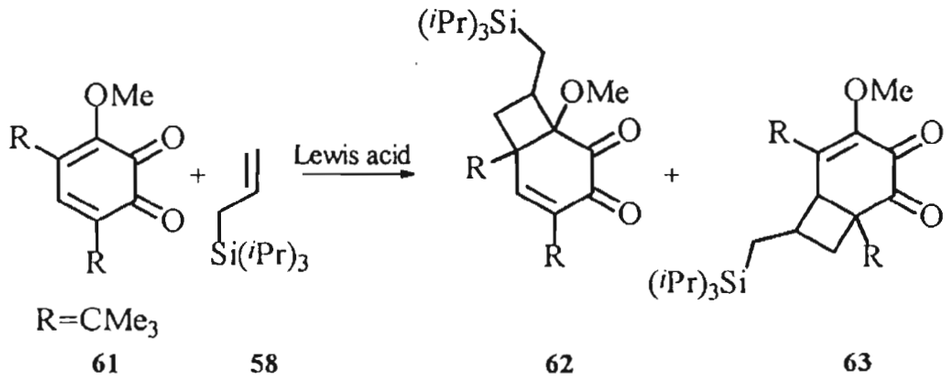
In presence of Lewis acids, allylsilanes participate as 1,2-dipoles in reactions with 3,5-di-*tert*-butyl-1,2-quinone to afford benzodioxin derivatives presumably *via* a sigmatropic rearrangement of the initially formed adduct (Scheme 1.19).[17]



18 **58** **59** **60**

Scheme 1.19

o-Quinones with electron releasing substituents are known to participate as carbon dipolarophiles towards allylsilanes leading to cyclobutane derivative (Scheme 1.20).[17]

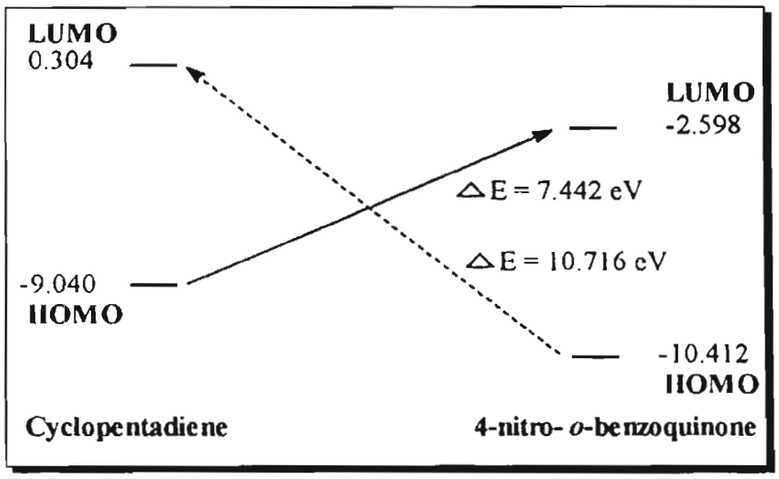


61 **58** **62** **63**

Scheme 1.20

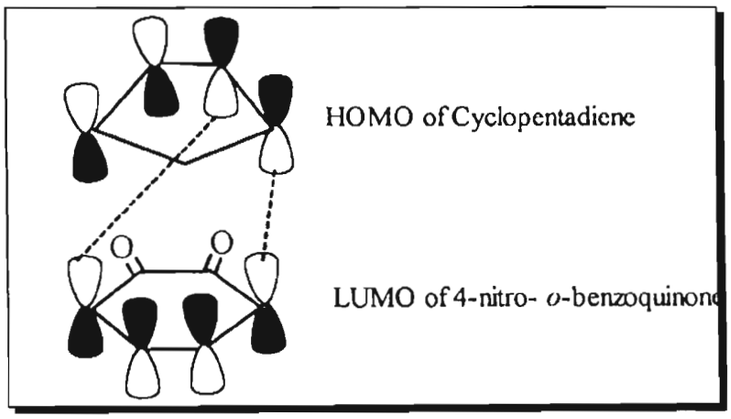
1.5 THEORETICAL CONSIDERATIONS

The postulates of Frontier Molecular Orbital theory (FMO)[39,40] regarding the interaction of molecular orbitals in pericyclic reactions, offer a rational way to understand the rate of reaction as well as chemo, regio, and stereoselectivities. The rate of a reaction is determined by the energy separation of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) of the reactants. [4π+2π] Cycloaddition reactions in which HOMO of the diene interacts with LUMO of the dienophile leading to the adduct is referred to as normal Diels-Alder reaction. If HOMO of the dienophile and LUMO of the diene interaction is favoured, it is referred to as an inverse electron demand Diels-Alder reaction. Semiempirical molecular orbital calculations are used to gain better understanding of the reactivity pattern of *o*-quinones. Thus MNDO and AM1 calculations using MOPAC programme were utilised to confirm that the cycloadditon reactions of *o*-quinones fall under the inverse electron demand Diels-Alder category. The orbital interactions in a typical reaction involving *o*-quinone is represented in figure 1.3 and 1.4.



HOMO-LUMO Energy levels of cyclopentadiene and 4-nitro-*o*-benzoquinone

Fig. 1.3



Frontier orbital interaction of cyclopentadiene and 4-nitro-*o*-benzoquinone

Fig. 1.4

1.6 DEFINITION OF THE PROBLEM

The chemistry of *o*-quinones is of considerable topical interest. In spite of the large amount of the work in this area, it is evident from the foregoing discussion that a number of facets of these interesting compounds remain unexplored. We have focussed our attention on some of these.

The first problem we have addressed is the reactivity of zwitterionic species derived from dimethyl acetylenedicarboxylate and triphenylphosphine towards *ortho* and *para* quinones.

The second problem has its genesis in the earlier observation of an anomalous reaction of *o*-quinones and 6,6-tetramethylene fulvene, which was explained by invoking the isomerization of the latter. It was of interest to confirm this isomerization and gain some insight into the cycloadditions of the isomerized fulvene.

The third phase of the work explores the possibility of synthesising substituted catechols by an expeditious protocol involving alkylation of catechols by carbinols. The catechols serve as precursors to *o*-quinones.

Finally, in our quest to examine the validity of a proposed biosynthesis of the tea pigment theaflavin, some preliminary experiments involving hydroxy-*o*-quinones were undertaken.

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CHAPTER 2

TRIPHENYLPHOSPHINE INDUCED ADDITION OF DIMETHYL ACETYLENEDICARBOXYLATE TO *ORTHO* AND *PARA* QUINONES

The contents of this chapter are divided into two parts. The first part (2.1) deals with triphenylphosphine induced addition of dimethyl acetylenedicarboxylate to *o*-quinones while the second part (2.2) covers the addition of dimethyl acetylenedicarboxylate to *p*-quinones in presence of triphenylphosphine.

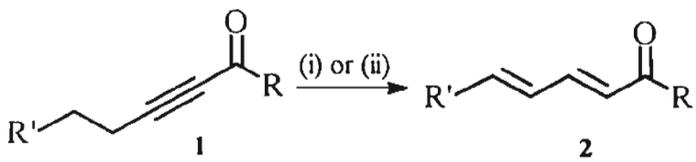
2.1 TRIPHENYLPHOSPHINE INDUCED ADDITION OF DIMETHYL ACETYLENEDICARBOXYLATE TO *o*-QUINONES.

2.1.1 INTRODUCTION

Phosphorus and its compounds have been extensively used in organic synthesis.[1] In presence of halogens, phosphorus compounds are known to bring about important functional group modifications. With the advent of Wittig's olefination[2] and its subsequent modifications, organophosphines have received special attention in synthetic methodology. Phosphines have been known to bring about transformations both catalytically and stoichiometrically. Among the phosphines, triphenylphosphine has emerged as the reagent of choice due to its stability, crystalline nature, low-toxicity and easy availability. A number of protocols for the conversion of alcohols to halides use triphenylphosphine in combination with N-halosuccinimides (Ph_3P-NBS, Ph_3P-NCS, PPh_3-NIS),[3] or carbon tetrahalides (Ph_3P-CCl_4, Ph_3P-CBr_4).[4] Triphenylphosphine plays a key role in transition metal chemistry, especially in the case of Pd, Ru, Rh and Re. Most of the transition metal chemistry makes use of the neutral ligand property of triphenylphosphine.

2.1.2 TRIPHENYLPHOSPHINE AS CATALYST

Triphenylphosphine finds use as a catalyst in various isomerization reactions. For example, Trost has exploited the isomerization of alkynones to dienones[6] and propiolic acid esters to conjugated esters[7] in presence of triphenylphosphine (Scheme 2.1.1).



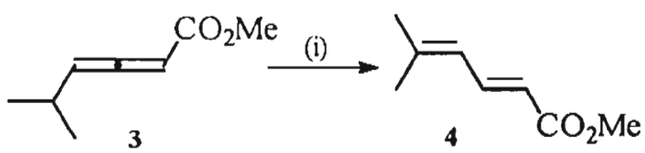
1 2

R= -Oallyl; (i) PPh_3, AcOH, Toluene, 110 °C, 83%.

R'= Alkyl or Aryl; (ii) PPh_3, Toluene, 80-110 °C, 69-88%.

Scheme 2.1.1

Triphenylphosphine induced isomerization of allenic esters to conjugated esters has also been shown to proceed in good yields (Scheme 2.1.2).[7]

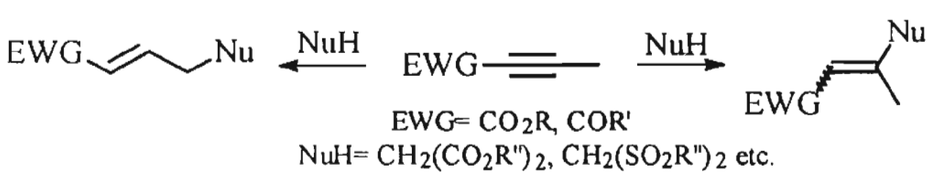


3 4

(i) PPh_3, Toluene, 60 °C.

Scheme 2.1.2

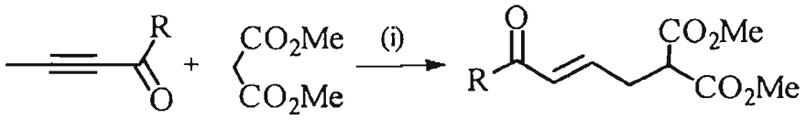
Nucleophilic addition to alkynones and alkyne esters in presence of triphenylphosphine has been reported to result in 1,4 or 1,5 addition (Scheme 2.1.3 and 2.1.4)[7]



EWG= CO_2R, COR'

NuH= $CH_2(CO_2R'')_2$, $CH_2(SO_2R'')_2$ etc.

Scheme 2.1.3



5a R=OMe
5b R=NMe$_2$
5c R=Ph

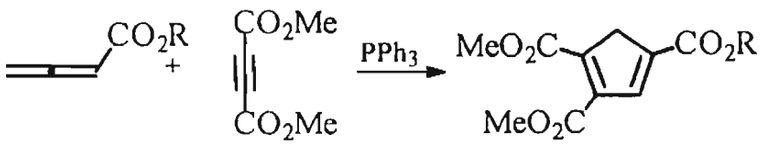
6

7a R=OMe
7b R=NMe$_2$
7c R=Ph

(i) PPh_3, AcOH, AcONa, Toluene, 80 °C, 63%.

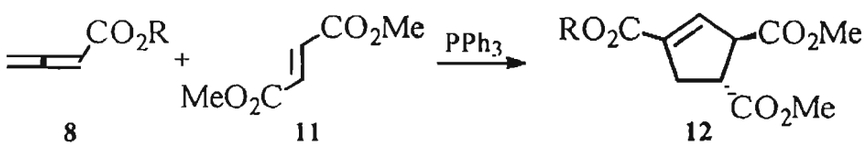
Scheme 2.1.4

Zwitterionic intermediates resulting from the addition of triphenylphosphine to allenic esters undergo [3+2] annulation with electron deficient alkenes and alkynes to form cyclopentadiene and cyclopentene derivatives respectively (Scheme 2.1.5 and 2.1.6).[8]



8 **9** **10**

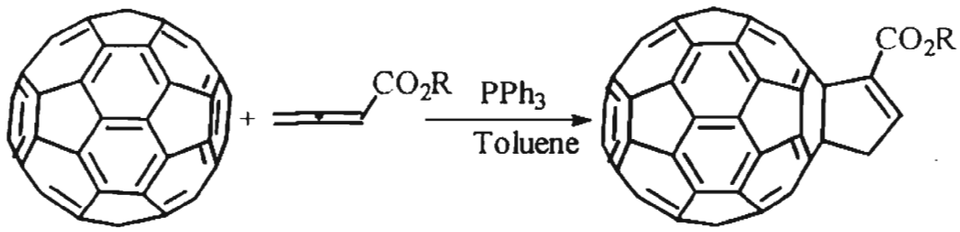
Scheme 2.1.5



8 **11** **12**

Scheme 2.1.6

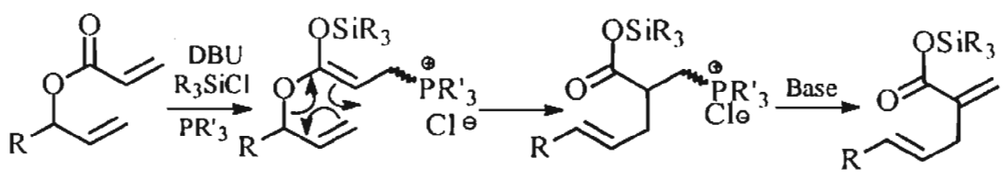
Allenes have been shown to add to fullerene in presence of triphenylphosphine to give similar cyclopentene derivatives (Scheme 2.1.7).[9]



13 **8** **14**

Scheme 2.1.7

The catalytic activity of triphenylphosphine is best illustrated in the [3,3] sigmatropic rearrangement of substituted vinyl esters (Scheme 2.1.8).[10]



15 **16** **17** **18**

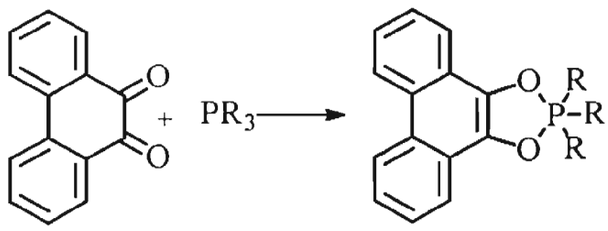
Scheme 2.1.8

2.1.3 REACTION WITH α-DIKETONES AND QUINONES

Reaction of triphenylphosphine with α-diketones has been reported to yield pentaoxyphosphorane derivatives.[11,12] Illustrative examples are given in scheme 2.1.9a and 2.1.9b.

19 **20**

Scheme 2.1.9a



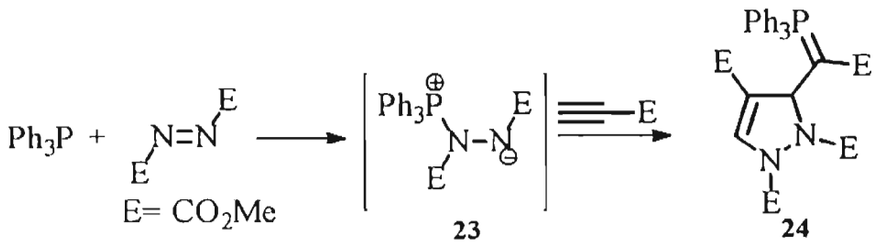
21 22

R = Alkyl or aryl

Scheme 2.1.9b

2.1.4 REACTION WITH DIMETHYL AZODICARBOXYLATE

The quasi 1,3-dipole **23**, generated by the addition of triphenylphosphine to dimethyl azodicarboxylate adds to methylpropiolate resulting in the formation of **24** (Scheme 2.1.10).[13]

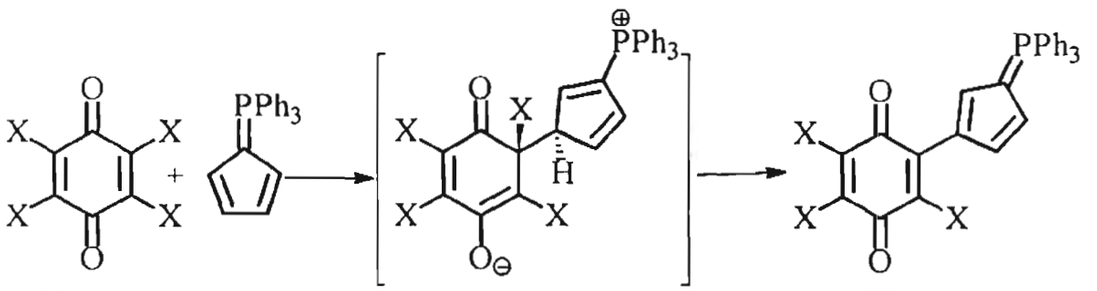


23 24

Scheme 2.1.10

2.1.5 REACTION WITH PHOSPHORANES

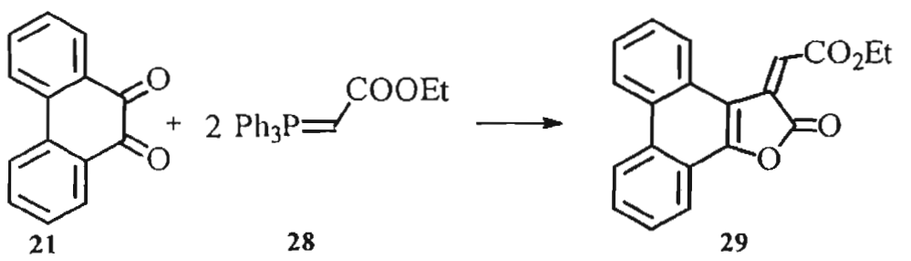
Triphenylphosphinocyclopentadienide has been shown to react with *p*-chloranil to yield zwitterionic dyes containing phosphoranes. Mechanism and kinetics of the reaction have been investigated (Scheme 2.1.11).[14]



25a-c X=Cl, Br, I **26a-c** **27a-c**

Scheme 2.1.11

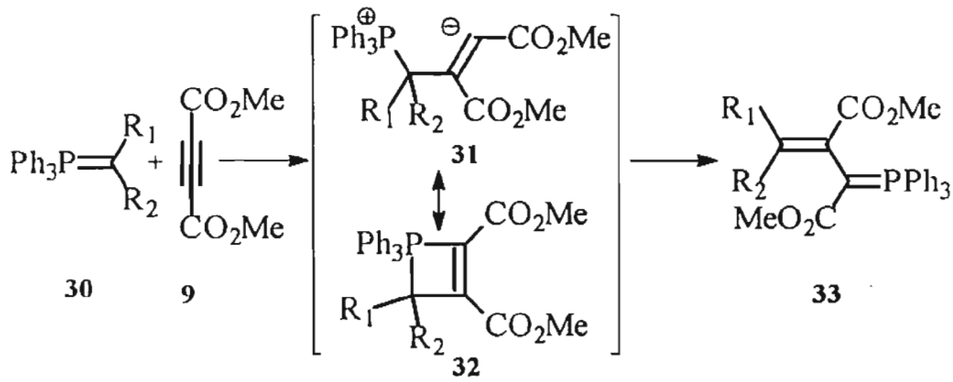
Alkylidene triphenylphosphoranes undergo facile addition to various quinones to form a variety of products.[15] For example, phenanthrene quinone reacts with an excess of stabilised Wittig ylide such as Ph_3P=CHCOOEt to give **29** (Scheme 2.1.12).



21 **28** **29**

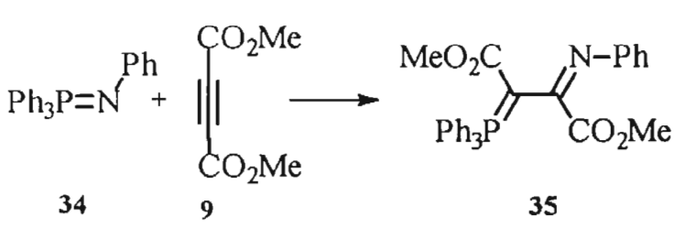
Scheme 2.1.12

Alkylidene triphenylphosphoranes are known to react with dimethyl acetylenedicarboxylate to produce ylides **33** *via* the betaine **31** or the intermediate phosphacyclobutene **32** (Scheme 2.1.13).[16]



Scheme 2.1.13

Iminophosphoranes are known to react with dimethyl acetylenedicarboxylate forming 1:1 adducts which have been assigned the structure **35** (Scheme 2.1.14).[17]

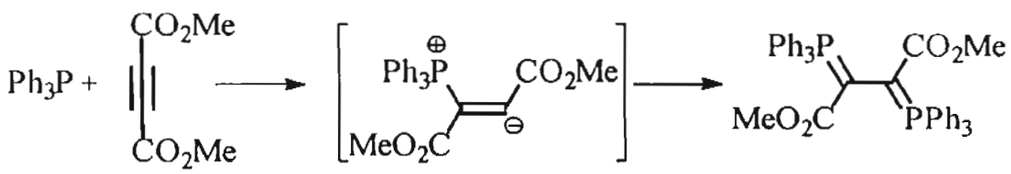


Scheme 2.1.14

2.1.6 REACTION WITH ACETYLENES

The reactivity of triphenylphosphine towards various acetylenes has been studied by Tebby. The results of these studies have shown that triphenylphosphine adds to acetylenes such as dimethyl acetylenedicarboxylate, dicyanoacetylene, dibenzoylacetylene etc. to generate zwitterionic intermediates and the chemistry of these zwitterionic intermediates have been studied in detail.

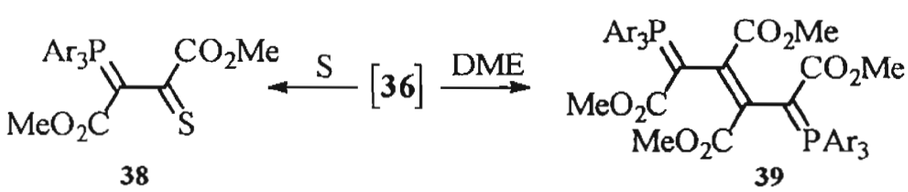
It has been shown that triphenylphosphine adds to dimethyl acetylenedicarboxylate to form a 2:1 dialkylidene diphosphorane adduct **37** in quantitative yield (Scheme 2.1.15).[18,19]



9 **36** **37**

Scheme 2.1.15

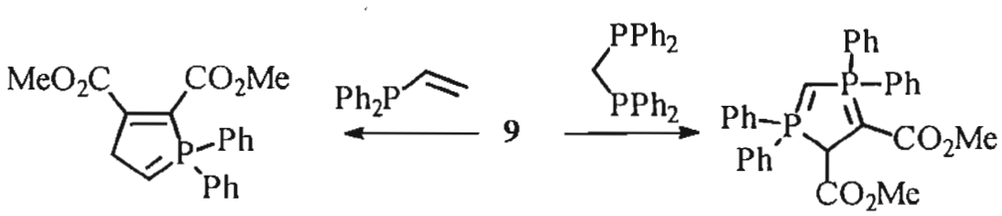
Reaction of **36** with chalcogens afforded the chalcogenated phosphorane **38**. In the absence of an excess of phosphine, **39** was isolated (Scheme 2.1.16). Dibenzoylacetylene also exhibited similar reactivity.[18]



38 **39**

Scheme 2.1.16

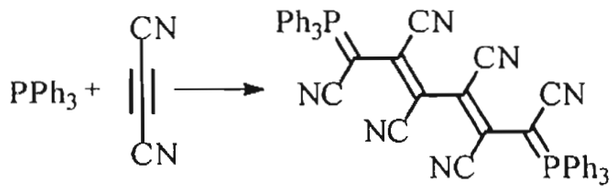
A similar reaction of dimethyl acetylenedicarboxylate was observed with vinyldiphenylphosphine[20] and bis(diphenylphosphino)methane[21] affording **40** and **41** respectively (Scheme 2.1.17).



40 **41**

Scheme 2.1.17

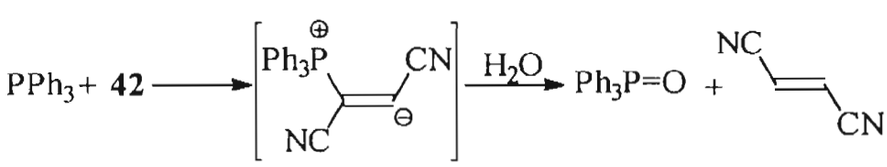
Reaction of dicyanoacetylene with triphenylphosphine yields a stable adduct which has been shown to be a 1,6-alkylidene diphosphorane **43.**[22] (Scheme 2.1.18).



42 **43**

Scheme 2.1.18

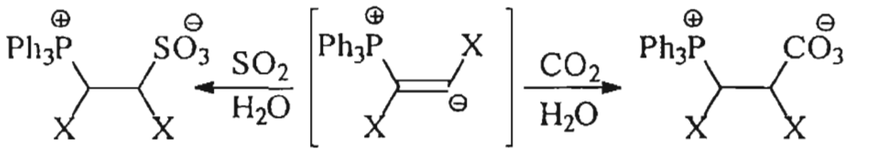
If the reaction is carried out in a protic solvent such as water, the solvent gets added to the zwitterionic species to form fumaronitrile and triphenylphosphine oxide (Scheme 2.1.19).[23]



44 **45**

Scheme 2.1.19

The zwitterionic species **44** can also be trapped as the betaine of a succinonitrile derivative **46** by sulfur dioxide in the presence of water.[23] Dimethyl acetylenedicarboxylate and triphenylphosphine under similar conditions afforded dimethyl succinate derivative **47**. The zwitterionic species **36** under the same conditions reacts with CO_2 to yield a similar type of betaine **48** as illustrated in scheme 2.1.20.[24,25]

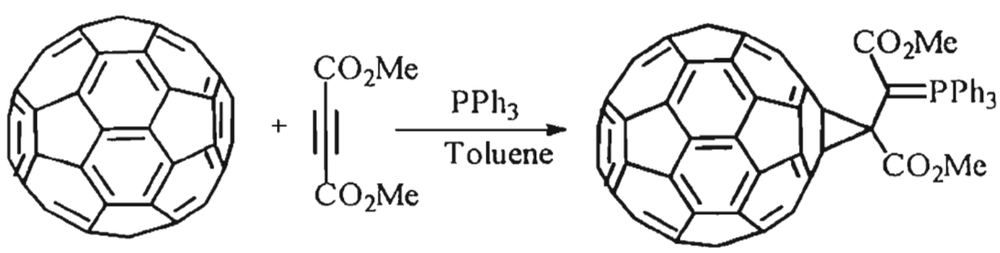


46 X= CN
47 X= CO_2Me **36** or **44** **48** X= CO_2Me

Scheme 2.1.20

2.1.6.1 Reaction with Fullerene

Recent reports indicate that the zwitterionic intermediate resulting from the reaction of triphenylphosphine with dimethyl acetylenedicarboxylate can also be trapped with fullerene (C_{60}) to afford **49** in moderate yields (Scheme 2.1.21).[26]

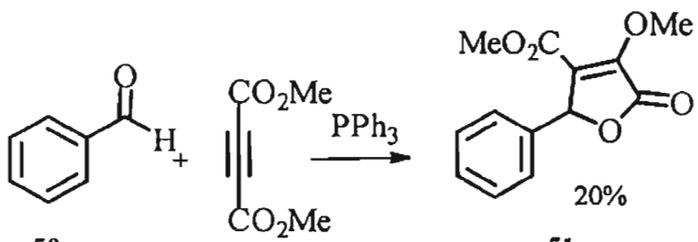


13 **9** **49**

Scheme 2.1.21

2.1.6.2 Reaction with benzaldehyde and other carbonyl compounds

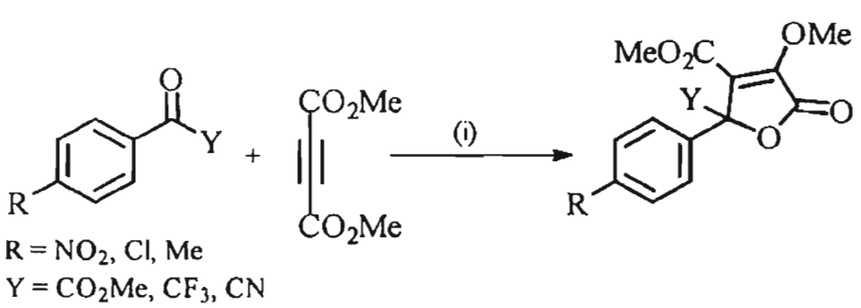
It has been reported by Winterfeldt that dimethyl acetylenedicarboxylate reacts with benzaldehyde in the presence of triphenylphosphine giving an unsaturated lactone **51** in 20% yield (Scheme 2.1.22).[27]



50 9 51

Scheme 2.1.22

In view of the lower yields obtained with benzaldehyde, Nozaki has recently reported a modification of the Winterfeldt protocol using activated carbonyl compounds such as α-ketoesters, α-ketonitriles and α-hydroxyketones.[#] The use of catalytic amount of triphenylphosphine afforded unsaturated lactones in moderate to high yields (Scheme 2.1.23).[28]



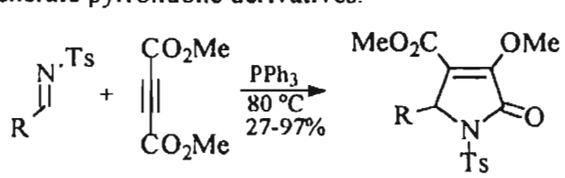
R = NO_2, Cl, Me
Y = CO_2Me, CF_3, CN

9 52

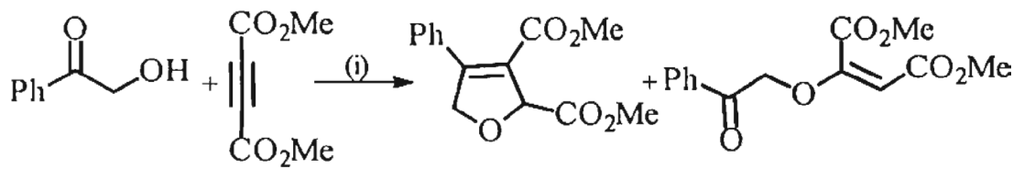
(i) Ph_3P, Toluene, 80 °C, 40-94%.

