# ĘL DIPOLAR CYCLOADDITION REACTIONS OF 1,2-DIONES AND RELATED CHEMISTRY

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

BY

**SHEELA K. C.**

UNDER THE SUPERVISION OF

**Dr. G. VIJAY NAIR**

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

MARCH, 2000

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MARCH, 2000

*DEDICATED TO*

*MY PARENTS AND TEACHERS*

## DECLARATION

I hereby declare that the matter embodied in the thesis entitled "*NOVEL DIPOLAR CYCLOADDITION REACTIONS OF 1,2-DIONES AND RELATED CHEMISTRY*" is the result of investigations carried out by me at the **Organic Chemistry Division of Regional Research Laboratory [CSIR], Trivandrum** under the supervision of **Dr. G. Vijay Nair** and the same has not been submitted elsewhere for a degree.

Sheela

Trivandrum — **SHEELA K. C.**

22 March 2000

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

डॉ.जी.विजय नायर
निदेशक
Dr. G. Vijay Nair, F . A . Sc
Director

22 March 2000

## CERTIFICATE

This is to certify that the work contained in the thesis entitled "*NOVEL DIPOLAR CYCLOADDITION REACTIONS OF 1,2-DIONES AND RELATED CHEMISTRY*" has been carried out by **Sheela K. C.** under my supervision at the **Organic Chemistry Division of Regional Research Laboratory [CSIR], Trivandrum** and the same has not been submitted elsewhere for any other degree.

G. Vijay Nair

**G. VIJAY NAIR**
**THESIS SUPERVISOR**

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*Trivandrum* ***SHEELA K. C.***

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## CONTENTS

## PREFACE

Heterocyclic compounds constitute one of the most important classes of organic compounds and it is estimated that approximately half of all known organic compounds, natural and unnatural, incorporate a heterocyclic structural component.

In view of the remarkable biological activity exhibited by many heterocyclic compounds, developing new synthetic methodologies for heterocyclic construction has been an area of immense interest. In recent years much attention has been focused on the application of 1,3-dipolar cycloadditions in heterocyclic synthesis. In this context 1,2-diones appeared particularly attractive due to their potential ability to undergo a range of cycloadditions. A systematic investigation of the dipolar cycloaddition reactions of various 1,2-diones such as 1,2-benzoquinones, isatins and cyclobutenediones with different dipoles and some aspects of the chemistry of the cycloadducts has been carried out and the results are presented in the thesis entitled **"NOVEL DIPOLAR CYCLOADDITION REACTIONS OF 1,2-DIONES AND RELATED CHEMISTRY"**.

The thesis is divided into three chapters. Relevant references are given at the end of each chapter.

A general introduction to the cycloaddition chemistry with special emphasis on the dipolar cycloadditions of 1,2-diones such as 1,2-benzoquinones, isatins and cyclobutene-1,2-diones are presented in Chapter 1. A definition of the present research problem is also incorporated.

The second chapter contains the results of our systematic investigation of the dipolar cycloaddition reactions of carbonyl ylides with various 1,2-diones. The photolytic rearrangement of the cycloadducts obtained by the

reaction between 3,5-di-*tert*-butyl-1,2-benzoquinone and carbonyl ylides are also incorporated. General information on experimental procedure is given in this chapter.

The third chapter deals with the dipolar cycloaddition reactions of azomethine ylides with various 1,2-diones.

It may be mentioned that each chapter of the thesis is presented as an independent unit and therefore the structural formulae, schemes and figures are numbered chapterwise.

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

## ABBREVIATIONS

| | | |
|---|---|---|
| AM1 | : | Austin Method 1 |
| br s | : | broad singlet |
| d | : | doublet |
| dd | : | double doublet |
| DMSO | : | Dimethyl sulfoxide |
| DDQ | : | 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone |
| DEPT | : | Distorsionless Enhancement by Polarization Transfer |
| HOMO | : | Highest Occupied Molecular Orbital |
| HRMS | : | High Resolution Mass Spectrum |
| h | : | hours |
| IR | : | Infrared |
| LUMO | : | Lowest Unoccupied Molecular Orbital |
| m | : | multiplet |
| min | : | minutes |
| mp | : | melting point |
| Me | : | Methyl |
| NMR | : | Nuclear Magnetic Resonance |
| nm | : | nanometer |
| RT | : | Room Temperature |
| *o* | : | ortho |
| *p* | : | para |
| Ph | : | phenyl |
| s | : | singlet |
| t | : | triplet |
| TMS | : | Tetramethylsilane |

# CHAPTER 1

# AN INTRODUCTION TO THE DIPOLAR CYCLOADDITION REACTIONS OF 1,2-BENZOQUINONES, ISATINS AND CYCLOBUTENEDIONES

## 1.1 GENERAL

The focal theme of the thesis is the dipolar cycloaddition reactions of 1,2-diones such as 1,2-benzoquinones, acenaphthenequinone, isatins and cyclobutenediones (Figure 1) with various dipoles along with some aspects of the chemistry of the cycloadducts. To put things in perspective, this chapter begins with a brief overview to the Diels-Alder type cycloadditions of 1,2-benzoquinones and this is followed by a comprehensive review of the dipolar cycloadditions of the 1,2-diones under consideration.

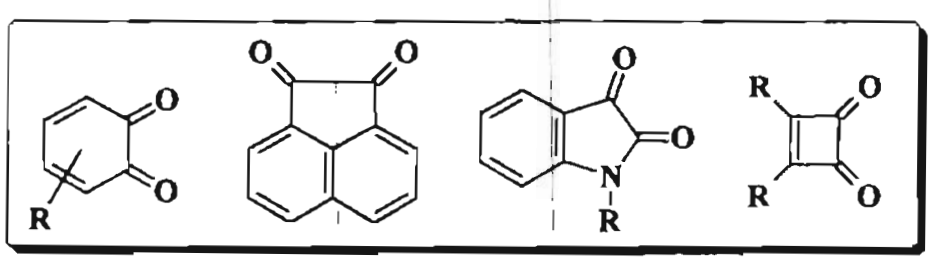



**Figure 1**

## 1.2 1,2-BENZOQUINONES

Compounds with quinonoid skeleton constitute an important and interesting class of organic molecules and they serve as versatile intermediates in organic synthesis. Among the quinonoid compounds, 1,2-benzoquinonoid functionality is present in a number of biologically active natural products.[1,2]

1,2-Benzoquinones can be prepared from phenols by oxidation with cerium(IV) sulfate in dilute acids,[4] Fremy's salt,[5] benzene seleninic anhydride,[6] iodosobenzene or iodoxybenzene.[7] The most commonly used method for the preparation of 1,2-benzoquinones involves oxidation of the corresponding catechols with appropriate oxidizing agents such as $Ag_2O$, $Ag_2CO_3$, $FeCl_3$, $NaIO_4$,[8] $MnO_2$ or sodium hypochlorite in the presence of phase transfer catalyst.[9]

### 1.2.1 [4π+2π] Cycloaddition Reactions of 1,2-Benzoquinones

The chemistry of 1,2-benzoquinones has been a subject of great interest both from the synthetic and theoretical standpoints because these are unique conjugated 1,2-diones that can exhibit diverse modes of cycloadditions. In cycloadditions, 1,2-benzoquinones can participate as carbodiene, heterodiene, dienophile or as heterodienophile as highlighted in Figure 2.

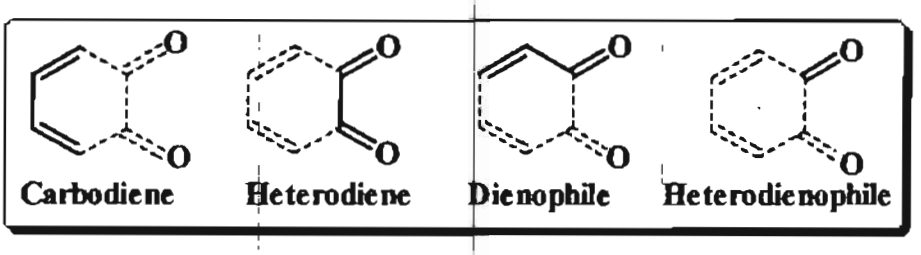


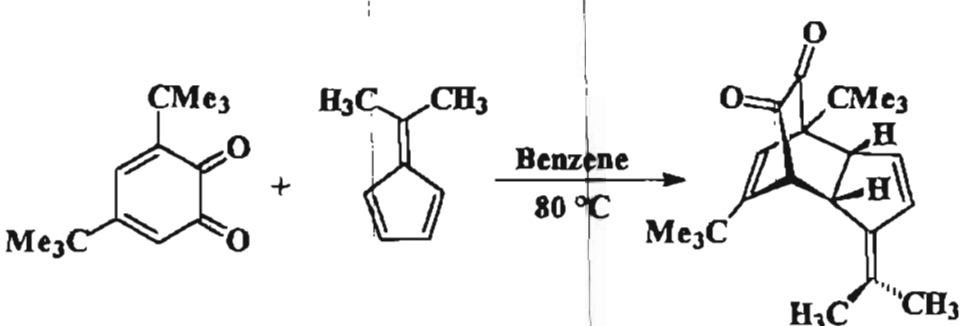

**Figure 2**

The electronic and steric features of the substituents on the quinone play an important role in the cycloaddition reactions of 1,2-benzoquinones. Recent investigations in our laboratory have highlighted the influence of these factors on the cycloaddition reactions of 1,2-benzoquinones.[11-14]

The different types of reactivity shown by 1,2-benzoquinones in [4π+2π] cycloaddition reactions are briefly outlined in the following sections.

**1,2-Benzoquinone as Carbodiene**

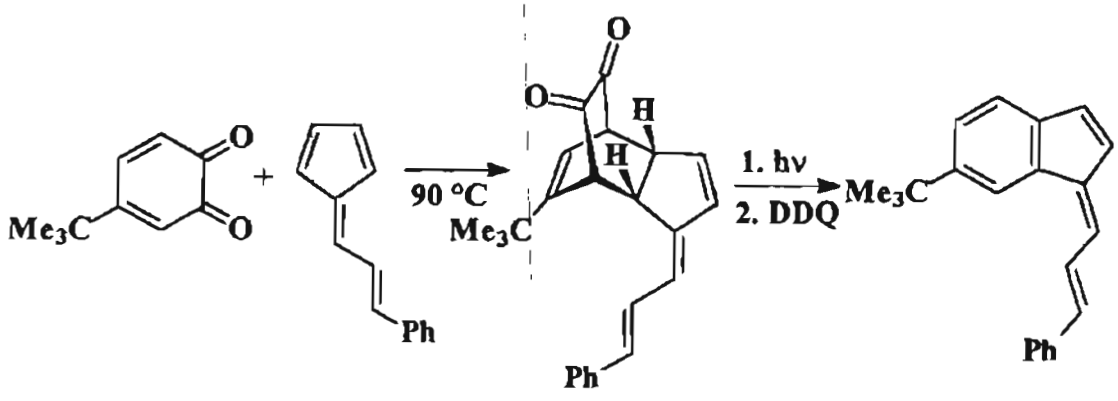
3,5-Di-*tert*-butyl-1,2-benzoquinone undergoes facile cycloaddition with pentafulvene **2** to afford bicyclo[2.2.2]octene dione **3** in good yield (Scheme 1).[11]




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

**Scheme 1**

Similarly 1,2-benzoquinones undergo inverse electron demand Diels-Alder reactions with 6-(2-phenylethenyl) fulvene. The bicyclo[2.2.2]octene diones resulting from these reactions undergo facile photolytic double decarbonylation reactions providing an efficient route to the synthesis of highly substituted indenes, which show interesting chemical and physical properties (Scheme 2).[12]

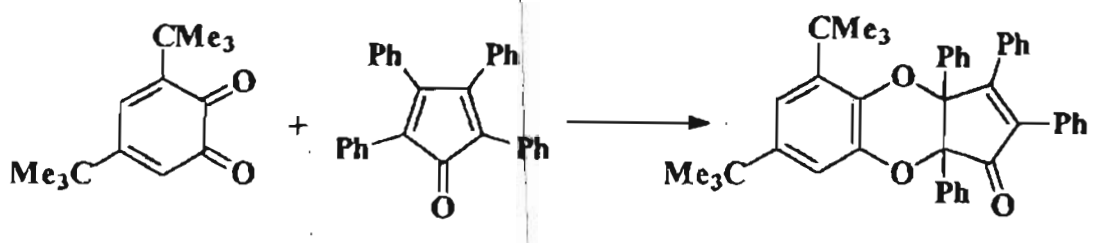



**4a** **5** **6** **7**

**Scheme 2**

**1,2-Benzoquinone as Heterodiene**

1,2-Benzoquinone has a highly activated heterodiene moiety and it participates in facile Diels-Alder reaction with tetracyclone **8** leading to the formation of benzodioxin derivatives (Scheme 3).[13]

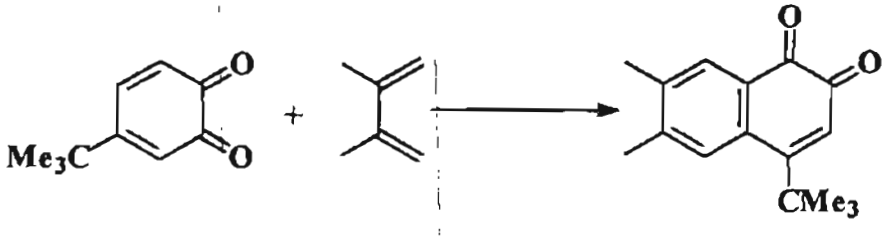



**1** **8** **9**

**Scheme 3**

**1,2 Benzoquinone as Dienophile**

1,2-Benzoquinone functions as an electron deficient dienophile in its reaction with 2,3-dimethyl butadiene (Scheme 4).[14]

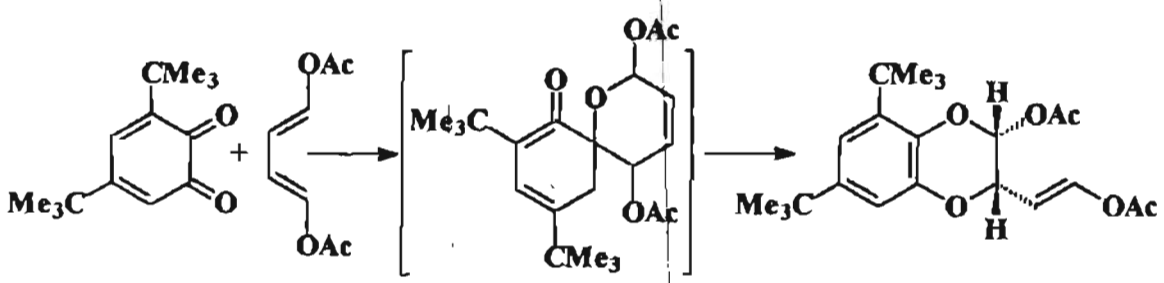



**4a** **10** **11**

**Scheme 4**

**1,2-Benzoquinone as Heterodienophile**

1,2-Benzoquinone can serve as a heterodienophile in cycloaddition reactions due to the presence of two activated carbonyl groups. An illustrative example is the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone with 1,4-diacetoxy-1,3-butadiene (Scheme 5).[15]




**1** **12** **13** **14**

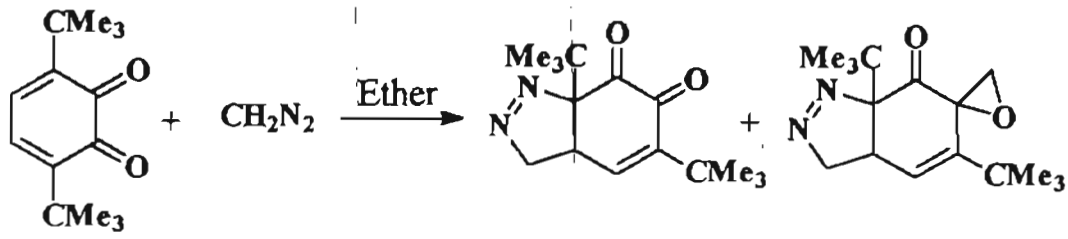
**Scheme 5**

**1.2.2 Dipolar Cycloaddition Reactions of 1,2-Benzoquinones**

The presence of two potentially dipolarophilic functionalities *viz.*, C=C and C=O, renders 1,2-benzoquinones very interesting from the vantage point of dipolar cycloaddition. Although such reactions can potentially lead to novel heterocyclic compounds, there has been very little information available on the reaction of 1,2-benzoquinones with various dipoles; the available data is restricted to the reactions of diazomethane, nitrile oxides and certain mesoionic compounds.[2,16]

**Reaction with Diazomethane**

The reaction of 3,6-di-*tert*-butyl-1,2-benzoquinone **15** with diazomethane has been reported to afford the corresponding indazole **16**. With excess of diazomethane, the spirooxirane **17** is also formed (Scheme 6).[17]

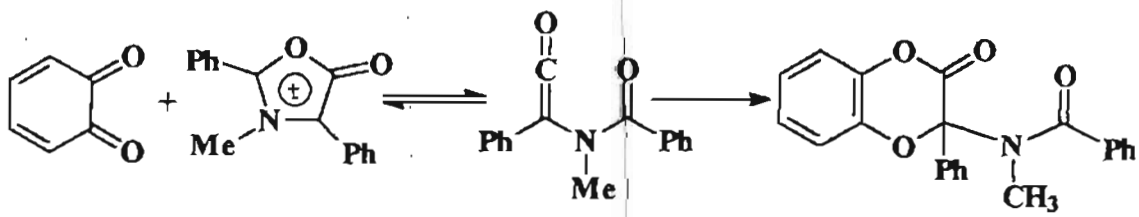


15 16 17

Scheme 6

**Reactions with Mesoionic Compounds**

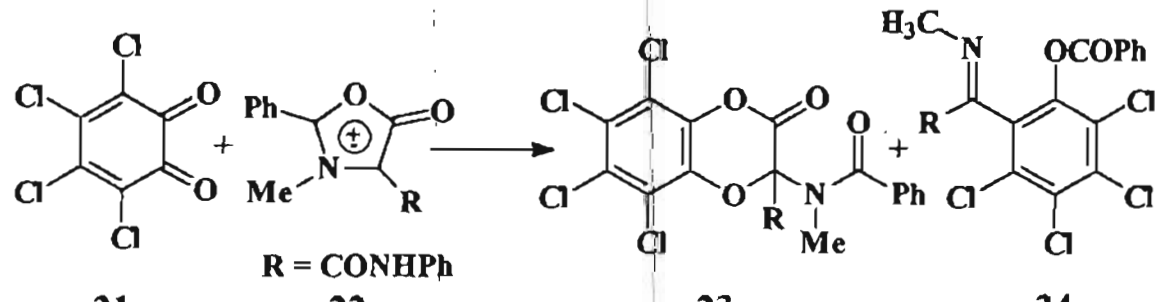
Mesoionic compounds have been extensively utilized as substrates in 1,3-dipolar cycloadditions. The anhydro-5-hydroxy-1,3-oxazolium hydroxide or münchnone **19** reacts with unsubstituted 1,2-benzoquinone **18**, affording the lactone **20**; evidently the open chain ketene form of münchnone participates in this reaction (Scheme 7).[18]



18 19 20

Scheme 7

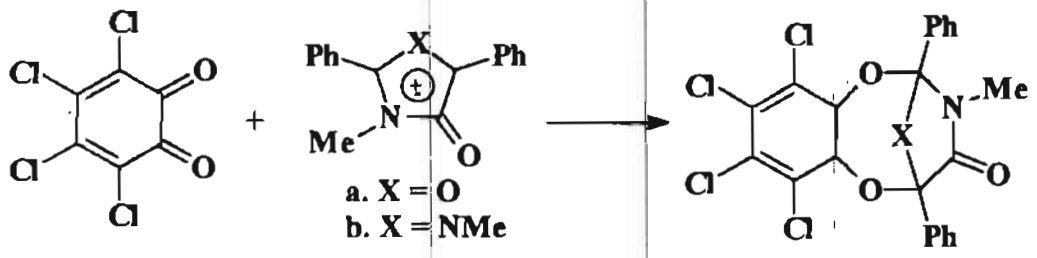
The reaction of münchnone **22** with *o*-chloranil **21** in $CH_3CN$ yielded only the lactone **23**, while the same reactants in benzene afforded **23** and **24** (Scheme 8).[19]



21 22 23 24

Scheme 8

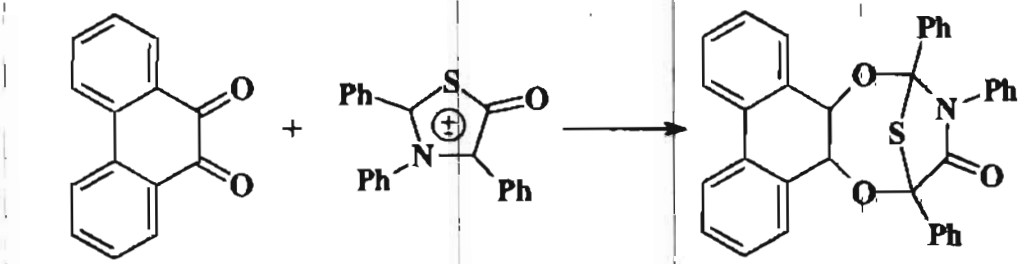
Interestingly, 3-methyl-5-(4-nitrophenyl)-1,3-oxazolium-4-olate **25a** and 1,3-diazolium-4-olate **25b** undergo [4+4] cycloaddition with *o*-chloranil, affording highly oxygenated heterocyclic systems **26(a-b)** (Scheme 9).[20]




**21** **25(a-b)** **26(a-b)**

**Scheme 9**

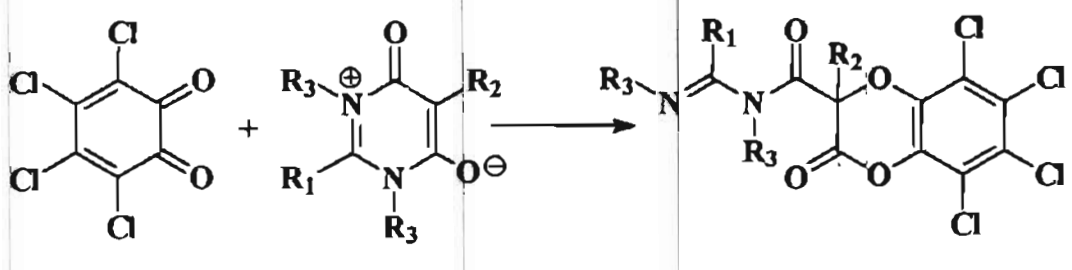
Similar reactivity was observed in the reaction of thioisomünchnone **28** with phenanthrenequinone **27** as shown in Scheme 10.[21]




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

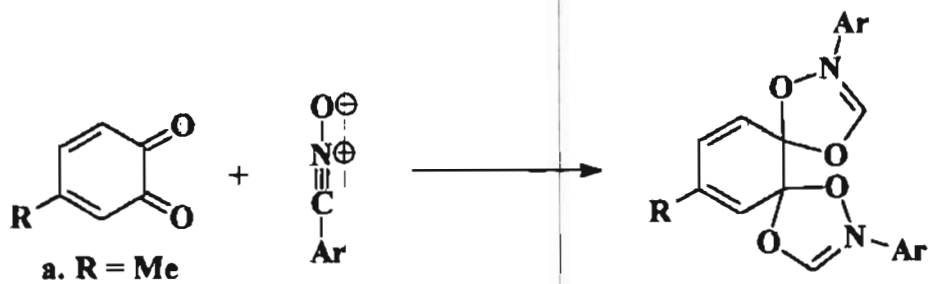
**Scheme 10**

*o*-Chloranil reacts with 1,3-disubstituted-3,6-dihydro-6-oxopyrimidinium-4-olates **30** affording the product **31**. The open chain ketene form of the dipole participates in this reaction (Scheme 11).[22,23]



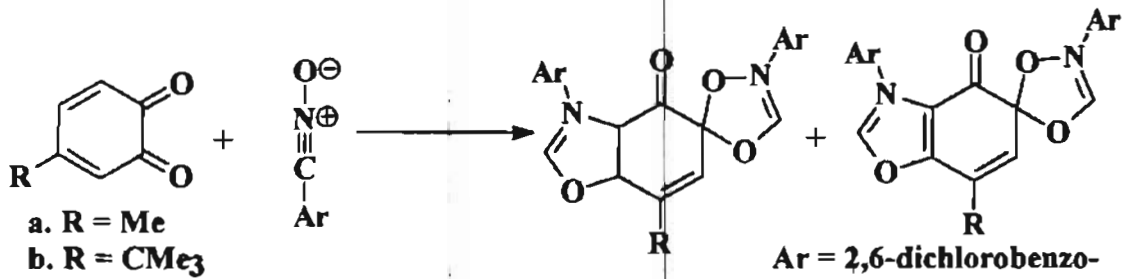

**21** **30** **31**

**Scheme 11**




**Scheme 14**

Reactions of **4(a-b)** with 2,6-dichlorobenzonitrile oxide **37b**, afforded the diadducts **39** and **40** by participation of one of the C=C and C=O bonds (Scheme 15).