Scheme 2.1.23

[#]In a recent report, N-tosylimines have been shown to add to zwitterionic intermediates to generate pyrrolidone derivatives.[29]



The reductive formation of dihydrofurans **54** along with the addition product **55**, from the intermediate zwitterion and α-hydroxyketone has also been reported. The intermediacy of an intramolecular Wittig reaction was invoked to explain the formation of **54**. Both the need for a stoichiometric amount of triphenylphosphine and the isolation of triphenylphosphine oxide support the intramolecular nature of the reaction (Scheme 2.1.24).[28]



53 **9** **54**(80%) **55**(10%)

(i) Ph_3P (1.9 eq.), Toluene, 80 °C, 24 h.

Scheme 2.1.24

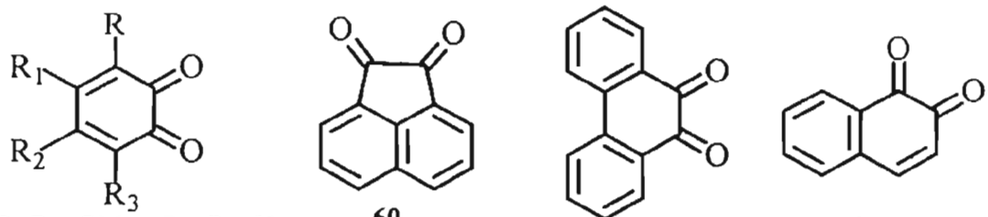
2.1.7 STATEMENT OF THE PROBLEM

Against the literature background given above and in the context of our general interest in the chemistry of *o*-quinones, especially the addition of dipolar species to quinones, it was of interest to explore the addition of zwitterionic intermediates to the latter. The absence of such studies served as an added incentive.

We have undertaken a thorough investigation of the addition of zwitterionic species generated from dimethyl acetylenedicarboxylate and triphenylphosphine to a number of *ortho* and *para* quinones and our results are discussed in the following sections.

2.1.8 RESULTS AND DISCUSSION

The quinones selected for the study are listed in the following figure.

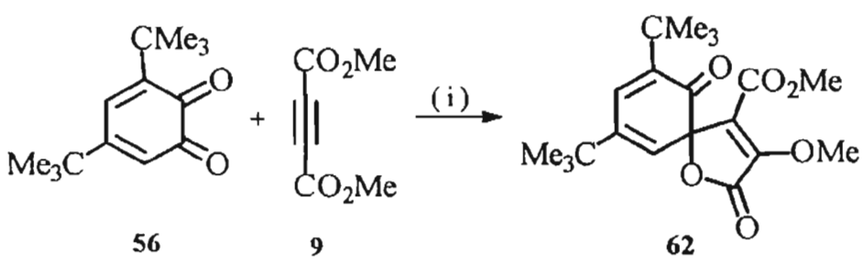


56 R=R_2=CMe_3; R_1=R_2=H
57 R=R_2=CMe_3; R_3=OMe; R_1=H
58 R_2=CMe_3; R=R_1=R_3=H
59 R=R_2=$CHPh_2$; R_3=OMe; R_1=H

60 **21** **61**

Figure 2.1.1

Our investigations were initiated with 3,5-di-*tert*-butyl-1,2-benzoquinone which on treatment with dimethyl acetylenedicarboxylate in presence of 50 mol% of triphenylphosphine in refluxing benzene afforded **62** in 48% yield (Scheme 2.1.25).[30]



56 **9** **62**

(i) PPh_3, Benzene, 80 °C, 48 h, 48%.

Scheme 2.1.25

The compound **62** was characterized by spectral and analytical data. The IR spectrum showed strong absorption at 1779 cm^{-1} due to the γ,δ-unsaturated lactone. A sharp band at 1738 cm^{-1} was due to the ester and the enone carbonyl of the quinone absorbed at 1680 cm^{-1}. The sharp

band at 1660 cm^{-1} was assigned to the double bond in the spirolactone moiety. In the ^{1}H NMR, the two *tert*-butyl groups resonated at δ 1.228 and δ 1.147 as singlets. The methoxy group α to the lactone was observed at δ 4.281 as a singlet and the methyl of the carbomethoxy group appeared at δ 3.643. The resonance signals of olefinic protons on the quinone moiety were visible as two doublets at δ 5.644 (J= 2.00 Hz) and δ 6.978 (J= 2.00 Hz). In the ^{13}C NMR spectrum of **62**, the spirocarbon resonated at δ 80.306. The enone carbonyl was observed at δ 192.114 and the lactone carbonyl at δ 160.923. The peak at δ 166.624 was assigned to the ester carbonyl. The *tert*-butyl methyls appeared at δ 29.257 and 28.527. The quaternary carbons on the *tert*-butyl groups were observed at δ 35.137 and δ 35.001. The methyl of the ester group resonated at δ 51.927 and the methyl of the enol ether at δ 60.338. The two olefinic carbons bearing protons on the quinone ring appeared at δ 135.951 and 122.773. The two tetrasubstituted olefinic carbons on the quinone ring appeared at δ 147.889 and 144.575 and the tetrasubstituted sp^2 carbons on the lactone ring gave signals at δ 149.503 and 122.314. The assigned structure was supported by analytical data and finally confirmed unambiguously by single crystal X-ray analysis.[#] (Figure 2.1.2)

[#]X-ray analysis was done by Dr. Nigam P. Rath of Missouri University, U. S. A.

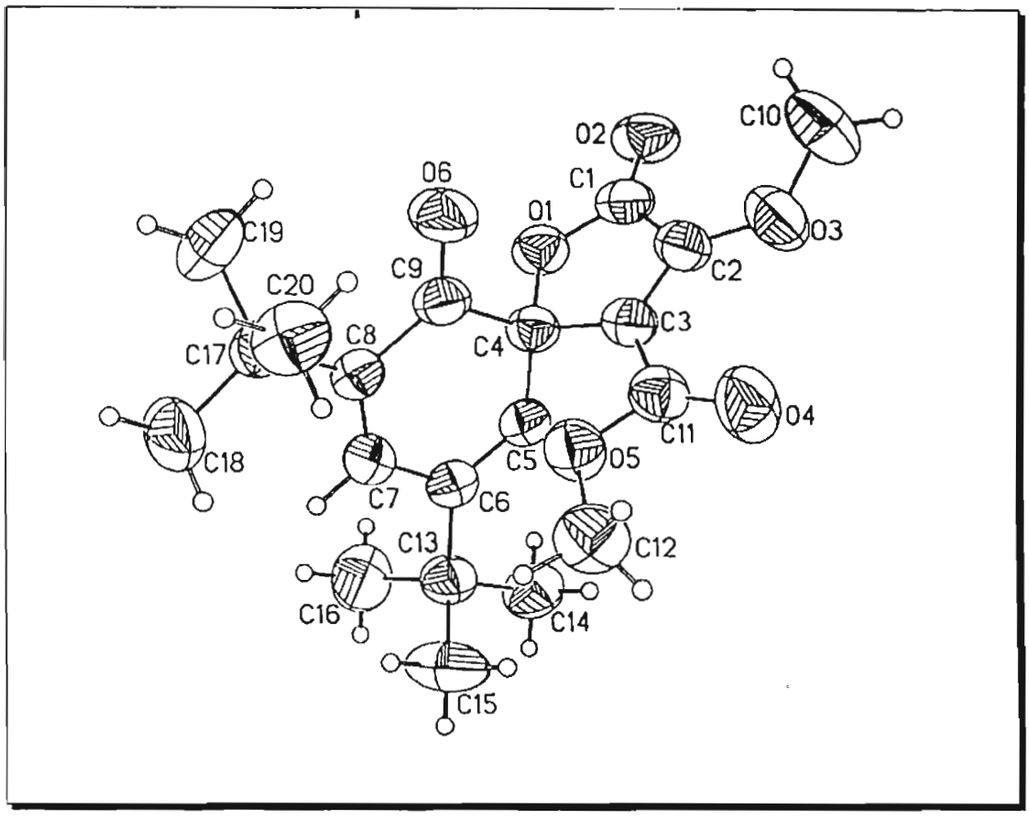
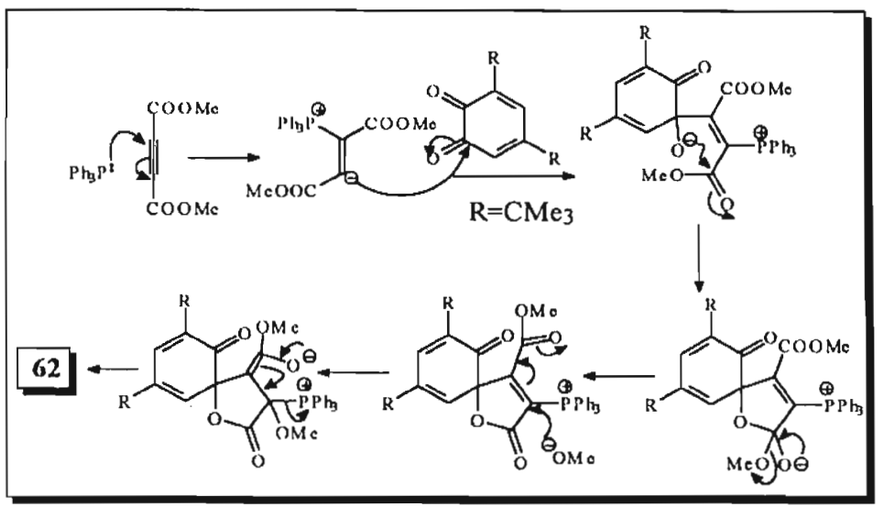


Figure 2.1.2

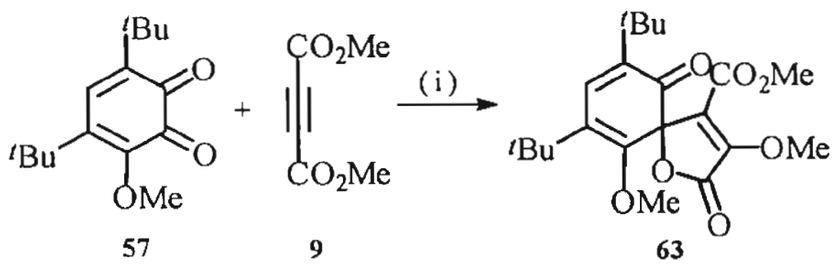
X-ray crystal structure of 62

The reaction involves the initial formation of a zwitterionic intermediate from triphenylphosphine and dimethyl acetylenedicarboxylate, which adds to the carbonyl of the quinone to yield a betaine. The betaine on subsequent cyclisation leads to the spirolactone (Scheme 2.1.26).



Scheme 2.1.26

Similar reactivity was observed with 3-methoxy-4,6-di-*tert*-butyl-1,2-benzoquinone which when treated with dimethyl acetylenedicarboxylate in presence of 50 mol% of triphenylphosphine gave 70 % of the spirolactone **63** (Scheme 2.1.27).



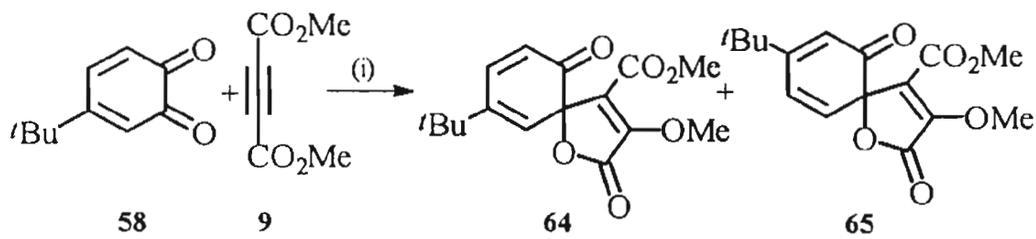
(i) PPh_3, Benzene, 80 °C, 4 h, 70%

Scheme 2.1.27

The IR spectrum of **63** showed strong absorptions at 1793, 1729 and 1681cm^{-1} due to the lactone, ester and the enone carbonyls respectively. In the ^{1}H NMR, the olefinic proton resonated as a singlet at δ 7.127. The methoxy group α to the lactone was observed at δ 4.291 as a singlet. In the ^{13}C NMR spectrum of **63**, the characteristic spirocarbon

of the lactone gave a signal at δ 83.331. The *tert*-butyl methyls appeared at δ 29.038 and δ 29.800 and the quaternary carbons were observed at δ 34.673 and δ 35.088. The enone, ester and the lactone carbonyls were observed at δ 190.17, 166.639 and 160.636 respectively. Other signals are also in good agreement with the assigned structure.

4-*tert*-Butyl-1,2-benzoquinone afforded an inseparable mixture of spirolactones **64** and **65** in 26% yield when treated with dimethyl acetylenedicarboxylate and triphenylphosphine in refluxing benzene for 5 h (Scheme 2.1.28).



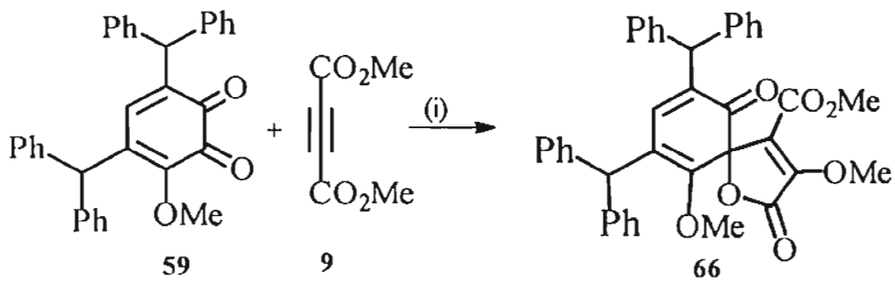
58 **9** **64** **65**

(i) PPh_3, Benzene, 80 °C, 5 h, 26%

Scheme 2.1.28

IR spectrum showed three carbonyls at 1782, 1729 and 1676 cm^{-1}. In the ^{1}H NMR, the *tert*-butyl groups resonated at δ 1.259 and 1.173 as two singlets. The six olefinic protons were seen between δ 7.232-5.717. In the ^{13}C NMR the two signals at δ 192.489 and 192.340 were attributed to the two enone carbonyls. The characteristic spirocarbons gave signals at δ 78.417 and 77.223. The *tert*-butyl carbons resonated at δ 35.738, 34.709, 28.326 and 27.988.

Analogous reaction was observed with 3-methoxy-4,6-bis(1,1-diphenylmethyl)-1,2-benzoquinone which on treatment with dimethyl acetylenedicarboxylate and triphenylphosphine in dry benzene at 80 °C for 1.5 h furnished the adduct **66** (Scheme 2.1.29).



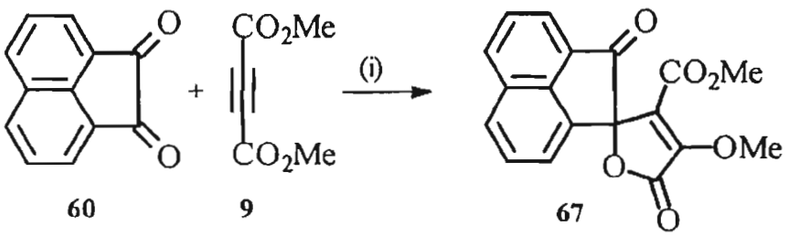
59 **9** **66**

(i) PPh_3, Benzene, 80 °C, 1.5 h, 46%

Scheme 2.1.29

The IR spectrum showed strong absorptions at 1782, 1732 and 1685 cm^{-1} due to the lactone, ester and the enone carbonyls respectively. ^1H NMR spectrum of **66** showed three methoxy groups as singlets at δ 3.403, 3.596 and 4.288. The olefinic proton on the quinone ring resonated at δ 6.526 and the two benzylic protons resonated as singlets at δ 5.361 and 5.597 respectively. The 20 aromatic protons were visible as multiplet in the region δ 7.243-6.904. In the ^{13}C NMR the two benzylic carbons appeared at δ 48.032 and 49.078. The characteristic spirocarbon signal was observed at δ 81.565. The carbonyls of enone, ester and the lactone were observed at δ 190.221, 166.194 and 160.227 respectively. All other signals were in agreement with the assigned structure.

Treatment of acenaphthenequinone with dimethyl acetylenedicarboxylate in presence of triphenylphosphine in dry benzene at 80 °C for 1 h afforded **67** (Scheme 2.1.30).



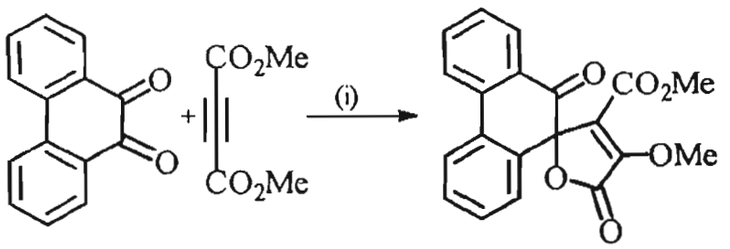
60 **9** **67**

(i) PPh_3, Benzene, 80 °C, 1 h, 55%

Scheme 2.1.30

The IR spectrum of **67** showed the lactone, ester and benzoyl carbonyls at 1780, 1735, 1705 cm^{-1} respectively. In the ^1H NMR the carbomethoxy methyl group resonated at δ 3.377 and the methoxy group α to the lactone carbonyl at δ 4.416. In the ^{13}C NMR spectrum, the characteristic spirocarbon was discernible at δ 85.222. The lactone, ester and the benzoyl carbonyls resonated at δ 160.858, 165.881 and δ 195.056 respectively. All other signals are in good agreement with the assigned structure.

The reaction of 9,10-phenanthrenequinone with dimethyl acetylenedicarboxylate also gave a similar spirolactone **68** in 78% yield. (Scheme 2.1.31).



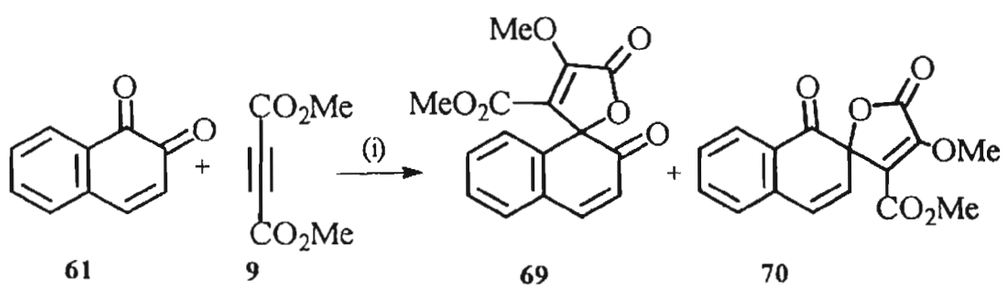
21 **9** **68**

(i) PPh_3, Benzene, 80 °C, 1 h, 78%.

Scheme 2.1.31

In this case also the spectral data are in agreement with the assigned structure.

Reaction of 1,2-naphthoquinone with dimethyl acetylenedicarboxylate gave a 1:1 regioisomeric mixture of the spirolactones **69** and **70** (Scheme 2.1.32).



61 **9** **69** **70**

(i) PPh_3, Benzene, 80 °C, 4 h, 46%.

Scheme 2.1.32

The IR spectrum of **69** showed absorptions at 1795, 1719 and 1695 cm^{-1} indicating the presence of the lactone, ester and the benzoyl carbonyls. In the ^1H NMR spectrum of **69**, the olefinic protons appeared as two doublets at δ 5.90 (*J*= 10.6 Hz) and δ 6.90 (*J*= 10.6 Hz). In the ^{13}C NMR the benzoyl carbonyl resonated at δ 190.761, the ester carbonyl at δ 166.087 and the lactone carbonyl was observed at δ 160.806. The characteristic spirocarbon resonance was seen at δ 79.029.

In the IR spectrum, **70** showed characteristic absorptions at 1779, 1709 and 1681 cm^{-1}. In the ^1H NMR, the olefinic protons resonated at δ 7.5 (*J*= 11 Hz) and 6.4 (*J*= 11 Hz) respectively. ^{13}C NMR spectrum showed the characteristic spirocarbon signal at δ 79.029. The three carbonyl carbons appeared at δ 190.761, 166.297 and 160.568.

2.1.9 EXPERIMENTAL DETAILS

Melting points were recorded on Toshniwal and Büchi melting point apparatus and are uncorrected. The infrared (IR) spectra were recorded on Perkin-Elmer-882 and Nicolet Impact 400D FT-IR spectrophotometers. NMR spectra were recorded on Jeol EX-90, Bruker-300 and Varian 500 NMR spectrophotometers. NMR spectra were obtained using chloroform-*d* as the solvent and chemical shifts are given in δ scale with tetramethylsilane as internal standard. Mass spectra were recorded on a Fisons GC-8000-MD-800 and AE1 MS-50-(IE) mass spectrometers. Elemental analyses were obtained on a Perkin-Elmer-2400 elemental analyser. Dimethyl acetylenedicarboxylate was purchased from Aldrich Chemical Co. and was used without further purification. Elemental analyses were carried out using Perkin Elmer analyzer. Solvents used were distilled and/or dried. Analytical thin layer chromatography was performed on glass plates coated with silica gel containing calcium sulphate as the binder. Gravity column chromatography was performed using silica gel (100-200 mesh) and mixtures of hexane-ethyl acetate were used for elution. Solvents were removed under vacuum using Büchi rotary evaporator.

7,9-Di-*tert*-butyl-3-methoxy-2,10-dioxo-1-oxa-spiro[4.5]deca-3,6,8-triene-4-carboxylic acid methyl ester (62)

To a refluxing mixture of 3,5-di-*tert*-butyl-1,2-benzoquinone (440 mg, 2.0 mmols) and dimethyl acetylenedicarboxylate (DMAD) (320 mg, 2.2 mmols) in dry benzene (10 mL) was added triphenylphosphine (262 mg, 1.0 mmol) and the heating was continued

for 48 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel. The unreacted quinone was eluted with 95:5 hexane-ethyl acetate and further elution with 80:20 hexane-ethyl acetate afforded the adduct **62** as yellow prisms (340 mg, 48%, the yield based on the reacted quinone was 60%). mp. 130-132 °C (CH_2Cl_2-hexane).

IR ν_{max} (KBr) : 2968, 2880, 1779, 1738, 1684, 1660, 1566, 1464, 1373, 1241, 1156, 810 cm^{-1}.

^1H NMR : 6.978 (d, 1H, *J*= 2.0 Hz), 5.644 (d, 1h, *J*= 2.0 Hz), 4.281 (s, 3H), 3.643 (s, 3H), 1.228 (s, 9H), 1.147 (s, 9H).

^{13}C NMR : 192.114, 166.624, 160.923, 149.503, 147.889, 144.575, 135.959, 122.781, 122.314, 80.306, 60.338, 51.927, 35.137, 35.001, 29.257, 28.527.

MS : 362 (M^+).

EIMS m/z (%) : 318 (M^+-CO_2, 53), 303 (M^+-CO_2Me, 100), 287 (81), 247 (9), 215 (17), 141 (12), 128 (15), 115 (21), 91 (15), 59 (16), 57 (72).

Anal. calcd. for $C_{20}H_{26}O_6$:C, 65.97, H, 7.22; Found: C, 66.28, H, 7.25%.

7,9-Di-*tert*-butyl-3,6-dimethoxy-2,10-dioxo-1-oxa-spiro[4.5]deca-3,6,8-triene-4-carboxylic acid methyl ester (63)

To a mixture of 3-methoxy-4,6-di-*tert*-butyl-1,2-benzoquinone (100 mg, 0.4 mmols) and DMAD (68 mg, 0.48 mmols) in refluxing dry benzene (5 mL) was added triphenylphosphine (52 mg, 0.2 mmols) and the refluxing was continued for 4 h. The residue after removal of the

solvent was purified by chromatography on silica gel using 90:10 hexane-ethyl acetate to afford **63** as a viscous yellow oil (107 mg, 70%).

IR ν_{max} (CCl_4) : 2962, 2874, 1793, 1729, 1681, 1655, 1566, 1459, 1388, 1232, 1171, 949, 880, 796 cm^{-1}.

^1H NMR : 7.127 (s, 1H), 4.291 (s, 3H), 3.673 (s, 3H), 3.606 (s, 3H), 1.271 (s, 9H), 1.218 (s, 9H).

^{13}C NMR : 190.170, 166.639, 152.315, 150.093, 140.023, 131.895, 127.677, 121.732, 83.331, 62.130, 60.325, 51.846, 35.089, 34.673, 29.800, 29.039.

EIMS m/z (%) : 392 (M^+, 6), 349 (23), 348 (62), 333 (71), 301 (74), 271 (23), 245 (18), 143 (29) 115 (29), 91 (28), 59 (32), 57 (100), 44 (70).

7-*tert*-Butyl-3-methoxy-2,10-dioxo-1-oxa-spiro[4.5]deca-3,6,8-triene-4-carboxylic acid methyl ester (64 and 65)

To a mixture of 4-*tert*-butyl-1,2-benzoquinone (500 mg, 3.05 mmols) and DMAD (520 mg, 3.66 mmol) in dry benzene (10 mL) at 80 °C was added triphenylphosphine (400 mg, 1.52 mmol) and the reaction mixture was refluxed for 5 h. The solvent was removed and the residue was chromatographed on silica gel using 80:20 hexane-ethyl acetate to afford an inseparable mixture of the spirolactones **64** and **65** as a viscous yellow oil (242 mg, 26%).