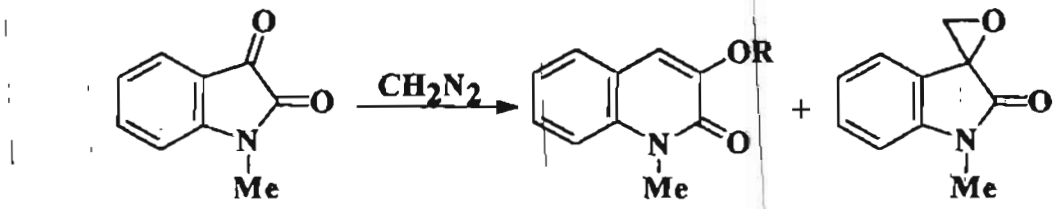

**Scheme 15**

## 1.3 ISATINS

Isatin and its derivatives have been used for the synthesis of a wide variety of compounds with interesting pharmacological activities.[28] Isatin is well known as an inhibitor of alkaline phosphatase activity. N-alkylated isatins act as antimicrobials,[28a] excitatory amino acid antagonists, immunomodulators and anti-cancer drugs,[28b] ulcer inhibitors, acetylcholinesterase inhibitors for the treatment of memory dysfunction, and reversible and competitive inhibitors of monoamine oxidase A and B.

The methods for the preparation of N-alkylated isatins have been reviewed.[29] It appears that reaction of isatins with alkyl halide in DMF in the presence of calcium hydride as a base is the easiest method for the preparation of N-alkyl isatins.[28c]

The reaction of N-methyl isatin with a slight excess of diazomethane has been reported to give the hydroxy quinoline **42a**. With excess of diazomethane, the epoxide **43** was isolated together with the quinolines **42a** and **42b** (Scheme 16).[30]




**41** **42(a-b)** **43**

**Scheme 16**

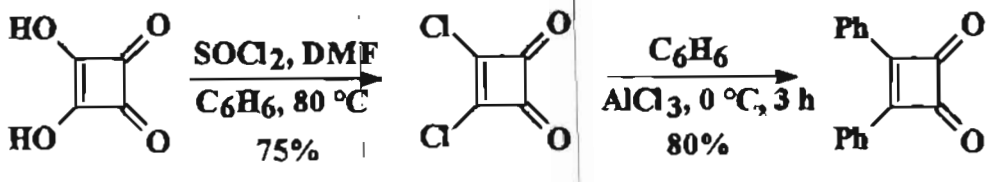
The mechanism of these reactions does not involve a 1,3-dipolar cycloaddition, instead diazomethane acts as a nucleophile, attacking the ketonic carbonyl group of the isatin.

## 1.4 CYCLOBUTENE-1,2-DIONES

1,2-Diones such as squaric acid and its derivatives have attracted considerable attention as versatile C-4 synthons for complex carbocyclic and heterocyclic construction.[31]

3,4-Diphenylcyclobutene-1,2-dione **46** can be readily prepared *via* the dichloride **45** obtainable by treatment of squaric acid **44** with thionyl chloride and a trace amount of N,N-dimethyl formamide. This dichloro

derivative on treatment with anhydrous $AlCl_3$ in benzene afforded the dione **46** (Scheme 17).[32]



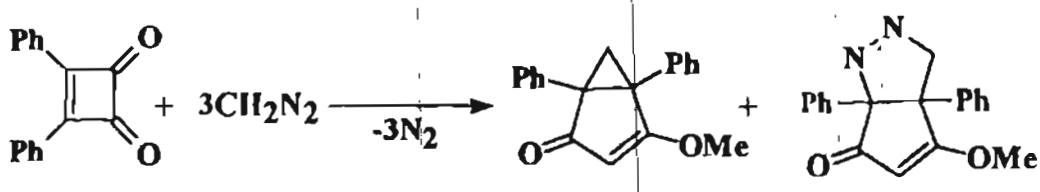

**44** **45** **46**

**Scheme 17**

Although the chemistry of cyclobutenediones has received considerable attention,[33] very little is known about their reactivity towards dipoles, the only known reports being concerned with the reaction of diazomethane and mesitonitrile oxide.

**Reaction with Diazomethane**

3,4-Diphenylcyclobutene-1,2-dione **46** reacts with excess diazomethane to give **47** and **48** (Scheme 18)[34]

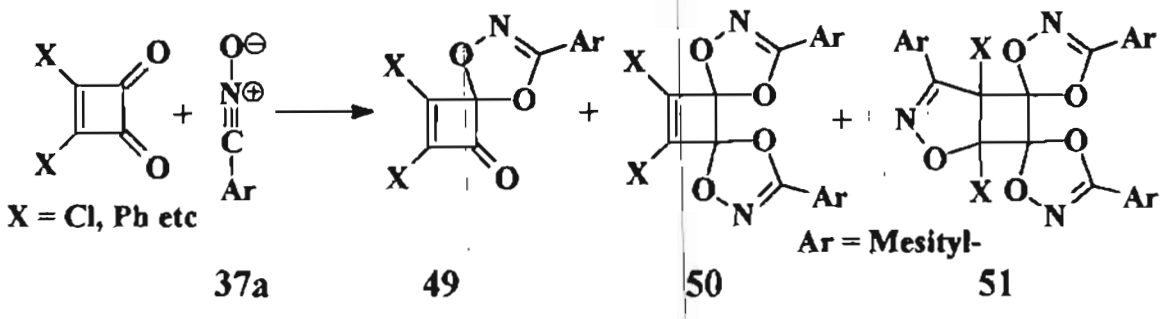



**46** **47** **48**

**Scheme 18**

**Reaction with Nitrile Oxide**

Cyclobutene-1,2-diones, despite their weak dipolarophilic behavior towards benzonitrile oxide, on prolonged heating (30-40 h) with excess mesitonitrile oxide **37a** afforded mono, bis and tris adducts (Scheme 19).[35] Interestingly, the 1,3-dipole preferentially attacks the C=O bond.




37a 49 50 51

**Scheme 19**

## 1.5 THEORETICAL CONSIDERATIONS

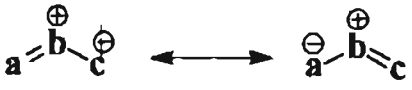
The Woodward-Hoffmann orbital symmetry rules apply only to concerted reactions and are based on the principle that a reaction takes place in such a way as to maintain maximum bonding throughout the course of the reaction.[36a]

The rate of a Diels-Alder reaction is determined largely by the degree of interaction between the highest occupied molecular orbital (HOMO) of one component and the lowest unoccupied molecular orbital (LUMO) of the other. The smaller the energy separation between these orbitals, the more readily the reaction proceeds. Electron withdrawing substituents on the double bond of the dienophile in a normal Diels-Alder reaction facilitate the reaction by lowering the energy of the LUMO and thus decreasing energy separation between LUMO of the dienophile and the HOMO of a given diene. Electron donating substituents on the diene accelerate the reactions by raising the energy level of the HOMO.

### 1,3-Dipolar Cycloaddition Reactions[36b,c]

The 1,3-dipole is defined as a species that is represented by zwitterionic octet structures and undergoes 1,3-cycloaddition to a multiple-bond system, the dipolarophile.

All 1,3-dipoles, in common, have a three atomic π orbital system containing four electrons analogous to an allyl anion. The 1,3-dipoles contain an -onium center atom **b**, whose charge compensates the negative charge distributed in the two all octet structures over the two termini **a** and **c** and the whole system can be considered as a heteroallyl anion, which bears no net charge (Scheme 20).

**Octet structures** 

**Scheme 20**

1,3-Dipolar cycloadditions are single step, four centered, concerted reactions, in which the two new σ bonds are formed simultaneously and are susceptible to electronic and steric influences, which affect the nature of the transition state. This is a 'thermally allowed' process on the basis of the Woodward-Hoffmann rules.

Depending on the relative disposition of 1,3-dipole and dipolarophile, 1,3-dipolar cycloadditions are classified into three types (Figure 3).

1. HOMO-controlled, in which the interaction of the dipole HOMO with dipolarophile LUMO is greatest.
2. Both HOMO and LUMO controlled, which involves large interaction between both frontier orbitals.
3. LUMO-controlled, in which the interaction of the dipole LUMO with the dipolarophile HOMO is greatest.

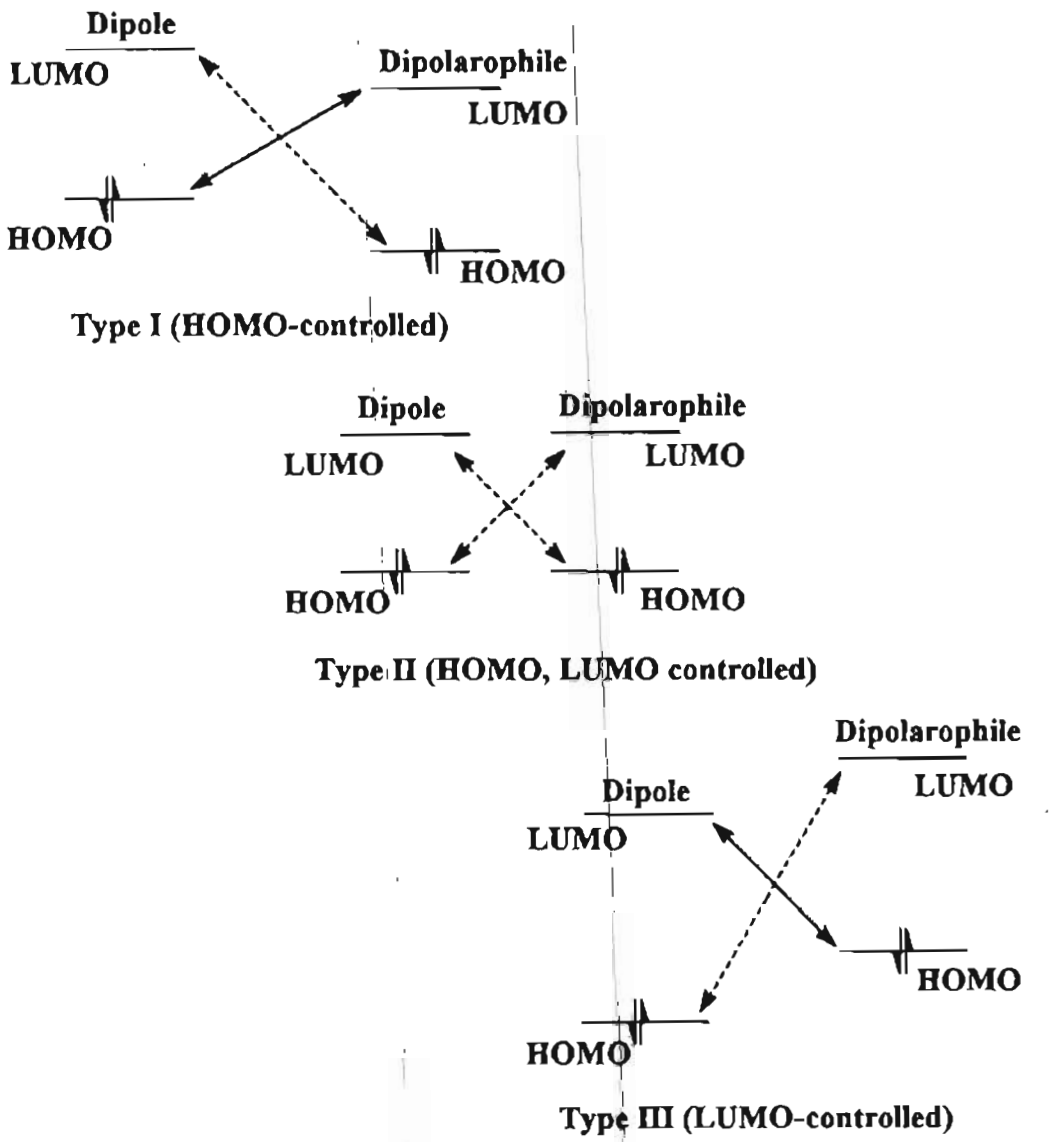
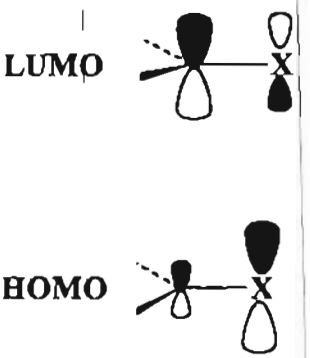



**Figure 3. Sustmann's classification of 1,3-dipolar cycloadditions**

The substituents that raise the dipole HOMO energy or lower the dipolarophile LUMO energy will accelerate HOMO-controlled reactions and decelerate LUMO-controlled reactions. Conversely, substituents, which lower the dipole LUMO energy or raise the dipolarophile HOMO energy, will accelerate LUMO-controlled reactions and decelerate HOMO-controlled reactions. HOMO, LUMO controlled reactions will be accelerated by an increase of either frontier orbital interaction.

The HOMOs and LUMOs of heterodienophiles (Figure 4) will, in general be located at energy levels similar to those of electron deficient dipolarophiles. All 1,3-dipoles have the larger coefficient at the anionic terminus in the HOMO and at the neutral terminus in the LUMO.





**52**

**Figure 4. Frontier orbitals of heterodipolarophiles**

Both of these interactions as well as the better overlap of carbon with carbon than with oxygen or nitrogen lead to preferential formation of **52**.[37] Coulombic and closed shell repulsion effects will also favor the formation of **52**.

## 1.6 STATEMENT OF THE PROBLEM

It is clear from the literature survey presented above that the information available on the dipolar cycloadditions of 1,2-benzoquinones with various dipoles is very limited. Earlier studies in our laboratory have unraveled the novel reactivity patterns of 1,2-benzoquinones towards aryl nitrile oxides.[27] A subject of continuing interest in this area has been the systematic investigation of the dipolar cycloaddition reactions of various 1,2-diones with different dipoles such as carbonyl ylides and azomethine ylides and the author's work in this area constitutes the subject matter of this

thesis. The 1,2-diones selected for our investigations are 1,2-benzoquinones, acenaphthenequinone, isatins and cyclobutene-1,2-diones (Figure 1).

The first phase of the present investigations was mainly concerned with the dipolar cycloaddition reactions of carbonyl ylides with these 1,2-diones. It is noteworthy that the dipolar cycloaddition reactions of carbonyl ylides with 1,2-dicarbonyl compounds have not been previously reported in the literature. The photochemical rearrangement of the cycloadducts resulting from the dipolar cycloaddition reactions of 3,5-di-*tert*-butyl-1,2-benzoquinone with different substituted carbonyl ylides was also investigated.

The second and final phase of the investigations involved the dipolar cycloaddition reactions of azomethine ylides with 1,2-diones.

Details of these studies are presented in the following chapters.

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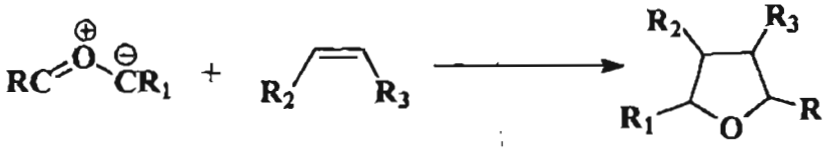
# CHAPTER 2

# DIPOLAR CYCLOADDITION REACTIONS OF CARBONYL YLIDES WITH 1,2-DIONES

## 2.1 INTRODUCTION

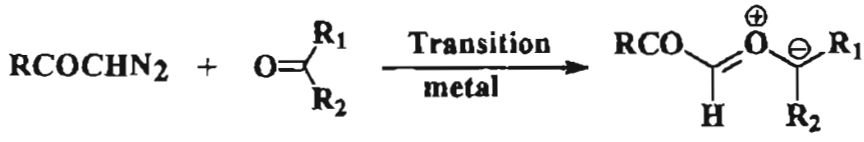
The 1,3-dipolar cycloadditions offer one of the most convergent approaches for the construction of five membered heterocycles.[1] The ease of generation of 1,3-dipoles, coupled with the highly regio and stereoselective nature of their cycloaddition reactions has resulted in a number of syntheses which utilize such a reaction as key step.[2] The stereoselective synthesis of highly substituted oxygen heterocycles, especially structurally complex tetrahydrofurans and tetrahydropyrans, has attracted considerable attention in recent years.[3,4] Conceptually the 1,3-dipolar cycloaddition of carbonyl ylides to π-bonds represents an attractive strategy for tetrahydrofuran formation (Scheme 1).[1]




1 2 3

**Scheme 1**

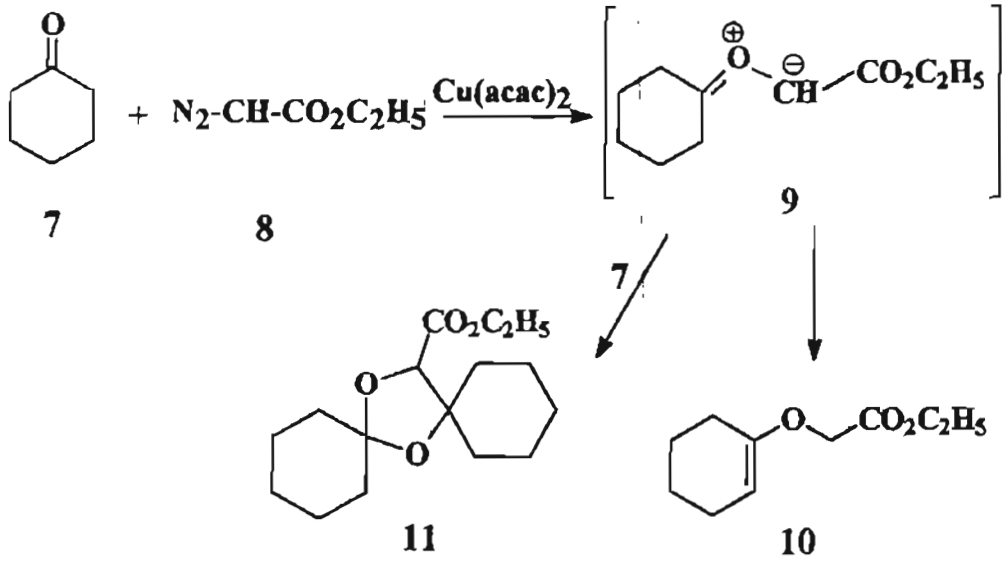
Carbonyl ylides can be generated by a number of methods.[5-10] The transition metal-catalyzed decomposition of an α-diazo ketone **4** in the presence of a carbonyl functionality **5** provides the simplest and the easiest route to these dipoles **6** (Scheme 2).[11-15]




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

**Scheme 2**

The earliest example of the reaction of a carbonyl ylide involves the demonstration by Kharasch that ethyl diazoacetate **8** undergoes decomposition in cyclohexanone to afford the enol ether **10** and the 2:1 adduct **11** of cyclohexanone and ethoxycarbonylcarbene (Scheme 3).[16]

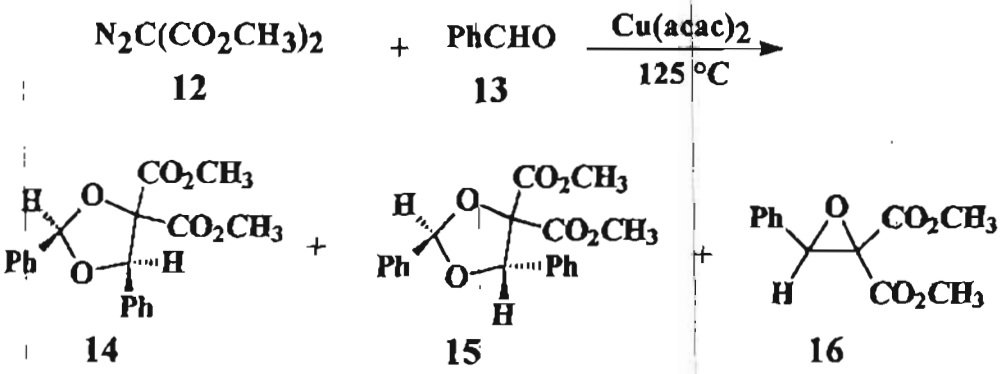



**7** **8** **9**

**11** **10**

**Scheme 3**

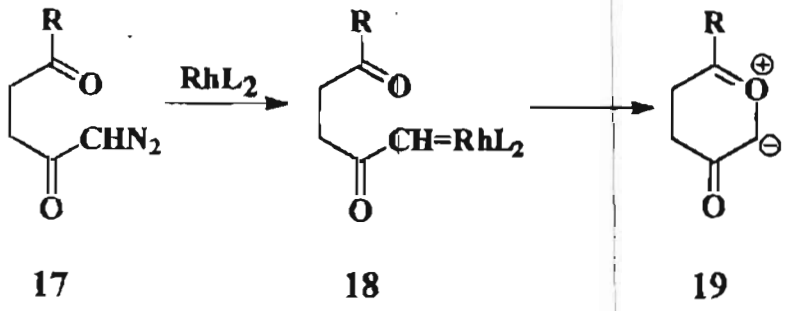
Copper-catalyzed decomposition of dimethyl diazomalonate in the presence of excess benzaldehyde, leads to the formation of two diastereomeric dioxolanes **14** and **15**, and the epoxide **16** (Scheme 4).[16c,d]




**Scheme 4**

Among all the catalysts that have been developed for carbene addition to π bonds, rhodium(II) carboxylates are the most effective for bimolecular reactions that employ diazo carbonyl compounds.[17] In general, the reactions can be carried out under mild conditions, often at 10 °C and the products are obtained in high yields.[18,19]

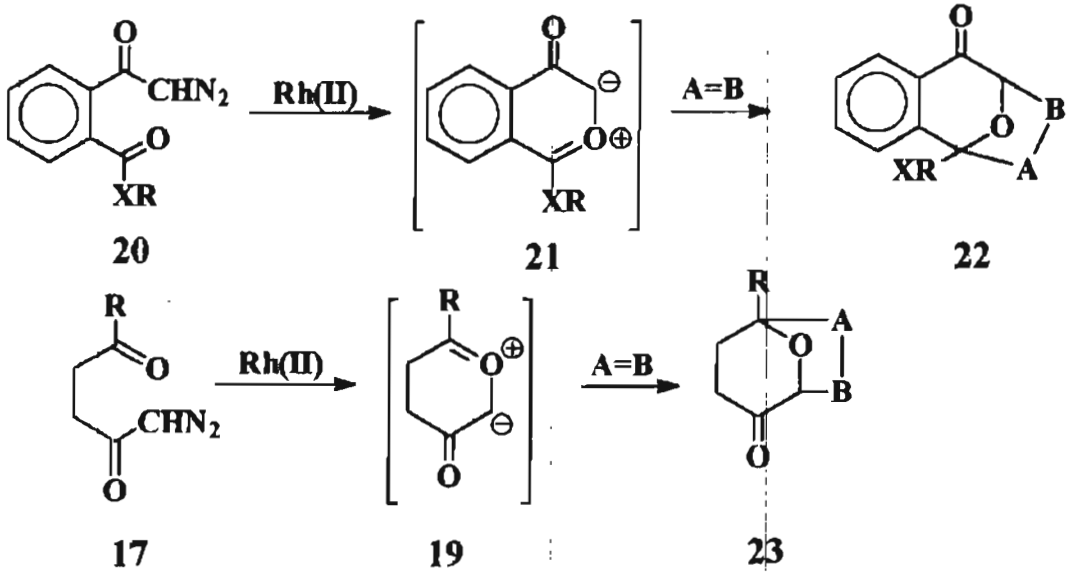
The rhodium(II) catalyzed decomposition of diazo carbonyl compounds is believed to involve a metallo-carbenoid intermediate **18** which retains the highly electrophilic properties associated with free carbenes.[20,21] Therefore, in an appropriate acyclic substrate, such an intermediate can be intercepted intramolecularly by the nonbonding electrons on the neighboring carbonyl to effect overall cyclization (Scheme 5).




**Scheme 5**

The two types of diazo ketones, which can undergo tandem cyclization-cycloaddition chemistry,[22] are shown in Scheme 6. First one

involves systems in which the diazo ketone and the remote carbonyl are attached in a 1,2-fashion on a benzene ring **20**.[23] This arrangement provides interatomic distances and bond angles that are ideal for dipole formation and the second system involves the 1-diazo-2,5-pentanedione backbone as the target.[24,25] With this system, the ylide **19** was formed by reaction of the less nucleophilic ketonic carbonyl on the rhodium carbenoid center. The tether utilized corresponds to a simple dimethylene chain, which introduces a certain conformational flexibility not available to the more rigid benzo systems.



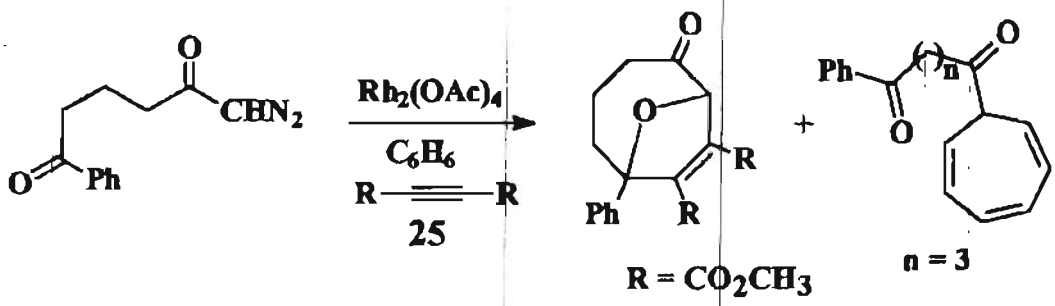

**Scheme 6**

The carbonyl ylides generated by the tandem intramolecular carbenoid-carbonyl cyclizations are known to react with both external and internal dipolarophiles including acetylenic and olefinic dipolarophiles, such as dimethyl acetylenedicarboxylate and N-phenylmaleimide.[25]

An attractive feature of the above tandem cyclization-cycloaddition process is the opportunity to control the stereochemistry of the product at several centers. The final product represents a highly functionalized rigid

bicyclic system that is amenable to subsequent synthetic elaboration. Application of this methodology to the synthesis of natural products is well established.[26-29]

Padwa has reported the formation of a seven membered carbonyl ylide intermediate,[30] where the connecting chain contains three methylene units. The rhodium(II) acetate catalyzed reaction of 1-diazo-6-phenyl-2,6-hexanedione **24** with dimethyl acetylenedicarboxylate **25** afforded a 2:1 mixture of products. The major product corresponds to the expected cycloadduct **26** (45%) whereas the minor component is identified as the cycloheptatriene **27** (22%) (Scheme 7).

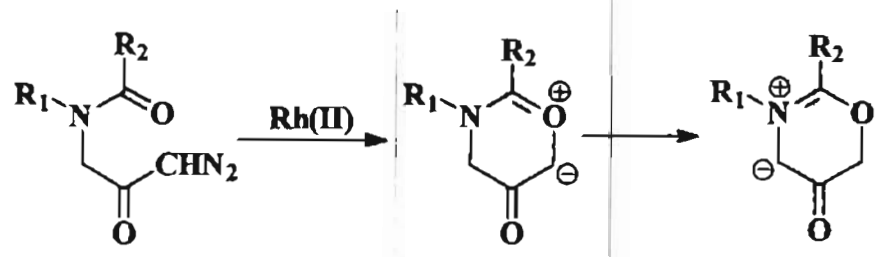



**24** **26** **27**

**Scheme 7**

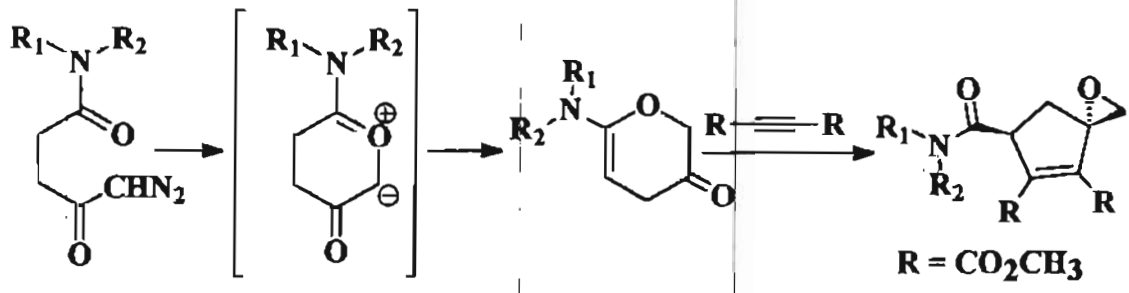
The formation of a mixture of products indicates that extending the tether to three methylene groups sufficiently retards the rate of intramolecular cyclization so as to allow the bimolecular reaction with benzene to occur. The minor component **27** is derived from a bimolecular addition of the rhodium carbenoid on to benzene, followed by ring tautomerization.

Padwa has also reported a 'dipole cascade process' which interconverts α-diazo ketones **28** to azomethine ylides **30** *via* the intermediacy of carbonyl ylides **29** (Scheme 8).[31]




**Scheme 8**

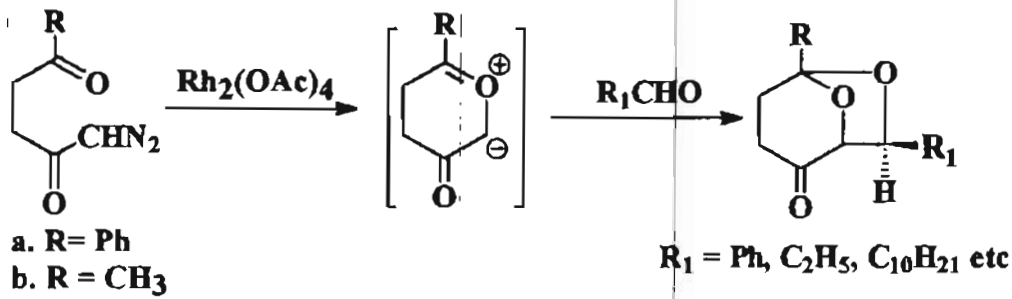
Rh(II) acetate catalyzed transformation of the closely related α-diazo ketoamide **31** to the ylide **32** and its cycloaddition to dimethyl acetylenedicarboxylate was also reported (Scheme 9).[32]




**Scheme 9**

**Cycloaddition with Aldehydes**

There is only one report on the trapping of this transient dipole with carbonyl compounds such as aldehydes (Scheme 10).[33]




**Scheme 10**

In the case of **17b**, trace amount of higher order cyloadduct derived by further dipolar cycloaddition of the carbonyl ylide across the keto group of the initially formed 1:1 cycloadduct was also formed.

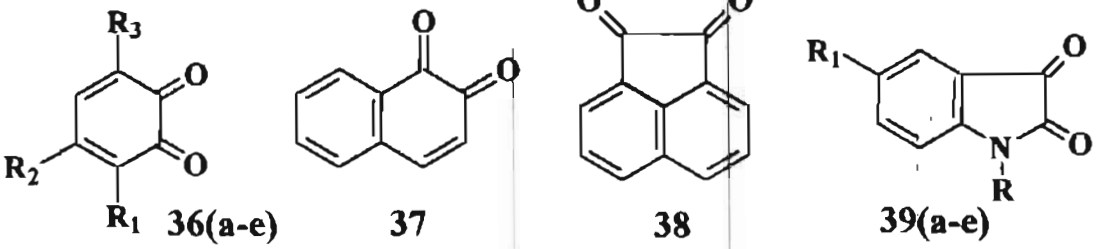
### 2.1.1 The Present Work

It is noteworthy that, although Padwa has studied the reactions of carbonyl ylides with electron rich and electron deficient dipolarophiles including benzaldehyde and alkyl aldehydes, there has been no work on the addition of carbonyl ylides to 1,2- and 1,4-diones.

Against the literature background presented above and in the context of the general interest in the chemistry of 1,2-diones,[34] especially their reactivity towards dienes, dienophiles and dipoles, it was obligatory to explore the cycloaddition reactions of carbonyl ylide dipoles with various 1,2-diones.

We have undertaken a detailed investigation of the cycloaddition reactions of various 1,2-diones such as substituted 1,2-benzoquinones, acenaphthenequinone and isatins with different carbonyl ylides and our results are discussed in this chapter. Preliminary results of our studies on the cycloaddition reactions of carbonyl ylide with a 1,4-dione are also presented.

The 1,2-diones and the α-diazo ketones selected for our investigations are shown in Figures 1 and 2 respectively.

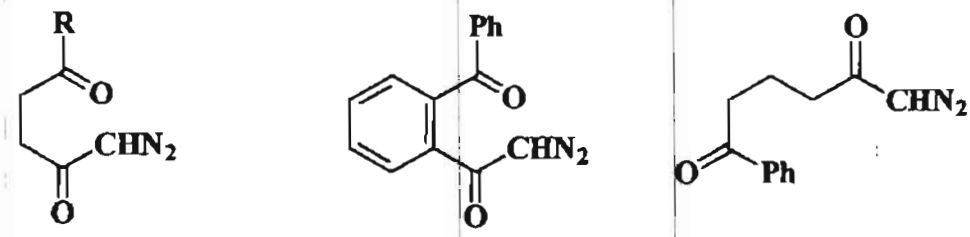


36(a-e) 37 38 39(a-e)

a. $R_1$ = H, $R_2$ = $R_3$ = $CMe_3$
b. $R_1$ = OMe, $R_2$ = $R_3$ = $CMe_3$
c. $R_1$ = OMe, $R_2$ = $CMe_3$, $R_3$ = H
d. $R_1$ = $R_3$ = H, $R_2$ = $CMe_3$
e. $R_1$ = OMe, $R_2$ = $R_3$ = $CHPh_2$

a. R = Ph, $R_1$ = H
b. R = Bn, $R_1$ = H
c. R = $CH_3$, $R_1$ = H
d. R = $R_1$ = H
e. R = H, $R_1$ = Br

**Figure 1**



17(a-e) 40 24

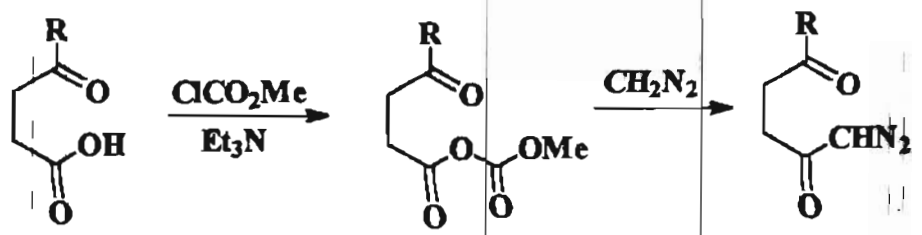
a. R = Ph
b. R = $CH_3$
c. R = $(C_5H_5)_2Fe$
d. R = *p*-$C_6H_4$-$CH_3$
e. R = *p*-$C_6H_4$-$OCH_3$

**Figure 2**

## 2.2 RESULTS AND DISCUSSION

### 2.2.1 Dipolar Cycloaddition Reactions of Carbonyl Ylides with 1,2-Benzoquinones

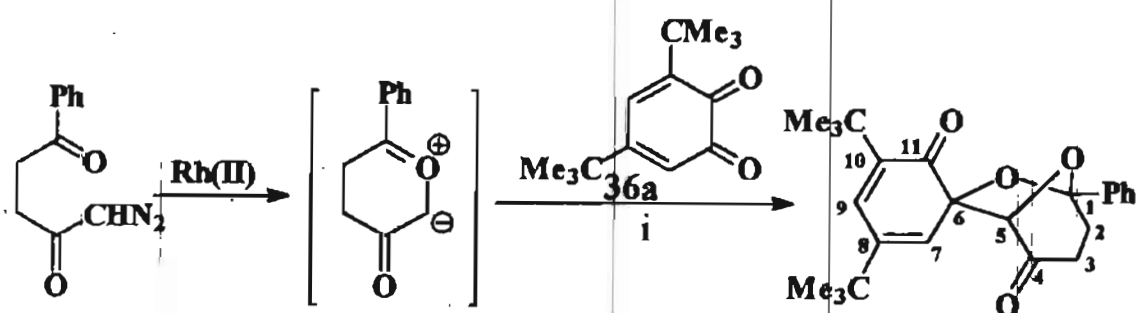
The diazo ketones required for our investigations were conveniently prepared from the corresponding carboxylic acids by the known procedure (Scheme 11).[33]



41 42 17

**Scheme 11**

*Our studies were initiated with the Rh(II) acetate catalyzed* cycloaddition reaction of 1-diazo-5-phenyl-2,5-pentanedione **17a** with 3,5-di-*tert*-butyl-1,2-benzoquinone **36a**. This reaction proceeded smoothly to afford a yellow crystalline product **43** in 76% yield (Scheme 12).[35]



**17a** **19a** **43 (76%)**

**i. Toluene, Argon, RT, 30 min**

**Scheme 12**

The structure of the product was assigned on the basis of spectral data. The IR spectrum of **43** showed two strong bands at 1735 and 1708 $cm^{-1}$ due to C-4 and C-11 carbonyls respectively. In the $^1H$ NMR spectrum, the phenyl protons appeared as a multiplet centered at δ 7.57. The C-7 proton resonated as a doublet at 5.85 (1H, $J$ = 2.1 Hz) and the C-9 proton appeared as a doublet at δ 6.76 (1H, $J$ = 2.1 Hz) due to allylic coupling. The bridgehead proton on C-5 appeared as a singlet at δ 4.58. The methylene protons

resonated as a multiplet centered at δ 2.54. The singlets at δ 1.18 and 1.11 were assigned to the two *tert*-butyl groups. In the $^{13}C$ NMR spectrum, the two carbonyl signals were observed at δ 201.85 and 199.33 and signals due to the two bridgehead carbons C-1 and C-5 appeared at δ 110.51 and 82.08 respectively. The characteristic spiro carbon C-6 was discernible at δ 87.90. All the other signals were in agreement with the proposed structure. Satisfactory elemental analysis was also obtained. Finally the structure assigned was confirmed unequivocally by single crystal X-ray determination (Figure 3).

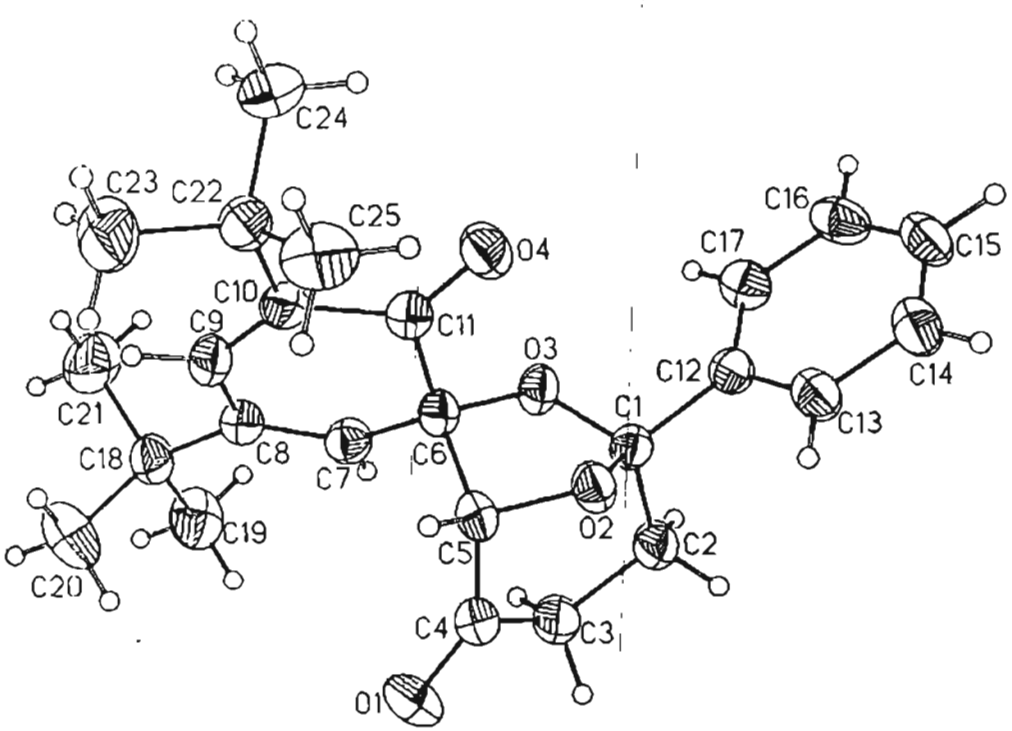
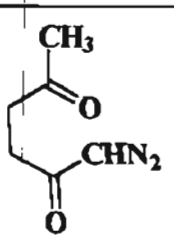
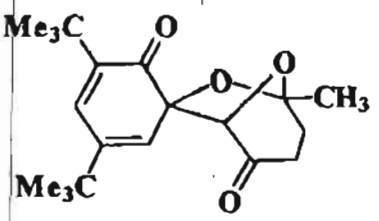
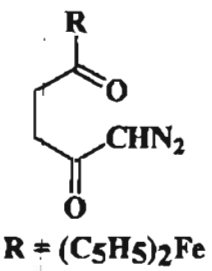
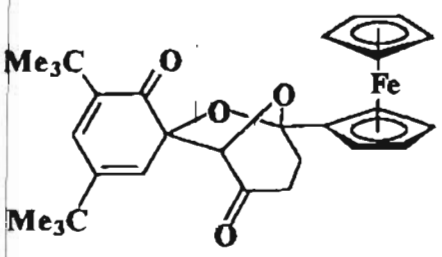
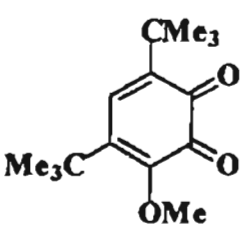
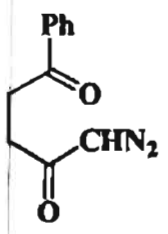
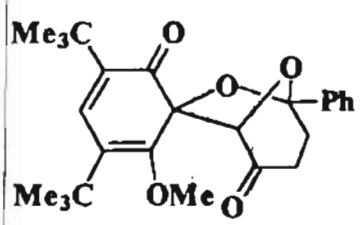
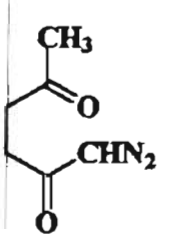
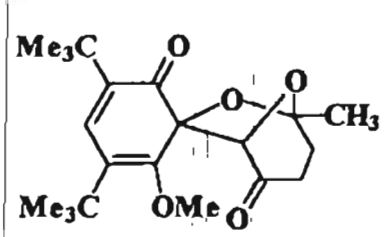



**Figure 3. X-ray crystal structure of 43**

Similarly **36a** and 3-methoxy-4,6-di-*tert*-butyl-1,2-benzoquinone **36b** underwent facile cycloaddition with other substituted diazo ketones, yielding the spiro acetals (**44-47**). The results obtained are summarized in Table 1.