IR ν_{max} (CCl_4) : 2965, 2874, 1782, 1729, 1676, 1656, 1575, 1452, 1437, 1390, 1237, 1196, 1148, 1067, 1003, 912, 788, 734 cm^{-1}.

^{1}H NMR : 7.232-7.192 (dd, 1H, *J*= 10.16 Hz; 1.82 Hz), 6.617 (d, 1H, *J*= 10.18 Hz), 6.251 (d, 1H, *J*= 10.26 Hz), 6.122 (s, 1H), 6.03 (d, 1H, *J*= 10.0 Hz), 5.717 (d, 1H, *J*= 1.99 Hz), 4.314 (s, 6H), 3.686 (s, 6H), 1.259 (s, 9H), 1.173 (s, 9H).

^{13}C NMR : 192.489, 192.340, 165.923, 163.758, 160.609, 149.696, 147.570, 141.938, 132.956, 128.428, 125.625, 125.036, 119.221, 78.417, 77.223, 60.017, 51.968, 51.889, 35.738, 34.709, 28.326, 27.988.

EIMS m/z (%) : 306 (M^+, 36), 291 (9), 277 (27), 274 (20), 262 (19), 259 (100), 247 (61), 231 (45), 203 (26), 175 (19), 163 (21), 147 (14), 135 (22), 115 (42), 91 (63), 79 (39), 77 (54), 65 (27), 59 (68).

7,9-Dibenzhydryl-3,6-dimethoxy-2,10-dioxo-1-oxa-spiro[4.5]deca-3,6,8-triene-4-carboxylic acid methyl ester (66)

To a mixture of 3-methoxy-4,6-bis(1,1-diphenylmethyl)-1,2-benzoquinone (250 mg, 0.53 mmol) and DMAD (108 mg, 0.76 mmol) in refluxing dry benzene was added triphenylphosphine (70 mg, 0.267 mmol) and the reaction mixture was stirred for 1.5 h. The solvent was removed and the residue was chromatographed on silica gel using 80:20 hexane-ethyl acetate to afford **66** as yellow crystals(125 mg, 46%).

IR ν_{max} (KBr) : 3038, 2950, 1782, 1732, 1685, 1655, 1599, 1497, 1452, 1390, 1230, 1171, 990, 705 cm^{-1}.

^{1}H NMR : 7.243-7.147 (m, 12 H), 7.021-6.904 (m, 8 H), 6.526 (s, 1H), 5.597 (s, 1H), 5.361 (s, 1H), 4.288 (s, 3H), 3.596, (s, 3H), 3.452 (s, 3H).

^{13}C NMR : 190.221, 166.194, 160.227, 152.016, 150.319, 144.403, 141.383, 141.267, 136.241, 128.923, 128.727, 128.550, 128.414, 128.259, 126.983, 126.912, 126.581, 126.521, 126.200, 120.286, 81.565, 63.292, 60.465, 52.444, 51.993, 49.078, 48.032.

Spirolactone 67

To a mixture of acenaphthenequinone (364 mg, 2.0 mmol) and DMAD (625 mg, 4.4 mmol) in dry benzene (15 mL) at 80 °C was added triphenylphosphine (262 mg, 1.0 mmol) and the reaction mixture was stirred for a period of 1 h. Benzene was removed and the residue on chromatographic separation on silica gel using 75:25 hexane-ethyl acetate gave the adduct **67** (353 mg, 55%). mp. 121-122 °C (Benzene-hexane).

IR ν_{max} (KBr) : 3015, 2957, 2870, 1780, 1735, 1705, 1653, 1607, 1469, 1456, 1437,1392, 1229, 1148, 1019, 797 cm^{-1}.

^{1}H NMR : 8.202 (d, 1H, *J*= 8.14 Hz), 8.080 (d, 1H, *J*= 6.934 Hz), 8.010 (d, 1H, *J*= 8.34 Hz), 7.822-7.771 (m, 1H, *J*= 7.351 Hz, *J*= 0.608 Hz), 7.700-7.649 (m, 1H, *J*= 7.13 Hz, *J*= 1.0 Hz), 7.504 (d, 1H, *J*= 6.88 Hz), 4.416 (s, 3H), 3.377 (s, 3H).

^{13}C NMR : 195.056, 165.881, 160.858, 149.348, 143.231, 132.356, 130.819, 128.548, 127.264, 123.164, 121.278, 85.222, 60.387, 52.088.

EIMS m/z (%) : 325 (M^+ +1, 1.7), 324 ($M^{+\cdot}$ 8.9), 309 (1), 280 (11), 265 (100), 237 (31), 194 (15), 179 (15), 150 (30), 138 (23), 126 (21), 75 (13), 59 (16), 44 (22).

Spirolactone 68

To a mixture of 9,10-Phenanthrenequinone (230 mg, 1.105 mmols) and DMAD (172 mg, 1.216mmol) in dry benzene (10 mL) at 80 °C was added triphenylphosphine (145 mg, 0.552 mmol) and the mixture was heated for 1 h. The solvent was removed under reduced pressure and the residue on chromatographic separation on silicagel using 80:20 hexane-ethyl acetate gave **68** as a yellow solid (304 mg, 78%).

IR ν_{max} (KBr) : 3068, 2955, 2860, 1780, 1734, 1707, 1657, 1600, 1462, 1390, 1276, 1229, 1171, 997, 916, 758, 730 cm^{-1}.

^1H NMR : 8.130-8.040 (m, 3H), 7.753-7.698 (m, 1H), 7.508-7.251 (m, 4 H), 4.366 (s, 3H), 3.400 (s, 3H).

^{13}C NMR : 190.107, 166.493, 160.778, 149.219, 136.658, 135.787, 131.901, 131.307, 130.412, 129.314, 128.726, 128.171, 128.111, 124.111, 123.691, 123.386, 81.083, 60.416, 52.059.

Spirolactones 69 and 70

To a refluxing mixture of 1,2-naphthoquionone (125 mg, 0.791 mmol) and DMAD (135 mg, 0.95 mmols) in dry benzene (5 mL) was added triphenylphosphine (104 mg, 0.396 mmol) and heating was continued for 4 h. The solvent was evaporated and the residue on radial

chromatography on a Chromatotron® using 90:10 hexane-ethyl acetate afforded the adduct **69** as a yellow solid (54 mg, 23%). Further elution with the same solvent mixture afforded the spirolactone **70** as a yellow solid (55 mg, 23%).

Data for **69**

IR ν_{max} (KBr) : 3018, 2968, 1795, 1719, 1695, 1663, 1628, 1603, 1458, 1385, 1243, 1171, 1007, 774 cm^{-1}.

^1H NMR : 8.00 (dd, 1H, *J*= 7.9 Hz, *J*= 1.3 Hz) 6.90 (d, 1H, *J*= 10.6 Hz), 5.90 (d, 1H, *J*= 10.6 Hz), 4.30 (s, 3H), 3.55 (s, 3H).

^{13}C NMR : 190.761, 166.087, 160.806, 149.320, 136.133, 135.417, 131.777, 129.062, 128.525, 128.435, 127.600, 126.944, 121.752, 79.029, 60.173, 52.028.

EIMS m/z (%) : 285 (M^+-Me, 0.5), 284 (2.5), 256 (M^+-CO_2, 75), 241 (M^+-CO_2Me, 100), 213 (18), 183 (10), 154 (19), 145 (23), 128 (17), 126 (51), 115 (12), 63 (10), 59 (6).

Data for **70**

IR ν_{max}(KBr) : 3030, 2969, 1779, 1709, 1681, 1658, 1576, 1444, 1397, 1228, 1196, 1171, 997, 838, 766 cm^{-1}.

^1H NMR : 7.5 (d, 1H, *J*= 11 Hz), 7.4 (m, 4H), 6.4 (d, 1H, *J*= 11 Hz), 4.3 (s, 3H), 3.5 (s, 3H).

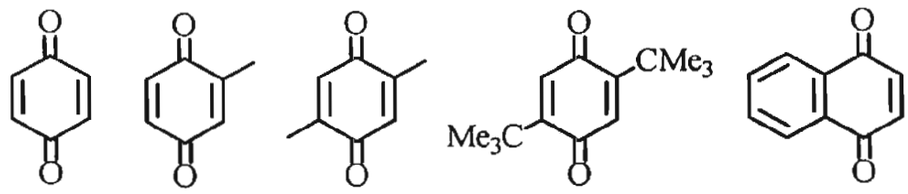
^{13}C NMR : 190.761, 166.297, 160.568, 149.112, 145.74, 136.163, 135.447, 131.807, 129.092, 128.435, 126.630, 127.003, 79.029, 60.173, 52.028.

EIMS m/z (%) : 285 (M^+-Me, 18), 284 (100), 254 (14), 253 (61), 226 (30), 223 (26), 195 (24), 166 (11), 139 (46), 138 (32), 126 (26), 86 (15), 63 (8), 59 (9).

2.2 ADDITION OF DIMETHYL ACETYLENE-DICARBOXYLATE TO *PARA*-QUINONES MEDIATED BY TRIPHENYLPHOSPHINE

2.2.1 INTRODUCTION

In view of the interesting results obtained by the addition of zwitterionic intermediates, generated from dimethyl acetylenedicarboxylate and triphenylphosphine, to *o*-quinones, a logical extension of this work was to explore the reactivity of *p*-quinones towards the zwitterionic intermediates. The quinones selected for the study are listed in the following figure.

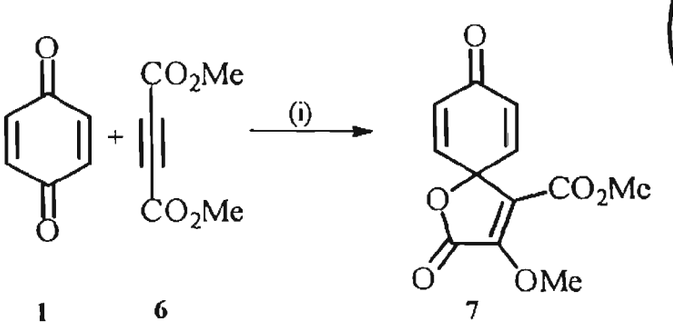


1 2 3 4 5

Figure 2.2.1

2.2.2 RESULTS AND DISCUSSION

Benzoquinone when treated with dimethyl acetylenedicarboxylate and 50 mol% triphenylphosphine in benzene at ambient temperature for 12 h afforded the adduct 7 in 88% yield (Scheme 2.2.1).



1 6 7

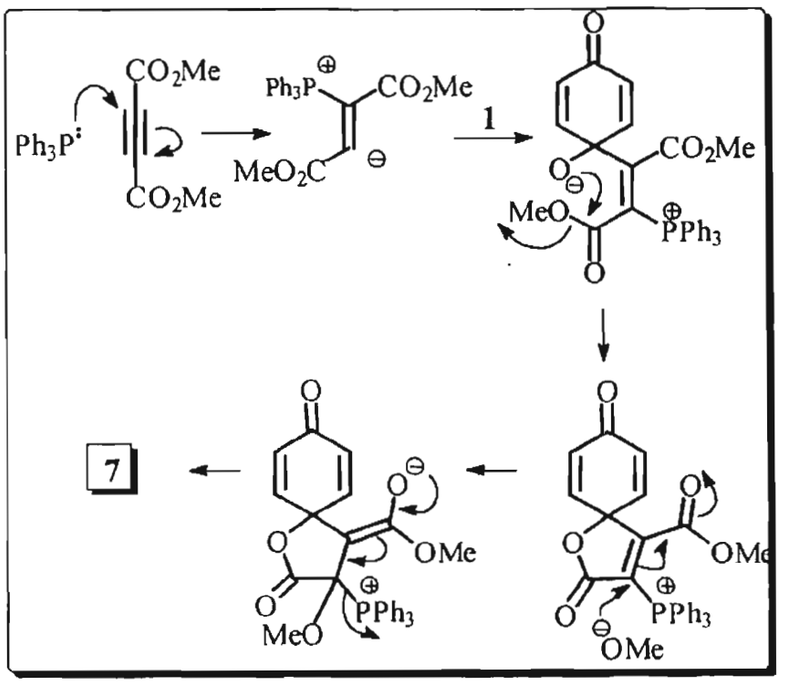
(i) PPh_3, Benzene, R.T., 12 h, 88%.

Scheme 2.2.1

The structure of the adduct was elucidated by analytical and spectroscopic methods. The IR spectrum of 7 showed a strong absorption at 1774 cm^{-1} indicating the presence of the lactone moiety. The peak at 1727 cm^{-1} is attributed to the carbomethoxy group and the one at 1680 cm^{-1} is due to the dienone. The sharp band at 1647 cm^{-1} was assigned to the double bond in the lactone ring. In the ^1H NMR, the four olefinic protons in the cyclohexadiene ring appeared as a multiplet between δ 6.542-6.370. The carbomethoxy group was observed as a singlet at δ 3.730 and the methoxy group adjacent to the lactone carbon resonated at δ 4.316. In the ^{13}C NMR a characteristic peak at δ 76.983 was assigned to the spirocarbon atom. The methyl of the -COOMe showed a signal at δ 52.381 and the -OMe α to the lactone carbonyl appeared at δ 60.314. The lactone carbon resonated at δ 160.369 and the ester carbon at δ 164.836 while the peak at δ 184.158 was assigned to

the carbonyl of the dienone. The sp^2 carbon α to the lactone gave a signal at δ 120.622 and the one β to the lactone appeared at δ 149.854. The α and β olefinic carbons in the dienone ring were observed at δ 131.566 and 142.266 respectively. Analytical data is in agreement with the proposed structure.

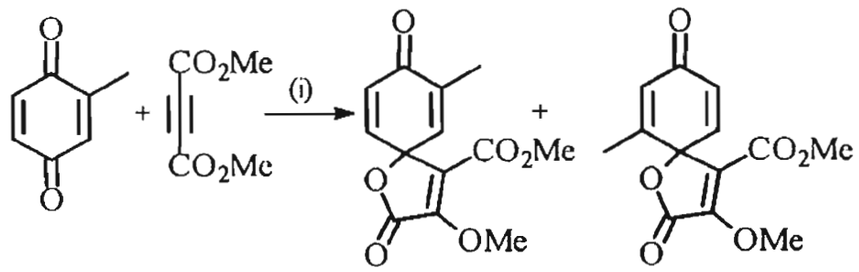
The reaction involves the initial formation of a zwitterionic intermediate from triphenylphosphine and dimethyl acetylenedicarboxylate, which then adds to the quinone carbonyl to yield a betaine. The betaine on subsequent cyclization leads to the spirolactone (Scheme 2.2.2).



Scheme 2.2.2

The reaction of other benzoquinones with dimethyl acetylenedicarboxylate and triphenylphosphine afforded similar

γ,δ–spirolactones. 2-methyl-1,4-benzoquinone gave a 1:4 regioisomeric mixture of the adducts **8** and **9** in 89% yield (Scheme 2.2.3).

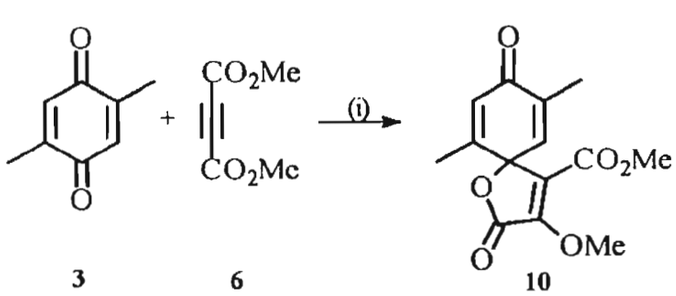


(i) PPh_3, Benzene, R.T., 12 h, 89% (1:4).

Scheme 2.2.3

8 showed strong IR absorptions at 1769 with a shoulder at 1782, 1719, and 1677 cm^{-1}. In the ^1H NMR of **8**, the methyl group was observed at δ 1.944. In the ^{13}C NMR, the lactone, ester and enone carbonyls were visible at δ 160.585, 165.086 and 184.979 respectively. The methyl carbon resonated at δ 15.802 and the spirocarbon appeared at δ 77.812. The carbon bearing the methyl group appeared at δ 138.905. The proposed structure was supported by satisfactory analytical data. Similar spectral and analytical data were obtained for **9**.

A similar spirolactone **10** was obtained with 2,5-dimethyl-1,4-benzoquinone (Scheme 2.2.4).

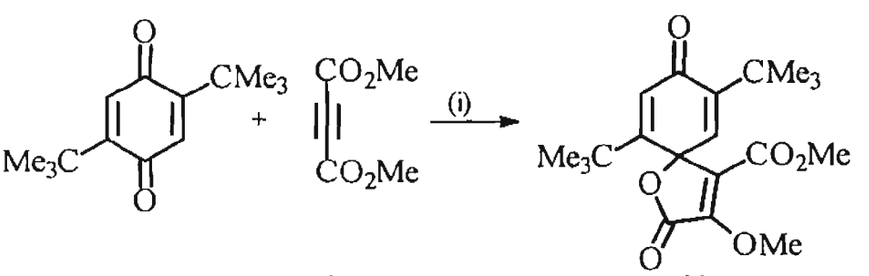


(i) PPh_3, Benzene, R.T., 24 h, 73%.

Scheme 2.2.4

The IR absorptions at 1772, 1719, and 1685 cm^{-1} were characteristic of the proposed spirolactone structure. Proton NMR spectrum of **10** showed two doublets at δ 6.278 (*J*= 1.46 Hz) and δ 6.231 (*J*= 1.74 Hz) due to the olefinic protons. The two methyl groups resonated as two doublets at δ 1.938 (*J*= 1.51Hz) and δ 1.821 (*J*= 1.42 Hz). In the ^{13}C NMR, the methyl groups resonated at δ 16.772 and δ 15.386. The spirocarbon was discernible at δ 79.63. The assigned structure was further supported by satisfactory elemental analysis.

2,5-di-*tert*-butyl-1,4-benzoquinone on reaction with dimethyl acetylenedicarboxylate and triphenylphosphine afforded a similar spirolactone **11** in 26% yield. Some unreacted quinone was recovered, and the yield of the lactone based on the reacted quinone was 39% (Scheme 2.2.5).



4 **6** **11**

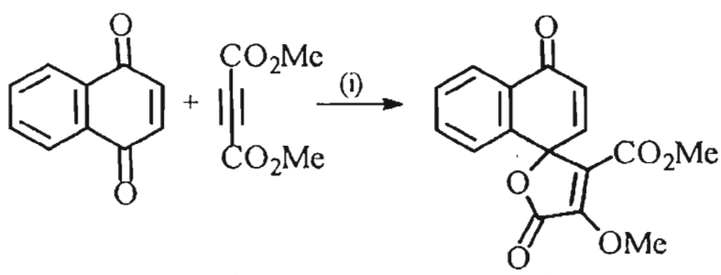
(i) PPh_3, Benzene, R.T., 24 h, 26%.

Scheme 2.2.5

As described for the other spirolactones, the IR spectrum of **11** showed three carbonyl absorptions at 1796, 1723 and 1667 cm^{-1} revealing the presence of the lactone, ester and the enone carbonyls respectively. The ^1H NMR showed two sharp singlets at δ 1.217 and δ 1.178 corresponding to the two *tert*-butyl groups. The olefinic protons resonated as singlets at δ 6.347 and δ 5.914. In the ^{13}C NMR, methyl

carbons of the *tert*-butyl group resonated at δ 30.834 and 28.755. The quaternary carbons of the *tert*-butyl groups appeared at δ 37.224 and 34.376. All other signals are also in agreement with the assigned structure.

1,4-naphthoquinone also undergoes a similar reaction when treated with DMAD and triphenylphosphine to afford the spirolactone **12** in 26% yield. The yield based on the reacted starting material was 70% (Scheme 2.2.6).



5 **6** **12**

(i) PPh_3, Benzene, 80 °C, 4 h, 26%.

Scheme 2.2.6

The IR spectrum of **12** showed the three carbonyl absorptions at 1761, 1706 and 1681 cm^{-1}. In the ^1H NMR the two olefinic protons appeared as a singlet at δ 6.6. The carbomethoxy and the methoxy protons resonated at δ 3.549 and δ 4.380 respectively. In the ^{13}C NMR the signal due to the spirocarbon was visible at δ 78.405. The three carbonyl carbons resonated at δ 183.525, 165.775 and δ 160.35. The two olefinic carbons bearing hydrogen resonated at δ 142.616 and 133.211. The structure was further supported by analytical data.

In conclusion, we have unraveled the reactivity of both *ortho* and *para* quinones towards the zwitterionic intermediate generated by the addition of triphenylphosphine to dimethyl acetylenedicarboxylate. These investigations have resulted in a facile synthesis of highly functionalised γ,δ-unsaturated spirolactones. In this context, it may be noted that γ,δ-unsaturated spirolactone moiety is present in a number of biologically active natural products such as chlorothricin, kijanolide and tetranolide.[31]

2.2.3 EXPERIMENTAL DETAILS

For general experimental details see Chapter 2, p-42.

3-Methoxy-2,8-dioxo-1-oxa-spiro[4.5]deca-3,6,9-triene-4-carboxylic acid methyl ester (7)

A mixture of benzoquinone (500 mg, 4.63 mmol) and dimethyl acetylenedicarboxylate (DMAD) (790 mg, 5.56 mmol) in dry benzene (10 mL) was purged with argon and stirred at room temperature. To this triphenylphosphine (606 mg, 2.31 mmols) was added and the reaction mixture was stirred for 12 h. Removal of the solvent and chromatography on silica gel using 80:20 hexane-ethyl acetate afforded 7 as colourless prisms (1.022 g 88%). mp. 120-122 °C (Benzene-hexane).

IR ν_{max} (KBr) : 3056, 3009, 2955, 1774, 1727, 1680, 1647, 1629, 1456, 1438, 1390, 1248, 1215, 1154, 1019, 930, 871, 760 cm^{-1}.

^1H NMR : 6.542-6.370 (m, 4 H), 4.316 (s, 3 H), 3.730 (s, 3H).

^{13}C NMR : 184.158, 164.836, 160.369, 149.854, 142.266, 131.566, 120.622, 76.983, 60.314, 52.381.

MS : 250(M^+).

Anal. calcd. for $C_{12}H_{10}O_6$:C: 57.61; H: 4.03. Found C: 57.53; H: 4.06%.

3-Methoxy-7-methyl-2,8-dioxo-1-oxa-spiro[4.5]deca-3,6,9-triene-4-carboxylic acid methyl ester (8) and 3-methoxy-6-methyl-2,8-dioxo-1-oxa-spiro[4.5]deca-3,6,9-triene-4-carboxylic acid methyl ester (9)

A mixture of 2-methyl-1,4-benzoquinone (500 mg, 4.1 mmol) and dimethyl acetylenedicarboxylate (700 mg, 4.9 mmol) under argon

atmosphere at ambient temperature in dry benzene (10 mL) was treated with triphenylphosphine (540 mg, 2.05 mmols) for 12 h. The solvent was removed and the residue on radial chromatography with 90:10 hexane-ethyl acetate afforded **8** as white needles (198 mg, 18%). mp. 116-118 °C (Benzene-hexane). Further elution with 90:10 hexane-ethyl acetate gave the spirolactone **9** as a white solid (775 mg, 71%).

Data for **8.**

IR ν_{max} (KBr) : 3029, 2962, 1782, 1769, 1719, 1677, 1641, 1454, 1386, 1250, 1204, 1176, 983, 884, 769 cm^{-1}.

^{1}H NMR : 6.467-6.434 (d, 1H, *J*= 9.9 Hz), 6.386-6.348 (dd, 1H, *J*= 9.92 Hz, *J*= 1.7 Hz), 6.621-6.279 (t, 1H, *J*= 1.39Hz), 4.306 (s, 3H), 3.711 (s, 3H), 1.831-1.826 (d, 3H, *J*= 1.39 Hz).

^{13}C NMR : 184.868, 165.267, 160.405, 150.958, 149.884, 142.469, 131.393, 130.066, 121.235, 78.989, 60.404, 52.522, 17.100.

Anal. calcd. for $C_{13}H_{12}O_6$: C: 59.09, H: 4.58, found. C: 59.53, H: 4.37%.

Data for **9**

IR ν_{max} (KBr) : 2961, 1768, 1707, 1676, 1645, 1438, 1394, 1235, 1205, 1156, 984, 893, 763 cm^{-1}.

^{1}H NMR : 6.453-6.444 (dd, 1H, *J*= 2.85 Hz), 6.403-6.370 (d, 1H), 6.259-6.249 (t, 1H, *J*= 2.91 Hz), 4.303 (s, 3H), 3.721 (s, 1H), 1.951-1.946 (d, 3H, *J*= 1.43 Hz).

^{13}C NMR : 184.979, 165.086, 160.586, 149.594, 142.041, 138.905, 137.181, 131.600, 121.195, 77.812, 60.279, 52.393, 15.802.

Anal. calcd. for $C_{13}H_{12}O_6$: C: 59.09, H: 4.58, found. C: 59.23, H: 4.55%.

3-Methoxy-6,9-dimethyl-2,8-dioxo-1-oxa-spiro[4.5]deca-3,6,9-triene-4-carboxylic acid methyl ester (10)

To a mixture of 2,5-dimethyl-1,4-benzoquinone (500 mg, 3.67 mmols) and DMAD (650 mg, 4.57 mmol) in dry benzene (10 mL) at room temperature under argon atmosphere was added triphenylphosphine (482 mg, 1.84 mmol) and the reaction mixture was stirred for 24 h. After the solvent was removed, the residue was chromatographed on silica gel. Elution with 95:5 hexane-ethyl acetate gave the unreacted quinone (99 mg). Further elution with 80:20 hexane-ethyl acetate afforded **10** as a white solid (752 mg, 73%). The yield based on the reacted quinone was 91%. The white solid was recrystallised from dichloromethane-hexane to give colourless needles. mp. 107-109 °C.

IR ν_{max} (KBr) : 2965, 2919, 1778, 1764, 1719, 1685, 1642, 1472, 1450, 1390, 1247, 1202, 979, 898, 770 cm^{-1}.

^1H NMR : 6.278-6.224 (dd, *J*= 11.81 Hz and 1.46 Hz) 4.296 (s, 3H) 3.716 (s, 3H), 1.938-1.932 (d, 3H, *J*= 1.51 Hz), 1.821-1.815 (d, 3H, *J*= 1.42 Hz).

^{13}C NMR : 185.474, 165.410, 160.499, 150.598, 149.483, 138.503, 137.298, 129.860, 121.494, 79.630, 60.250, 52.420, 16.772, 15.386.

EIMS m/z (%) : 278 (M^+, 12), 246 (25), 235 (37), 219 (32), 203 (41), 191 (61), 175 (30), 163 (17), 147 (22), 131 (31), 103 (39), 77 (67), 59 (100), 51 (42).

Anal. calcd. for $C_{14}H_{14}O_6$ C: 60.43; H: 5.07; Found C: 60.33; H: 5.1%.

6,9-Di-*tert*-butyl-3-methoxy-2,8-dioxo-1-oxa-spiro[4.5]deca-3,6,9-triene-4-carboxylic acid methyl ester (11)

A mixture of 2,5-di-*tert*-butyl-1,4-benzoquinone (500 mg, 2.272 mmols) and DMAD (388 mg, 2.726 mmols) in dry benzene(10 mL) at room temperature under argon atmosphere was treated with triphenylphosphine (298 mg, 1.136 mmols) and the reaction mixture was stirred for 24 h. The residue obtained after the removal of the solvent was chromatographed on silica gel using 95:5 hexane-ethyl acetate to give the unreacted quinone (251 mg) and further elution with 90:10 hexane-ethyl acetate yielded **11** as light yellow crystals (214 mg, 26%). mp. 121-123 °C (CH_2Cl_2-hexane).

IR ν_{max} (KBr) : 2962, 2874, 1796, 1723, 1667, 1631, 1458, 1371, 1249, 1209, 1175, 980, 791 cm^{-1}.

^1H NMR : 6.347 (s, 1H), 5.914 (s, 1H), 4.257 (s, 3H), 3.666 (s, 3H), 1.217 (s, 9H), 1.178 (s, 9H).

^{13}C NMR : 186.092, 165.834, 160.627, 157.251, 149.128, 146.909, 140.133, 131.322, 123.4, 82.259, 60.064, 52.132, 37.224, 34.376, 30.834, 28.755.

Anal. calcd. for : $C_{20}H_{26}O_6$ C: 66.28; H: 7.25. Found: C: 66.37; H: 7.48%.

Spirolactone 12

Triphenylphosphine (420 mg, 1.60 mmol) was added to a refluxing mixture of 1,4-naphthoquinone (500 mg, 3.16 mmol) and DMAD (542 mg, 3.81 mmol) in dry benzene (10 mL) and the heating was continued for 4 h. The solvent was removed and the residue on chromatographic separation on silica gel using 95:5 hexane-ethyl acetate

removed the unreacted quinone (300 mg,). Further elution with 80:20 hexane-ethyl acetate afforded the product **12** (250 mg, 26%). The yield based on the reacted starting material was 66%. The product was recrystallised from dichloromethane-hexane to give light yellow crystals. mp. 180-182 °C.

IR ν_{max} (KBr) : 3062, 3019, 2961, 1761, 1706, 1681, 1643, 1593, 1451, 1385, 1297,1195, 1087, 979, 763 cm^{-1}.

^{1}H NMR : 8.180-8.151 (dd, 1H, *J*= 7.54Hz and *J*= 1.09 Hz), 7.622-7.504 (m. 2H), 7.229-7.204 (d, 1H, *J*= 7.62 Hz), 6.600 (s, 2H), 3.549 (s, 3H), 4.380 (s, 3H).

^{13}C NMR : 183.525, 165.775, 160.352, 149.376, 142.616, 136.868, 133.211, 131.894, 131.385, 129.769, 127.192, 1275.398, 123.481, 78.405, 60.532, 52.272.

Anal. calcd. for $C_{16}H_{12}O6$: C, 64.00; H; 4.03. Found: C, 63.87; H, 3.99%.

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CHAPTER 3

ISOMERIZATION OF 6,6-TETRAMETHYLENE FULVENE TO 1-CYCLOPENTENYL CYCLOPENTADIENE AND ITS CYCLOADDITION

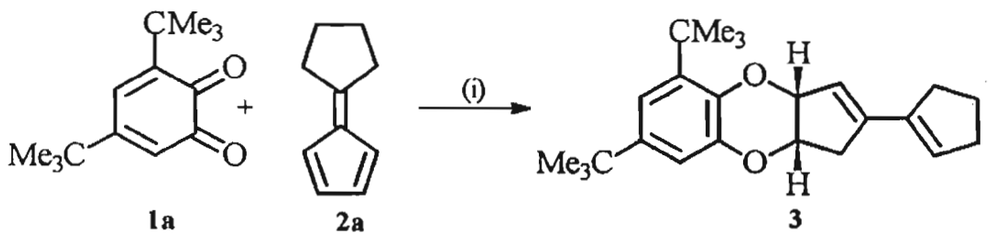
3.1 INTRODUCTION

As mentioned in the general introduction (Chapter 1), *o*-quinones can exhibit multiple reactivity and these have been investigated with various dienes,[1] fulvenes,[2] dipolarophiles,[3] etc.

Studies in our laboratory exploring the reactivity profile of *o*-benzoquinones with 6,6-dialkyl, 6-aryl, 6,6-diaryl, 6,6-arylalkyl fulvenes revealed that generally *o*-benzoquinones act as carbodienes in their reactions leading to the formation of bicyclo[2.2.2]octenediones.[2]

For example, reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone with 6-substituted fulvenes afforded the bicyclo[2.2.2]diones exclusively.

Interestingly, however, the cycloaddition reaction of *o*-benzoquinones with 6,6-tetramethylene fulvene proceeded in a completely different route. For example, 3,5-di-*tert*-butyl-1,2-benzoquinone (**1a**) reacted with 6,6-tetramethylene fulvene (**2a**), to afford a product, the structure of which was unambiguously established as **3** by single crystal X-ray analysis (Scheme 3.1).[2b]

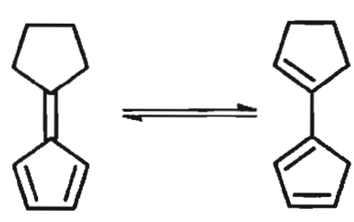


1a **2a** **3**

(i) Toluene, Sealed tube, 110 °C, 85%.

Scheme 3.1

The benzodioxin adduct **3** was formed, presumably by the cycloaddition of 1-cyclopentenylcyclopentadiene **4**, generated by the isomerization of 6,6-tetramethylene fulvene **2a** under the experimental conditions (Scheme 3.2).



2a **4**

Scheme 3.2

In this context, it was of interest to isolate **4** and investigate its cycloaddition chemistry. To put things in perspective, a brief discussion

of the reactivity profile of fulvenes, especially pentafulvenes, is given in the following section.

Fulvenes are an important class of compounds[4] both from the standpoint of theory[5] and organic synthesis.[6] Pentafulvenes are easily obtained by the condensation of cyclopentadiene with carbonyl compounds. Their reactivity profile, cycloaddition profile in particular, has been extensively investigated during the last two decades.[4]

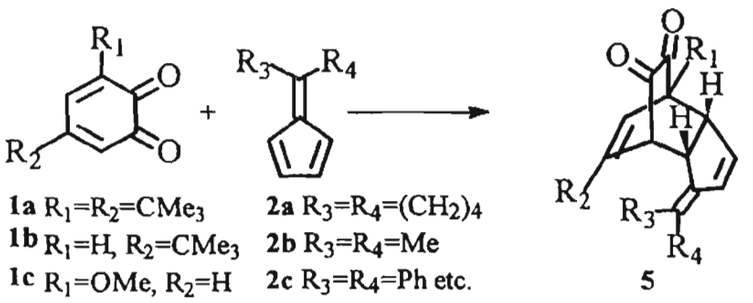
3.2 REACTIVITY OF FULVENES

In cycloaddiiton reactions, fulvenes can participate as 2π, 4π or 6π components.The reactivity profile depends on the nature of the dienophile.[7]

Vinyl fulvenes can be considered as higher homologues of fulvenes.[8] Studies on the cycloaddition reactions of 6-styrenyl fulvene have been reported from our laboratory with various dienes and dienophiles.[9]

3.2.1 Reaction of pentafulvenes with *o*-quinones

It has been shown in our laboratory that *o*-quinones react with various fulvenes such as 6-alkyl, 6-aryl, 6,6-dialkyl, 6,6-diaryl and 6-styrenylfulvenes to give bicyclooctene-8,9-dione derivatives (Scheme 3.3).[2,9] The resulting adducts are amenable to a number of transformations leading to interesting products.[9,10]



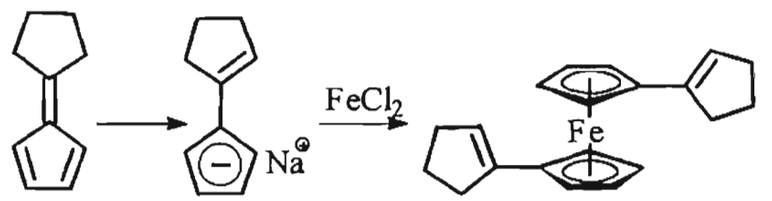
1a $R_1=R_2=CMe_3$ **2a** $R_3=R_4=(CH_2)_4$
1b $R_1=H$, $R_2=CMe_3$ **2b** $R_3=R_4=Me$
1c $R_1=OMe$, $R_2=H$ **2c** $R_3=R_4=Ph$ etc.

5

Scheme 3.3

3.3 REARRANGEMENT OF PENTAFULVENES

6,6-tetramethylene fulvene is known to form cyclopentylidine-cyclopentenyl anion when treated with sodium. The anion is trapped with ferrous chloride to give 1,1'-dicyclopentenylferrocene (Scheme 3.4). [11,4c]

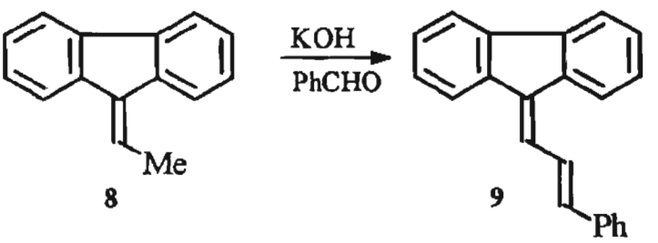


2a **6** **7**

Scheme 3.4

The acidic nature of the hydrogens at the 7-position of fulvenes is best illustrated by the fact that 6,6-dimethylfulvene forms the anion when treated with triphenylmethylsodium or sodamide in liquid ammonia. This isopropylidenecyclopentadienide anion gave the corresponding ferrocene derivative, *viz.*, 1,1'-diisopropenylferrocene.[12,13]

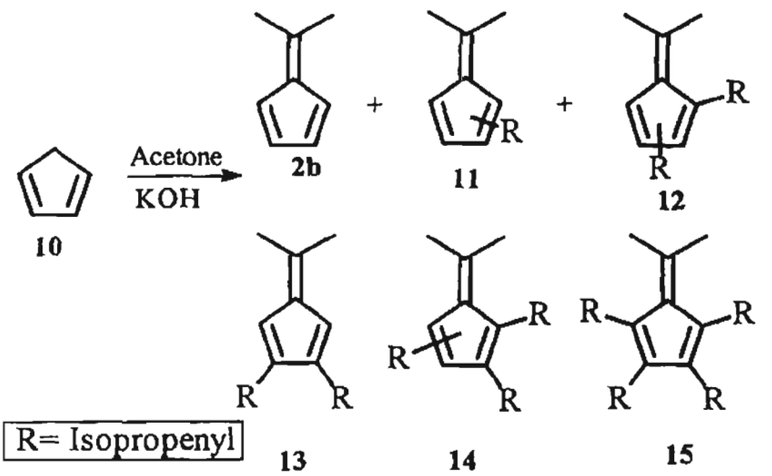
Ethylidene fluorene can be condensed with aldehydes in presence of KOH to give vinyl fulvenes, thus attesting the acidic nature of the methyl hydrogens (Scheme 3.5).[14]



8 9

Scheme 3.5

The reaction of cyclopentadiene with excess of acetone gave mono-, di-, tri- and tetraisopropenyl fulvenes in addition to the expected 6,6-dimethyl fulvene (Scheme 3.6). When the reaction is carried out in ethanol, product resulting from the addition of the solvent was observed.[15]



10 2b 11 12 13 14 15

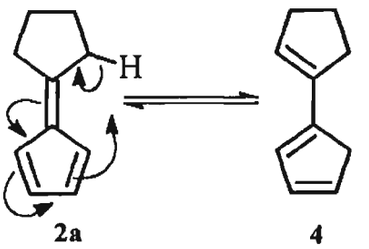
Scheme 3.6

3.4 STATEMENT OF THE PROBLEM

In view of the assumption that 6,6-tetramethylene fulvene rearranges to cyclopentenyl cyclopentadiene during the reaction with *o*-quinone, it was necessary to isolate the rearranged product and investigate its cycloadditions. These studies are presented in this chapter.

3.5 RESULTS AND DISCUSSION

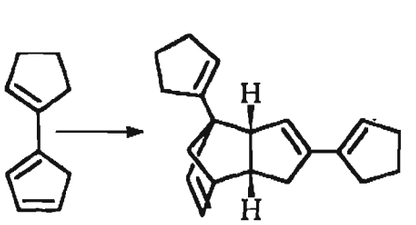
Our initial attempts to isolate or trap the isomerized product from 6,6-tetramethylene fulvene with reactive dienophiles such as maleic anhydride were unsuccessful. The fulvene was heated over a period of time and treated with the dienophile. In most of the experiments the normal Diels-Alder adducts from the fulvene and the dienophile were isolated. Later on the isomerization of **2a** was found to occur in presence of acid (Scheme 3.7).



2a **4**

Scheme 3.7

Theoretical studies revealed that the isomerized 6,6-tetramethylene fulvene *viz.*, 1-cyclopentenylcyclopentadiene is more stable than the fulvene by 4.9 kcal/mol. Even though the magnitude of energy difference between **2a** and **4** is not very large, it is sufficient to provide the driving force for such a facile rearrangement of **2a** to the isomerized fulvene **4**. The isomerized fulvene being a very reactive cyclopentadiene undergoes rapid dimerization to afford **16** (Scheme 3.8).



4 **16**

Scheme 3.8

In order to gain insight into the reactivity profile of **4,** its cycloaddition with a number of dienophiles was investigated. The dienes and dienophiles used in the investigation are listed in figure 3.1. In most cases cycloaddition products resulting from **4** as well as those from the dimer were isolated.

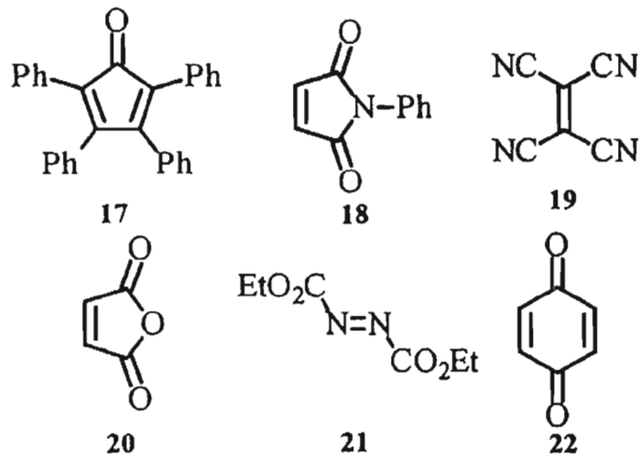
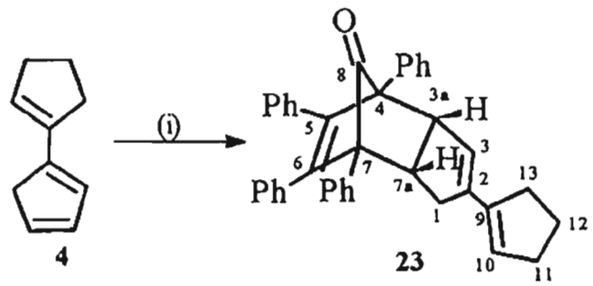


Figure 3.1

Reaction of tetracyclone with the isomerized fulvene **4** in refluxing benzene for 40 h, afforded the adduct **23** in 30% yield. The isomerized fulvene participated as the 2π component and tetracyclone as the 4π component (Scheme 3.9).[16]



(i) Tetracyclone (17), Benzene, 80 °C, 40 h, 30%.

Scheme 3.9

The structure of the adduct **23** was confirmed by spectral and analytical data. In the IR spectrum, the bridge carbonyl group was observed at 1770cm^{-1}. In the ^{1}H NMR spectrum, the 20 aromatic protons appeared as four multiplets in the region δ 7.51-6.53. The olefinic protons appeared at δ 5.90 and δ 5.60. The ring junction proton on C_{3a} appeared at δ 4.35 as a doublet. The other ring junction proton on C_{7a} was observed at δ 3.65 as a multiplet. The two protons on C_1 were observed at δ 2.98-2.81 as a multiplet. The methylene protons on C_{12} were seen as a multiplet between δ 1.96-1.81. The four methylene protons on C_{11} and C_{13} appeared as multiplets between δ 2.62-2.27. In the ^{13}C NMR spectrum, the carbonyl carbon was seen at δ 201.538. The two bridgehead quaternary carbons (C_4 and C_7) were observed at δ 66.816 and 65.972 and the ring junction carbon atoms, C_{3a} and C_{7a} were observed at δ 52.936 and 42.291. The presence of four methylene carbons has been shown by DEPT NMR experiments. The methylene carbon adjacent to the ring junction (C_1) resonated at δ 36.699. The methylene carbon C_{12}, appeared at δ 23.237. The other two methylene carbons C_{11} and C_{13}, on the cyclopentenyl ring were observed at δ 33.343 and 32.932. All the aromatic carbons and the olefinic carbons appeared as a cluster in the region δ 130.439-124.471. From the hetero COSY NMR studies, the two olefinic carbons (C_2 & C_9) were observed at δ 129.624 and 124.471. The two tetrasubstituted sp^2 carbons (C_5 and C_6) on the bicyclo ring appeared at δ 142.746 and 141.016. The proton-proton connectivity was well established with the 2D COSY NMR studies. The structure of the adduct was supported by satisfactory

elemental analysis and finally confirmed by single crystal X-ray analysis[#] (Figure 3.2).

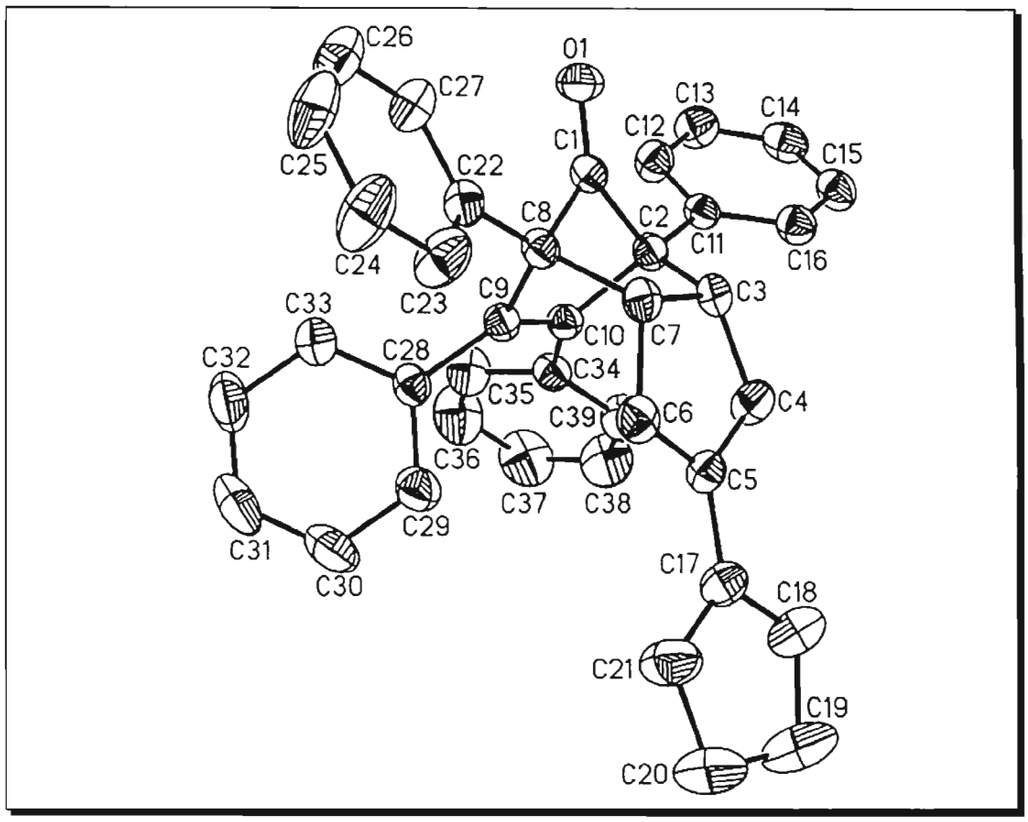


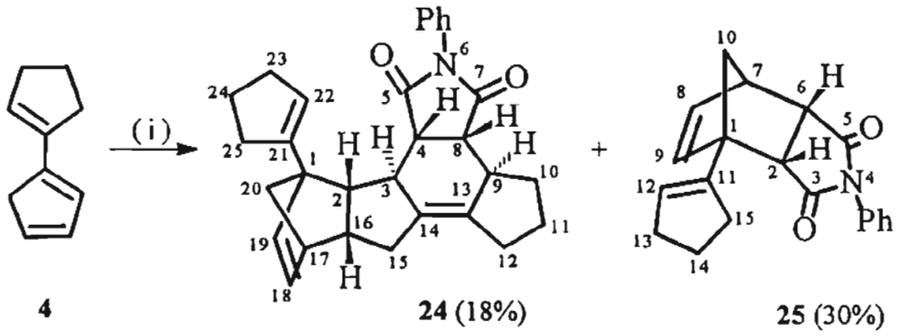
Figure 3.2

X-ray Crystal structure of 23

When treated with N-phenylmaleimide, the isomerized fulvene **4** afforded Diels-Alder adduct **25** resulting from the 1-cyclopentenyl cyclopentadiene and also the adduct **24** from the dimer of the isomerized fulvene. The isomerized fulvene undergoes spontaneous dimerization under the experimental conditions in a Diels-Alder fashion and the dimer

[#] X-ray crystal analysis was done by Dr. Nigam P. Rath of Missouri University, U. S. A.

subsequently undergoes cycloaddition with N-phenylmaleimide to yield the adduct **24** (Scheme 3.10).



4 **24** (18%) **25** (30%)

(i) N-Phenylmaleimide (**18**), Benzene, 80 °C, 4 h.

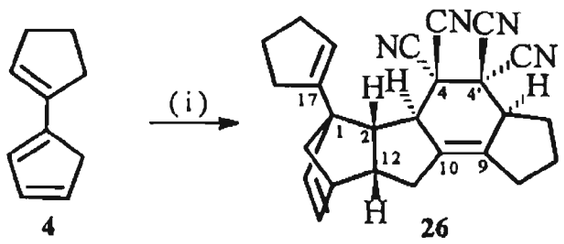
Scheme 3.10

The adduct **24** from the dimer of the isomerized fulvene showed characteristic absorptions in IR spectra at 1780 and 1714 cm^{-1}. In the ^1H NMR the aromatic protons were seen as two multiplets at δ 7.4-7.2. The olefinic protons were visible at δ 6.2 as a multiplet and at δ 5.65 as a broad singlet. The doublet of doublet at δ 3.35 was assigned to the bridgehead proton on C_{17}. All the other protons appeared as a multiplet between δ 3.25-0.90. In the ^{13}C NMR spectrum, two imide carbonyls gave signals at δ 177.932 and 176.858. The aromatic carbon signals were assigned at δ 133.358, 126.377, 128.256 and 128.943. The three olefinic carbons (C_{18}, C_{19} and C_{22}) resonated at δ 131.886, 137.475 and 123.572 respectively. The two tetrasubstituted olefinic carbons (C_{13} and C_{14}) were visible at δ 145.919 and 136.431. The olefinic carbon C_{21} resonated at δ 140.369. The bridgehead quaternary carbon (C_1) appeared at δ 59.189 and the bridgehead methylene carbon (C_{20}) appeared at δ 56.503. The methine carbons C_4 & C_8 resonated at δ 47.344 and 46.210 and the

signals at δ 44.629 and 43.913 were assigned carbons labeled C_3 and C_9. The ring junction carbon atoms (C_2 and C_{16}) were observed at δ 50.029 and 40.959.

The IR spectrum of **25** showed absorptions at 1776 and 1713 cm^{-1} indicating the presence of imide carbonyl group. In the ^1H NMR of **25**, the aromatic protons appeared at δ 7.4-7.1 as a multiplet. The broad singlet at δ 6.35 was assigned to the two olefinic protons on C_8 and C_9. The olefinic proton on C_{12} was seen at δ 5.9 as a broad triplet. The three protons, one on the bridgehead (C_7) and the two on the ring junction (C_2 and C_6) were observed at δ 3.5 as a multiplet. The four protons on C_{13} and C_{15} were visible as a multiplet between δ 2.7 and 2.25. The protons on C_{10} and C_{14} resonated between δ 2.2 and 1.65 as a multiplet. In the ^{13}C NMR spectrum, the two imide carbonyls were observed at δ 176.321 and 175.604. The aromatic carbons gave signals at δ 133.985, 128.734, 126.824 and 126.407. The tetrasubstituted olefinic carbon (C_{11}) resonated at δ 141.801 and the olefinic carbons C_8, C_9 and C_{12} were assigned values δ 137.088, 131.807 and 128.227. The bridgehead quaternary carbon was discernible at δ 59.368 and the signal at δ 56.593 was assigned to the other bridgehead carbon. The two carbons α to the olefinic bond in cyclopentenyl ring were observed at δ 33.351 and 32.516. The bridge carbon appeared at δ 45.166. The two carbons at the ring junction resonated at δ 48.358 and 47.553. The signal at δ 23.148 was assigned to the methylene carbon β to the olefinic bond in the cyclopentenyl ring. The high-resolution mass spectrum showing M^+ peak at 305.14092 is also in accordance with the proposed structure.

When more reactive dienophiles such as maleic anhydride, tetracyanoethylene and diethyl azodicarboxylate were used, the adducts from the dimer were obtained. When tetracyanoethylene was treated with the isomerized fulvene **4** in benzene at room temperature, the adduct **26** from the dimer **16** was isolated in 52% yield (Scheme 3.11).



4 **26**

(i) TCNE (**19**), Benzene, RT, 45 min., 52%.

Scheme 3. 11

The IR spectrum of **26** showed a weak absorption at 2252 cm^{-1} indicating the presence of -CN group. In the ^1H NMR spectrum, the olefinic protons were seen at δ 6.321-6.309 as a doublet and at δ 5.719 as a triplet. The cyanide carbons were discernible in the ^{13}C NMR at δ 111.788 and 110.833. The tetrasubstituted olefinic carbon (C_{17}) appeared at δ 138.28 and the carbons C_9 and C_{10} were observed at δ 142.63 and 137.088. The bridgehead quaternary carbon (C_1) was seen at δ 58.592. The two quaternary carbons bearing nitrile groups(C_4 and $C_{4'}$) gave signals at δ 44.003 and 43.883. The ring junction carbon atoms (C_2 and C_{12}) appeared at δ 47.821 and 47.314. The structure assigned was supported by satisfactory analytical data and finally confirmed by single crystal X-ray analysis[#] (Figure 3.3).

[#] X-ray crystal analysis was done by Prof. Paul G. Williard of Brown University, U. S. A.