**Table 1**. Cycloaddition reactions of carbonyl ylides with *o*-quinones **36(a-b)**

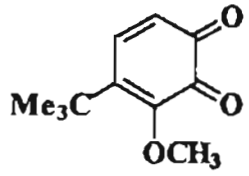
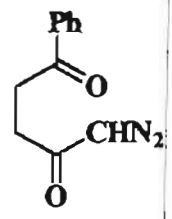
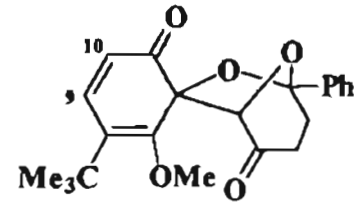
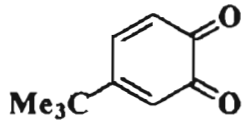
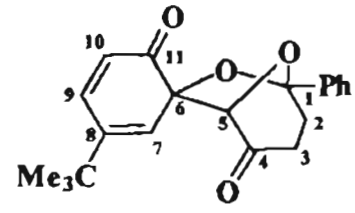
| Entry | 1,2-Benzoquinone | Diazo ketone | Product | Yield (%)[a] |
|---|---|---|---|---|
| 1 |  **36a** |  **17b** |  **44** | 53 |
| 2 | |  $R = (C_5H_5)_2Fe$ **17c** |  **45** | 42 |
| 3 |  **36b** |  **17a** |  **46** | 63 |
| 4 | |  **17b** |  **47** | 48 |

Reaction conditions: $Rh_2(OAc)_4$, Toluene, Argon, RT, 30 min., [a]Isolated yield.

The cycloadducts (**44-47**) were characterized by spectroscopic methods. All these compounds showed two carbonyl absorptions each in the IR spectrum and they showed typical proton and carbon signals in the $^1H$ and $^{13}C$ NMR spectra.

Reactions of 3-methoxy-4-*tert*-butyl-1,2-benzoquinone **36c** and 4-*tert*-butyl-1,2-benzoquinone **36d** with the diazo ketone **17a** furnished similar spiro oxabicyclic derivatives. The results are given in Table 2.

**Table 2**. Cycloaddition reactions of carbonyl ylide with *o*-quinones **36(c-d)**

| Entry | 1,2-Benzoquinone | Diazo ketone | Product | Yield (%)[a] |
|---|---|---|---|---|
| 1 |  **36c** |  **17a** |  **48** | 48 |
| 2 |  **36d** | |  **49** | 55 |

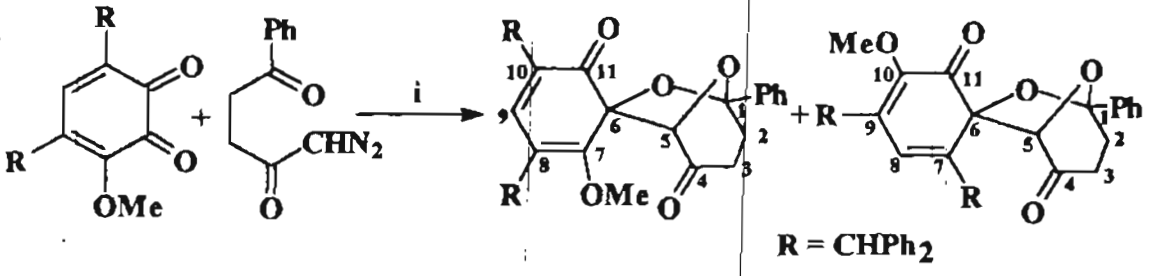
Reaction conditions: $Rh_2(OAc)_4$, Toluene, Argon, RT, 30 min. [a]Isolated yield.

The structure of the product in each case was ascertained from the spectral data. The IR spectrum of **48** showed two carbonyl absorptions at 1732 and 1682 $cm^{-1}$. Compound **48** showed typical $^1H$ and $^{13}C$ NMR signals as in **43**. The doublets at δ 6.79 (1H, $J$ = 7.3 Hz) and 5.33 (1H, $J$ = 7.3 Hz) were assigned to the C-9 and C-10 protons respectively. The two carbonyl carbons resonated at δ 205.92 and 195.81 in the $^{13}C$ NMR spectrum. The signal due to the spiro carbon was discernible at δ 88.98. Cycloadduct **48** gave satisfactory elemental analysis also.

In the IR spectrum of **49**, the two carbonyls absorbed at 1735 and 1691 $cm^{-1}$. In the $^1H$ NMR spectrum, the bridgehead proton appeared as a

singlet at δ 4.57. The olefinic proton on C-9 displayed a double doublet at δ 7.05 (1H, $J$ = 2.3 Hz and 10.2 Hz) whereas the C-7 and C-10 protons resonated as separate doublets at δ 5.90 (1H, $J$ = 2.0 Hz) and 6.02 (1H, $J$ = 10.2 Hz) respectively. The $^{13}C$ NMR spectrum showed two signals at δ 201.39 and 198.25 corresponding to C-4 and C-11 carbonyl groups respectively.

3-Methoxy-4,6-bis(1,1-diphenylmethyl)-1,2-benzoquinone **36e** on treatment with the diazo ketone **17a** in the presence of Rh(II) afforded a mixture of regioisomers in 77% yield (Scheme 13).




**36e** **17a** **50** 77% (1:1.1) **51**

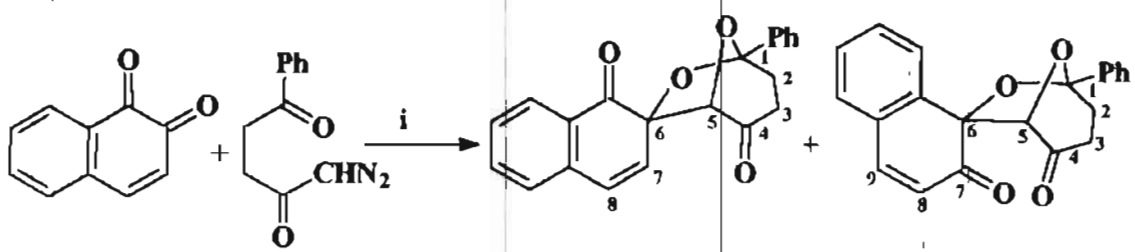
**i. $Rh_2(OAc)_4$, Toluene, Argon, RT, 30 min**

**Scheme 13**

The products were separated by silica gel column chromatography and characterized by spectral data. The IR spectrum of **50** showed two strong bands at 1732 and 1675 $cm^{-1}$ due to the C-4 and the C-11 carbonyl groups respectively. In the $^1H$ NMR spectrum, the bridgehead proton resonated as a singlet at δ 4.70. The signal due to the methoxy protons appeared as a sharp singlet at δ 3.13. The singlet at 6.42 is due to the C-9 proton. The $^{13}C$ NMR spectrum with resonance signals at δ 204.78 and 196.58 also revealed the presence of two carbonyls.

The IR spectrum of **51** showed two strong bands at 1739 and 1695 $cm^{-1}$ due to the C-4 and C-11 carbonyl groups respectively. In the $^1H$ NMR spectrum, the C-8 proton resonated as a singlet at δ 6.29. The signal due to the bridgehead proton appeared as a singlet at δ 4.38 and the methoxy protons at δ 3.67. The $^{13}C$ NMR spectrum also showed the presence of two carbonyl groups at δ 203.82 and 195.99.

A similar reaction was observed with 1,2-naphthoquinone **37** and the carbonyl ylide **17a** leading to the mixture of regioisomers **52** and **53** in 45% yield (Scheme 14). The major product isolated was the cycloadduct **53** (39%).




**37** **17a** **52** (45%) **53**

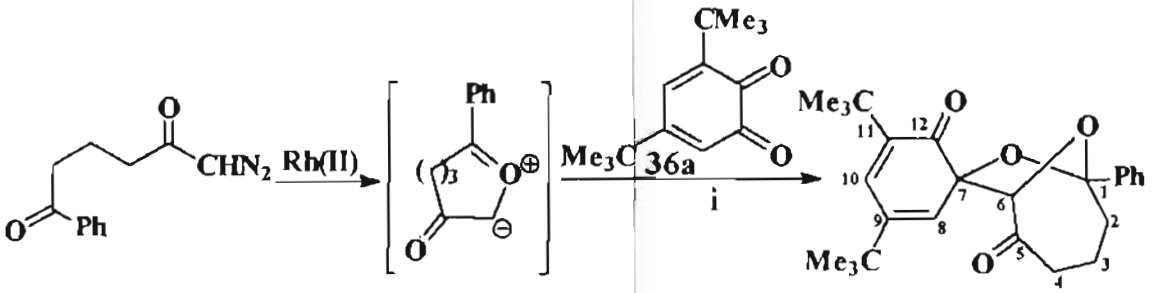
**i. $Rh_2(OAc)_4$, Toluene, Argon, RT, 40 min**

**Scheme 14**

The IR spectrum of **52** showed two carbonyl absorptions at 1729 and 1688 $cm^{-1}$. In the $^1H$ NMR spectrum, the bridgehead proton resonated as a singlet at δ 4.51. The C-7 and C-8 protons appeared as doublets at δ 6.11 (1H, $J$ = 9.8 Hz) and 6.52 (1H, $J$ = 9.8 Hz) respectively. In the $^{13}C$ NMR spectrum, the C-4 carbonyl was visible at δ 203.83 and the other carbonyl at 190.40. The signals due to the two methylene carbons C-2 and C-3 were discernible at δ 33.43 and 34.57 respectively. All the other signals were in agreement with the proposed structure.

The IR spectrum of **53** showed two carbonyl absorptions at 1731 and 1694 $cm^{-1}$. In the $^1H$ NMR spectrum, the bridgehead proton resonated as a singlet at δ 4.52. The C-8 and C-9 protons resonated as doublets at δ 6.07 (1H, $J$ = 9.9 Hz) and 6.71 (1H, $J$ = 9.9 Hz) respectively. In the $^{13}C$ NMR spectrum, the two carbonyls C-4 and C-7 resonated at δ 201.17 and 195.96 respectively.

Subsequent to the above investigations, we turned our attention to the generation of a seven membered carbonyl ylide and its reactivity towards 1,2-benzoquinones. Treatment of the diazo ketone **24** with 3,5-di-*tert*-butyl-1,2-benzoquinone **36a** in the presence of Rh(II) acetate resulted in the formation of a yellow solid **55** in 37% yield. Trace amount of 3,5-di-*tert*-butyl-catechol was also observed in the reaction mixture (Scheme 15).




**24** **54** **55** (37%)

**i. Benzene, Argon, RT, 60 min**

**Scheme 15**

The structure of the adduct **55** was elucidated by spectroscopic methods. The IR spectrum of **55** showed two carbonyl absorptions at 1708 and 1695 $cm^{-1}$. In the $^1H$ NMR spectrum, the C-8 and C-10 protons appeared as doublets at δ 5.69 (1H, $J$ = 2.0 Hz) and 6.70 (1H, $J$ = 2.0 Hz) respectively. The singlet at δ 4.53 was assigned to the bridgehead proton. In the $^{13}C$ NMR spectrum, the two carbonyl signals were visible at δ 210.89 and 198.89. The

presence of three methylene carbons has been confirmed by DEPT-135 NMR experiments. All the other signals were in agreement with the assigned structure.

## 2.2.2 Theoretical Calculations

In order to explain the observed mode of cycloaddition and regioselectivity in the above reactions, we have carried out some AM1 calculations using PC SPARTAN Graphical Interface Package for Molecular Mechanics and Molecular Orbital Models.[36] The correlation diagram for the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone **36a** with the carbonyl ylide **17a** is illustrated as an example in Figure 4.

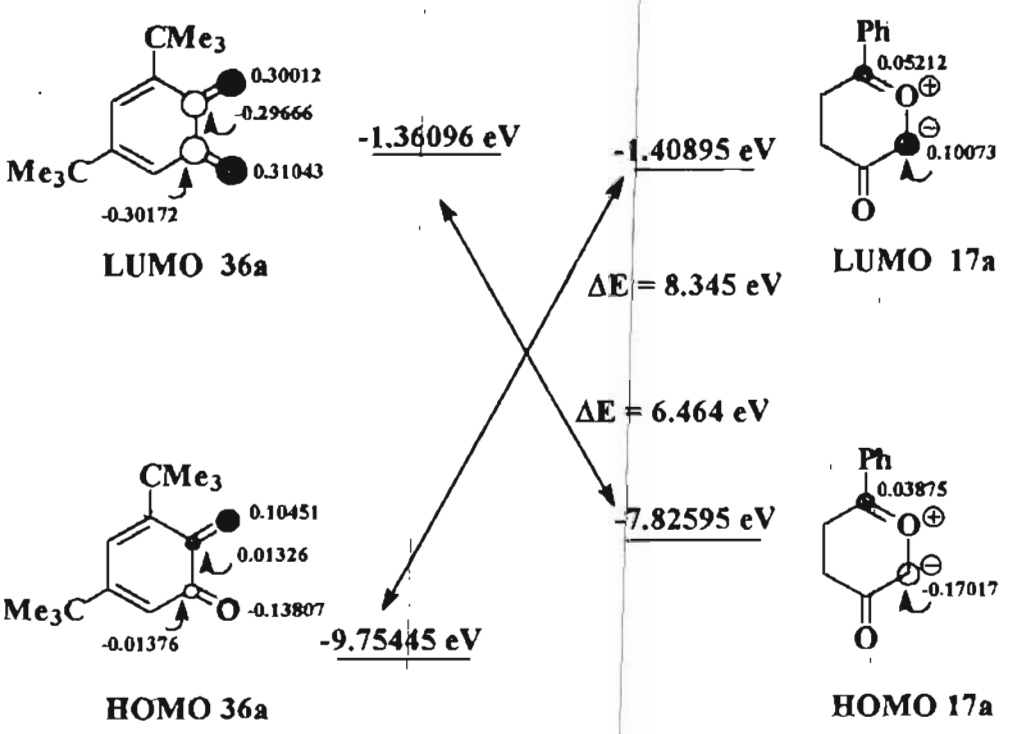


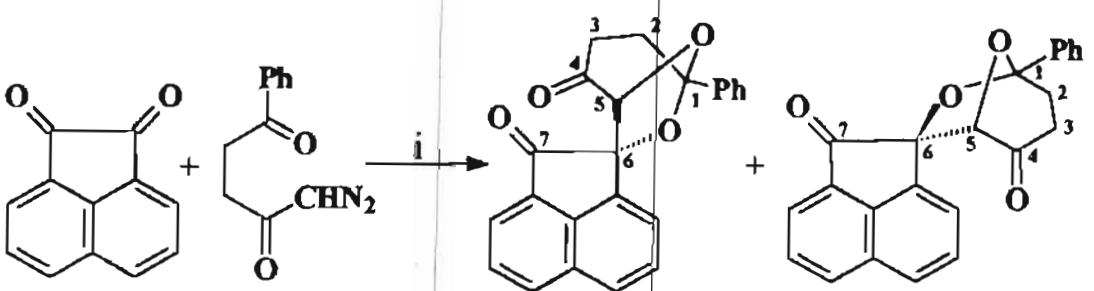

**Figure 4**. Molecular orbital correlation diagrams of 3,5-di-*tert*-butyl-1,2-benzoquinone **36a** and the carbonyl ylide **17a**.

Frontier molecular orbital theory correctly rationalizes the regiochemistry of the product in this 1,3-dipolar cycloaddition. The most

favorable FMO interaction is between the HOMO of the dipole and the LUMO of the dipolarophile. The HOMO(**36a**)-LUMO(**17a**) interaction is unimportant due to large energy gap.

## 2.2.3 Dipolar Cycloaddition Reactions of Carbonyl Ylides with Acenaphthenequinone

In the second phase of our investigations, cycloaddition of carbonyl ylides with acenaphthenequinone was undertaken. Acenaphthenequinone **38** on treatment with the diazo ketone **17a**, derived from 3-benzoyl propionic acid in the presence of a catalytic amount of Rh(II) acetate at room temperature under argon atmosphere underwent facile cycloaddition to afford a mixture of isomers **56** and **57** in the ratio 1.3:1 (Scheme 16). These were separated by silica gel column chromatography.




**38** **17a** **56** 67% (1.3:1) **57**

**i. $Rh_2(OAc)_4$, Toluene, Argon, RT, 3 h**

**Scheme 16**

The products were characterized on the basis of spectral data. The IR spectrum of **56** showed a strong band at 1730 $cm^{-1}$ due to overlapping of the C-4 and C-7 carbonyl groups. In the $^1H$ NMR spectrum, the bridgehead proton on C-5 resonated as a singlet at δ 4.54. In the $^{13}C$ NMR spectrum, the signals due to the two carbonyls C-4 and C-7 appeared at δ 202.34 and

198.25 respectively. The characteristic spiro carbon signal was discernible at δ 86.79. The two bridgehead carbons C-1 and C-5 resonated at δ 111.22 and 87.60 respectively. All the other signals were in agreement with the assigned structure. Finally the structure was confirmed unambiguously by single crystal X-ray structure determination (Figure 5).

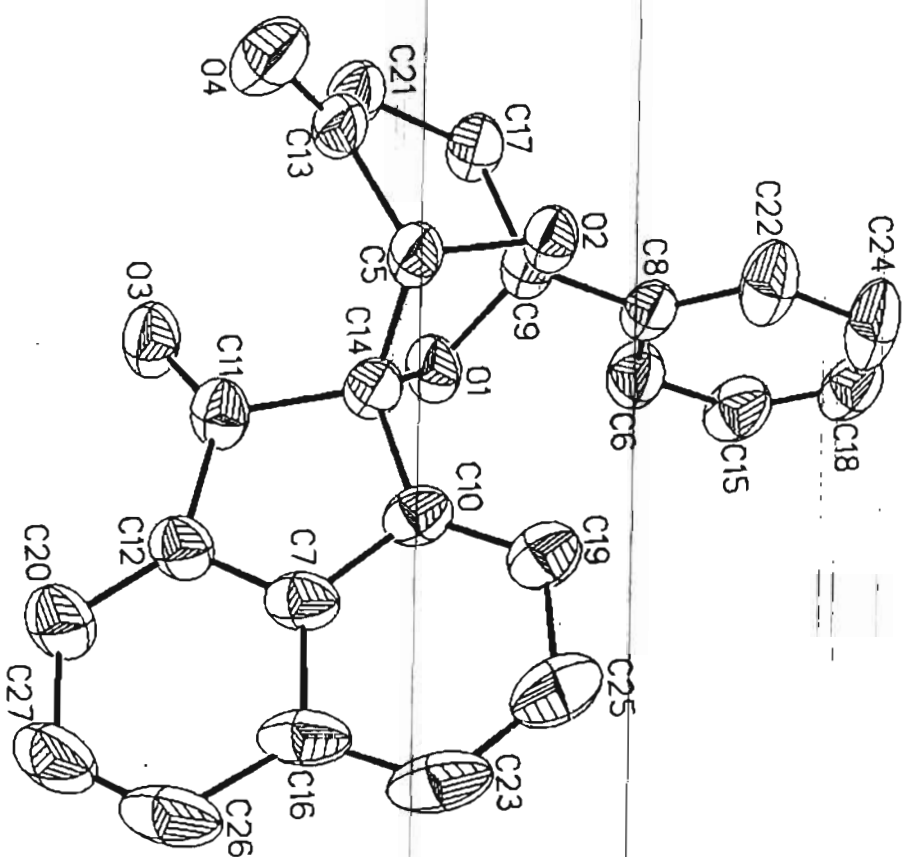



**Figure 5. X-ray crystal structure of 56**

The IR spectrum of **57** showed strong band at 1730 $cm^{-1}$ due to overlapping of the two carbonyl groups. In the $^{1}H$ NMR spectrum, the bridgehead proton on C-5 appeared as a singlet at δ 4.63. The signal due to the four methylene protons appeared as separate multiplets centered at 2.85 and 2.71, integrating for two protons each. In the $^{13}C$ NMR spectrum, the

two carbonyls resonated at δ 202.72 and 199.36 and the bridgehead carbons were discernible at δ 110.51 and 85.25. The spiro carbon displayed a characteristic signal at δ 98.12 and the two methylene carbons were visible at δ 33.90 and 33.56. Final proof for the stereochemistry of the cycloadduct **57** was obtained by single crystal X-ray analysis (Figure 6).