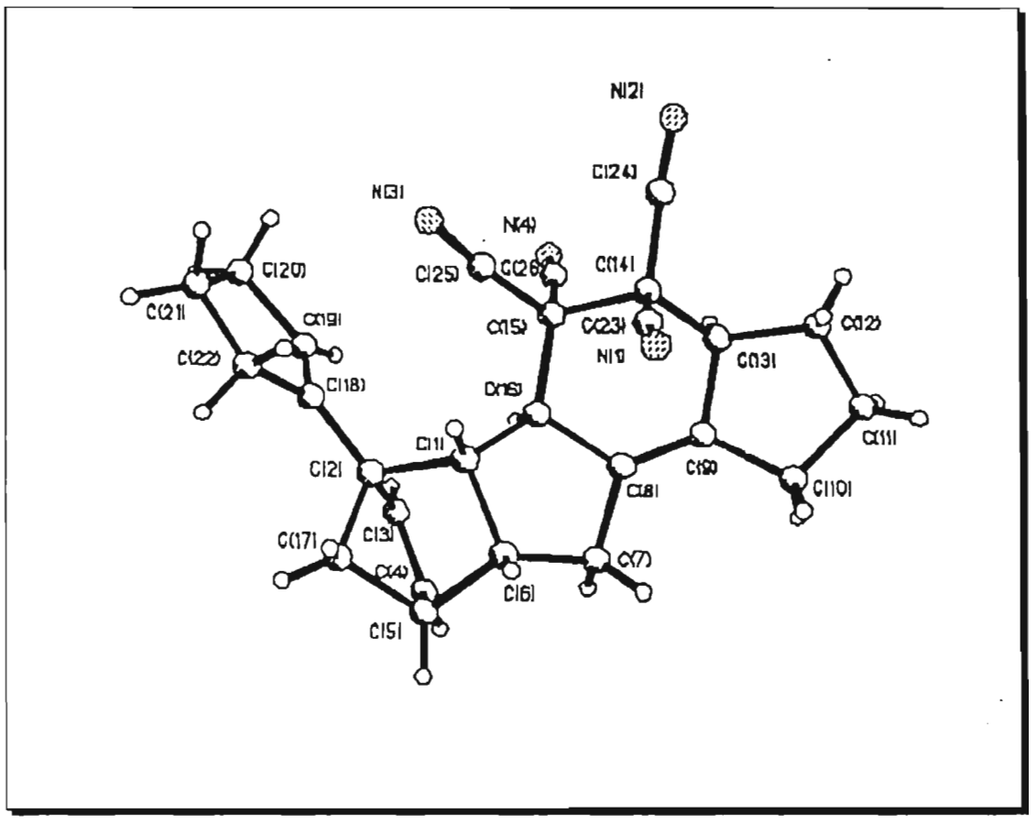
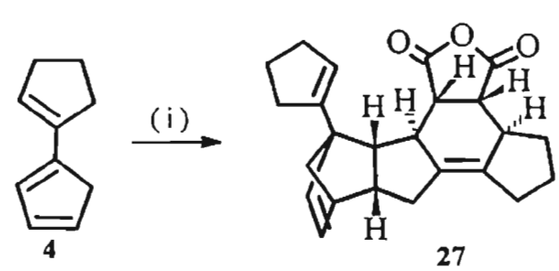


Figure 3.3

X-ray crystal structure of 26

A similar adduct **27** from the dimer **16** was obtained in 66% yield when the isomerized fulvene **4** was refluxed with maleic anhydride in benzene for 5 h (Scheme 3.12).



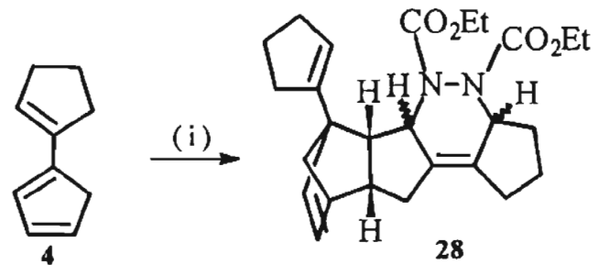
4 **27**

(i) Maleic anhydride (**20**), Benzene, 80 °C, 5 h, 66%.

Scheme 3.12

The IR spectrum of **27** showed characteristic absorption of succinic anhydride moiety at 1849 and 1775 cm^{-1}. In the ^{1}H NMR the olefinic proton on the cyclopentenyl ring resonated as a broad singlet at δ 5.553 and the other two olefinic protons appeared as multiplets at δ 6.20-6.11 and δ 6.066–6.026. The bridgehead proton appeared as a doublet of doublet at δ 3.587. The three multiplets between δ 2.50-1.50 account for the 18 aliphatic protons. The ^{13}C NMR showed two signals at δ 172.896 and 171.845 due to the two carbonyls. The bridgehead quaternary carbon resonated at δ 59.155 and the bridge methylene carbon at δ 56.620. The other methylene carbons were seen at δ 53.197, 49.904, 47.356, 47.029, 44.332, 43.914 and 40.258. The assigned structure was supported by HRMS.

Analogous to the reaction of maleic anhydride, diethyl azodicarboxylate when treated with **4** in benzene at room temperature for 1h afforded the adduct **28** in 46% yield (Scheme 3.13).



4 **28**

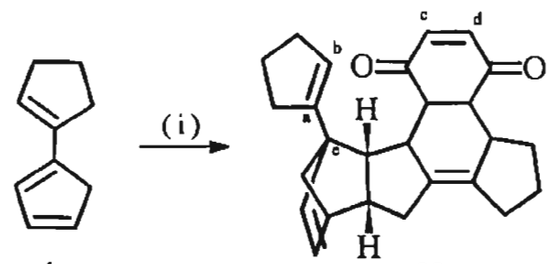
(i) Diethyl azodicarboxylate (**21**), Benzene, RT., 1 h, 46%.

Scheme 3.13

The IR spectrum of **28** showed a strong absorption at 1735 and 1720 cm^{-1} indicating the presence of -COOEt carbonyl. In the proton NMR, the olefinic protons appeared as a multiplet between δ 6.399-6.251 and as a broad signal at δ 5.834. In the ^{13}C NMR peaks at

δ 155.841, 155.557, 155.437 and 155.243 were due to the carboethoxy groups indicating the presence of an isomeric mixture. The resonance due to bridge methylene carbon was observed at δ 58.325 and the bridgehead quaternary carbon gave signal at δ 61.408. The carbons adjacent to nitrogen gave signals at δ 58.834, 57.910, 57.225 and 56.927. Other resonances are also in agreement with the assigned structure.

Reaction of the isomerized fulvene **4** with *p*-benzoquinone in benzene at ambient temperature afforded a similar adduct **29** in 44% yield (Scheme 3.14).



4 **29**

(i) *p*-Benzoquinone (**22**), RT., 24 h, 44%.

Scheme 3.14

IR spectrum of **29** showed an absorption at 1684 cm^{-1} indicating the presence of the enone moiety. ^1H NMR showed a multiplet between δ 6.565-6.448 due to the two enone protons. The olefinic protons appeared at δ 5.416 and between δ 6.197-6.085. The multiplet between δ 3.301-3.210 was assigned to the protons adjacent to the carbonyl groups. Aliphatic protons appeared as a series of multiplets between δ 2.265-1.453. In the ^{13}C NMR, the two carbonyl groups appeared at δ 201.481 and 199.529. The two olefinic carbons C_c and C_d of the enone resonated at δ 136.827 and 137.408. The bridgehead quaternary carbon

(C_c) appeared at δ 58.935. Other signals are also in agreement with the assigned structure.

3.6 THEORETICAL CALCULATIONS

The MNDO and AM1 calculations using MOPAC programme were carried out to get some insight into the mode of addition of isomerized fulvene to various dienes and dienophiles. The molecular orbital coefficient relations obtained from the calculations were in good agreement with the observed experimental data.

The isomerization of 6,6-tetramethylene fulvene to 1-cyclopentenyl cyclopentadiene can be rationalized by the fact that the latter is stabilized by 4.9 kcal/mol. The MMX energy difference is approximately 6.77 kcal/mol, which is also in agreement with the observed isomerization.

The HOMO-LUMO energies of isomerized fulvene, diene and various dienophiles were calculated and are summarised in table 1. The HOMO-LUMO energy level interactions in the formation of the adducts from isomerized fulvene and its dimer are shown in figure 3.4 and 3.5 respectively.

Table 1

Entry	Reactant	HOMO (*eV*)	LUMO (*eV*)
1	6,6-Dimethyl fulvene	-8.8912	-0.5575
2	Cyclopentenyl cyclopentadiene	-8.5037	-0.2271
3	Dimer **16**	-8.828	0.1415
4	2,4-Cyclopentadien-1-one	-9.709	-0.9219
5	N-Phenyl maleimide	-9.4231	-1.0844

Entry	Reactant	HOMO (*eV*)	LUMO (*eV*)
6	Tetracyanoethylene	-1.4754	-2.4959
7	Maleic anhydride	10.9586	-1.5085
8	Diethyl azodicarboxylate	-0.8331	-0.6438
9	*p*-Benzoquinone	-0.9586	-1.5085

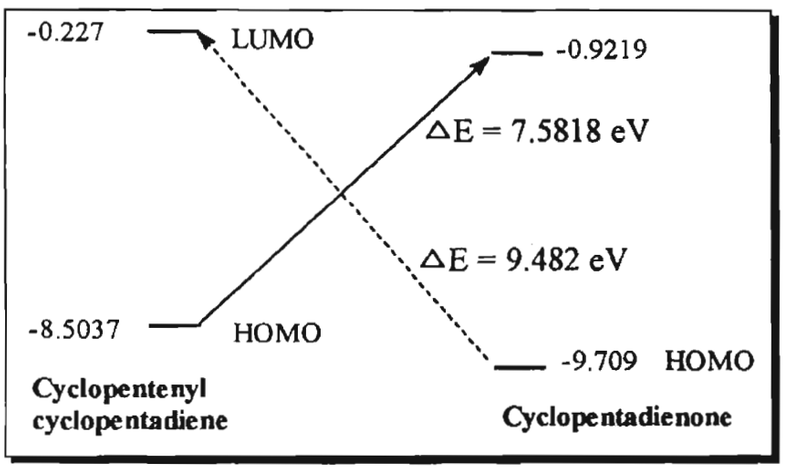


Figure 3.4

HOMO-LUMO energy levels of cyclopentenyl cyclopentadiene and cyclopentadienone

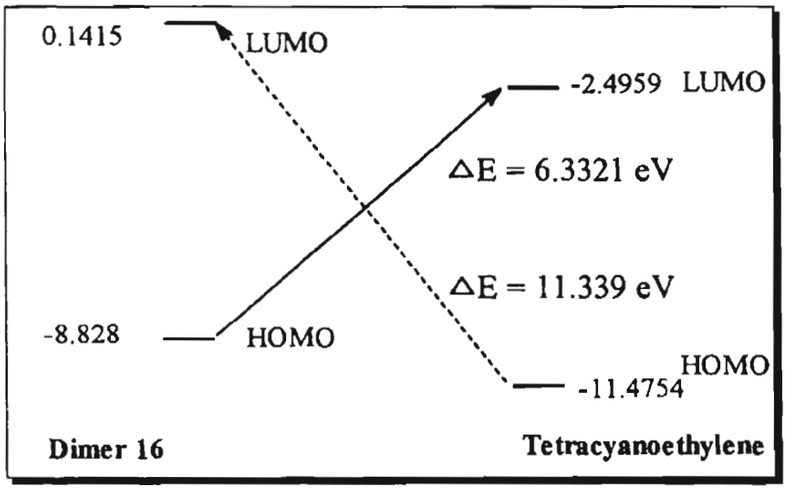


Figure 3.5

HOMO-LUMO energy levels of 16 and tetracyanoethylene

The molecular orbital calculations support the cycloaddition profile shown by cyclopentenyl cyclopentadiene with dienophiles and the interaction is illustrated in figure 3.6.

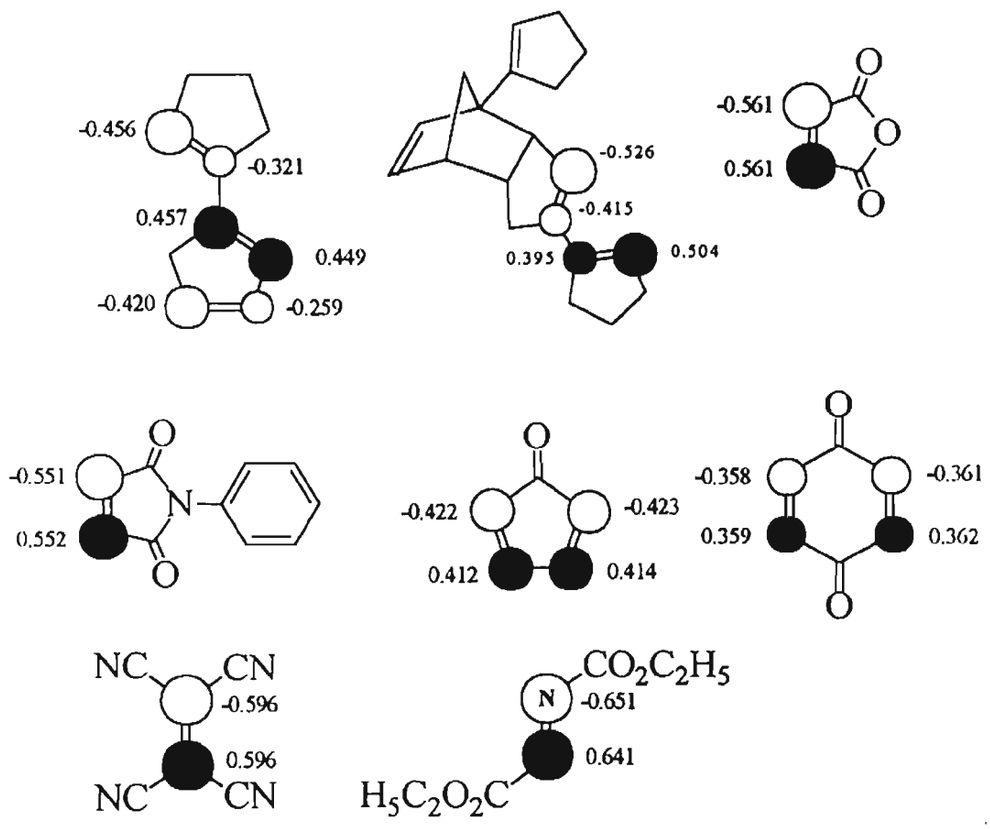


Figure 3.6

It can be seen that the molecular orbital coefficients of the dimer (-0.526 and 0.504) were comparable with those of maleic anhydride (-0.551and 0.552), TCNE, (-0.0596 and 0.596), and DEAD (-0.651 and 0.641). Hence the cycloaddition of these reactive dienophiles occurs with the dimer of the isomerized fulvene. On the other hand, the molecular orbital coefficients of isomerized fulvene were comparable with that of tetracyclone. In the reaction of tetracyclone and **4**, the latter offers a

2π system in which the $HOMO_{diene}$ and $LUMO_{dienophile}$ participates in $[4\pi+2\pi]$ cycloaddition.

The molecular orbital coefficients of N-phenylmaleimide falls in the range of isomerized fulvene and the dimer, which on reaction resulted in the formation of both the adducts, one with the dimer and the other with the isomerized fulvene (Figure 3.7).

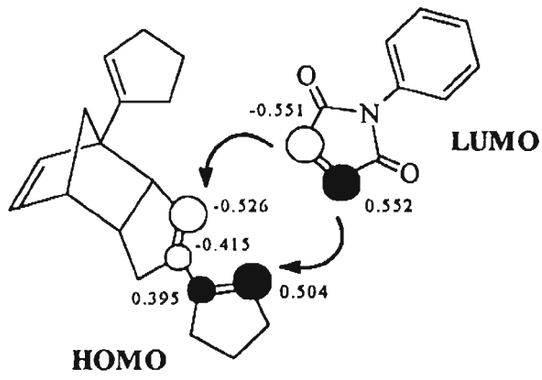


Figure 3.7

In conclusion, we have shown that isomerization of 6,6-tetramethylene fulvene occurs to give cyclopentenyl cyclopentadiene **4**. The dimerization of **4** and the cycloaddition of the resulting dimer **16** with various dienophiles afforded polycyclic ring systems, which may be of value in the construction of complex polyquinane frameworks.

3.7 EXPERIMENTAL DETAILS

For general experimental details see Chapter 2. p-42. Cyclopentadiene was freshly cracked from the dimer.

1-Cyclopent-1-enyl-1,3-cyclopentadiene (4) and 2,4-dicyclopent-1-enyl-3a,4,7,7a-tetrahydro-1H-4,7-methanoindene (16)

Pyrrolidine (2.556 g, 35.9 mmol) was added dropwise to a mixture of cyclopentanone (1.951 g, 23.2 mmol) and cyclopentadiene (4.02 g, 60.1 mmol) at ice temperature and stirring was continued in an ice-bath. After 1h, the resulting mixture was neutralised with acetic acid and stirred for further 30 minutes. The mixture was diluted with water and extracted with ether (4x 25 mL). The combined organic extracts were washed with water (3X25 mL), saturated bicarbonate (25 mL), again with water and finally with brine. The combined ether layer was dried over sodium sulfate and the solvent was removed. The crude product obtained when chromatographed on silica gel using hexane afforded the isomerized fulvene **4** as a viscous colourless oil (2.81 g, 91%). On standing at room temperature the isomerized fulvene dimerizes to **16**.

The isomerized fulvene **4** is unstable owing to facile dimerization, hence spectral data could not be obtained.

Data for **16**

IR ν_{max} (CCl_4) : 3049, 2962, 2929, 2897, 2847, 1613, 1452, 1344, 1249, 1027, 926, 818, 771 cm^{-1}.

^1H NMR : 6.0 (m, 2H), 5.5 (m, 3H), 3.2 (m, 1H), 2.8 (m, 2H), 2.3 (m, 8H), 1.9 (m, 4H), 1.4 (m, 4H).

^{13}C NMR : 135.95, 135.80, 132.22, 132.10, 131.83, 131.74, 127.92, 126.19, 54.89, 54.71, 50.41, 50.20, 46.30, 45.58, 41.43, 34.87, 34.57, 32.87, 32.72, 23.08.

2-Cyclopent-1-enyl-4,5,6,7-tetraphenyl-3a,4,7,7a-tetrahydro-1H-4,7-methanoinden-8-one (23)

A mixture of isomerized fulvene **4** (500 mg, 3.78 mmol) and tetracyclone (800 mg, 2.08 mmol) was heated in benzene (10 mL) at 80 °C under argon atmosphere for 40 h. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography. Elution with hexane gave the dimer of the isomerized fulvene (77 mg). Further elution with 98:2 hexane-ethyl acetate afforded **23** as colurless prisms (590 mg, 30%). mp. 184-186 °C (CH_2Cl_2-hexane).

λ_{max} : 229 nm.

IR ν_{max} (KBr) : 3070,3046, 2932, 2901, 2851, 1770, 1601, 1491, 1442, 1186, 1078, 981, 735, 700 cm^{-1}.

^{1}H NMR : 7.51-7.42 (m, 2H), 7.42-7.20 (m, 8H), 7.0-6.80 (m, 6H), 6.70-6.53 (m, 4H), 5.90 (s, 1H), 5.60 (s, 1H), 4.35- 4.25 (d, 1H), 3.65- 3.55 (m, 1H), 3.98-2.81 (m, 2H), 2.62-2.27 (m, 4H), 1.96-1.81 (m, 2H).

^{13}C NMR : 201.538, 145.299, 142.746, 141.016, 139.369, 136.087, 135.822, 135.272, 134.873, 130.439, 130.065, 129.373, 129.624, 128.238, 127.592, 127.427, 127.256, 127.175, 126.753, 126.533, 124.471, 66.816, 65.972, 52.936, 42.291, 36.699, 33.343, 32.932, 23.237.

Anal. Calcd.. for $C_{39}H_{32}O$: C, 90.66; H, 6.24; Found: C, 91.07; H, 6.22%.

Crystallographic data for 23

Triclinic, P1, a= 9.4620 (10) Å, b= 12.6260 (10) Å, c=13.569 (2) Å, α= 63.970 (10)°, β= 84.120 (10)°, γ= 87.070 (10)°, V= 1448.9 (3) $Å^3$, Z= 2, Density= 1.184 Mg/m^3, Temp.= 298 K, R1= 0.0561, wR2= 0.1247, Formula weight= 516.65, No. of unique reflections= 4738, Radiation source= MoKα (λ= 0.71073Å).

1-Cyclopent-1-enyl-4-phenyl-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene-3,5-dione 24 and 25

A mixture of isomerized fulvene (200 mg, 0.757 mmol) and N-phenylmaleimide (150 mg, 0.86 mmol) in benzene (5 mL) was heated at 80 °C for 4 h. The solvent was evaporated off and the residue was purified by silica gel chromatography. Elution with 90:10 hexane-ethyl acetate afforded **24** as a semisolid (100 mg, 30%). Further elution with 80:20 hexane-ethyl acetate gave **25** as colourless needles (85 mg, 18%). mp. 121-123 °C (CH_2Cl_2-hexane).

Data for **24**

IR ν_{max} (KBr) : 3060, 2959, 2869, 1780, 1714, 1601, 1501, 1434, 1315, 1242, 1181, 754 cm^{-1}.

^1H NMR : 7.4-7.1 (m, 5H), 6.2 (m 2H), 5.65 (s, 1H), 3.35 (dd, 1H), 3.25 (m, 2H), 2.85 (s, 1H), 2.4 (m, 6H), 2.0 (m, 8H), 1.6 (d, 4H).

^{13}C NMR : 177.932, 176.858, 145.919, 140.369, 137.475, 136.431, 133.358, 131.986, 128.943, 128.256, 126.377, 123.572, 59.189, 56.503, 53.311, 50.029, 47.344, 46.210, 44.629, 43.913, 40.959, 33.292, 32.486, 32.128, 29.383, 28.399, 26.698, 23.357.

Data for **25**

IR ν_{max} (KBr) : 3060, 2955, 2851, 1776, 1713, 1598, 1500, 1456, 1382, 1186, 1077, 744 cm^{-1}.

^{1}H NMR : 7.4-7.1 (m, 5H), 6.35 (s, 2H), 5.9 (m, 1H), 3.5 (m, 3H), 2.5 (m, 4H), 2.0 (m, 2H), 1.8 (d, 2H).

^{13}C NMR : 176.321, 175.604, 141.801, 137.088, 133.985, 131.807, 128.734, 128.227, 126.824, 126.407, 59.368, 56.593, 48.358, 47.553, 45.166, 33.358, 32.516, 23.148.

HRMS Calcd. for $C_{20}H_{19}O_2N$: 305.14157; Found: 305.14092.

Diels-Alder adduct 26

To a solution of **4** (300 mg, 1.136 mmol) in benzene (6 mL) under argon atmosphere was added tetracyanoethylene (160 mg, 1.25 mmol). After 45 minutes, the solvent was removed and the residue on chromatographic separation on silica gel using 93:7 hexane-ethyl acetate afforded the adduct **26** as colourless cubes (232 mg, 52%). mp. 204-206 °C (CH_2Cl_2-hexane).

IR ν_{max} (KBr) : 3078, 2976, 2902, 2853, 2252, 1625, 1469, 1433, 1316, 1292, 1184, 1042, 969, 822, 794, 747 cm^{-1}.

^{1}HNMR : 6.32-6.30 (m, 2H), 5.72-5.71 (t, 1H), 3.00-2.90 (m, 5H), 2.60-2.27 (m, 8H), 1.96-1.50 (m, 8H).

^{13}C NMR : 142.63, 138.28, 137.08, 136.61, 131.59, 126.37, 111.78, 110.83, 58.59, 56.20, 55.13, 47.82, 47.31, 46.00, 45.76, 44.00, 43.88, 32.69, 31.35, 28.99, 22.67, 22.19.

Anal. Calcd. for $C_{26}H_{24}N_4$: C, 79.56; H, 6.16; N, 14.27. Found: C, 79.437; H, 6.159; N, 14.005%.

Crystallographic data for 26

Monoclinic, $P2_{1/n}$, a= 7.850(2)Å, b= 18.988(4)Å, c= 14.065(3)Å, α= 90°, β= 90.45°, γ= 90°, Z = 4, Density= 1.244Mg/m^3, Temp.= 293 K, R1= 0.1404, wR2= 0.3444, Formula weight= 392.49, No. of unique reflections= 4361, Radiation source= Mo Kα (λ= 0.71073 Å).

Diels -Alder adduct 27

A mixture of **4** (200 mg, 0.757 mmol) and maleic anhydride (90 mg, 0.918 mmol) in 3 mL benzene was refluxed at 80 °C for 5 h. The residue after the removal of the solvent was chromatographed on silica gel. Elution with 90:10 hexane-ethyl acetate furnished **27** as colourless crystals (181 mg, 66%). mp. 156-158 °C (CH_2Cl_2-hexane).

IR ν_{max} (KBr) : 3056, 2955, 2867, 1849, 1775, 1519, 1438, 1383, 1263, 1196, 1081, 1007, 966, 926 cm^{-1}.

^{1}H NMR : 5.553 (brs, 1H), 6.200-6.113 (m, 1H), 6.066-6.026 (m, 1H), 3.587 (dd, 1H), 3.360-3.213 (m, 2H), 3.153 (m, 1H), 2.8 (brs, 1H), 2.5-1.5 (m, 18H).

^{13}C NMR : 172.896, 171.845, 145.729, 140.902, 137.395, 136.856, 134.041, 123.828, 59.155, 56.620, 53.197, 49.904, 47.356, 47.029, 44.331, 43.914, 40.257, 33.314, 32.585, 32.146, 29.356, 28.486, 26.329, 23.410.

HRMS calcd. for $C_{24}H_{26}O_3$: 362.18820; Found : 362.18864.

Diels-Alder adduct 28

To a solution of **4** (300 mg, 2.272 mmol) in 3mL benzene was added diethyl azodicarboxylate (400 mg, 2.52 mmol) and stirred at room temperature for 1 h. The solvent was evaporated and the residue was purified by chromatography on silica gel using 90:10 hexane-ethyl acetate mixture to afford **28** as dark yellow oil (232 mg, 46%).

IR ν_{max} (KBr) : 3052, 2956, 2867, 2866, 1735, 1720, 1464, 1443, 1409, 1376, 1327, 1272, 1175, 1148, 1100, 1039, 766 cm^{-1}.

^{1}H NMR : 6.251 (brs, 2H), 5.834-5.794 (m, 1H), 4.197-4.051 (m, 4H), 3.755 (m, 1H), 2.781-2.61 (m, 4H), 2.29-2.12 (m, 7H), 1.836-1.476 (m, 8H), 1.284-1.223 (m, 6H).

^{13}C NMR : 155.841, 155.557, 155.437, 155.243, 144.536, 140.068, 139.716, 136.734, 136.149, 134.572, 134.050, 130.914, 129.990, 124.195, 62.110, 61.322, 58.834, 58.317, 57.910, 57.477, 57.225, 56.927, 49.369, 47.331, 45.390, 33.200, 32.737, 29.027, 26.435, 23.539, 22.092, 14.586.

Diels-Alder adduct 29

A mixture of **4** (300 mg, 2.27 mmol) and *p*-benzoquinone (270 mg, 2.5 mmol) in 5 mL dry benzene was stirred at room temperature for 24 h. The solvent was then removed under reduced pressure and the residue on chromatographic separation on silica gel using 95:5 hexane-ethyl acetate afforded **29** as a viscous light-yellow oil (185 mg, 44%).

IR ν_{max} (CCl_4) : 3053, 2954, 2863, 1684, 1607, 1447, 1379, 1297, 1260, 1203, 1084, 1040, 912, 733 cm^{-1}.

^1H NMR : 6.565-6.448 (m, 2H), 6.197-6.085 (m, 2H), 5.419-5.413 (m, 1H), 3.301-3.210 (m, 3H), 3.048 (m, 1H), 2.804 (brs, 1H), 2.265-2.209 (m, 5H), 1.911-1.356 (m, 13H).

^{13}C NMR : 201.481, 199.529, 145.895, 141.814, 141.106, 140.061, 137.408, 136.827, 136.345, 130.308, 123.407, 58.935, 56.858, 55.243, 52.632, 51.773, 51.141, 49.067, 46.933, 44.011, 40.467, 33.274, 32.507, 30.954, 27.145, 23.384, 23.231.

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CHAPTER 4

MISCELLANEOUS REACTIONS OF *o*-BENZOQUINONES

This chapter is divided into two parts 4.1 and 4.2. In the first part (4.1), a facile alkylation of catechols leading to *bis* substituted catechols which are precursors to novel *o*-benzoquinones is described. In the second part, some preliminary studies aimed at the synthesis of a model for the tea pigment theaflavin is presented.