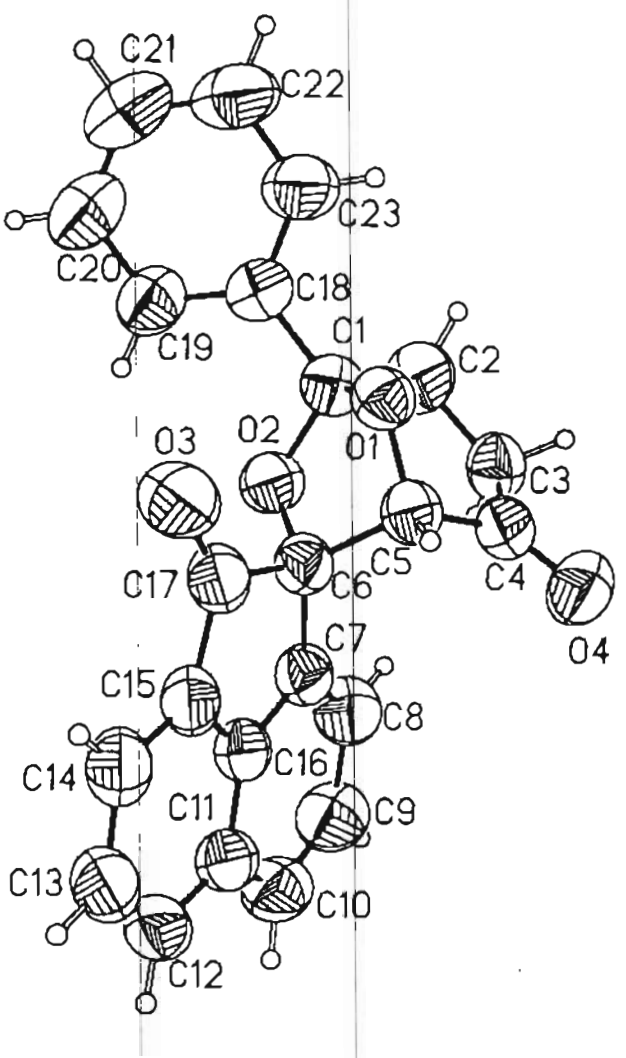
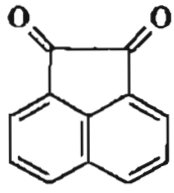
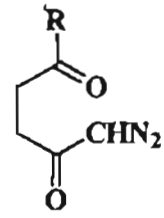
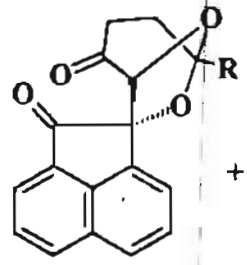
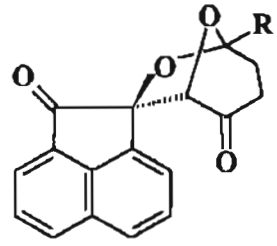
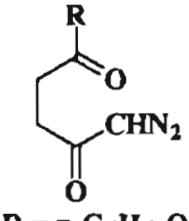
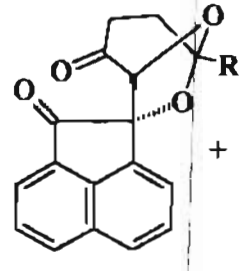
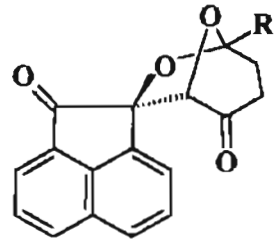



**Figure 6. X-ray crystal structure of 57**

Similarly, acenaphthenequinone underwent smooth cycloaddition with other substituted diazo ketones yielding the spiro oxobicyclic derivatives in good yields. These results are summarized below (Table 3).

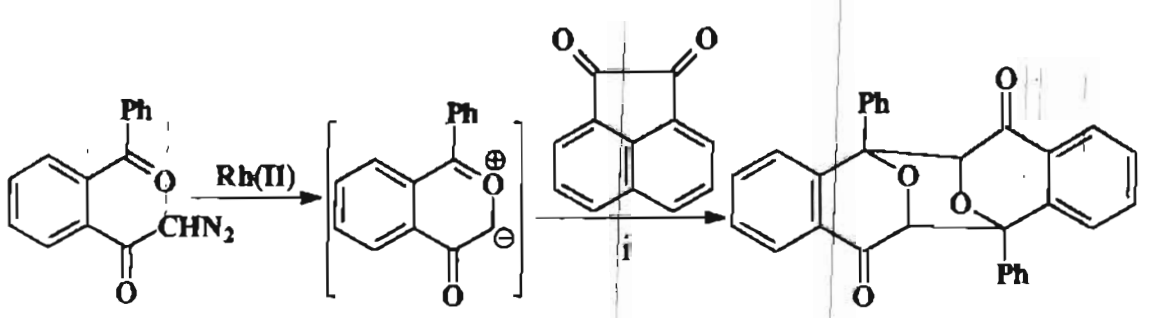
**Table 3**. Cycloaddition reactions of carbonyl ylides with **38**

| Entry | 1,2-Dione | Diazo ketone | Products | Yield (%)[a] |
|---|---|---|---|---|
| 1 |  **38** |  R = *p*-$C_6H_4$-$CH_3$ **17d** |  **58** +  **59** | 68 (2.8:1) |
| 2 |  **38** |  R = *p*-$C_6H_4$-$OCH_3$ **17e** |  **60** +  **61** | 61 (1:1.6) |

Reaction conditions: $Rh_2(OAc)_4$, Toluene, Argon, RT, 3 h. [a]Isolated yield.
Ratio of isomers are given in paranthesis.

The cycloadducts **58-61** showed spectroscopic data comparable to those of **56** and **57**.

Attempted reaction between the diazo ketone **40** and acenaphthenequinone in the presence of Rh(II) acetate did not succeed; a dimer **63** derived from head-to-tail coupling of the transient carbonyl ylide dipole together with unreacted acenaphthenequinone was isolated from this reaction (Scheme 17). As expected, the blank reaction also gave the dimer **63**.




**40** **62** **63** (84%)

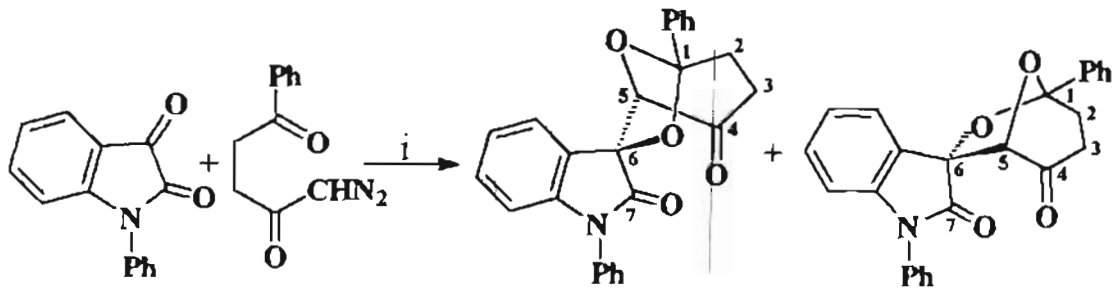
**i. Toluene, Argon, RT, 3 h**

**Scheme 17**

The product was characterized on the basis of spectral data. The IR spectrum of **63** showed strong carbonyl absorption at 1701 $cm^{-1}$. In the $^1H$ NMR spectrum, the bridgehead protons resonated as a sharp singlet at δ 4.23. In the $^{13}C$ NMR spectrum, the signal due to the carbonyl group appeared at δ 197.82. Satisfactory elemental analysis was also obtained.

## 2.2.4 Dipolar Cycloaddition Reactions of Carbonyl Ylides with Isatins

Subsequently, we focused our attention on the cycloaddition profile of carbonyl ylide with isatin. 1-phenylisatin **39a** when treated with the diazo ketone **17a** and a catalytic amount of Rh(II) acetate in dry toluene at ambient temperature under argon atmosphere for 3 h afforded the adduct **64** in 75% yield along with <10% of **65** (Scheme 18).



**39a** **17a** **64** (75%) **65** (<10%)

**i. $Rh_2(OAc)_4$, Toluene, Argon, RT, 3 h**

**Scheme 18**

The products were separated by silica gel column chromatography and characterized by spectral analysis. The IR spectrum of **64** showed a strong band at 1733 $cm^{-1}$ due to overlapping of the C-4 and C-7 carbonyl groups. In the $^1H$ NMR spectrum, the bridgehead proton resonated as a singlet at δ 4.63. One of the four methylene protons appeared as a separate multiplet in the region δ 3.38 while the other three protons were discernible as multiplet centered at 2.61. In the $^{13}C$ NMR spectrum of **64**, the spiro carbon signal appeared at 83.04. The C-4 carbonyl was observed at δ 202.40 and the lactam carbonyl at δ 171.04. The bridgehead carbons C-1 and C-5 resonated at δ 109.77 and 87.61 respectively. The two methylene carbons C-2 and C-3 gave signals at δ 33.73 and 35.55 respectively. Finally the structure assigned was established unequivocally by single crystal X-ray analysis (Figure 7).

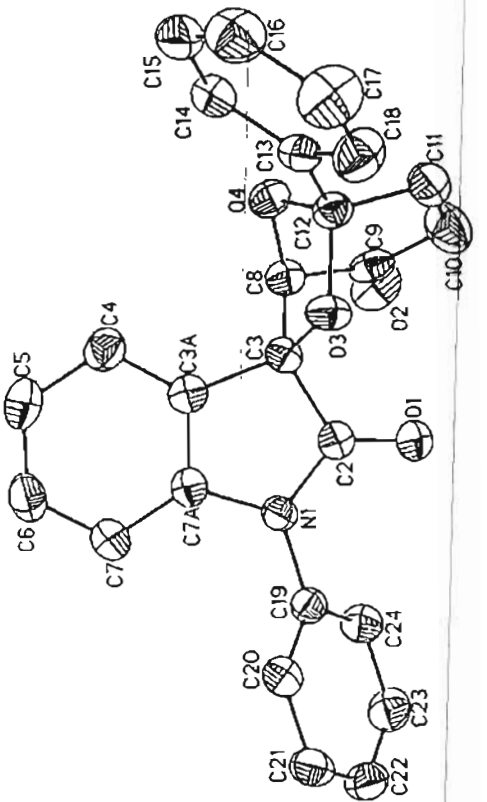
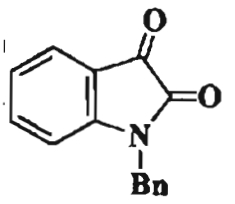
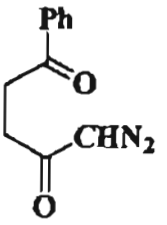
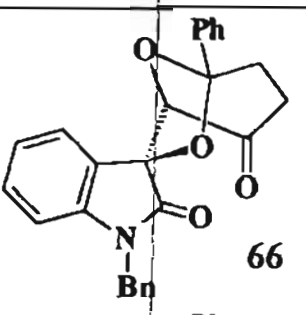
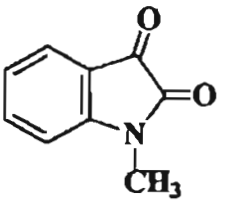
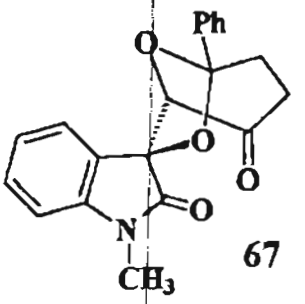
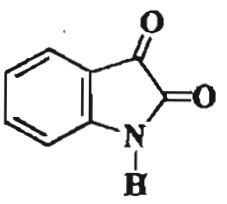
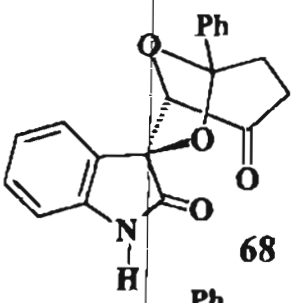
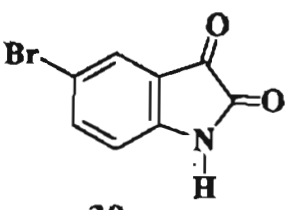
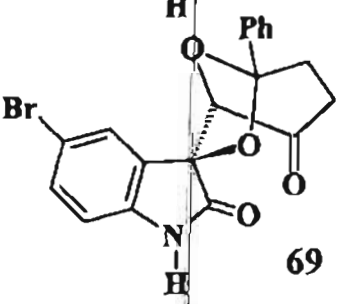



**Figure 7. X-ray crystal structure of 64**

The IR spectrum of **65** showed two carbonyl absorptions at 1718 and 1684 $cm^{-1}$. In the $^{1}H$ NMR spectrum, the characteristic bridgehead proton resonated as a singlet at δ 4.84. The resonance signals of the four methylene protons were visible as a multiplet centered at δ 2.81. In the $^{13}C$ NMR spectrum of **65**, the signal due to the C-4 carbonyl was discernible at δ 202.60 and the lactam carbonyl at δ 173.52. The characteristic spiro carbon signal was observed at δ 81.64 and the bridgehead carbons C-1 and C-5 were visible at δ 110.39 and 85.34 respectively. The two methylene carbons appeared at δ 33.28 and 33.04. All the other signals were in agreement with the assigned structure.

Similar reactivity of the carbonyl ylide **17a** was observed with other isatins **39(b-e)** yielding the spiro oxindoles as a single isomer in good yields and the results are summarized in Table 4.

**Table 4**. Cycloaddition reactions of carbonyl ylide with isatins **39(b-e)**

| Entry | Isatin | Diazo ketone | Product | Yield (%)[a] |
|---|---|---|---|---|
| 1 |  **39b** |  **17a** |  **66** | 78 |
| 2 |  **39c** | |  **67** | 83 |
| 3 |  **39d** | |  **68** | 71 (80) |
| 4 |  **39e** | |  **69** | 70 (81) |

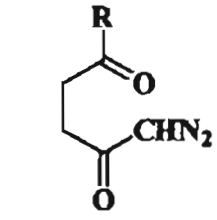
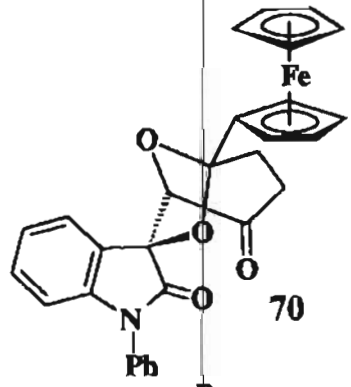
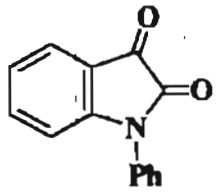
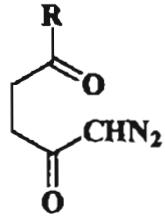
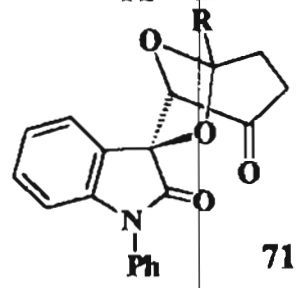
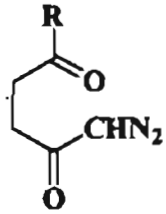
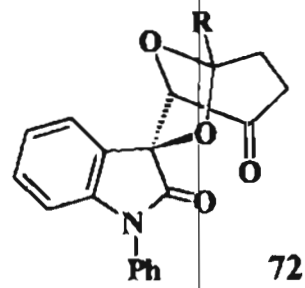
Reaction conditions: $Rh_2(OAc)_4$, Toluene, Argon, RT, 3 h. [a]Isolated yield. Yield based on recovered isatins is given in paranthesis.

The cycloadducts **66-69** were characterized by spectroscopic methods. All these compounds showed typical proton and carbon signals in the $^1H$ and $^{13}C$ NMR spectra. In the $^1H$ NMR spectra of **68** and **69**, the -NH protons

resonated as singlets at δ 10.53 and 10.51 (exchangeable with $D_2O$) respectively.

Similarly, 1-phenylisatin underwent smooth cycloaddition with other substituted diazo ketones yielding the spiro oxindoles and the results are summarized in Table 5.

**Table 5.** Cycloaddition reactions of the diazo ketones **17(c-e)** with **39a**

| Entry | Isatin | Diazo ketone | Product | Yield (%)[a] |
|---|---|---|---|---|
| 1 | |  R = $(C_5H_5)_2Fe$ **17c** |  **70** | 33 (45) |
| 2 |  **39a** |  R = *p*-$C_6H_4$-$CH_3$ **17d** |  **71** | 51 (59) |
| 3 | |  R = *p*-$C_6H_4$-$OCH_3$ **17e** |  **72** | 39 (45) |

Reaction conditions: $Rh_2(OAc)_4$, Toluene, Argon, RT, 3 h. [a]Isolated yield. Yield based on recovered isatin is given in paranthesis.

Diagnostic spectral data were obtained for the cycloadducts **70-72**. All these compounds also gave satisfactory high resolution mass.

The 1,2-diones **73-76** failed to give any cycloadduct with carbonyl ylides. In all these cases, the diones were recovered quantitatively (Figure 8).

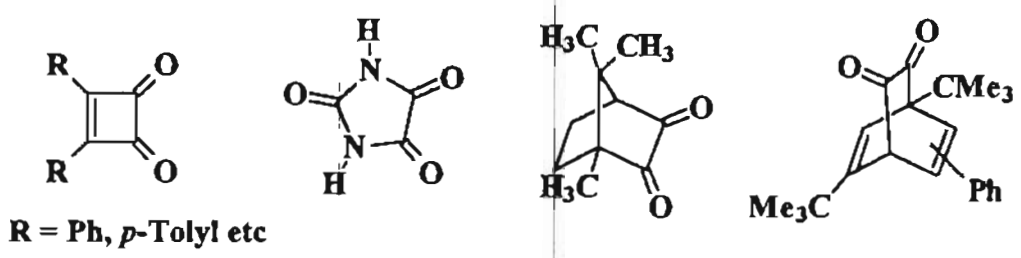
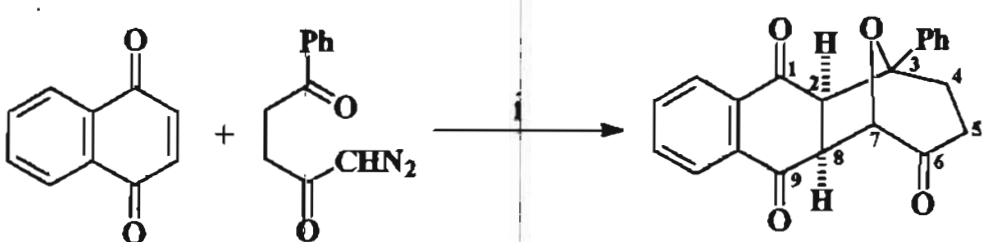



**Figure 8**

## 2.2.5 Dipolar Cycloaddition Reaction of Carbonyl Ylide with 1,4-Naphthoquinone

In view of the interesting results obtained in the dipolar cycloaddition reactions of carbonyl ylides with various 1,2-diones, some preliminary studies were conducted with 1,4-diones as exemplified by 1,4-naphthoquinone **77**.

Rh(II) acetate catalyzed cycloaddition of 1-diazo-5-phenyl-2,5-pentanedione **17a** with **77** proceeded smoothly to afford a colorless crystalline product **78** in 30% yield (Scheme 19).




**77** **17a** **78** (30%)

**i. $Rh_2(OAc)_4$, Toluene, Argon, RT, 3 h**

**Scheme 19**

The structure of the product was elucidated by spectroscopic methods. The IR spectrum of **78** showed two strong bands at 1738 and 1688 $cm^{-1}$ due to the carbonyl groups. In the $^1H$ NMR spectrum, the proton on C-2 and C-8 resonated as doublets at δ 3.63 (1H, $J$ = 8.1 Hz) and δ 3.86 (1H, $J$ = 8.1 Hz) respectively. The bridgehead proton on C-7 appeared as a singlet at δ 5.08. In the $^{13}C$ NMR spectrum, the three carbonyls resonated at δ 205.27, 194.47 and 192.92. The signal at δ 96.06 was assigned to the C-3 carbon. The two methylene carbons appeared at δ 36.88 and 32.68. The presence of these two methylene carbons has been confirmed by DEPT-135 NMR studies. All the other signals were in agreement with the assigned structure. The structure was finally established unequivocally by single crystal X-ray analysis (Figure 9).

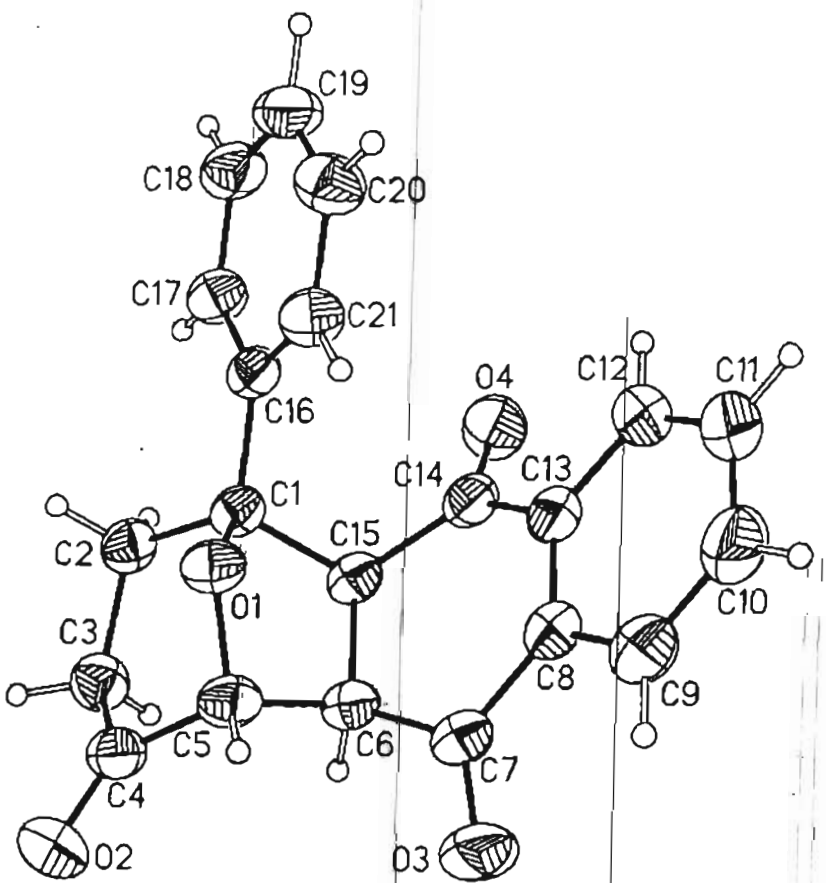
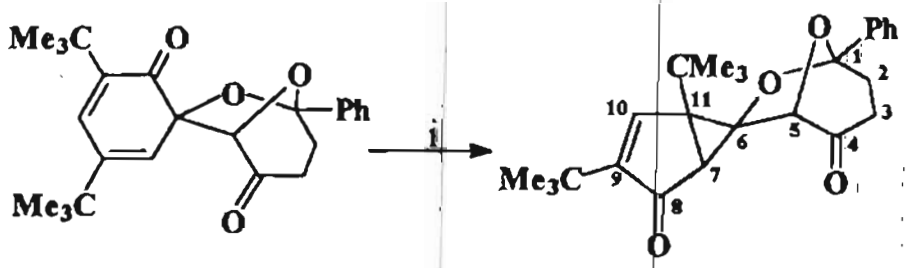



**Figure 9. X-ray crystal structure of 78**

The product of cycloaddition of carbonyl ylide with 1,4-naphthoquinone is a novel heterocyclic compound which is potentially amenable to a number of synthetic transformations. Further studies of the cycloaddition of different 1,4-diones and carbonyl ylides are currently being explored in detail by other members of our group.

## 2.3 Photochemical Rearrangement of the cycloadducts

The photolysis of the cycloadduct **43** in $CH_3CN$ in a Rayonet Photochemical Reactor using quartz filter at 350 nm afforded a colorless crystalline product in 94% yield. This has been characterized as **79** (Scheme 20).




**43** **79** (94%)

**i. hν, $CH_3CN$, Argon, 12 min**

**Scheme 20**

The IR spectrum of **79** showed two strong carbonyl absorptions at 1741 and 1689 $cm^{-1}$ due to the C-4 and C-8 carbonyls respectively. In the $^1H$ NMR spectrum, the aromatic protons appeared as a multiplet centered at δ 7.43 integrating for five protons. The C-10 proton displayed a sharp singlet at δ 7.01. The signals due to the bridgehead protons on C-5 and C-7 appeared as sharp singlets at δ 4.39 and 2.65 respectively. The sharp singlet

at δ 1.16 and 1.01 are due to the two *tert*-butyl groups. In the $^{13}C$ NMR spectrum, the spiro carbon resonated at δ 85.44. The signals due to the two carbonyls C-4 and C-8 appeared at δ 200.28 and 198.74 respectively and the two bridgehead carbons C-1 and C-5 were observed at δ 110.90 and 80.29 respectively. The C-7 carbon was discernible at δ 46.77. All the other signals were in agreement with the assigned structure. Finally the structure assigned was confirmed unequivocally by single crystal X-ray determination (Figure 10).

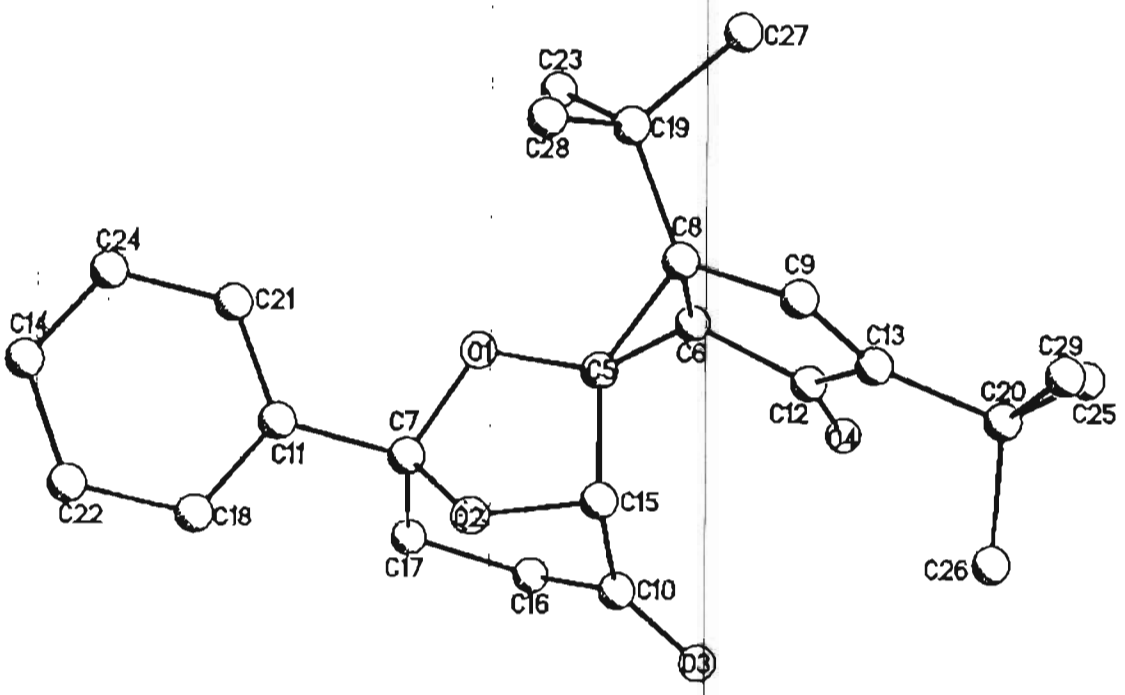
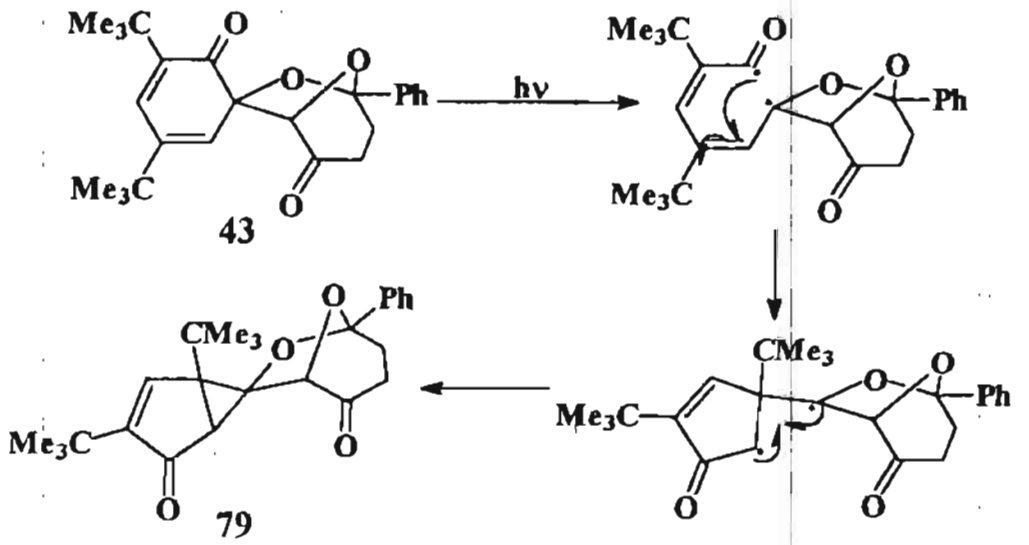


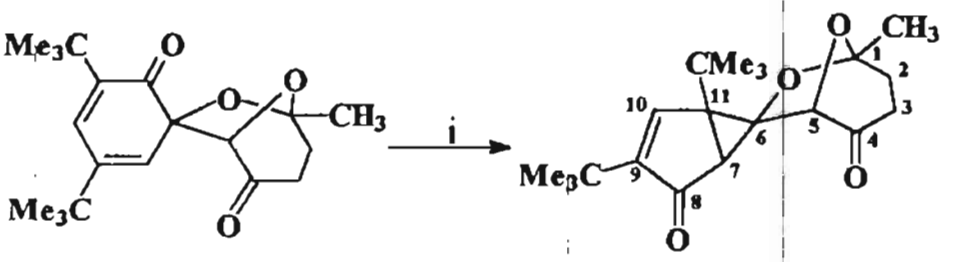

**Figure 10. X-ray crystal structure of 79**

A mechanistic rationalization as outlined in Scheme 21 may be invoked for the photolytic rearrangement of the cycloadduct **43.** The preferred pathway involves a bond-switching mechanism, probably *via* the $\pi\pi^*$ singlet state.[37]



Scheme 21

Similarly the cycloadduct **44**, when subjected to photolysis in acetonitrile in a quartz tube at 350 nm, using a Rayonet Photochemical Reactor afforded a compound which was identified as **80** (74%) on the basis of spectral data (Scheme 22).



**44** **80** (74%)

***i. hν, $CH_3CN$, Argon, 20 min***

***Scheme 22***

The IR spectrum of **80** showed two strong bands at 1736 and 1688 $cm^{-1}$ due to the C-4 and C-8 carbonyls respectively. The $^1H$ NMR spectrum exhibited two signals at δ 1.14 and 1.13 integrating for eighteen protons, corresponding to the two *tert*-butyl groups. The signal at δ 4.20 has

been assigned to the bridgehead proton on C-5. The methyl proton was discernible at δ 1.60. The olefinic proton C-10 displayed a singlet at δ 7.02. The signal due to the C-7 proton was discernible at δ 2.53 as a sharp singlet. The $^{13}C$ NMR spectrum showed two signals at δ 200.28 and 199.00 corresponding to the C-4 and C-8 carbonyl groups respectively. All the other signals were comparable to those of **79**.

In conclusion, it has been shown that carbonyl ylides undergo facile cycloaddition to 1,2-diones thus offering an efficient method for the synthesis of novel spiro oxabicyclic derivatives. In all cases the cycloaddition is highly regio and stereoselective. Interestingly in the case of 1,2-benzoquinones, the ylide preferentially adds to the more electron deficient of the two carbonyls of each quinone. Such preference is precedent in the reactivity of dicarbonyl compounds towards dipolar species.[34] In the case of 1,2-benzoquinones **36e** and **37**, mixtures of regioisomers are obtained. The reaction of carbonyl ylide with acenaphthenequinone proceeds in a highly stereoselective fashion. With isatins too, the reaction is regio and stereoselective and affords novel spiro oxindole derivatives in good yields. It is anticipated that the products of cycloaddition may exhibit some interesting biological properties. It has been shown that the cycloadducts obtained by the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone with the carbonyl ylides **19(a-b)** undergo facile photochemical rearrangement.

## 2.4 EXPERIMENTAL DETAILS

All the reactions were carried out in oven dried glasswares under an atmosphere of argon unless otherwise mentioned. Melting points were recorded on a Toshniwal or Büchi-530 melting point apparatus and are uncorrected. The IR spectra were recorded on Bomem MB series FT-IR spectrophotometer, using potassium bromide pellets. NMR spectra were recorded on Bruker-300 MHz FT NMR spectrometer using chloroform-d as the solvent unless otherwise mentioned. The chemical shifts are given in the δ scale with tetramethylsilane as internal standard. Elemental analyses were carried out using Perkin-Elmer 2400 CHN analyzer. High-resolution mass spectra were done using Finnigan MAT model 8430 instrument. Solvents used for experiments (toluene, benzene, acetonitrile and ether) were distilled and dried according to literature procedures.

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

**Synthesis of Diazo ketones: Typical experimental procedure**

The preparation of 1-diazo-5-phenyl-2,5-pentanedione **17a** from 3-benzoyl propionic acid described below, is illustrative of the general procedure for the synthesis of α-diazo ketones.

***1-Diazo-5-phenyl-2,5-pentanedione (17a)***[25a]

To a solution containing 1.78 g (1 mmol) of 3-benzoyl propionic acid and 0.9 mL (1.05 mmol) of methyl chloroformate in 50 mL of ether was added 1.5 mL of triethylamine. The resulting white suspension was stirred at room temperature under argon for 2 h. The precipitated triethylamine hydrochloride was removed by filtration and the resulting pale yellow solution was immediately treated with 25 mmol of freshly prepared diazomethane in ether (20 mL) at 0 °C. The reaction mixture was maintained at 0 °C for 8 h and then at room temperature and stirred overnight. The solvent was removed and the resulting yellow oil was chromatographed on a silica gel column by using 10% ethyl acetate in hexane as the eluent to give 1.36 g of 1-diazo-5-phenyl-2,5-pentanedione **17a** (67%).

Yellow solid; recrystallized from hexane-dichloromethane.

mp : 55-56 °C.

IR (KBr) $\nu_{max}$ : 3100, 2920, 2110, 1690, 1645, 1360, 755 $cm^{-1}$.

$^1H$ NMR : δ 8-7.80 (m, 2H), 7.50-7.30 (m, 3H), 5.30 (s, 1H), 3.25 (t, 2H), 2.65 (t, 2H).

**General Procedure for the Rhodium(II)-catalyzed Cycloaddition Reaction of 1-Diazo alkanediones with various Dipolarophiles.**

A 5 mL toluene solution containing 1.2 equivalent of the appropriate diazo alkanedione was purged with argon. To this solution was added a catalytic amount (2 mg) of $Rh_2(OAc)_4$ and stirred under argon atmosphere at room temperature for 3 min 1 equivalent of the appropriate dipolarophile was added to it and the reaction mixture was allowed to stir at room temperature until nitrogen evolution ceased (30 min). The solvent was removed under reduced pressure and the residue subjected to silica gel

column chromatography using the appropriate hexane-ethyl acetate mixture as the eluent to give the pure cycloadducts. The products were identified on the basis of their spectral data.

***(1S,1'S,5'S)-3,5-Bis(1,1-dimethylethyl)-5'-phenylspiro[3,5-cyclohexadiene-1,7'-[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (43)***

Treatment of 1-diazo-5-phenyl-2,5-pentanedione **17a** (0.243 g, 1.2 mmol) with 3,5-di-*tert*-butyl-1,2-benzoquinone **36a** (0.220 g, 1 mmol) in the presence of a catalytic amount of rhodium(II) acetate at room temperature for 30 min followed by purification of the residue using a Chromatotron® afforded the cycloadduct **43** (76%, 0.298 g).

Yellow crystals; recrystallized from hexane-dichloromethane.

mp : 207-209 °C.

IR (KBr) $\nu_{max}$ : 2555, 1735, 1708, 1640, 1276, 1128, 1074, 946, 778, 703 $cm^{-1}$.

$^1H$ NMR : δ 7.72-7.42 (m, 5H), 6.76 (d, 1H, *J* = 2.1 Hz), 5.85 (d, 1H, *J* = 2.1 Hz), 4.58 (s, 1H), 2.66-2.42 (m, 4H), 1.18 (s, 9H), 1.11 (s, 9H).

$^{13}C$ NMR : δ 201.85, 199.33, 147.49, 144.75, 138.72, 133.69, 128.70, 128.20, 125.29, 122.54, 110.51, 87.90, 82.08, 35.67, 34.56, 33.26, 29.25, 28.37.

Anal. Calcd for $C_{25}H_{30}O_4$: C, 76.11; H, 7.66. Found: C, 75.61; H, 7.95.

**Crystal data for 43**: $C_{25}H_{30}O_4$. M. 394.49, triclinic, space group $P\bar{1}$, unit cell dimensions a = 5.9075(1) Å, α = 97.315(1)°; b = 9.7892(1) Å, β = 97.692 (1)°; c = 19.2052(2) Å ; γ = 91.79°, R indices (all data) RI = 0.0860, wR2 = 0.1427, volume, Z = 1090.36(2) $Å^3$, 2, D calc = 1.202 $Mg/m^3$, absorption coefficient = 0.080 $mm^{-1}$, λ = 0.71073 Å. 20474

reflections measured, 4673 unique [$R_{(int)}$ = 0.06] which were used in all calculations. (Sheldrick, G. M., Siemens, Analytical X-ray Division, Madison, WI, 1995).

***(1S,1'S,5R)-3,5-Bis(1,1-dimethylethyl)-5'-methylspiro[3,5-cyclohexadiene-1,7'-[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (44)***

Rhodium(II) acetate catalyzed reaction of 1-diazohexane-2,5-dione **17b** (0.168 g, 1.2 mmol) with 3,5-di-*tert*-butyl-1,2-benzoquinone **36a** (0.220 g, 1 mmol) in 5 mL of toluene at room temperature for 30 min according to the general procedure followed by silica gel column chromatography afforded the cycloadduct **44** (0.178 g) in 54% yield.

Yellow crystals; recrystallized from hexane-dichloromethane.

mp : 166-168 °C.

IR (KBr) $\nu_{max}$ : 2974, 2881, 1732, 1679, 1487, 1367, 1277, 1167, 1101, 1067, 988, 922, 893 $cm^{-1}$.

$^1H$ NMR : δ 6.76 (s, 1H), 5.70 (s, 1H), 4.32 (s, 1H), 2.49-2.38 (m, 2H), 2.26-2.14 (m, 2H), 1.85 (s, 3H), 1.23 (s, 9H), 1.09 (s, 9H).

$^{13}C$ NMR : δ 201.81, 199.84, 151.47, 146.94, 144.49, 133.81, 123.10, 110.45, 87.75, 81.90, 34.66, 34.57, 34.00, 32.81, 29.31, 28.43, 23.13.

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.71; H, 8.62.

***Cycloadduct 45***

3,5-Di-*tert*-butyl-1,2-benzoquinone **36a** (0.050 g, 0.23 mmol) was added to a solution of 1-diazo-5-ferrocenyl-2,5-pentanedione **17c** (0.845 g, 0.27 mmol) and Rh(II) acetate in dry toluene (3 mL) at room temperature under argon atmosphere and stirred for 30 min. The solvent was removed in

*vacuo*. Purification of the residue on a silica gel column gave **45** (0.048 g, 42%).

Orange crystals; recrystallized from hexane-dichloromethane.

mp : 181-183 °C.

IR (KBr) $\nu_{max}$ : 2962, 1742, 1701, 1485, 1378, 1276, 1142, 1094, 1027, 926, 791 $cm^{-1}$.

$^1H$ NMR : δ 6.74 (s, 1H), 5.74 (s, 1H), 4.84 (s, 1H), 4.67 (s, 1H), 4.47 (s, 1H), 4.27 (s, 2H), 4.19 (s, 5H), 2.78-2.52 (m, 4H), 1.23 (s, 9H), 1.09 (s, 9H).

$^{13}C$ NMR : δ 202.10, 199.71, 146.71, 144.54, 133.49, 123.61, 111.08, 96.23, 87.35, 84.40, 82.08, 69.03, 68.76, 68.00, 67.96, 34.58, 32.89, 32.81, 29.32, 28.35.

***(1S,1'S,5'S)-3,5-Bis(1,1-dimethylethyl)-6-methoxy-5'-phenyl spiro [3,5-cyclohexadiene-1,7'-[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (46)***

Rhodium(II) acetate catalyzed reaction of the diazo ketone **17a** (0.145 g, 0.72 mmol) and 3-methoxy-4,6-di-*tert*-butyl-1,2-benzoquinone **36b** (0.150 g, 0.6 mmol) in toluene (5 mL) at room temperature for 30 min followed by silica gel column chromatography afforded the cycloadduct **46** (0.160 g) in 63% yield.

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 168-170 °C.

IR (KBr) $\nu_{max}$ : 2962, 1735, 1688, 1627, 1445, 1303, 1270, 1135, 1067, 939, 892, 757 $cm^{-1}$.

$^1H$ NMR : δ 7.74-7.40 (m, 5H), 6.92 (s, 1H), 4.59 (s, 1H), 3.88 (s, 3H), 2.69-2.50 (m, 4H), 1.23 (s, 9H) 1.17 (s, 9H).

$^{13}$C NMR : δ 203.51, 197.57, 151.73, 141.38, 139.46, 136.97, 132.02, 128.69, 128.21, 125.21, 110.77, 93.39, 82.03, 62.54, 35.31, 34.89, 33.90, 32.95, 30.16, 29.18.

***(1S,1'S,5'R)-3,5-Bis(1,1-dimethylethyl)-6-methoxy-5'-methyl spiro[3,5-cyclohexadiene-1,7'-[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (47)***

Rhodium(II) acetate catalyzed reaction of 0.168 g (1.2 mmol) of α-diazo ketone **17b** with 0.250 g (1 mmol) of 3-methoxy-4,6-di-*tert*-butyl-1,2-benzoquinone **36b** in toluene (5 mL) at room temperature under argon atmosphere for 30 min followed by purification of the residue by silica gel column chromatography afforded the cycloadduct **47** (0.174 g, 48%).

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 156-158 °C.

IR (KBr) $\nu_{max}$ : 2962, 1732, 1685, 1645, 1569, 1481, 1379, 1298, 1173, 1053, 989, 839 cm$^{-1}$.

$^{1}$H NMR : δ 6.92 (s, 1H), 4.33 (s, 1H), 3.78 (s, 3H), 2.56-2.44 (m, 2H), 2.26-2.24 (m, 2H), 1.88 (s, 3H), 1.21 (s, 18H).

$^{13}$C NMR : δ 203.26, 198.21, 152.24, 141.23, 137.21, 131.79, 110.91, 93.39, 82.00, 62.36, 34.91, 34.56, 32.49, 30.29, 29.32, 24.13.

Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 70.05; H, 8.50.

***(1S,1'S,5'S)-5-(1,1-dimethylethyl)-6-methoxy-5'-phenyl spiro[3,5-cyclohexadiene-1,7'-[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (48)***

Treatment of 1-diazo-5-phenylpentane-2,5-dione **17a** (0.242 g, 1.2 mmol) with 3-methoxy-4-*tert*-butyl-1,2-benzoquinone **36c** (0.194 g, 1 mmol) in the presence of a catalytic amount of rhodium(II) acetate

according to the general procedure, followed by silica gel column chromatography gave the cycloadduct **48** (0.177 g, 48%).

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 164-166 °C.

IR (KBr) $\nu_{max}$ : 2956, 1732, 1682, 1645, 1574, 1384, 1260, 1084, 992, 887, 760 $cm^{-1}$.

$^1H$ NMR : δ 7.78-7.40 (m, 5H), 6.79 (d, 1H, *J* = 7.3 Hz), 5.33 (d, 1H, *J* = 7.3 Hz), 4.48 (s, 1H), 3.60 (s, 3H), 2.69-2.53 (m, 4H), 1.16 (s, 9H).

$^{13}C$ NMR : δ 205.92, 195.81, 158.57, 139.71, 138.49, 135.36, 129.12, 128.62, 125.77, 111.52, 88.98, 82.20, 55.99, 34.30, 33.54, 29.60.

Anal. Calcd for $C_{22}H_{24}O_5$: C, 71.72; H, 6.57. Found: C, 71.81; H, 6.61.

***(1S,1'S,5'S)-5-(1,1-Dimethylethyl)-5'-phenyl spiro[3,5-cyclohexadiene-1,7'-[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (49)***

Rhodium(II) acetate catalyzed reaction of 0.221 g (1.09 mmol) of the α-diazo ketone **17a** with 0.150 g (0.91 mmol) of 4-*tert*-butyl-1,2-benzoquinone **36d** in toluene (5 mL) at room temperature under argon atmosphere for 30 min followed by silica gel chromatography of the residue afforded the cycloadduct **49** (0.186 g, 55%).

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 112-113 °C.

*IR (KBr)* $\nu_{max}$ : *2977, 1735, 1691, 1450, 1367, 1279, 1114, 1025, 937, 772* $cm^{-1}$.

$^1H$ NMR : δ 7.71-7.37 (m, 5H), 7.05 (dd, 1H, *J* = 2.3 and 10.2 Hz), 6.02 (d, 1H, *J* = 10.2 Hz), 5.90 (d, 1H,

J = 2.0 Hz), 4.57 (s, 1H), 2.68-2.44 (m, 4H), 1.12 (s, 9H).