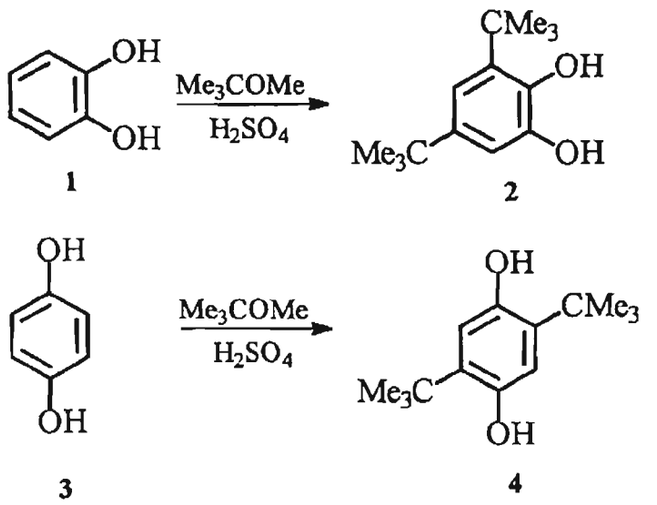
4.1 AN EFFICIENT SYNTHESIS OF CATECHOLS: PRECURSORS OF NOVEL *o*-BENZOQUINONES

4.1.1 INTRODUCTION

As already mentioned in the general introduction (Chapter 1), the chemistry of quinones has evoked enormous interest, but much of this interest has been focused on *p*-quinones. This may be attributed to their stability and easy accessibility from quinols and phenols. On the other hand, *o*-quinones are comparatively less stable and are not readily available and therefore their chemistry has been underinvestigated. The parent 1,2-benzoquinone can only be prepared *in situ* by the oxidation of catechol at low temperature. Oxidation of phenols with Fremy's salt, ceric ammonium nitrate etc. are also suitable methods for the preparation of *o*-quinones. The most general and satisfactory method is the oxidation of the corresponding catechols by oxidants such as MnO_2, Ag_2CO_3 and $NaIO_4$. The limiting factor, however, is the availability of substituted catechols. It may be recalled that the chemistry of the stable tetrasubstituted *o*-quinones such as chloranil, bromanil and phenanthrene quinone has been investigated. Other stable *o*-quinones such as 3,5-di-*tert*-butyl and 2,6-di-*tert*-butyl-1,2-benzoquinones have also been studied in some detail. We have been interested in a comprehensive study of the chemistry of *o*-quinones. But our studies were hampered by the limited number of stable *o*-quinones available.[1] To alleviate this difficulty it was planned to devise an easy route to substituted catechols, the latter being precursors of the desired *o*-quinones.

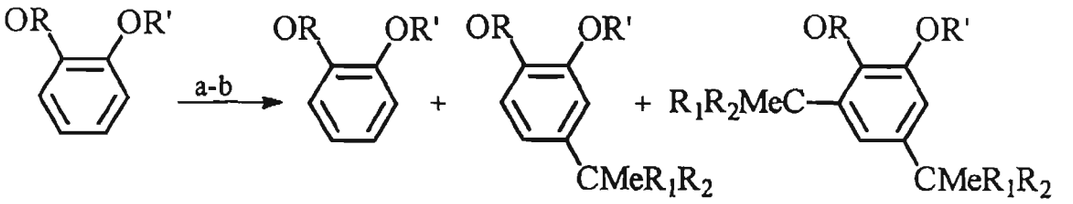
4.1.2 Alkylation of catechols

Literature survey reveals that alkylation of phenols and polyhydric benzenes has been achieved by using olefins, secondary or tertiary alcohols and even *tert*-butylethers in presence of acid catalysts. For example, di-*tert*-butylcatechol was obtained by treating *tert*-butyl methyl ether with catechol in presence of sulfuric acid. Quinol gave 2,5-di-*tert*-butylquinol in 72% yield (Scheme 4.1.1).[2]



Scheme 4.1.1

The alkylation of polyhydric benzenes such as catechol was shown to give a mixture of ring alkylated products which on methylation afforded 2-methoxyphenol, alkyl-3,4-dimethoxybenzene, 3,5-dialkyl veratrole etc. (Scheme 4.1.2).[3]

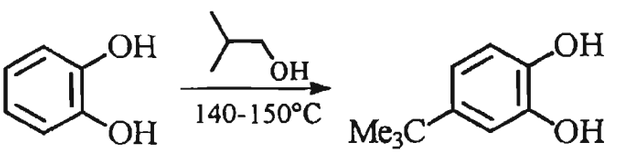


R=H; R'=H | R=H; R'=Me | R=H; R'=Me, R=R'=H, R_1=R_2=Me, Pentyl | R=H; R'=Me, R=R'=H, R_1=R_2=Me, Pentyl

a) R_1R_2MeCOH, H_3PO_4
b) Methylation

Scheme 4.1.2

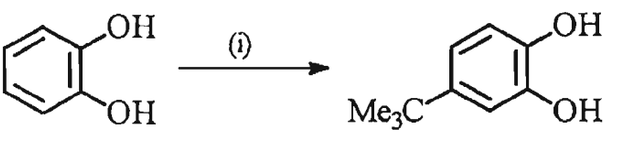
Acids such as CF_3SO_3H, have been used effectively for the alkylation of catechols and quinols.[4] Tertiary butylation of catechols has been achieved by reaction with *sec*-butyl alcohol at high temperature to give 4-*tert*-butyl catechol in low yields (Scheme 4.1.3).[5]



1 5

Scheme 4.1.3

The yield of *tert*-butyl catechol was improved by the use of *tert*-butanol in presence of phosphoric acid as the catalyst at 140 °C (Scheme 4.1.4).

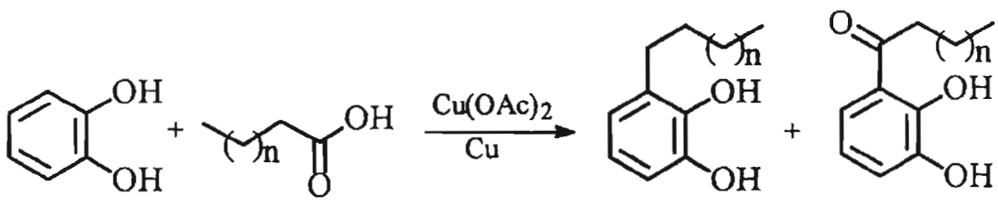


1 5

(i) Me_3COH, H_3PO_4, 140 °C.

Scheme 4.1.4

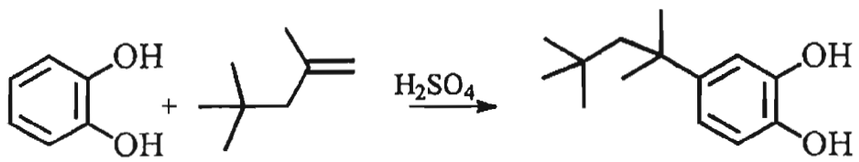
Higher fatty acids such as stearic acid in presence of copper acetate and copper afforded a mixture of the alkyl and acyl catechols (Scheme 4.1.5).[6]



1 6 7 8

Scheme 4.1.5

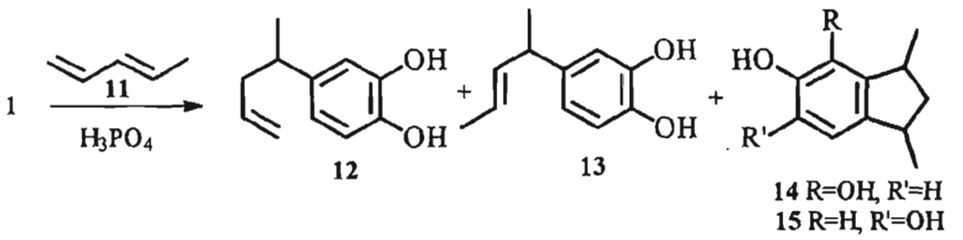
In presence of acid, alkenes are known to bring about alkylation of phenols and polyhydric benzenes.[7] For example, di-*tert*-butylene in presence of sulfuric acid afforded 4-*tert*-octyl catechol in high yield (Scheme 4.1.6).



1 9 10

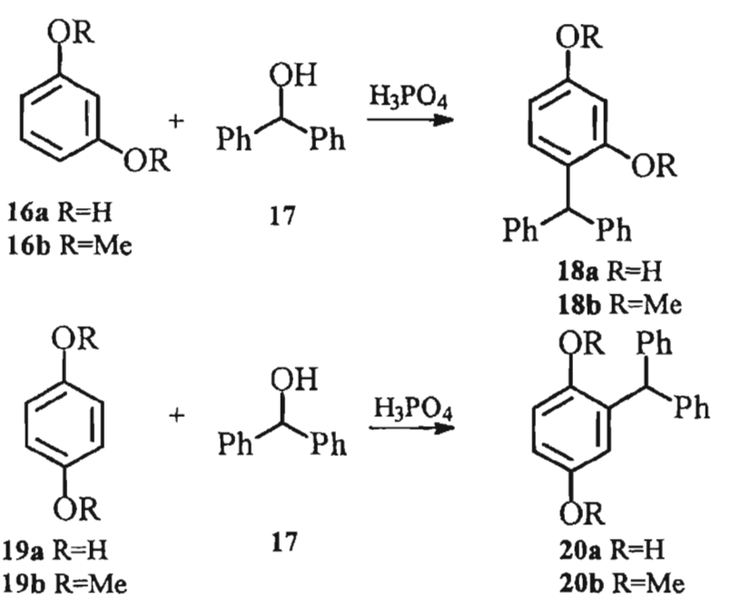
Scheme 4.1.6

Another interesting example is the reaction of catechol with 1,3-pentadiene in presence of phosphoric acid or aluminium chloride leading to the indane derivatives in addition to the normal alkylated products. This is illustrated in scheme 4.1.7.[8]



Scheme 4.1.7

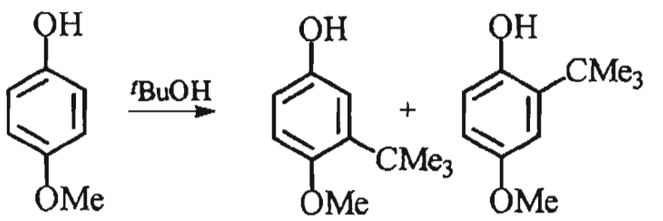
It has been shown that alkylation of polyhydric benzenes can be achieved with benzhydrols in presence of acids.[9] For example, resorcinol, quinol and their dimethyl ethers condensed with benzhydrol in presence of phosphoric or sulfuric acid to yield mono alkylated hydroxy triphenylmethanes in 77-89% yield (Scheme 4.1.8).[10]



Scheme 4.1.8

4.1.3 Alkylation using clay and other catalysts

Alkylation of phenols and polyhydric benzenes under catalysis by acid clays is known. An example is the alkylation of catechol with *tert*-butanol to give alkyl catechols along with a mixture of undesired ethers.[11] Fujita demonstrated the preparation of mono-isopropylphenol with aluminium exchanged hectorite catalyst with high selectivity and conversion.[12] A highly selective alkylation of substituted phenol with *tert*-butanol in presence of clay supported Lewis acid under non-polar and polar solvents has been known.[13] Thus in hexane, 2-*tert*-butyl and 3-*tert*-butyl-4-methoxyphenol were formed in the ratio 99:1 while in *tert*-butanol a reversal of the isomer ratio (1:99) was observed (Scheme 4.1.9).

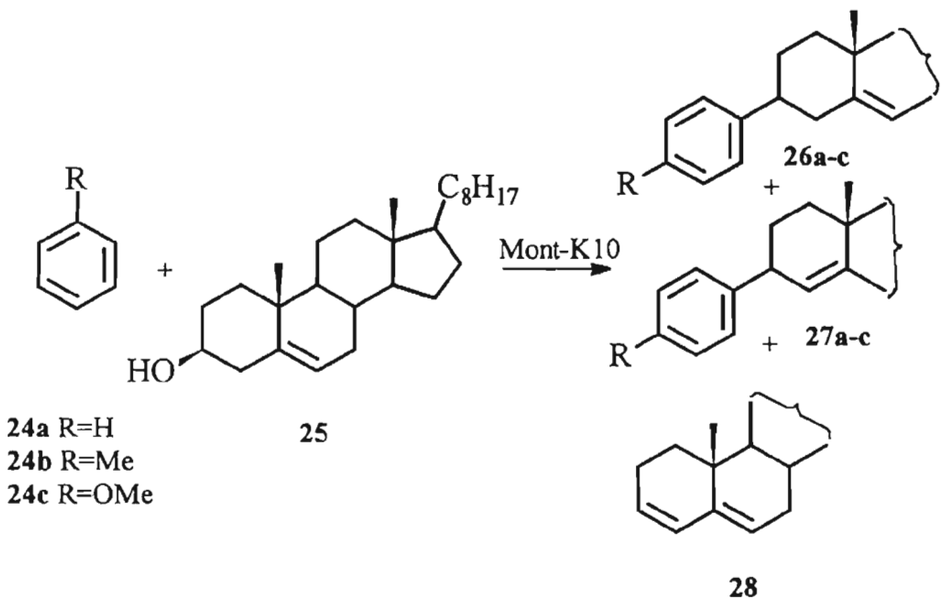


21 **22** **23**

Hexane: 1:99; ^{t}Butanol: 99:1

Scheme 4.1.9

Alkylation of benzene, anisole and other electron rich aromatics with cholesterol in presence of clay catalyst, Montmorillonite K 10, to afford the isomeric alkyl aromatics together with dienes and other products has been reported recently (Scheme 4.1.10).[14]

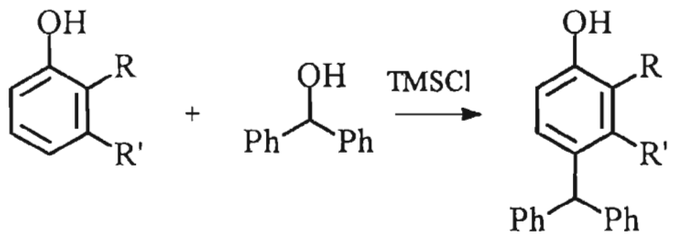


24a R=H
24b R=Me
24c R=OMe

25

Scheme 4.1.10

Trimethylsilyl chloride has been used effectively to bring about alkylation of phenols with benzhydrol to afford the alkylated triphenylmethane derivatives in high yields (Scheme 4.1.11).[15]



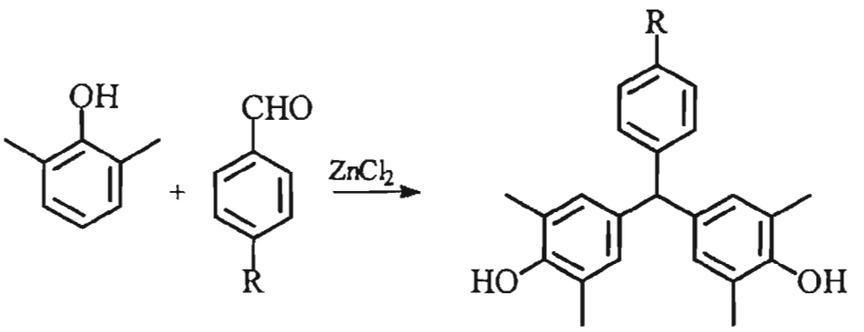
29a R=R'=H
29b R=Me, R'=H
29c R=R'=Me

17

30a R=R'=H
30b R=Me, R'=H
30c R=R'=Me

Scheme 4.1.11

Polyhydroxytriphenylmethane derivatives were also prepared by the condensation of aldehydes with phenols in presence of Lewis acids such as $ZnCl_2$ (Scheme 4.1.12).[16]



31 **32** **33**

Scheme 4.1.12

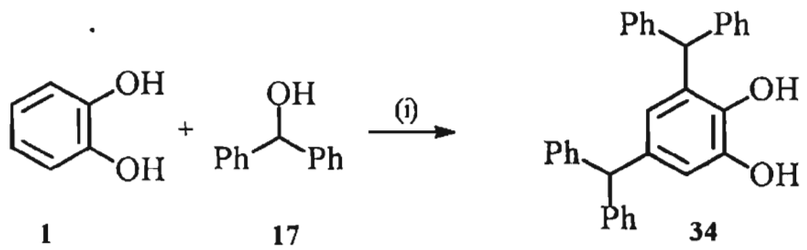
4.1.4 STATEMENT OF THE PROBLEM

It is obvious from the foregoing discussion that although the C-alkylation of phenols has been investigated in detail, only limited attention has been paid to the alkylation of catechols, especially using carbinols. Against this background, we have carried out some studies aimed at the alkylation of catechol with various carbinols with a view to obtain substituted catechols that would serve as precursors for novel *o*-benzoquinones.

4.1.5 RESULTS AND DISCUSSION

4.1.5.1 Acid catalyzed reactions

Our studies were initiated with the reaction of catechol with benzhydrol in presence of sulfuric acid. Treatment of catechol with benzhydrol in presence of conc. H_2SO_4 at 20 °C smoothly afforded the 3,5-bis(diphenylmethyl)-1,2-benzenediol **34** in 100% yield (Scheme 4.1.13).



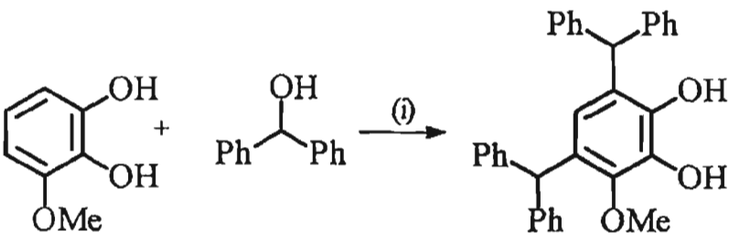
1 **17** **34**

(i) H_2SO_4, AcOH, 20 °C - RT, 12 h, 100%.

Scheme 4.1.13

In the ^1H NMR spectrum of **34,** the aromatic protons of the phenyl ring were observed as two sets of multiplets between δ 7.368 and 6.899. The two protons on the tetrasubtituted ring appeared at δ 6.345 and the two benzylic protons were discernible at δ 5.455. The -OH protons appeared at δ 2.456 as a broad singlet. In the ^{13}C NMR, the benzylic carbons resonated at δ 52.031 and the signals at δ 144.022, 142.423, 134.428, 129.528, 128.270, 126.247 and 117.457 were attributed to the aromatic carbons.

The alkylation of 3-methoxycatechol with benzhydrol in presence of sulfuric acid afforded 3-methoxy-4,6-bis(diphenylmethyl)catechol **36** in 89% yield (Scheme 4.1.14).



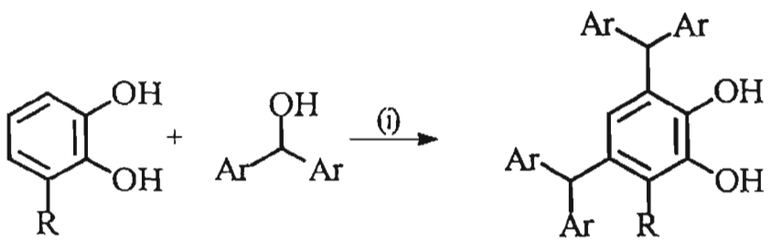
35 **17** **36**

(i) H_2SO_4, AcOH, 20 °C - RT, 13 h, 89%.

Scheme 4.1.14

In the ^1H NMR of **36**, the aromatic proton on the pentasubstituted ring appeared as singlet at 6.006 and the two benzylic protons at δ 5.701. The two phenolic protons were observed at δ 5.611 and δ 5.283 and the methoxy protons resonated at δ 3.507. In the ^{13}C NMR, the methoxy carbon resonated at δ 61.071 and the benzylic carbons at δ 49.825 and 49.401.

A similarly substituted catechol resulted in the reaction between 3-methoxycatechol and 4,4'-dimethoxybenzhydrol **38** in 93% yield (Scheme 4.1.15).



35 R=OMe **37** Ar = 4-Methoxyphenyl **38** R=OMe
Ar = 4-Methoxyphenyl

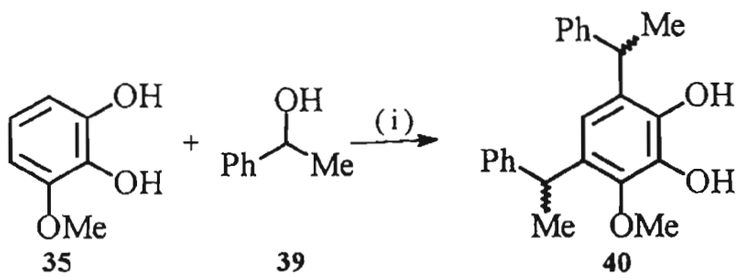
(i) H_2SO_4, AcOH, 20 °C - RT, 12 h, 93%.

Scheme 4.1.15

In the ^{1}H NMR of **38**, the aromatic proton on the pentasubstituted ring appeared as singlet at 5.901 and the two benzylic protons resonated at δ 5.599 and 5.553. The two phenolic protons were observed at δ 5.633 and δ 5.226 and the protons of the methoxy groups were observed at δ 3.765 and 3.513. In the ^{13}C NMR, the methoxy carbon resonances were observed at δ 60.951, 55.270 and 54.971.The benzylic carbons gave signals at δ 48.484 and 47.931.

Reaction of **17** and **35** with other alcohols such as 2-phenyl-2-propanol and 1-phenylethanol afforded corresponding substituted catechols in high yields.

1-Phenylethanol on treatment with 3-methoxycatechol in presence of sulfuric acid afforded the bis alkylated catechol **40** in 75% yield (Scheme 4.1.16).



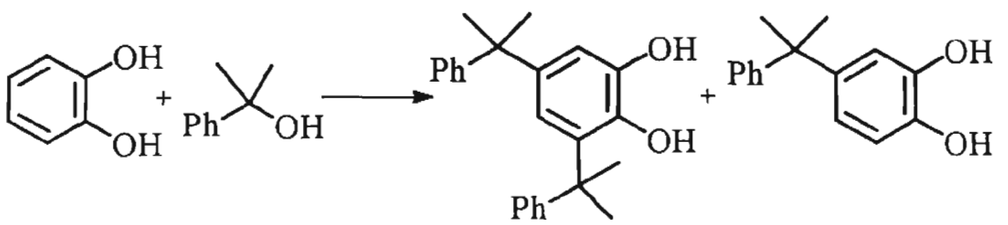
(i) H_2SO_4, AcOH, 20 °C - RT, 16 h, 75%.

Scheme 4.1.16

In the ^{1}H NMR of **40**, the phenolic hydroxyls were observed at δ 5.975 and 5.470. The methoxy group resonated at δ 3.472. The aromatic proton on the pentasubstituted ring appeared at δ 6.669 and the other aromatic protons were visible as a multiplet between δ 7.237-7.110. The two methyl groups resonated as a multiplet between δ 1.587-1.502. The benzylic protons appeared as a multiplet

between δ 4.426-4.333. In the ^{13}C NMR, the two methyl groups gave signals at δ 22.103 and 20.856 and the benzylic carbons appeared at δ 38.198, 38.174, 37.802 and 37.753 indicating that the product is a mixture of stereoisomers.

The reaction of 2-phenyl-2-propanol with catechol in presence of sulfuric acid afforded both the mono and bis alkylated catechols (Scheme 4.1.17).



1 **41** **42** (22%) **43** (32%)

(i) H_2SO_4, AcOH, 20 °C - RT, 48 h.

Scheme 4.1.17.

In the ^1H NMR of **42**, the methyl groups resonated at δ 1.668 and 1.577 as two singlets. The two -OH groups resonated at δ 5.404 and 4.147. The two protons on the tetrasubstituted phenyl ring appeared at δ 6.870 and the ten aromatic protons were visible as a multiplet between δ 7.280-7.129. In the ^{13}C NMR, the two methyl carbons appeared at δ 30.899 and 29.388 and the quaternary carbons at δ 42.659 and 41.898.

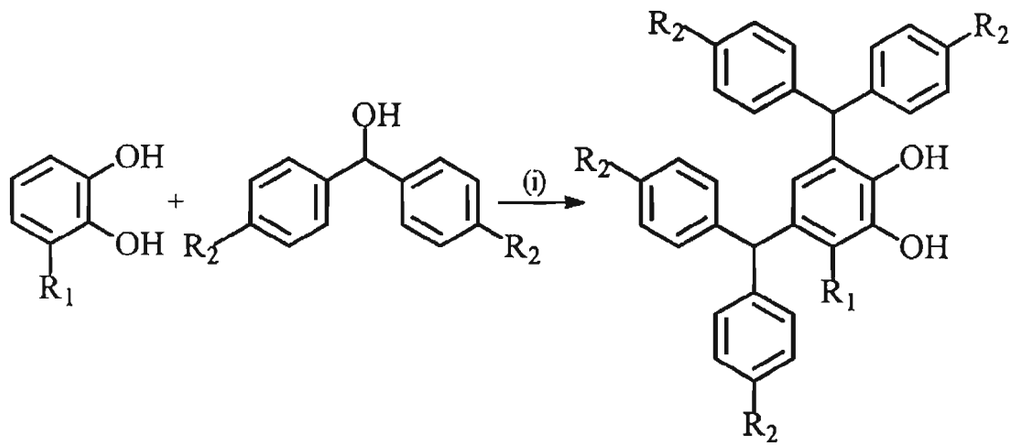
In the ^1H NMR of **43**, the methyl groups were observed at δ 1.553 as overlapping singlets and the two -OH protons appeared at δ 5.9 and 5.8 as broad singlets. The three aromatic protons of catechol were visible between δ 6.63-6.59 as a multiplet and the five phenyl

protons were observed as a multiplet between δ 7.188-7.093. In the ^{13}C NMR, the signal at δ 30.699 was due to the two methyl groups and the quaternary carbon appeared at δ 42.306. The three methine carbons on the catechol ring appeared at δ 114.678, 115.025, 119.300.

4.1.5.2 Montmorillonite catalyzed alkylations

Montmorillonite K 10 has been used as a versatile, convenient and ecofriendly catalyst for many synthetic transformations. It has been used as a catalyst in rearrangements such as Claisen Rearrangement, Fries rearrangement etc. Alkylation of phenols has been shown to proceed with Montmorillonite to give substituted phenols in very high yield and selectivity. We have now used Montmorillonite K 10 as catalyst for the synthesis of substituted catechols.

Reaction of catechol and benzhydrol in the presence Montmorillonite in dichloromethane at ambient temperature for 2 h afforded **34** in quantitative yield. Similar results were obtained with other catechols and benzhydrols in presence of Montmorillonite K 10; dialkyl catechols were formed in almost quantitative yields (Scheme 4.1.18).



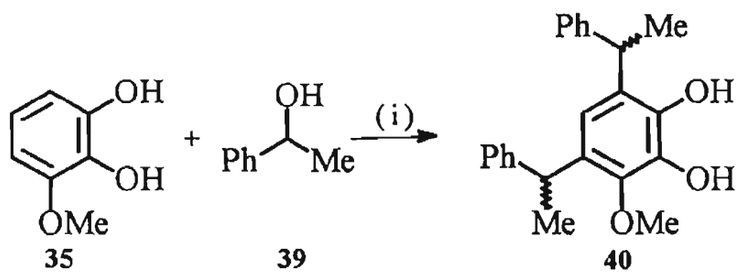
1 R_1=H **17** R_2=H **34** R_1=R_2=H(2 h, 100%)
35 R_1=OMe **37** R_2=OMe **36** R_1=OMe, R_2=H(2 h, 98%)
38 R_1=R_2=OMe (3 h, 100%)

(i) Montmorillonite K 10, R.T., CH_2Cl_2, 2-3 h, 98-100%.