$^{13}$C NMR : δ 201.69, 198.69, 147.50, 141.17, 138.58, 128.76, 128.16, 125.49, 125.28, 124.79, 111.00, 86.20, 83.04, 35.16, 34.56, 33.26, 28.34.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.79; H, 6.65%.

***Cycloadducts 50 and 51***

Treatment of 1-diazo-5-phenylpentane-2,5-dione (0.103 g, 0.51 mmol) with the quinone **36e** (0.200 g, 0.42 mmol) in the presence of a catalytic amount of rhodium(II) acetate afforded a mixture of two products. Chromatography of the mixture on silica gel using 3% ethyl acetate in hexane as the eluent afforded **50** (0.099 g) in 36% yield.

***(1S,1S',5'S)-3,5-Bis(diphenylmethyl)-6-methoxy-5'-phenyl spiro[3,5-cyclohexadiene-1,7'-[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (50)***

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 161-163 °C.

IR (KBr) $\nu_{max}$ : 3030, 2924, 1732, 1675, 1495, 1452, 1065, 980, 762, 707 cm$^{-1}$.

$^1$H NMR : δ 7.66-6.83 (m, 25H), 6.42 (s, 1H), 5.47 (s, 1H), 5.24 (s, 1H), 4.70 (s, 1H), 3.13 (s, 3H), 2.82-2.80 (m, 1H), 2.54-2.41 (m, 3H).

$^{13}$C NMR : δ 204.78, 196.58, 159.88, 144.05, 141.54, 141.34, 141.19, 140.05, 137.41, 129.10, 128.71, 128.53, 128.45, 128.29, 128.07, 126.65, 126.35, 126.20, 124.53, 123.32, 112.09, 90.77, 90.10, 62.31, 49.01, 47.61, 33.92, 33.24.

Further elution using 5% ethyl acetate in hexane afforded the cycloadduct **51** *(0.112 g, 41%).*

***Cycloadduct 51***

*Yellow crystals; recrystallized from hexane-ethyl acetate.*

mp : 92-94 °C.

IR (KBr) $\nu_{max}$ : *3030, 2943, 1739, 1695, 1494, 1446, 1305, 1128,* 1072, 1029, 789, 699 $cm^{-1}$.

$^1H$ NMR : δ 7.70-6.75 (m, 25H), 6.29 (s, 1H), 5.59 (s, 1H), *5.41 (s, 1H), 4.38 (s, 1H), 3.67 (s, 3H), 2.71-2.58* (m, 4H).

$^{13}C$ NMR : δ 203.82, 195.99, 152.81, 142.48, 142.22, 141.44, 141.18, 140.74, 139.17, 136.26, 129.27, 128.77, 128.71, 128.57, 128.42, 128.19, 127.60, 126.81, 126.64, 126.31, 125.31, 124.81, 111.19, 90.70, 82.67, 62.73, 48.33, 47.56, 33.14, 32.82.

Anal. Calcd for $C_{44}H_{36}O_5$: C, 81.97; H, 5.63. Found: C, 81.94; H, 5.75.

***Cycloadducts 52 and 53***

Rhodium(II) acetate catalyzed reaction of 0.242 g (1.2 mmol) of the α-diazo ketone **17a** with 0.158 g (1 mmol) of 1,2-naphthoquinone **37** in toluene (5 mL) at room temperature under argon atmosphere for 40 min followed by removal of the solvent afforded a yellow residue which was subjected to silica gel column chromatography. The minor component was identified as the cycloadduct **52** (6%)

***Cycloadduct 52***

Colorless semisolid

IR (neat) $\nu_{max}$ : 3068, 1729, 1688, 1451, 1304, 1193, 932, 785 $cm^{-1}$.

$^1$H NMR : δ 7.94-7.17 (m, 9H), 6.52 (d, 1H, $J$ = 9.8 Hz), 6.11 (d, 1H, $J$ = 9.8 Hz), 4.51 (s, 1H), 2.95-2.47 (m, 4H).

$^{13}$C NMR : δ 203.83, 190.40, 140.37, 136.56, 135.42, 134.28, 129.82, 128.81, 128.75, 128.43, 127.69, 127.52, 127.16, 124.82, 111.27, 89.19, 85.70, 34.57, 33.43.

The major fraction isolated from the column contained the cycloadduct **53** (0.130 g, 39%).

***Cycloadduct 53***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 164-166 °C.

IR (KBr) $\nu_{max}$ : 3056, 2942, 1731, 1694, 1593, 1452, 1303, 1216, 1128, 1061, 933, 764 cm$^{-1}$.

$^1$H NMR : δ 7.86-7.18 (m, 9H), 6.71 (d, 1H, $J$ = 9.9 Hz), 6.07 (d, 1H, $J$ = 9.9 Hz), 4.52 (s, 1H), 2.69-2.46 (m, 4H).

$^{13}$C NMR : δ 201.17, 195.96, 138.57, 136.37, 134.66, 130.93, 128.87, 128.71, 128.58, 128.14, 127.66, 127.48, 127.44, 125.24, 111.11, 85.37, 83.64, 35.64, 33.46.

Anal. Calcd for $C_{21}H_{16}O_4$: C, 75.88; H, 5.17. Found: C, 75.79; H, 4.81.

***(1S,1'S,5'S)-3,5-Bis(1,1-dimethylethyl)-5'-phenylspiro[3,5-cyclohexadiene-1,8'-[6,8]dioxabicyclo[4.2.1]nonane]-2,2'-dione (55)***

3,5-Di-*tert*-butyl-1,2-benzoquinone **36a** (0.025 g, 0.11 mmol) was added to a solution of the diazo ketone **24** (0.030 g, 0.14 mmol) and a catalytic amount of Rh(II) acetate in dry toluene (2 mL) at room temperature under argon atmosphere and stirred for 60 min. The solvent was removed in *vacuo* and the residue on silica gel column chromatography afforded **55** (0.017 g) in 37% yield.

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 200-202 °C.

IR (KBr) $\nu_{max}$ : 2968, 1708, 1695, 1663, 1466, 1370, 1274, 1134, 970, 889, 754 $cm^{-1}$.

$^1H$ NMR : δ 7.54-7.32 (m, 5H), 6.70 (d, 1H, *J* = 2.0 Hz), 5.69 (d, 1H, *J* = 2.0 Hz), 4.53 (s, 1H), 2.97-2.89 (m, 1H) 2.46-2.27 (m, 2H), 2.11-1.84 (m, 3H), 1.13 (s, 9H), 1.10 (s, 9H).

$^{13}C$ NMR : δ 210.89, 198.89, 146.50, 143.96, 142.95, 133.46, 127.73, 124.76, 122.98, 115.86, 89.41, 81.85, 42.58, 42.32, 34.73, 34.45, 29.30, 28.37, 18.16.

***Cycloadducts 56 and 57***

To a solution of 1-diazo-5-phenylpentane-2,5-dione **17a** (0.242 g, 1.2 mmol) and a catalytic amount of $Rh_2(OAc)_4$ in toluene (3 mL) was added 0.182 g (1 mmol) of acenaphthenequinone **38** under argon atmosphere and resulting solution was stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the residue purified by silica gel column chromatography (hexane-ethyl acetate) to give **56** (0.134 g, 38%) and **57** (0.104 g, 29%) in 67% overall yield in 1.3:1 ratio.

***(1R,1'R,5'R)-5-Phenylspiro[acenaphthylene-1-(2H),7'[6,8]dioxabicyclo[3.2.1]octane]-2,2'-dione (56)***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 194-196 °C.

IR (KBr) $\nu_{max}$ : 3065, 2930, 1730, 1606, 1494, 1278, 1131, 1031, 935, 788, 704 $cm^{-1}$.

$^1$H NMR : δ 8.11-7.30 (m, 11H), 4.54 (s, 1H), 3.50-3.37 (m, 1H), 2.78-2.69 (m, 2H), 2.62-2.51 (m, 1H).

$^{13}$C NMR : δ 202.34, 198.25, 140.77, 139.60, 138.32, 132.19, 131.06, 130.30, 128.93, 128.70, 128.31, 125.66, 124.88, 122.28, 120.79, 111.22, 87.60, 86.79, 35.70, 33.87.

Anal. Calcd for $C_{23}H_{16}O_4$: C, 77.52; H, 4.53. Found: C, 77.60; H, 4.37.

***Cycloadduct 57***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 172-174 °C.

IR (KBr) $\nu_{max}$ : 3071, 2970, 1730, 1605, 1502, 1312, 1138, 1068, 910, 785 cm$^{-1}$.

$^1$H NMR : δ 8.20-7.28 (m, 11H), 4.63 (s, 1H), 2.88-2.83 (m, 2H), 2.73-2.68 (m, 2H).

$^{13}$C NMR : δ 202.72, 199.36, 141.98, 138.93, 134.98, 133.18, 132.32, 131.77, 130.47, 128.81, 128.43, 128.18, 126.48, 125.43, 122.33, 121.72, 110.51, 98.12, 85.25, 33.90, 33.56.

Anal. Calcd for $C_{23}H_{16}O_4$: C, 77.52; H, 4.53. Found: C, 77.12; H, 4.47.

**Crystal data for 57**: $C_{23}H_{16}O_4$. M. 356.36, monoclinic, space group P2(1)/c, unit cell dimensions a = 14.1914(5) Å, α = 90°; b = 14.2803(5) Å, β = 104.410(3)°; c = 8.7367(3) Å, γ = 90°, R indices (all data) R1 = 0.0864, wR2 = 0.1984, volume, Z = 1714.85(10) Å$^3$, 4, D calc = 1.380 Mg/m$^3$, absorption coefficient = 0.094 mm$^{-1}$, reflections collected = 28171.

***Cycloadducts 58 and 59***

Treatment of the diazo ketone **17d** (0.106 g, 0.49 mmol) with acenaphthenequinone **38** (0.075 g, 0.41 mmol) according to the general procedure afforded a mixture of two isomeric cycloadducts. Removal of the solvent followed by silica gel column chromatography afforded **58** (0.076 g, 50%) and **59** (0.027 g, 18%) in 68% yield in the ratio 2.8:1.

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 230-231 °C.

IR (KBr) $\nu_{max}$ : 3068, 2924, 1718, 1716, 1603, 1491, 1351, 1288, 1130, 1050, 922, 812, 770 $cm^{-1}$.

$^1H$ NMR : δ 8.12-7.21 (m, 10H), 4.54 (s, 1H), 3.49-3.37 (m, 1H), 2.78-2.68 (m, 2H), 2.61-2.51 (m, 1H), 2.39 (s, 3H).

$^{13}C$ NMR : δ 202.64, 198.47, 140.86, 138.50, 136.82, 132.29, 131.17, 130.38, 129.08, 128.33, 125.74, 124.94, 122.36, 120.94, 111.45, 87.70, 86.89, 35.78, 34.00, 21.29.

Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.82; H, 4.90. Found: C, 77.78; H, 4.88.

***Cycloadduct 59***

Colorless crystals; recrystallized from hexane-ethyl acetate

mp : 201-203 °C.

IR (KBr) $\nu_{max}$ : 3043, 2912, 1735, 1710, 1604, 1430, 1398, 1262, 1128, 1073, 930, 786 $cm^{-1}$.

$^1H$ NMR : δ 8.62-7.23 (m, 10H), 4.70 (s, 1H), 2.94-2.90 (m, 2H), 2.80-2.76 (m, 2H), 2.39 (s, 3H).

$^{13}$C NMR : δ 203.00, 199.50, 142.23, 138.73, 136.32, 135.17, 133.41, 132.52, 131.95, 130.72, 129.08, 128.64, 128.41, 127.54, 126.66, 125.67, 122.52, 121.94, 110.85, 96.50, 85.51, 34.07, 33.82, 21.42.

Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.82; H, 4.90. Found: C, 77.83; H, 4.87.

***Cycloadducts 60 and 61***

Rhodium(II) acetate catalyzed reaction of diazo ketone **17e** (0.278 g, 1.2 mmol) and acenaphthenequinone (0.182 g, 1 mmol) in dry toluene (5 mL) at room temperature for 3 h and purification of the residue by silica gel chromatography afforded 1:1.6 mixture of cycloadducts **60** (0.091 g, 24%) and **61** (0.144 g, 37%) in 61% yield.

***Cycloadduct 60***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 190-191 °C.

IR (KBr) $\nu_{max}$ : 3061, 1731, 1718, 1437, 1174, 1032, 770 cm$^{-1}$.

$^1$H NMR : δ 8.13-7.35 (m, 8H), 6.93 (d, 2H, $J$ = 8.6 Hz), 4.53 (s, 1H), 3.84 (s, 3H), 3.43-3.40 (m, 1H), 2.75-2.68 (m, 2H), 2.59-2.57 (m, 1H).

$^{13}$C NMR : δ 202.54, 198.38, 159.85, 140.80, 138.46, 132.20, 131.93, 131.13, 130.35, 128.96, 128.26, 126.32, 125.67, 122.28, 121.88, 120.87, 113.65, 111.31, 87.70, 86.85, 55.12, 35.70, 33.93.

Anal. Calcd for $C_{24}H_{18}O_5$: C, 74.60; H, 4.70. Found: C, 74.75; H, 4.64.

***Cycloadduct 61***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 166-168 °C.

IR (KBr) $\nu_{max}$ : 3030, 2930, 1730, 1717, 1608, 1519, 1252, 1050, 827, 790 $cm^{-1}$.

$^1H$ NMR : δ 8.12-7.40 (m, 8H), 6.96 (d, 2H, $J$ = 8.7 Hz), 4.70 (s, 1H), 3.83 (s, 3H), 2.94-2.90 (m, 2H), 2.83-2.79 (m, 2H).

$^{13}C$ NMR : δ 203.04, 199.74, 160.02, 142.03, 131.85, 131.13, 130.52, 129.38, 128.48, 128.22, 127.13, 126.50, 122.39, 121.73, 113.57, 110.58, 85.35, 85.22, 55.16, 33.58, 33.53.

Anal. Calcd for $C_{24}H_{18}O_5$: C, 74.60; H, 4.70. Found: C, 75.21; H, 4.88.

***Dimer 63***

Rhodium(II) acetate catalyzed reaction of 0.082 g (0.32 mmol) of α-diazo ketone **40** and 0.050 g (0.27 mmol) of acenaphthenequinone in toluene (5 mL) at room temperature under argon atmosphere for 60 min gave the head-to-tail dimer **63** (0.061 g) in 84% yield. Acenaphthenequinone recovered quantitatively.

Colorless crystals; recrystallized from hexane+ethyl acetate.

mp : 146-148 °C.

IR (KBr) $\nu_{max}$ : 3089, 2878, 1751, 1701, 1589, 1334, 1222, 1147, 1060, 973, 768 $cm^{-1}$.

$^1H$ NMR : δ 8.06-8.03 (m, 2H), 7.89-7.86 (m, 2H), 7.35-7.25 (m, 3H), 7.18-7.16 (m, 2H), 4.23 (s, 1H).

$^{13}C$ NMR : δ 197.82, 142.63, 135.75, 133.06, 128.87, 128.66, 127.72, 123.66, 96.22, 59.57.

Anal. Calcd for $C_{30}H_{20}O_4$: C, 81.07; H, 4.54. Found: C, 80.54; H, 4.43.

***Cycloadducts 64 and 65***

Treatment of 0.217 g (1.07 mmol) of diazo ketone **16a** and 0.200 g (0.89 mmol) of 1-phenylisatin **39a** in toluene (5 mL) in the presence of a catalytic amount of rhodium(II) acetate at room temperature under argon atmosphere for 3 h according to the general procedure afforded a mixture of two products which were separated by silica gel column chromatography. The major product was a colorless solid (0.267 g, 75%) whose structure was assigned as **64**.

***1S,3'R,5S)-5-phenyl-1'-(phenyl)spiro[6,8-dioxabicyclo[3.2.1]octane-7,3'-[3H]indole]-2,2'(1'H)-dione (64)***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 191-193 °C.

IR (KBr) $\nu_{max}$ : 3055, 2943, 1733, 1611, 1591, 1496, 1361, 1297, 1195, 1055, 904, 754, 696 $cm^{-1}$.

$^1H$ NMR : δ 7.69-6.92 (m, 13H), 6.79 (d, 1H, $J$ = 7.7 Hz), 4.63 (s, 1H), 3.40-3.32 (m, 1H), 2.75-2.48 (m, 3H).

$^{13}C$ NMR : δ 202.40, 171.04, 142.61, 139.41, 133.65, 129.64, 128.47, 128.43, 126.33, 124.94, 124.03, 111.57, 109.77, 87.61, 83.04, 35.55, 33.73.

Anal. Calcd for $C_{25}H_{19}N_1O_4$: C, 75.48; H, 4.78; N, 3.52. Found: C, 75.29; H, 4.69; N, 3.57.

**Crystal data for 64**: $C_{25}H_{19}N_1O_4$. M. 397.41, orthorhombic, space group Pbca, unit cell dimensions a = 18.0300(4) Å, b = 9.8921(2) Å, c = 21.5710(6) Å, $\alpha = \beta = \gamma = 90°$, R indices (all data) R1 = 0.1068, wR2 = 0.1077, volume, Z = 3847.29(16) $Å^3$, Z = 8, D calc = 1.372 $Mg/m^3$, absorption coefficient = 0.093 $mm^{-1}$, T = 213(2) K, λ = 0.71073 Å, 36868

reflections measured, 3648 unique [$R_{(int)}$ = 0.11] which were used in all calculations.

The minor component was identified as the cycloadduct **65** (0.029 g) in <10% yield.

***Cycloadduct 65***

Pale yellow semisolid

IR (neat) $\nu_{max}$ : 3030, 2912, 1718, 1684, 1593, 1449, 1356, 1229, 997, 745, 688 $cm^{-1}$.

$^1H$ NMR : δ 7.80-7.02 (m, 13H), 6.78 (d, 1H, *J* = 7.8 Hz), 4.84 (s, 1H), 2.89-2.74 (m, 4H).

$^{13}C$ NMR : δ 202.60, 173.52, 144.22, 138.61, 133.64, 130.73, 129.41, 128.87, 128.16, 128.07, 126.26, 125.54, 122.92, 121.18, 110.39, 109.87, 85.34, 81.64, 33.28, 33.04.

***(1S,3'R,5S)-5-phenyl-1'-(phenylmethyl)spiro[6,8-dioxabicyclo[3.2.1]octane-7,3'-[3H]indole]-2,2'(1'H)-dione (66)***

A solution containing 0.153 g (0.76 mmol) of diazo ketone **16a** and 0.150 g (0.63 mmol) of 1-benzylisatin **39b** in toluene (5 mL) was treated with a catalytic amount of rhodium(II) acetate according to the general procedure. The mixture was allowed to stir at room temperature under argon atmosphere for 3 h and the solvent was removed under reduced pressure. Chromatography of the resulting solid on silica gel using 8% ethyl acetate in hexane as the eluent afforded the cycloadduct **66** (0.202 g) in 78% yield.

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 218-220 °C.

IR (KBr) $\nu_{max}$ : 3062, 2930, 1727, 1487, 1365, 1057, 990, 747$cm^{-1}$.

$^1$H NMR : δ 7.65-6.85 (m, 13H), 6.65 (d, 1H, $J$ = 7.7 Hz), 4.86 (s, 2H), 4.51 (s, 1H), 3.45-3.37 (m, 1H), 2.75-2.65 (m, 2H), 2.58-2.51 (m, 1H).

$^{13}$C NMR : δ 202.15, 171.78, 141.84, 139.67, 135.21, 130.34, 129.12, 129.02, 128.59, 128.00, 127.55, 125.15, 124.63, 123.70, 111.69, 109.58, 87.78, 83.20, 44.44, 35.92, 33.97.

Anal. Calcd for $C_{26}H_{21}N_1O_4$: C, 75.89; H, 5.15; N, 3.41. Found: C, 75.69; H, 4.99; N, 3.47.

***(1S,3'R,5S)-5-phenyl-1'-(methyl)spiro[6,8-dioxabicyclo[3.2.1]octane-7,3'-[3H]indole]-2,2'(1'H)-dione (67)***

A solution containing 0.150 g (0.74 mmol) of diazo ketone **16a** and 0.100 g (0.62 mmol) of 1-methylisatin **39c** in toluene (5 mL) was treated with a catalytic amount of rhodium(II) acetate and the mixture was allowed to stir at room temperature under argon atmosphere for 3 h. Removal of the solvent under reduced pressure followed by silica gel chromatography afforded 0.172 g of the cycloadduct **67** in 83% yield.

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 217-219 °C.

IR (KBr) $\nu_{max}$ : 2999, 1735, 1710, 1612, 1495, 1375, 1127, 1027, 749, 692 cm$^{-1}$.

$^1$H NMR : δ 7.65-6.88 (m, 8H), 6.78 (d, 1H, $J$ = 7.7 Hz), 4.48 (s, 1H), 3.48-3.36 (m, 1H), 3.20 (s, 3H), 2.72-2.63 (m, 2H), 2.57-2.46 (m, 1H).

$^{13}$C NMR : δ 201.85, 171.19, 142.54, 139.39, 130.20, 128.91, 128.72, 128.30, 124.84, 124.32, 123.42, 111.22, 108. 24, 87.20, 82.71, 35.78, 33.73, 26.48.

Anal. Calcd for $C_{20}H_{17}N_1O_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.59; H, 5.04; N, 3.88.

***(1S,3'R,5S)-5-phenylspiro[6,8-dioxabicyclo[3.2.1]octane-7,3'-[3H]indole]-2,2'(1'H)-dione (68)***

A mixture containing 0.164 g (0.81 mmol) of diazo ketone **16a** and 0.100 g (0.67 mmol) of isatin **39d** in toluene (5 mL) was treated with a catalytic amount of $Rh_2(OAc)_4$ and allowed to stir at room temperature under argon atmosphere for 3 h. Removal of the solvent under reduced pressure followed by silica gel chromatography of the residue afforded **68** (0.155 g, 71%; yield based on recovered isatin (0.011 g) was 80%).

Colorless spongy solid

mp : 248-250 °C.

IR (KBr) $\nu_{max}$ : 3193, 3099, 1732, 1712, 1622, 1473, 1287, 1024, 915, 753, 698 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$) : δ 10.53 (s, 1H), 7.67-6.95 (m, 8H), 6.83 (d, 1H, $J$ = 7.7 Hz), 4.45 (s, 1H), 3.39-3.28 (m, 1H), 2.63-2.47 (m, 3H).