Scheme 4.1.18

The spectral data of the catechols obtained were identical with those of the products obtained in acid catalyzed reactions (See section 4.1.5.1 and also experimental section).

The reaction of 1-phenylethanol with 3-methoxycatechol in presence of montmorillonite afforded 82% of the corresponding catechol **40** as mixture of isomers (Scheme 4.1.19).



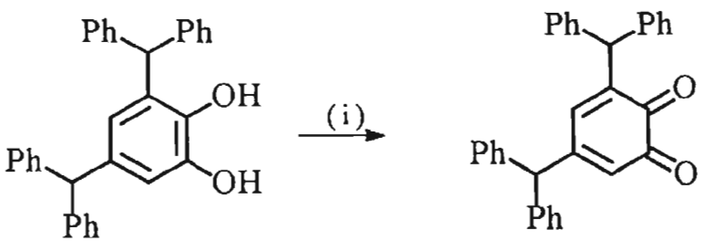
(i) CH_2Cl_2, Montmorillonite K 10., 5 h, 82%.

Scheme 4.1.19

4.1.5.3 Novel *o*-quinones from catechols

The catechols were converted to the corresponding novel *o*-benzoquinones by oxidation with sodium periodate in dichloromethane-water system.

The oxidation of **34** was performed with sodium periodate at ambient temperature in 1:1 CH_2Cl_2 - water in the presence of catalytic amount of tetrabutylammonium bromide to give the quinone **44** in 92% yield (Scheme 4.1.20).



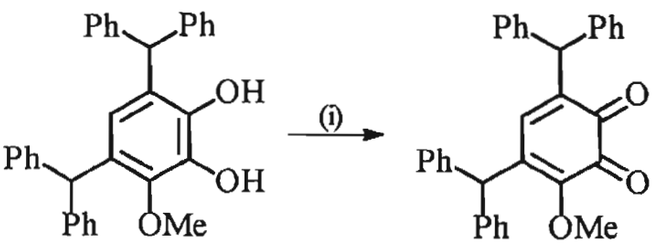
34 **44**

(i) $NaIO_4$, CH_2Cl_2: Water, $Bu_4N^+Br^-$, R.T., 5 h, 92%.

Scheme 4.1.20

In the ^1H NMR of **44**, the aromatic protons appeared as two sets of multiplets between δ 7.359-6.932. The olefinic protons resonated at δ 5.867 as a singlet and the two benzylic protons were observed as a singlet at δ 5.191. In the ^{13}C NMR, the quinone carbonyls resonated at δ 180.048 and the benzylic carbon gave signal at δ 52.949.

Oxidation of **36** with sodium periodate gave the quinone **45** in 90% yield (Scheme 4.1.21).

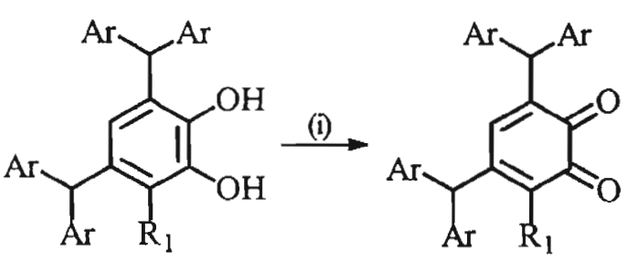


36 **45**

(i) $NaIO_4$, CH_2Cl_2: Water, RT., 6 h, 90%.

Scheme 4.1.21

The oxidation of **38** afforded the corresponding quinone **46** in 97% yield (Scheme 4.1.22).

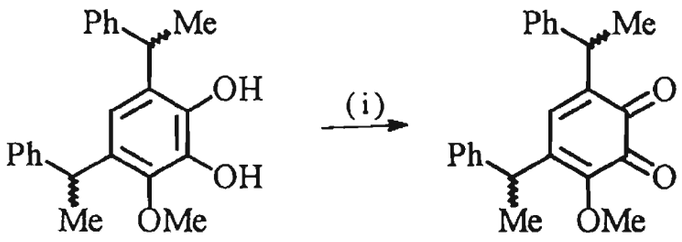


38 R_1=OMe, Ar = 4-Methoxyphenyl **46**

(i) $NaIO_4$, CH_2Cl_2: Water, RT., 5 h, 97%.

Scheme 4.1.22

The oxidation of **40** gave the quinone **47** in low yield as a mixture of stereoisomers (Scheme 4.1.23). Spectral data of **45, 46** and **47** were in good agreement with the structures assigned.

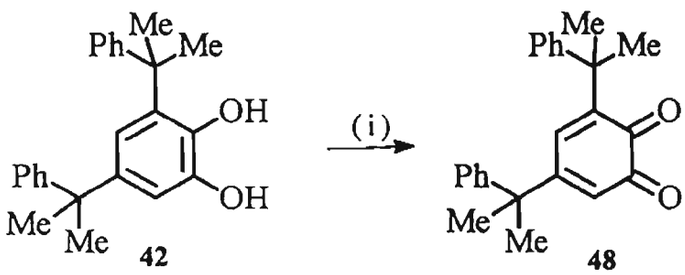


40 **47**

(i) $NaIO_4$, CH_2Cl_2: Water, RT., 3 h, 30%.

Scheme 4.1.23

Similarly, quinone **48** was obtained by the oxidation of **42** with sodium periodate (Scheme 4.1.24). In this case also the spectral data were in complete agreement with the assigned structure.



42 **48**

(i) $NaIO_4$, CH_2Cl_2: Water, RT., 24 h, 93%.

Scheme 4.1.24

In conclusion, we have developed a facile alkylation of catechols with benzhydrols to afford *bis* alkylated catechols using sulfuric acid or Montmorillonite K 10 as catalyst. In view of the experimental simplicity and ecofriendly nature of the clay catalyst, the latter method is preferred over the conventional acid catalyzed alkylation. The alkylated catechols on oxidation afforded novel *o*-benzoquinones.

4.1.6 EXPERIMENTAL DETAILS

For general experimental details see Chapter 2, p-42. Benzhydrols used were prepared from the corresponding benzophenones by reduction with sodium borohydride. Montmorillonite K 10 clay (Aldrich) was activated before use at 85 °C for 3 h and 100 wt % of the clay was used in the reactions.

Acid catalyzed reactions

General Experimental Procedure

A mixture of catechol and benzhydrol in acetic acid at 20 °C was treated with 5 equivalents of conc. H_2SO_4 and the reaction mixture was stirred at room temperature for 12-16 h (In the reaction of 2-phenyl-2-propanol, the reaction time was 48 h). The viscous mixture was then added to ice and the precipitated product if any, was collected by filtration and recrystallised. In the case of certain catechols, the products did not precipitate. These were extracted with ether or dichloromethane and chromatographed on silica gel using hexane-ethyl acetate mixtures to afford the pure product. Melting points are reported for recrystallized compounds.

3,5-Bis(diphenylmethyl)benzene-1,2diol (34)

To a mixture of catechol (1.10 g, 10.0 mmol) and benzhydrol (4.05 g, 22.0 mmol) in 100 mL acetic acid at 20 °C was added conc. H_2SO_4 (4.9 g, 50 mmol) dropwise and the resulting mixture was stirred for 12 h at room temperature. The viscous mixture was added to ice and the precipitated product was filtered by suction and

recrystallized from benzene-hexane to give **34** as colourless needles (4.40 g, 100%). mp. 197-198 °C (Benzene-hexane).

IR ν_{max} (KBr) : 3486, 3296, 3082, 3023, 1614, 1602, 1510, 1493, 1445, 1299, 1220, 1150, 746, 700 cm^{-1}.

^1H NMR ($CDCl_3$-Acetone d_6) : 7.368-7.149 (m, 12H), 6.921-6.899 (m, 10H), 6.345 (s, 2H), 5.455 (s, 2H), 2.456 (brs, 2 OH).

^{13}C NMR ($CDCl_3$-Acetone-d_6) : 144.022, 142.423, 134.428, 129.528, 128.270, 126.246, 117.457, 52.031.

3-Methoxy-4,6-bis(diphenylmethyl)benzene-1,2-diol (36)

To 3-methoxycatechol (1.0 g, 7.14 mmol) and benzhydrol (2.76 g, 15.7 mmol) in 100 mL acetic acid was added conc. H_2SO_4 (3.5 g, 35.7 mmol) and the reaction mixture was stirred at room temperature for 13 h. The resulting mixture was added to crushed ice and the precipitated product was collected by filtration and the light yellow product was recrystallised from dichloromethane-hexane mixture to give **36** as colourless needles (3.0 g, 89%). mp. 138-140 °C (CH_2Cl_2-hexane).

IR ν_{max} (KBr) : 3555, 3503, 3340, 3057, 3024, 1598, 1493, 1457, 1427, 1363, 1274, 1241, 1069, 986, 746, 700 cm^{-1}.

^1H NMR : 7.216-7.117 (m, 12H), 7.000-6.950 (m, 8H), 6.006 (s, 1H), 5.701 (s, 2H), 5.611 (brs, 1H, OH), 5.283 (brs, 1H, OH), 3.507 (s, 3H).

^{13}C NMR : 143.686, 142.851, 136.080, 129.045, 128.043, 127.983, 126.062, 126.062, 125.943, 123.363, 61.071, 49.825, 49.401.

3-Methoxy-4,6-bis(4,4'-dimethoxydiphenylmethyl)benzene-1,2-diol (38)

To a mixture of 3-methoxycatechol (300 mg, 2.14 mmol) and 4,4'-dimethoxybenzhydrol (1.045 g, 4.28 mmol) in 10 mL acetic acid was added conc. H_2SO_4 (1.05 g, 10.7 mmol) at 20 °C. The reaction mixture was stirred for another 12 h and added to ice. The product was extracted with ether and the combined ether extracts were washed with water, saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4. The residue obtained after the removal of the solvent, on chromatography afforded **38** as a semisolid (1.18 g, 93%).

IR ν_{max} (KBr) : 3387, 2948, 2827, 1607, 1506, 1465, 1243, 1175, 1027, 818, 589 cm^{-1}.

^{1}H NMR : 7.056-6.692 (m, 16H), 5.901 (s, 1H), 5.633 (brs, 1H, OH), 5.599 (s, 1H), 5.553 (s, 1H), 5.226 (brs, 1H, OH), 3.765 (s, 12H), 3,513 (s, 3H).

^{13}C NMR : 157.858, 157.708, 143.649, 140.689, 136.299, 135.265, 132.158, 129.918, 129.632, 128.588, 126.474, 122.889, 113.781, 113.486, 113.345, 60.951, 54.970, 48.483, 47.930.

3-Methoxy-4,6-bis (1-phenylethyl)benzene-1,2-diol (40)

To a mixture of 3-methoxycatechol (140 mg, 1.0 mmol) and 1-phenylethanol (293 mg, 2.4 mmol) in 5 mL acetic acid was added

conc. H_2SO_4 (490 mg, 5 mmol) at 20 °C and then stirred at room temperature for 16 h. The reaction mixture was added to ice and worked up as described in the earlier experiment. The residue was chromatographed on silica gel to give **40** as a semi solid (262 mg, 75%).

IR ν_{max} (KBr) : 3388, 2960, 2929, 1615, 1600, 1493, 1460, 1415, 1284, 1207, 1107, 949, 700 cm^{-1}.

^1H NMR : 7.237-7.110 (m, 2H), 6.689-6.676 (d, 1H), 5.975 (brs, 1H, OH), 5.470 (brs, 1H, OH), 4.426-4.333 (m, 4H), 3.472 (s, 3H), 1.587-1.502 (m, 6H).

^{13}C NMR : 146.785, 145.895, 143.440, 140.948, 136.105, 129.813, 128.362, 128.229, 128.180, 127.528, 127.372, 125.930, 125.767, 117.524, 117.309, 61.014, 38.198, 38.174, 37.802, 37.753, 22.103, 20.856.

3,5-Bis(2-phenyl-2-propyl)benzene-1,2-diol (42) and 4-(2-phenyl-2-propyl)benzene-1,2-diol (43)

To a mixture of catechol (3.25 g, 29.5 mmol) and 2-phenyl-2-propanol (10.0 g, 69.9 mmol) in 50 mL acetic acid was added conc. H_2SO_4 (14.5 g, 148 mmol) dropwise at 20 °C and stirred for 48 h. The reaction mixture was added to ice and extracted with dichloromethane (5x50 mL). The combined organic extracts were washed with water (2x100 mL), saturated aqueous $NaHCO_3$ (1x50 mL), brine and dried over Na_2SO_4. The solvent was removed and the residue on chromatography on silica gel using 90:10 hexane-ethyl acetate afforded **42** (2.25 g, 22%). Further elution with 80:20 hexane-ethyl

acetate gave **43** (2.155 g, 32%). **42** and **43** were recrystallised from CH_2Cl_2-hexane to give colourless crystals, mp. 99-100 °C and 92-93 °C respectively.

Data for **42**

IR ν_{max} (KBr) : 3499, 3339, 3055, 2970, 1619, 1597, 1489, 1424, 1391, 1298, 1193, 1135, 972, 788, 767, 700 cm^{-1}.

^1H NMR : 7.280-7.120 (m, 10H), 6.869 (d, 1H, J = 1.65 Hz), 6.699 (d, 1H, J = 1.78 Hz), 5.404 (s, 1H, OH), 4.147 (s, 1H, OH), 1.668 (s, 6H), 1.578 (s, 6H).

^{13}C NMR : 150.802, 148.452, 144.990, 143.297, 138.386, 135.293, 129.092, 127.873, 126.825, 126.657, 125.938, 125.473, 115.864, 112.658, 42.659, 41.898, 30.899, 29.388.

EIMS : 346,(m+, 26), 331 (47), 253 (36), 165 (23), 119 (50), 103 (67), 91 (100), 78 (79), 77 (82), 41(85).

Data for **43**

IR ν_{max} (KBr) : 3487, 3357, 3055, 2967, 1599, 1514, 1453, 1357, 1286, 1192, 1114, 793, 705 cm^{-1}.

^1H NMR : 7.188-7.093 (M, 5H), 6.637-6.596 (M, 3H), 5.8 (brs, 1H, OH), 5.7 (brs, 1H, OH), 1.553 (s, 6H).

^{13}C NMR : 150.672, 144.186, 142.739, 141.019, 127.933, 126.659, 125.542, 119.300, 115.025, 114.678, 42.306, 30.699.

Montmorillonite K 10 catalyzed reactions

3,5-Bis(1,1-diphenylmethyl)catechol (34)

A mixture of catechol (220 mg, 2.0 mmol) and benzhydrol (810 mg, 4.4 mmol) in 20 mL dry dichloromethane was treated with activated Montmorillonite K 10 (810 mg) and the mixture stirred for 3 h. The catalyst was filtered off, the solvent was removed and the residue filtered through a short column of silica gel using dichloromethane to afford **34** (880 mg, 100%). Recrystallised from benzene-hexane mixture. mp. 197-198 °C.

3-Methoxy-4,6-bis(1,1-diphenylmethyl)benzene-1,2-diol (36)

To a mixture of 3-methoxycatechol (150 mg, 1.07 mmol) and benzhydrol (445 mg, 2.41 mmol) in 10 mL dry dichloromethane was added activated catalyst (445 mg) and stirred for 2 h. The reaction mixture on usual work up afforded **36** (502 mg, 100%). mp. 138-140 °C (CH_2Cl_2-hexane).

3-Methoxy-4,6-bis[(4,4'-dimethoxydiphenyl)methyl]benzene-1,2-diol (38)

To a mixture of 3-methoxy catechol (200 mg, 1.429 mmol) and 4,4'-dimethoxybenzhydrol (766 mg, 3.14 mmol) in 15 mL dry dichloromethane was added activated catalyst (766 mg) and stirred for 3 h. The reaction mixture on usual work up afforded **38** as a viscous oil (844 mg, 100%).

3-Methoxy-4,6-bis(1-phenylethyl)benzene-1,2-diol (40)

A mixture of 3-methoxycatechol (110 mg, 0.714 mmol) and 1-phenylethanol (192 mg, 1.573 mmol) in 10 mL dry dichloromethane was treated with activated catalyst (192 mg) and stirred for 5 h. Usual work up procedure afforded **40** as a semisolid (204 mg, 82%).

Oxidation of the catechols to *o*-quinones

General Experimental procedure

The catechol in 1:1 mixture of dichloromethane-water was treated with 3 equivalents of solid sodium periodate at room temperature. (In the oxidation of **34**, catalytic amount of tetrabutylammonium bromide was also employed to effect fast oxidation). The reaction mixture was diluted with water and extracted with dichloromethane. The combined organic extracts were washed with water, brine and dried over sodium sulfate. The solvent was removed and the residue was filtered through a short pad of silica gel to afford the respective quinones.

3,5-Bis(1,1-diphenylmethyl)-1,2-benzoquinone (44)

Treatment of **34** (250 mg, 0.566 mmol) with sodium periodate (364 mg, 1.7 mmol) in dichloromethane-water (1:1, 40 mL) in presence of 20 mg of tetrabutylammonium bromide for 5 h followed by work up as described in the general procedure gave **44** as dark purple coloured crystals (230 mg, 92%). mp 194-196 °C (CH_2Cl_2-Diethyl ether).

IR ν_{max} (KBr) : 3060, 3023, 1666, 1660, 1640, 1599, 1563, 1493, 1451, 1289, 1078, 1040, 746, 698 cm^{-1}.

^1H NMR : 7.359-7.335 (m, 10H), 6.953-6.932 (m, 8H), 5.867 (s, 2H), 5.192 (s, 1H).

^{13}C NMR : 180.048, 157.694, 139.659, 130.710, 129.086, 128.851, 127.640, 52.949.

3-Methoxy-4,6-bis(1,1-diphenylmethyl)-1,2-benzoquinone (45)

To a mixture of **36** (100 mg, 0.211 mmol) in dichloromethane-water mixture (1:1, 10 mL) was added sodium periodate (136 mg, 0.636 mmol) and stirred for 6 h. The reaction mixture was worked up and the product chromatographed on silica gel using 85:15 hexane-ethyl acetate to afford **45** as a red solid (90 mg, 90%).

IR ν_{max} (CCl_4) : 3059, 3026, 1666, 1600, 1493, 1449, 1309, 1064, 979, 745, 700 cm^{-1}.

^1H NMR : 7.271-7.181(m, 14H), 7.006-6.914 (m, 6H), 6.382 (s, 1H), 5.734 (s, 1H), 5.404 (s, 1H), 3.828 (s, 3H).

^{13}C NMR : 178.464, 176.952, 148.503, 140.856, 140.584, 140.414, 139.769, 137.775, 128.690, 128.645, 128.589, 128.340, 127.926, 127.102, 126.592, 60.416, 49.035, 48.193.

3-Methoxy-4,6-bis[(4,4'-dimethoxydiphenyl)methyl]-1,2-benzoquinone (46)

A solution of **38** (660 mg, 1.115 mmol) in CH_2Cl_2-water (1:1, 10 mL) was added sodium periodate (715 mg, 3.34 mmol) and stirred at room temperature for 5 h. Usual work up and

chromatography on silica gel using 80:20 hexane-ethyl acetate afforded **46** as a red semisolid (638 mg, 97%).

IR ν_{max} (CCl_4) : 3026, 2969, 2935, 1667, 1628, 1599, 1490, 1451, 1379, 1317, 1109, 1027, 759, 702 cm^{-1}.

^1H NMR : 6.915-6.694 (m, 16H), 6.316 (s, 1H), 5.595 (s, 1H), 5.267 (s, 1H), 3.798-3.747 (3 singlets, 15H).

^{13}C NMR : 178.421, 176.847, 158.296, 157.865, 147.843, 140.848, 140.227,138.308, 132.744, 131.699, 129.338,129.237, 128.850, 113.763, 113.420, 60.132, 54.751, 54.699, 47.245, 46.420.

3-Methoxy-4,6-bis(1-phenylethyl)-1,2-benzoquinone (47)

To a solution of **40** (174 mg, 0.5 mmol) in dichloromethane-water (1:1, 10 mL) was added sodium periodate (339 mg, 1.58 mmol) and stirred for 3 h. Usual work up and chromatography afforded **47** (mixture of isomers) as a red semisolid (50 mg, 30%).

IR ν_{max} (CCl_4) : 2999, 2941, 2904, 2836, 1667, 1609, 1509, 1365, 1454, 1381, 1250, 1178, 1033, 980, 819 cm^{-1}.

^1H NMR : 7.326-6.964 (m, 20H), 6.522 (dd, 2H, J = 5.34 Hz, J= 1.02 Hz), 4.486 (q, 2H), 4.008 (q, 2H), 3.888 (s, 3H), 3.885 (s, 3H), 1.463 (d, 3H, J = 7.23 Hz), 1.407 (d, 3H, J= 7.23 Hz), 1.345 (d, 3H, J = 7.2Hz), 1.268 (d, 3H, J= 7.2 Hz).

^{13}C NMR : 178.616, 176.928, 147.322, 142.830, 142.723, 142.631, 140.713, 135.671, 135.476, 128.543, 128.276, 128.186, 127.268, 127.203, 127.094,

126.829, 126.265, 60.261, 37.892, 39.71, 36.094, 19.457, 16.561.

3,5-Bis(2-phenyl-2-propyl)-1,2-benzoquinone (48)

42 (100 mg, 0.289 mmol) in dichloromethane-water mixture (1:1, 10 mL) was treated with sodium periodate (185 mg, 0.865 mmol) for 24 h. Usual work up and chromatography on silica gel using 90:10 hexane-ethyl acetate afforded **48** as a dark green solid (93 mg, 93%). mp 140-141 °C (CH_2Cl_2- Diethyl ether).

IR ν_{max} (KBr) : 3062, 2975, 2920, 1662, 1624, 1597, 1570, 1505, 1466, 1364, 1263, 1025, 877, 765, 700 cm^{-1}.

^{1}H NMR : 7.381-7.020 (m, 10H), 6.456 (d, 1H, J = 1.99 Hz), 6.388 (d, 1H, J = 1.97 Hz), 1.583 (s, 6H), 1.415 (s, 6H).

^{13}C NMR : 180.222 179.225, 161.882, 148.504, 146.504, 146.645, 144.270, 135.939, 128.862, 128.124, 127.151, 126.239, 125.868, 125.344, 122.694, 43.940, 41.933, 28.186, 27.093.

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4.2 STUDIES TOWARDS THE SYNTHESIS OF A MODEL FOR THEAFLAVIN

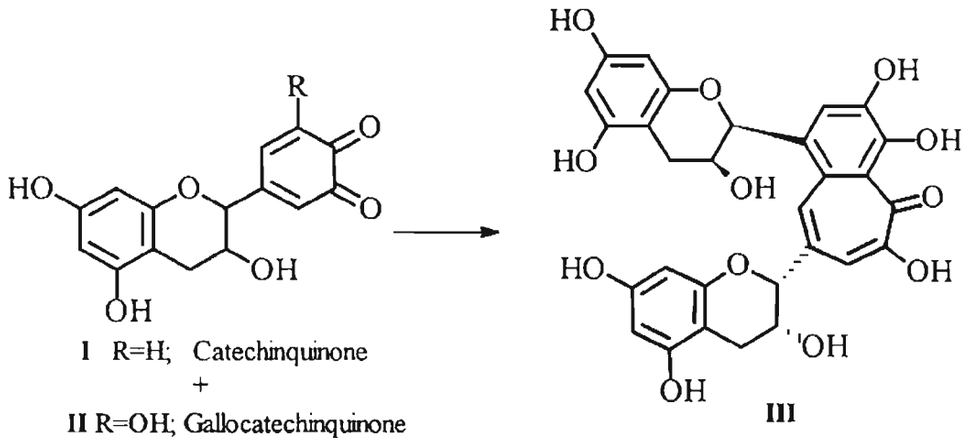
4.2.1 INTRODUCTION

Oxidative processes aided by enzymes are well known in biological systems and often play a crucial role in the biosynthesis of natural products. Enormous amount of work has been carried out to elucidate the course of such processes and their intricate details leading to the formation of many natural products. Biosynthesis of natural products makes use of the unique properties of enzymes in biological systems.

Perhaps, the most important class of compounds studied in the area of oxidative coupling, cleavage and other processes are phenols and related compounds. Phenols are known to undergo facile oxidation and oxidative coupling in presence of biological catalysts as well as chemocatalysts leading to functionally diverse molecules, which often show biological activity. One-electron oxidants and other oxidising agents have been used in such processes.[1]

Polyhydroxy aromatic compounds form a large and interesting class of natural products and the phenolic functionality is present in a wide variety of compounds. Polyhydroxy compounds in general, and polyhydroxy benzenes in particular, are susceptible to oxidation. This makes the synthesis of polyhydroxy compounds a real challenge to synthetic organic chemists. In most of the syntheses of polyhydroxy natural products such as flavones, isoflavones, anthocyanins etc., prior protection of the hydroxyl group is found to be essential.

The tea pigment, theaflavin **III**, found in green tea leaves, possesses unique and interesting structural features such as polyhydroxy benzenoid and troponoid skeletons. The presumed biosynthesis of **III** involves the cycloaddition of catechin quinone **I** and gallocatechin quinone **II** followed by further transformations (Scheme 4.2.1).[2]

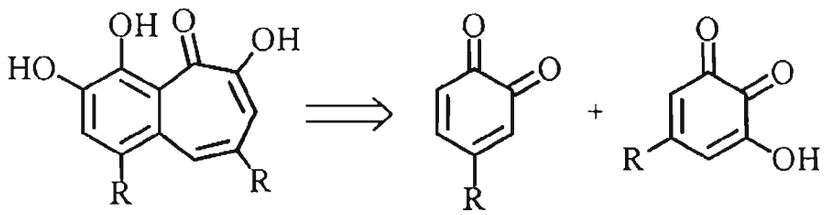


Scheme 4.2.1

It was surmised that the key structural fragment of theaflavin, 2,1',2'-trihydroxy-4,4'-disubstituted benzotropolone, can conceivably be constructed by the reaction of a suitably substituted 1,2-benzoquinone and 3-hydroxy-1,2-benzoquinone. In the context of our interest in the chemistry of *o*-quinones, especially their cycloadditions,[3] it was of interest to study the cycloaddition chemistry of 3-hydroxy-1,2-benzoquinone with a view to carrying out a model synthesis of the benzotropolone fragment of **III**.

It may be noted that the strategy conceived was analogous to the proposed biosynthesis in which a substituted *o*-quinone and 3-hydroxy-1,2-quinone undergo condensation to give the skeleton of **III**.[2] The corresponding pyrogallol derivative serves as the precursor for the

3-hydroxy-*o*-quinone and a catechol as the precursor for the quinone (Scheme 4.2.2).

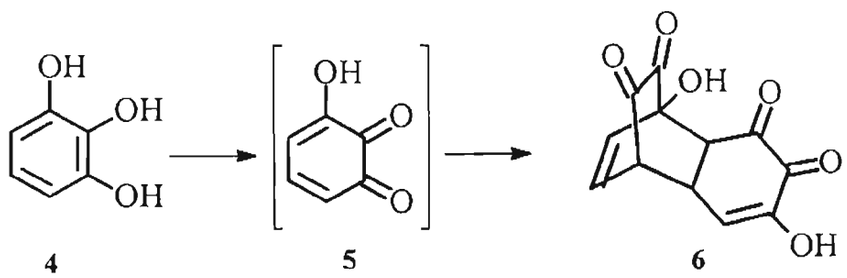


1 2 3

Scheme 4.2.2

4.2.2 REACTIVITY OF 3-HYDROXY-*o*-QUINONES

The chemistry of 3-hydroxy-1,2-quinones has been known in some detail. Salfeld has shown that 3-hydroxy-1,2-quinone generated by the oxidation of the corresponding pyrogallols with isoamyl nitrate or silver oxide undergoes dimerisation to give **6** (Scheme 4.2.3).[4,5]

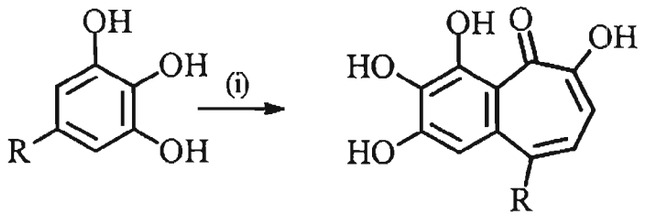


4 5 6

Scheme 4.2.3

Interestingly, polyhydroxy tropolone ring systems such as purpurogallins have been obtained by the oxidation of pyrogallols with a variety of oxidising agents. Thus pyrogallol on oxidation with potassium iodate or potassium periodate leads to the formation of purpurogallin. Analogous formation of substituted purpurogallin derivatives is known

when 5-substituted pyrogallols are oxidised. 5-*tert*-butyl pyrogallol and methyl gallate gave 4-substituted purpurogallin by the elimination of one of the substituents at the 5-position (Scheme 4.2.4).[6-9]



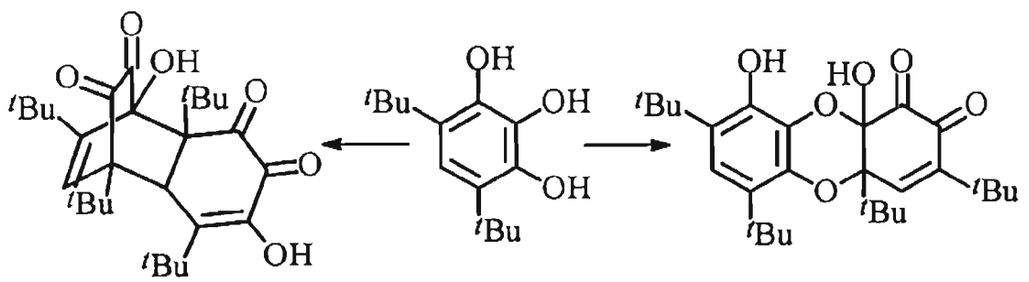
4 R=H,
7a R=^{t}Bu
7b R=CO_2Me

8 R=H,
8a R=^{t}Bu
8b R=CO_2Me

(i) KIO_3, Water.

Scheme 4.2.4

In contrast, the oxidation of 4,6-disubstituted pyrogallols afforded the dimers of the corresponding 3-hydroxy-*o*-quinones. The formation of these dimers from 4,6-di-*tert*-butyl pyrogallol is shown in scheme 4.2.5.[10]

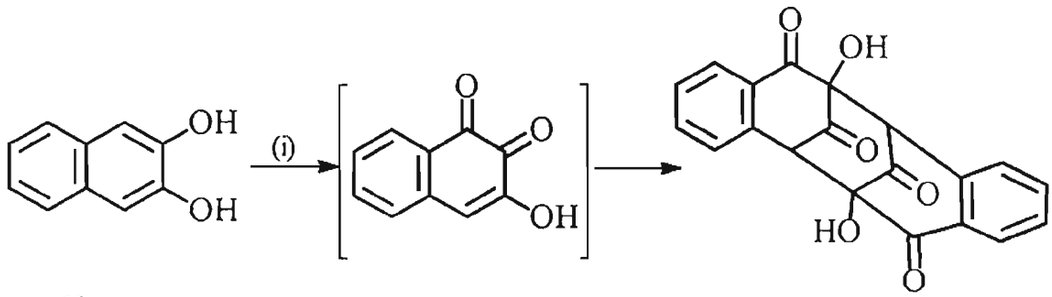


10 **9** **11**

Scheme 4.2.5

Teuber has shown another interesting mode of reactivity of 3-hydroxy-*o*-quinone in which the 3-hydroxy-*o*-quinone acts as inherent dipoles and they undergo dimerisation by dipolar cycloaddition. For

example, 3-hydroxy-1,2-naphthoquinone afforded the dimer **14** resulting from the dipolar cycloaddition (Scheme 4.2.6).[11]

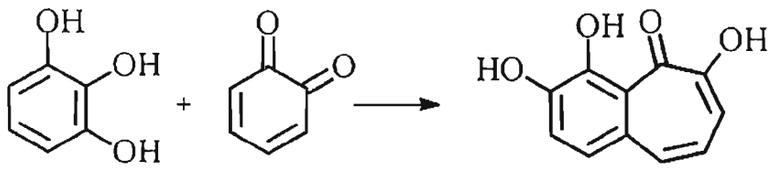


12 **13** **14**

(i) Fremy's salt, Acetone-H_2O.

Scheme 4.2.6

Deoxypurpurogallin derivatives have been prepared by the oxidation of corresponding pyrogallols with three fold excess of quinone as the oxidising agent. Horner has used this strategy for the preparation of benzodihydroxytropolones using benzoquinone as the oxidising agent and this is illustrated in scheme 4.2.7.[8,9]



4 **15** **16**

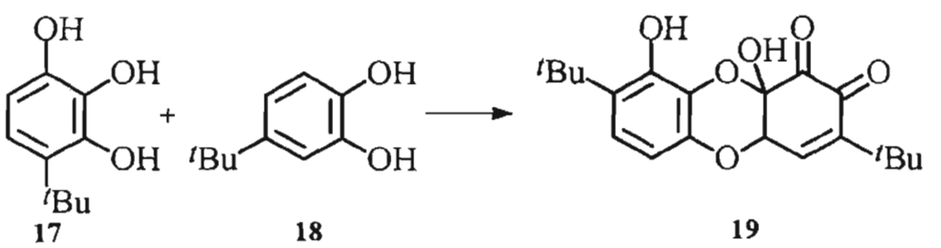
Scheme 4.2.7

4.2.3 STATEMENT OF THE PROBLEM

As mentioned earlier, the proposed biosynthesis of theaflavin invokes the cycloaddition of a hydroxy-*o*-quinone with another *o*-quinone followed by further transformations. It was of interest to examine the validity of this proposal. With this, some preliminary experiments aimed at synthesizing a model for the key benzotropolone fragment was undertaken. A 3-hydroxy-1,2-benzoquinone, generated by the oxidation of the corresponding pyrogallol, and an *o*-benzoquinone were selected as precursors for the study.

4.2.4 RESULTS AND DISCUSSION

The present studies were initiated with the reaction of 4-*tert*-butyl pyrogallol and 4-*tert*-butyl quinone. A 1:1 mixture of 4-*tert*-butyl pyrogallol and 4-*tert*-butyl catechol was oxidised with four equivalents of Ag_2CO_3 as the oxidizing agent. It was anticipated that the initially formed 3-hydroxy-*o*-quinone would be trapped by the quinone formed from the catechol to yield a benzotropolone derivative. However, instead of the expected product, the dimer **19** of the 3-hydroxy-o-quinone was found to be the only isolable product (Scheme 4.2.8).

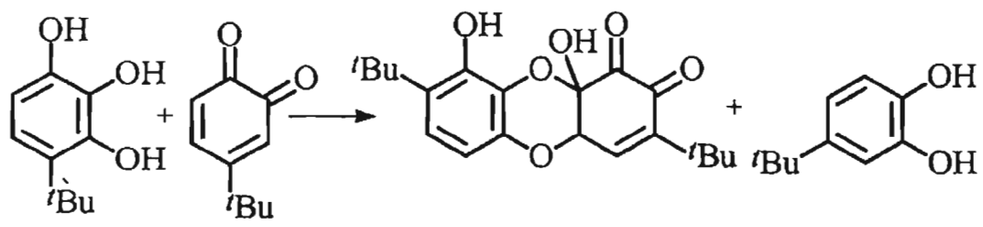


17 **18** **19**

Scheme 4.2.8

In the IR spectrum of **19**, the absorptions due to the hydroxyl groups were observed at 3404 and 3354 cm^{-1} and the absorptions at 1755 and 1683 cm^{-1} were attributed to the carbonyl groups. In the ^1H NMR, the proton adjacent to the oxygen atom appeared at δ 3.488 (J = 6.72 Hz) and the olefinic proton resonated at δ 7.156 (J = 6.69 Hz) as a doublet. The *tert*-butyl groups gave two singlets at δ 1.270 and 1.245.

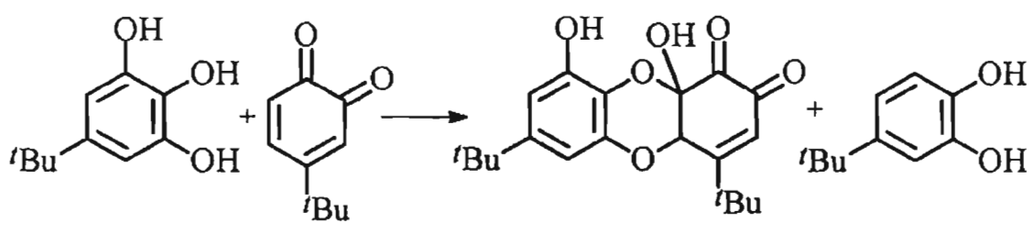
A subsequent experiment was conducted with the quinone as the oxidizing agent. Thus 4-*tert*-butyl pyrogallol was treated with 4-*tert*-butyl-1,2-benzoquinone at room temperature. In this case also, instead of the expected product, the dimer **19** was isolated along with **18** (Scheme 4.2.9).



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

Scheme 4.2.9

The reaction was then carried out with the 5-*tert*-butyl pyrogallol and 4-*tert*-butyl-1,2-benzoquinone. As in the previous case, the dimer **22** from the corresponding 3-hydroxy-*o*-benzoquinone was isolated along with 4-*tert*-butyl catechol **18** (Scheme 4.2.10).

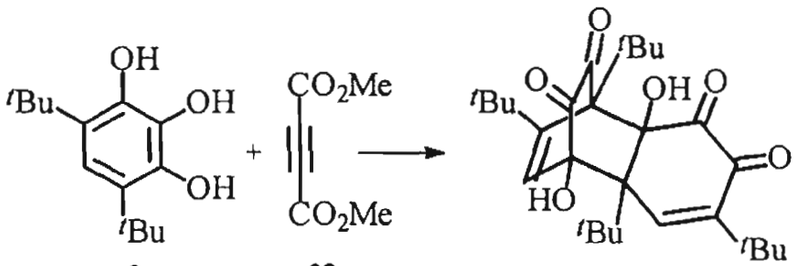


21 **20** **22** **18**

Scheme 4.2.10

In the IR spectrum of **22**, the hydroxyl groups gave absorption at 3408 cm^{-1}. In the ^{1}H NMR, the proton adjacent to the oxygen atom appeared at δ 3.958 and the olefinic proton resonated at δ 6.474. The aromatic protons resonated at δ 7.361 and 7.261. In the ^{13}C NMR, the carbonyl groups gave signals at δ 196.892 and 193.140. The quaternary carbon bearing hydroxyl was observed at δ104.814 and the other carbon on the ring junction appeared at δ 87.474. The *tert*-butyl groups gave signals at δ 29.945 and 29.101 and the quaternary carbons were visible at δ 41.390 and 36.121.

In a second phase, attempts were made to trap the reactive 3-hydroxy-1,2-benzoquinone with a variety of dienophiles. Thus 4,6-di-*tert*-butyl pyrogallol was oxidized in the presence of dienophiles such as dimethyl acetylenedicarboxylate, styrene and phenyl acetylene. 4,6-Di-*tert*-butyl pyrogallol when treated with dimethyl acetylenedicarboxylate in presence of Ag_2CO_3 afforded the yellow dimer **24** derived from the 3-hydroxy-*o*-quinone (Scheme 4.2.11).

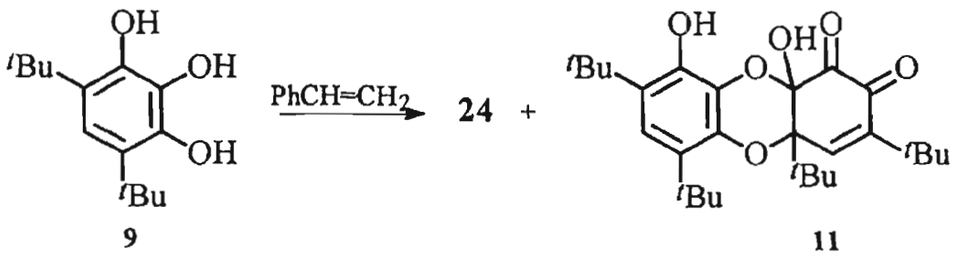


9 **23** **24**

Scheme 4.2.11

In the IR spectrum of **24**, the hydroxyl groups were observed at 3513 and 3471 cm^{-1} and the carbonyl groups gave absorptions at 1752 and 1686 cm^{-1}. In the proton NMR spectrum, the two olefinic protons were observed at 6.764 and 6.713. The *tert*-butyl groups appeared at δ 1.389, 1.174, 1.151 and 1.138. In the ^{13}C NMR, the carbonyl groups resonated at δ 184.946 and 180.458. The carbons bearing hydroxyl gave signals at δ 94.588 and 81.509.

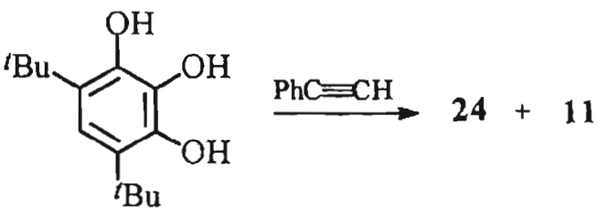
Similar results were obtained when **9** was oxidised with Ag_2CO_3 in the presence of styrene; both the dimers of the 3-hydroxy-*o*-quinone **11** and **24** resulted and these were separated by chromatography. Even in the presence of ten fold excess of styrene the dimers were the only isolable products and these were characterised as usual by spectral analysis (Scheme 4.2.12).



9 11

Scheme 4.2.12

Similar results were obtained when **9** was oxidized with Ag_2CO_3 in presence of an excess of phenyl acetylene (Scheme 4.2.13).



9

Scheme 4.2.13

In conclusion, it can be seen that the 3-hydroxy-*o*-quinone is too reactive to be trapped by another dienophile. The fast dimerization of the hydroxyquinone generated *in situ* precludes the cycloaddition reaction with the added dienophiles. In view of the discouraging results obtained, this line of investigation was discontinued. It appears that a fresh look at some of the results reported in the literature is necessary.

4.2.5 EXPERIMENTAL DETAILS

For general experimental details see Chapter 2, p-42.

Reaction of 4-*tert*-butyl pyrogallol:

Dimer 19

To a solution of 4-*tert*-butyl pyrogallol (100mg, 0.55 mmols) and 4-*tert*-butyl catechol (100 mg, 0.61 mmols) in 5 mL dichloromethane at ice temperature was added Ag_2CO_3 (606 mg, 2.2 mmols) and the reaction mixture was stirred for 2 h. It was then filtered through a column of celite to remove inorganic materials. The solvent was removed and the residue on chromatographic separation on silica gel using 95:5 hexane-ethyl acetate afforded the dimer **19** (33 mg, 33%). (The *tert*-butyl-1,2-quinone being unstable decomposed during chromatography).

IR ν_{max} (KBr) : 3404, 3354, 3097, 3070, 2959, 2870, 1755, 1683, 1607, 1508, 1479, 1467, 1366, 1282, 1200, 1158, 1040, 953, 813, 710 cm^{-1}.

^1H NMR : 7.156 (d, 1H, J = 6.69Hz), 6.883-6.763 (m, 2H), 4.2 (brs, 1H), 4.29 (brs 1H), 3.488 (d, J = 6.72Hz), 1.270 (s, 9H), 1.245 (s, 9H).

^{13}C NMR : 192.075, 168.460, 152.232, 147.320, 146.542, 141.658, 138.418, 128.795, 120.700, 119.960, 100.576, 82.948, 36.491, 34.347, 31.357, 28.179.

To a solution of 4-*tert*-butyl pyrogallol (280 mg, 1.53 mmols) in 5 mL dichloromethane was added 4-*tert*-butyl-1,2-benzoquinone (500 mg, 3.05 mmols) in dichloromethane at ice temperature and the reaction mixture was stirred for 30 min. The solvent was removed and the residue on chromatography afforded **19** as white solid. (98 mg, 18%) and 4-*tert*-butyl catechol (300mg, 60%).

To a solution of 4-*tert*-butyl pyrogallol (280 mg, 1.53 mmols) in 5 mL dichloromethane was added a solution of 4-*tert*-butyl-1,2-benzoquinone (750mg, 4.57 mmol) in 5 mL dichloromethane and the reaction mixture was stirred at ice temperature for 30 min. The solvent was removed and the residue on chromatographic separation on silica gel afforded the dimer **19** (90mg, 16%) and catechol (576 mg, 75%).

Reaction of 5-*tert*-butyl pyrogallol:

Dimer 22

To a solution of 5-*tert*-butyl pyrogallol (100 mg, 0.55 mmols) in 5 mL of dichloromethane was added a solution of 4-*tert*-butyl-1,2-quinone (181 mg, 1.1 mmols) in 5 mL dichloromethane at ice temperature and the reaction mixture was stirred for 30 min. The solvent was removed and chromatography of the residue afforded the dimer **22** (30 mg, 30%) and the catechol (110mg 59%).

IR ν_{max} (KBr) : 3408, 2966, 2908, 1747, 1680, 1600, 1363, 1299, 1225, 1164, 1040, 866 cm^{-1}.

^{1}H NMR : 7.361(s, 1H), 7.261 (s, 1H), 6.474 (s, 1H), 5.298 (s, 1H), 4.055 (s, 1H), 3.958 (s, 1H), 1.259 (s, 9H), 0.88 (s, 9H).

^{13}C NMR : 196.892, 193.140, 173.576, 128.364, 125.796, 104.814, 87.474, 41.391, 36.121, 29.945, 29.101.

To a solution of 5-*tert*-butyl pyrogallol (100mg, 0.55 mmols) in 5 mL water was added a solution of 4-*tert*-butyl-1,2-benzoquinone (270 mg, 1.64 mmols) in 5 mL water and the reaction mixture was stirred at ice temperature for 30 min. It was extracted with dichloromethane (3x25 mL). The combined organic layers were washed with water and brine and dried over sodium sulphate. Removal of the solvent followed by chromatography afforded the dimer **22** (36 mg, 36%) and catechol.

Reaction of 4,6-di-*tert*-butyl pyrogallol.

Dimer 24

To a mixture of 4,6-di-*tert*-butyl pyrogallol (200mg, 0.84 mmols) and dimethyl acetylenedicarboxylate (143 mg, 1.01 mmols) in 10 mL benzene was added Ag_2CO_3 (463 mg, 1.68 mmols) and the reaction mixture was stirred at room temperature for 3 h. The inorganic materials were removed by filtering through a short column of celite and the crude product was chromatographed on silica gel to afford **24** as a yellow solid (67 mg, 34 %).mp. 201-202 °C.

Data for **24**

IR ν_{max} (KBr) : 3551, 3513, 3471, 2959, 2912, 2874, 1752, 1686, 1485, 1431, 1366, 1300, 1223, 1093, 1046, 972 cm^{-1}.

^{1}H NMR : 6.764 (s, 1H), 6.713 (s, 1H), 5.483 (brs, 1H), 4.3 (brs, 1H), 1.389 (s, 9H), 1.174 (s, 9H), 1.151 (s, 9H), 1.138 (s, 9H).

^{13}C NMR : 184.946, 180.458, 149.966, 149.646, 147.782, 141.660, 134.789, 116.626, 94.588, 81.509, 40.150, 35.322, 34.659, 34.248, 29.934, 29.706, 28.506, 26.263.

EIMS : 473 (M^{+}+1, 5.5), 472 (M^{+}, 18), 280 (3), 249 (8), 238 (51), 223 (67), 208 (34), 207 (100), 193 (13), 179 (22), 135 (11), 152 (49), 151 (37), 137 (15), 123 (9), 109 (12), 57 (66).

Dimers 24 and 11

To a mixture of 4,6-di-*tert*-butyl pyrogallol (500 mg, 2.1 mmols) and styrene (437 mg, 2 mmols) in 5 mL dichloromethane was added Ag_2CO_3 (1.16g, 4.2 mmols) and stirred at room temperature for 2h. The inorganic materials were removed by filtered through a short column of celite and chromatographed on silica gel to afford **24** as a yellow solid (191mg, 38% mp. 201-202 °C) and **11** as a white solid (162 mg, 32%). mp. 179-180 °C.

Data for **11**

IR ν_{max} (KBr) : 3532, 3513, 3466, 2965, 2912, 2874, 1745, 1725, 1613, 1484, 1424, 1366, 1297, 1222, 1194, 1110, 981, 871, 696 cm^{-1}.

^1H NMR : 7.020 (s, 1H), 7.004 (s, 1H), 5.445 (s, 1H, OH), 4.349 (s, 1H, OH), 1.354 (s, 9H), 1.340 (s, 9H), 1.304 (s, 9H), 0.902 (s, 9H).

^{13}C NMR : 191.567, 169.501, 158.080, 146.377, 145.532, 141.118, 132.770, 131.523, 130.722, 121.302, 99.448, 83.330, 38.124, 34.830, 34.729, 31.877, 29.972, 29.445, 27.439.

EIMS : 473 (M^++1, 4), 472 (M^+, 14), 249 (14), 238 (42), 223 (34), 208 (30), 207 (100), 193 (8), 179 (19), 152 (35), 137 (15), 109 (11), 57 (50).

To a mixture of 4,6-di-*tert*-butyl pyrogallol (500 mg, 2.1 mmols) and styrene (2.2g, 21 mmols) in 10 mL dichloromethane was added Ag_2CO_3 (1.16g, 4.2 mmols) and the reaction mixture was stirred at room temperature for 2 h. The inorganic materials were removed by filtration through celite and the crude product was chromatographed on silica gel to afford **11** (130mg, 26%).

To a mixture of 4,6-di-*tert*-butyl pyrogallol (476 mg, 2.0 mmols) and phenyl acetylene (242 mg, 2.4mmols) in 10 mL benzene was added Ag_2CO_3 (1.1g, 4.mmols) and the reaction mixture was refluxed for 2 h. The inorganic materials were removed by filtration through celite and the crude product was chromatographed on silica gel to afford **11** (200 mg, 43%).

4.2.6 REFERENCES

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SUMMARY

The thesis entitled ***"NOVEL REACTIONS OF o-QUINONES AND RELATED CHEMISTRY"*** embodies the results of extensive investigations undertaken to gain insight into the reactivity of *o*-benzoquinones and related systems.

A general introduction to the chemistry of *o*-quinones is presented in Chapter 1. A definition of the problem is also incorporated in this chapter.

The second chapter describes the addition of a zwitterionic intermediate, generated by the addition of triphenylphosphine to dimethyl acetylenedicarboxylate, to *ortho* and *para* quinones. The addition of the zwitterionic intermediate to 3,5-di-*tert*-butyl-1,2-benzoquinone afforded highly functionalised γ,δ-unsaturated spirolactone **62** in moderate yield. The structure of the adduct was confirmed by single crystal X-ray analysis. The reaction was found to be general and similar spirolactones (e.g. **63**, **64**, **65**, **66**, **67** and **68**) are obtained with other *o*-quinones. The reaction of 1,2-naphthoquinone with the zwitterionic intermediate afforded two regioisomeric spirolactones **69** and **70** in 1:1 ratio. The addition of the zwitterionic intermediate to *p*-quinones also afforded similar adducts in moderate to good yields (e.g. **7**, **8**, **9**, **10**, **11** and **12**). A rationalization of the course of the reaction is also incorporated in the respective sections.

In the third chapter, the isomerization of 6,6-tetramethylene fulvene to 1-cyclopentenylcyclopentadiene **4**, and its cycloaddition reactions is described. A rationalization for this investigation is given in the introductory part of this chapter. Isomerization of

6,6-tetramethylene fulvene to 1-cyclopentenylcyclopentadiene **4** and the cycloaddition reactions of the latter are unprecedented. Thus, reaction of **4** with tetracyclone afforded the adduct **23** and the structure of the adduct was confirmed by single crystal X-ray analysis. In the case of more reactive dienophiles such as tetracyanoethylene, maleic anhydride, diethyl azodicarboxylate and *p*-benzoquinone, **4** undergoes rapid dimerization to **16** and the adducts from the dimer were isolated (e.g. **26**, **27**, **28** and **29**). For example, the reaction of tetracyanoethylene afforded the adduct **26** and its structure was confirmed unambiguously by X-ray analysis. Interestingly, the reaction of N-phenylmaleimide gave both adducts **24** and **25**, arising from the cycloaddition of **16** and **4** respectively.

Chapter 4 deals with some miscellaneous reactions of *o*-quinones. In the first part (*4.1*) the synthesis of substituted catechols by the alkylation of catechols with benzhydrols and other alcohols in presence of acids or eco-friendly clay catalyst Montmorillonite K 10 is described. Alkylation of catechols with benzhydrols in presence of acid afforded nearly quantitative yields of the corresponding *bis* alkylated catechols (**34** **36**, and **38**). Alkylation with 1-phenylethanol and 2-phenyl-2-propanol also afforded corresponding *bis* alkylated catechols (**40**, **42** and **43**). Montmorillonite K 10 is effectively used for similar *bis* alkylation in quantitative yields (e.g. **34**, **36** and **38**). These *bis* alkylated catechols are oxidized with sodium periodate to the corresponding novel *o*-benzoquinones **44**, **45**, **46** and **48** in very high yields.

Second part (*4.2*) deals with some attempts towards the synthesis of a model for the tea pigment theaflavin. Keeping in mind the suggested biosynthetic pathway, substituted pyrogallol and substituted o-quinone

were reacted. The desired product was not formed, instead the intermediate 4(5)-*tert*-butyl-3-hydroxy-*o*-quinone was found to undergo dimerization to the respective dimers (e.g. **19, 20**). Attempts to trap the reactive 3-hydroxy-*o*-quinone derived from 4,6-di-*tert*-butyl pyrogallol by dienophiles such as dimethyl acetylenedicarboxylate, styrene and phenyl acetylene also failed; formation of the respective dimers **11** and **24** from the 3-hydroxy-*o*-quinone was observed in these cases also.

In conclusion, we have uncovered a novel reactivity profile of *o*-quinones in the addition of zwitterionic intermediates to give highly functionalised spirolactones. The addition of the zwitterionic species to *p*-quinones also resulted in similar spirolactones. New insight was gained on the isomerization of 6,6-tetramethylene fulvene to 1-cyclopentenylcyclopentadiene; cycloadditions of the latter provided a new entry into novel polycyclic molecular frameworks, which may be transformed into polyquinane derivatives. A novel synthesis of *o*-quinones, which are otherwise difficult to synthesise, has been achieved from the corresponding catechols obtained by the alkylation of catechols with benzhydrols in presence of acids or eco-friendly clay catalyst Montmorillonite K 10. Even though the approach to the synthesis of a model for theaflavin was inconclusive, it can be seen that the intermediate 3-hydroxy-*o*-quinone is so reactive as to be trapped with added dienophiles; the formation of dimers from the 3-hydroxy-*o*-quinones was the only observable reaction.

LIST OF PUBLICATIONS

1. Nair,V.; Kumar, S.; Anilkumar, G.; **Nair; J. S.** *Diels Alder Reactions of o-Benzoquinones with 6-Substituted Fulvenes: Facile Synthesis of 1-aryl and 1,1-diarylmethylene-4,7-ethanoindene-8,9-diones.* ***Tetrahedron*** **1995**, *51* (33), 9155.

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