$^{13}$C NMR (DMSO-$d_6$): δ 201.63, 172.84, 140.98, 139.33, 130.03, 129.27, 128.65, 128.21, 124.78, 124.19, 122.49, 110.81, 110.36, 87.17, 82.98, 35.63, 33.67.

HRMS Calcd for $C_{19}H_{15}N_1O_4$: 321.10009. Found: 321.10011.

evaporated *in vacuo*. The residue obtained was chromatographed on a silica gel column to afford **70** (0.045 g, 33%) as an orange solid. Yield based on recovered 1-phenylisatin (0.016 g) was 45%.

Orange crystals; recrystallized from hexane-dichloromethane.

mp : 217-219 °C.

IR (KBr) $\nu_{max}$ : 3083, 2946, 1736, 1615, 1500, 1366, 1108, 1035, 830, 751 $cm^{-1}$.

$^1H$ NMR : δ 7.53-6.85 (m, 9H), 4.59 (s, 1H), 4.47 (s, 2H), 4.31 (s, 2H), 4.24 (s, 5H), 3.20-3.14 (m, 1H), 2.92-2.87 (m, 2H), 2.72-2.66 (m, 1H).

$^{13}C$ NMR : δ 204.13, 171.54, 143.00, 133.72, 130.28, 129.62, 129.01, 128.36, 126.36, 124.63, 123.97, 112.06, 109.92, 87.67, 85.41, 69.30, 69.11, 67.15, 33.30, 32.54.

HRMS Calcd for $C_{29}H_{23}N_1O_4Fe$: 505.09791. Found: 505.09765.

***(1S,3'R,5S)-5-(4-methyl)-phenyl-1'(phenyl)spiro[6,8-dioxabicyclo[3.2.1]octane-7,3'-[3H]indole]-2,2'(1'H)-dione (71)***

A solution containing the diazo ketone **16d** (0.174 g, 0.81 mmol) and 1-phenylisatin (0.150 g, 0.67 mmol) in dry toluene (5 mL) was treated with a catalytic amount of $Rh_2(OAc)_4$ under argon atmosphere at room temperature and stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography using hexane-ethyl acetate (85:15) and afforded **71** (0.141 g, 51%; yield based on recovered 1-phenylisatin (0.020 g) was 59%).

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 215-217 °C.

IR (KBr) $\nu_{max}$ : 3064, 2952, 1743, 1722, 1614, 1495, 1465, 1371, 1294, 1102, 1053, 815, 749 $cm^{-1}$.

$^1H$ NMR : δ 7.57-6.91 (m, 12H), 6.79 (d, 1H, $J$ = 7.8 Hz), 4.60 (s, 1H), 3.42-3.31 (m, 1H), 2.72-2.46 (m, 3H), 2.39 (s, 3H).

$^{13}C$ NMR : δ 201.89, 170.82, 142.50, 138.47, 136.54, 133.65, 130.05, 129.49, 128.99, 128.75, 128.23, 126.25, 124.82, 124.70, 123.85, 111.57, 109.59, 87.51, 82.85, 35.60, 33.64, 21.18.

HRMS Calcd for $C_{26}H_{21}N_1O_4$: 411.14677. Found: 411.14706.

***(1S,3'R,5S)-5-(4-methoxy)-phenyl-1'(phenyl)spiro[6,8-dioxabicyclo[3.2.1]octane-7,3'-[3H]indole]-2,2'(1'H)-dione (72)***

To a solution containing the diazo ketone **16e** (0.093 g, 0.40 mmol) and catalytic amount of $Rh_2(OAc)_4$ in dry toluene (2 mL) was added 1-phenylisatin (0.075 g, 0.33 mmol) at room temperature under argon atmosphere and allowed the reaction mixture to stir for 3 h. Removal of the solvent under reduced pressure followed by silica gel chromatography afforded the cycloadduct **72** (0.056 g, 39%; yield based on recovered 1-phenylisatin (0.010 g) was 45%).

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 187-189 °C.

IR (KBr) $\nu_{max}$ : 3064, 2946, 1735, 1611, 1504, 1375, 1248, 1049, 838, 751 $cm^{-1}$.

$^1H$ NMR : δ 7.64-6.94 (m, 12H), 6.82 (d, 1H, $J$ = 7.7 Hz), 4.63 (s, 1H), 3.86 (s, 3H), 3.45-3.33 (m, 1H), 2.75-2.51 (m, 3H).

$^{13}$C NMR : δ 201.99, 170.87, 159.90, 142.55, 133.68, 131.70, 130.09, 129.52, 128.80, 128.27, 126.29, 124.72, 123.88, 113.67, 111.53, 109.64, 87.59, 82.91, 55.13, 35.58, 33.67.

HRMS Calcd for $C_{26}H_{21}N_1O_5$: 427.14182. Found: 427.14197.

***Cycloadduct 78***

The rhodium(II)-catalyzed reaction of 0.153 g (0.75 mmol) of **16a** with 0.100 g (0.63 mmol) of 1,4-naphthoquinone **77** was carried out in dry toluene (3 mL) according to the general procedure and afforded the cycloadduct **78** (0.062 g) in 30% yield.

Colorless crystals; recrystallized from hexane-dichloromethane.

mp : 183-185 °C.

IR (KBr) $\nu_{max}$ : 3090, 3056, 2962, 1738, 1688, 1593, 1274, 1035, 768, 707 cm$^{-1}$.

$^1$H NMR : δ 7.98-7.02 (m, 9H), 5.08 (s, 1H), 3.86 (d, 1H, *J* = 8.1 Hz), 3.63 (d, 1H, *J* = 8.1 Hz), 2.75-2.61 (m, 3H), 2.49-2.43 (m, 1H).

$^{13}$C NMR : δ 205.27, 194.47, 192.92, 138.86, 136.33, 134.23, 133.83, 127.63, 127.52, 126.63, 126.10, 125.32, 96.06, 87.02, 58.94, 55.02, 36.88, 32.68.

**Crystal data for 78:** $C_{21}H_{16}O_4$. M. 332.34, monoclinic, space group P2(1)/n, unit cell dimensions a = 5.5993(1) Å , α = 90°; b = 25.3337(4) Å, β = 100.081(1)°; c = 11.2166(2) Å , γ = 90°, R indices (all data) R1 = 0.0474, wR2 = 0.0983, volume, Z = 1566.52(5) Å$^3$ , 4, Dcalc = 1.409 Mg/m$^3$, absorption coefficient = 0.097 mm$^{-1}$, λ = 0.71073 Å, 28308

reflections measured, 3187 unique [$R_{(int)}$ = 0.027] which were used in all calculations.

***Compound 79***

A solution of the cycloadduct **43** ($\lambda_{max}$ = 387 nm, 0.050 g, 0.13 mmol) in dry acetonitrile (30 mL) was purged with argon for 15 min in a quartz vessel and irradiated for 12 min inside a Rayonet Photochemical Reactor using 350 nm lamp. The yellow reaction mixture becomes colorless. The solvent was evaporated off and the residue purified by silica gel column chromatography using 8% ethyl acetate in hexane as the eluent to afford **79** (0.047 g) in 94% yield.

Colorless crystals; recrystallized from hexane-ethyl acetate.

$\lambda_{max}$ : 339, 264 nm.

mp : 148-150 °C.

IR (KBr) $\nu_{max}$ : 2959, 1741, 1689, 1450, 1367, 1277, 1123, 1048, 931, 768 $cm^{-1}$.

$^1H$ NMR : δ 7.50-7.36 (Ar, 5H), 7.01 (s, 1H), 4.39 (s, 1H), 2.86-2.80 (m, 1H), 2.65 (s, 1H), 2.56-2.45 (m, 2H), 2.34-2.29 (m, 1H), 1.16 (s, 9H), 1.01 (s, 9H).

$^{13}C$ NMR : δ 200.28, 198.74, 152.58, 151.55, 138.33, 128.90, 128.32, 124.77, 110.90, 85.44, 80.29, 46.77, 38.18, 35.97, 32.83, 32.10, 30.44, 28.58.

***Compound 80***

A solution of the cycloadduct **44** (0.035 g, 0.10 mmol) in dry acetonitrile (25 mL) was purged with argon for 15 min in a quartz vessel and irradiated for 20 min inside a Rayonet Photochemical Reactor using 350 nm lamp. The yellow reaction mixture becomes colorless. The solvent was

evaporated off and the residue purified by gel column chromatography and afforded **80** (0.026 g, 74%).

Colorless crystals; recrystallized from hexane-ethyl acetate.

IR (KBr) $\nu_{max}$ : 2968, 1736, 1688, 1362, 1265, 1175, 1093, 1043, 859 $cm^{-1}$.

$^1H$ NMR : δ 7.02 (s, 1H), 4.20 (s, 1H), 2.75-2.63 (m, 1H), 2.53 (s, 1H), 2.43-2.35 (m, 1H), 2.24-2.13 (m, 2H), 1.60 (s, 3H), 1.14 (d, 18H, $J$ = 5.2 Hz).

$^{13}C$ NMR : δ 200.28, 199.00, 152.50, 151.40, 110.25, 85.63, 80.01, 46.63, 36.22, 36.04, 32.18, 32.00, 31.80, 28.60, 28.47, 23.29.

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# CHAPTER 3

# DIPOLAR CYCLOADDITION REACTIONS OF AZOMETHINE YLIDES WITH 1,2-DIONES

## 3.1 INTRODUCTION

In the Huisgen classification of dipoles, azomethine ylides belong to the allyl type and are regarded as azomethinium betaines without a double bond in the sextet structure but with internal octet stabilization.[1] These dipoles are bent even in the ground state.[1,2] This property accounts in part for the characteristic stereochemical aspects of 1,3-dipolar cycloadditions of azomethine ylides.

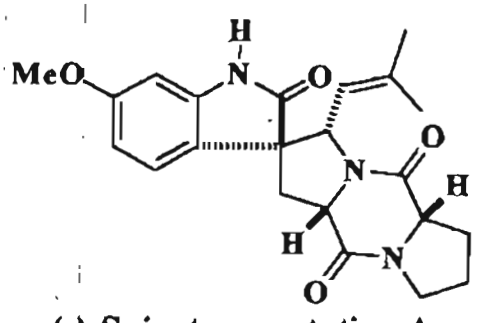
The 1,3-dipolar cycloaddition reactions of azomethine ylides are invariably stereospecific with respect to both the dipole and the dipolarophile.[1,2]

According to Sustmann's classification of 1,3-dipolar cycloadditions,[3] substituents that raise the dipole HOMO energy or lower the dipolarophile LUMO energy will accelerate HOMO-controlled reactions. Calculations of the energies of the various orbitals involved in different types of cycloadditions on this basis revealed that the ylides including azomethine ylides are all electron rich species characterized by relatively high energy

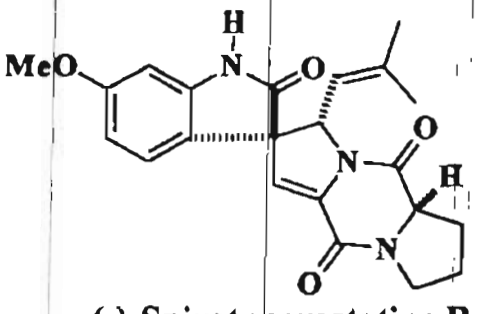
HOMOs and LUMOs. Such species react preferentially with electron-deficient alkenes because such a pair of reactants has a narrow dipole HOMO-dipolarophile LUMO gap.[3-7]

Azomethine ylides have proven to be extraordinarily rich in their chemistry. The synthetic utility of their 1,3-dipolar cycloadditions to a wide range of dipolarophiles has made available a variety of mono, bi, and tricyclic heterocycles.[8]

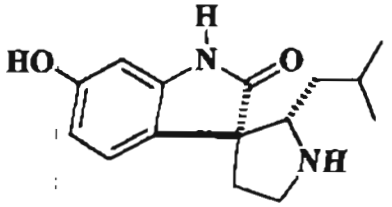
It is worthy of note that polycyclic nitrogen containing heterocycles form the basic skeleton of numerous alkaloids and therapeutic agents.[9,10] Pyrrolidine, pyrrolizidine and oxindole alkaloids constitute a class of compounds with significant biological activity and the spiro[pyrrolidine/oxindole] ring system is common to most oxindole alkaloids.[11] Spiropyrrolidinyl-oxindole skeletons are present in spirotryprostatine A and spirotryprostatine B,[12] the potent inhibitors of mammalian cell cycle at G2/M phase. Other examples of 3,3'-spirooxindole skeleton are found in (+)-Elacomine[13] and (-)-Horsfiline[14] (Figure 1).



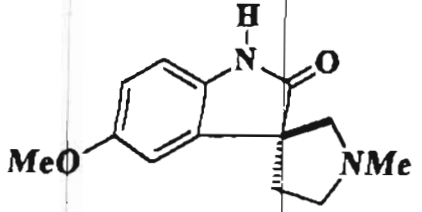

**(-)-Spirotryprostatine A**




**(-)-Spirotryprostatine B**




***(+)-Elacomine***




***(-)-Horsfiline***

**Figure 1**

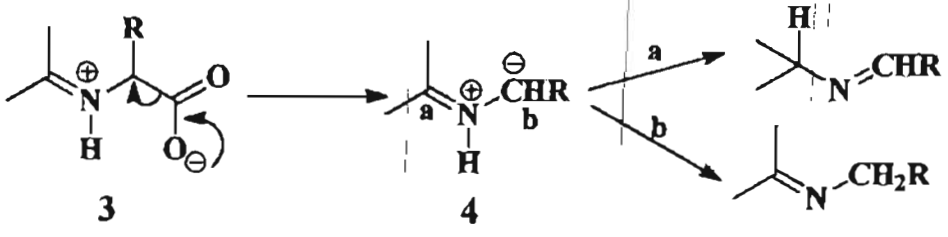
A number of methods, including thermal or photolytic ring opening of aziridines,[15] desilylation,[16] or dehydrohalogenation of iminium salts,[17] tandem reaction of carbenoids with simple imines,[18] and proton abstraction from imine derivatives of α-amino acids[19] have been developed for the generation of azomethine ylides. Since they are unstable species, they are prepared *in situ* in low concentrations.

Grigg *et al.* reported the formation of azomethine ylides from α-amino acid esters.[19] In this reaction, the imine derivative of an α-amino acid ester bearing at least one enolizable hydrogen α to the ester **1** is in equilibrium with the azomethine ylide **2** which may be trapped by a variety of dipolarophiles (Scheme 1).

**Scheme 1**

Recently, these workers have reported an interesting and general method for the preparation of azomethine ylides which involves decarboxylative transamination of α-amino acids.[20]

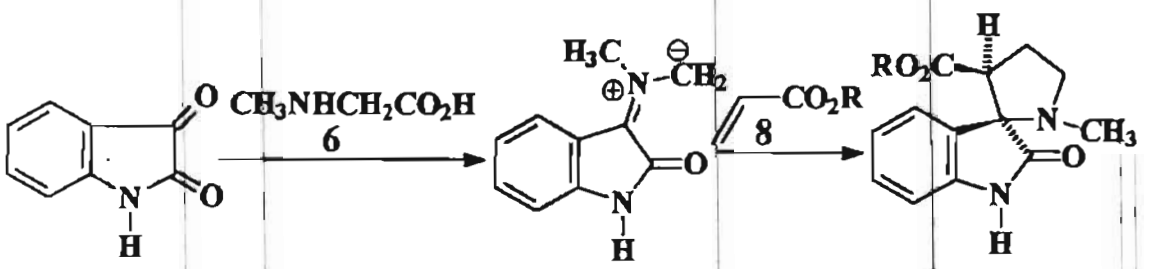
The mechanism of decarboxylative transamination is shown in Scheme 2. It is conceivable that the imine undergoes decarboxylation *via* the zwitterionic form **3** generating the 1,3-dipole **4**.[20]



**Scheme 2**

The final location of the proton in the neutral imine product would then depend on a kinetically controlled proton transfer to the site in the dipole (**6**; **a** or **b**) with the greatest electron density.

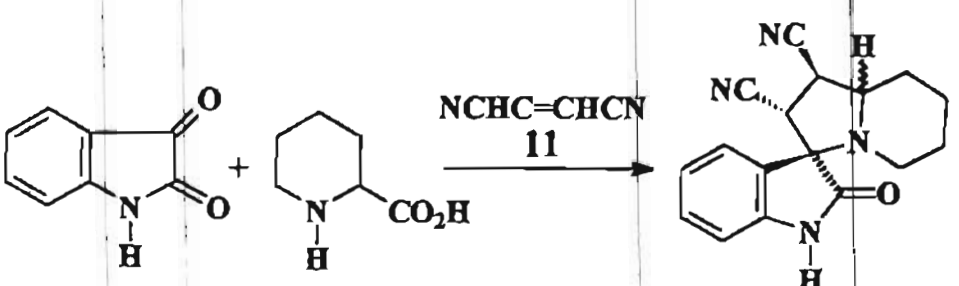
Solution phase azomethine ylides resulting from the condensation of 1,2-dicarbonyl compounds with α-amino acids or amines and their cycloaddition reactions with maleimides and acrylic esters were studied by Grigg.[20,21] For example, isatin **5**, sarcosine **6** and menthyl/methyl acrylate **8** react regio and stereospecifically in boiling acetonitrile to give a single cycloadduct in good yield *via* the azomethine ylide **7** (Scheme 3).[21]




**5** **7** **9**

**Scheme 3**

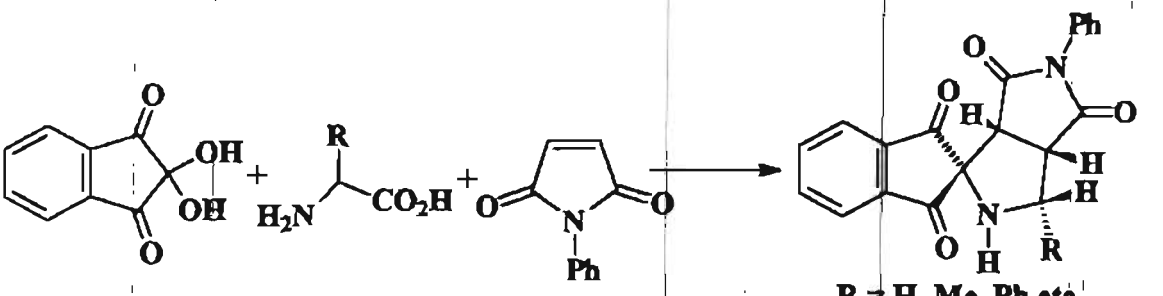
When isatin, pipecolic acid **10** and fumaronitrile **11** were heated in MeOH, the cycloadduct **12** was obtained in 76% yield (Scheme 4).[20b]




**5** **10** **12**

**Scheme 4**

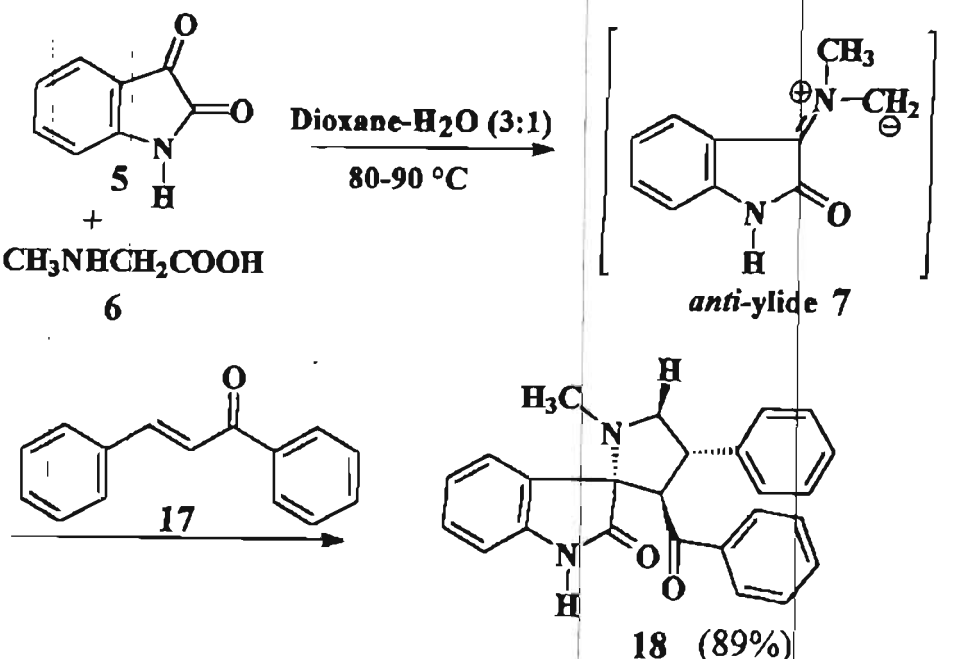
When ninhydrin was allowed to react with α-amino acids in methanol at room temperature for 12-18 h in the presence of N-phenyl maleimide **15**, the cycloadducts **16** were formed stereospecifically *via* an *endo* transition state in 50-80% yield (Scheme 5).[20b]




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

**Scheme 5**

Recently it has been reported that an azomethine ylide **7**, generated by the decarboxylative condensation of isatin with sarcosine, was trapped by a *trans* chalcone **17** to afford the heterocycle **18** (Scheme 6).[22]




**Scheme 6**

The product was purified by silica gel column chromatography and characterized by spectral analysis. The IR spectrum of **22** showed bands characteristic to -OH, $-CO_2Me$ and $-CONCH_3$ at 3562, 1728 and 1702 $cm^{-1}$ respectively. In the $^1H$ NMR spectrum, the -OH proton resonated at δ 2.08 as a sharp singlet (exchangeable with $D_2O$). The methyl protons of the ester appeared as a sharp singlet at δ 3.93. The methylene protons on C-5 appeared as separate doublets at δ 4.15 ($J$ = 8.7 Hz) and 3.69 ($J$ = 8.7 Hz). The methyl protons on the lactam nitrogen appeared as a sharp singlet at δ 2.85 and the other $-NCH_3$ protons resonated at δ 2.06 as a singlet (Figure 2). In the $^{13}C$ NMR spectrum, the two carbonyl carbons C-2 and C-9 appeared at δ 175.84 and 170.31 respectively. The signal due to the methoxy carbon was seen at δ 52.16 and the spiro carbon C-3 at δ 77.92. The methylene carbon C-5 appeared at δ 62.42 and the three quaternary carbons of the cyclopropane ring resonated at δ 65.03, 54.59 and 42.74 respectively. These assignments are supported by DEPT-135 NMR studies (Figures 3 and 4).

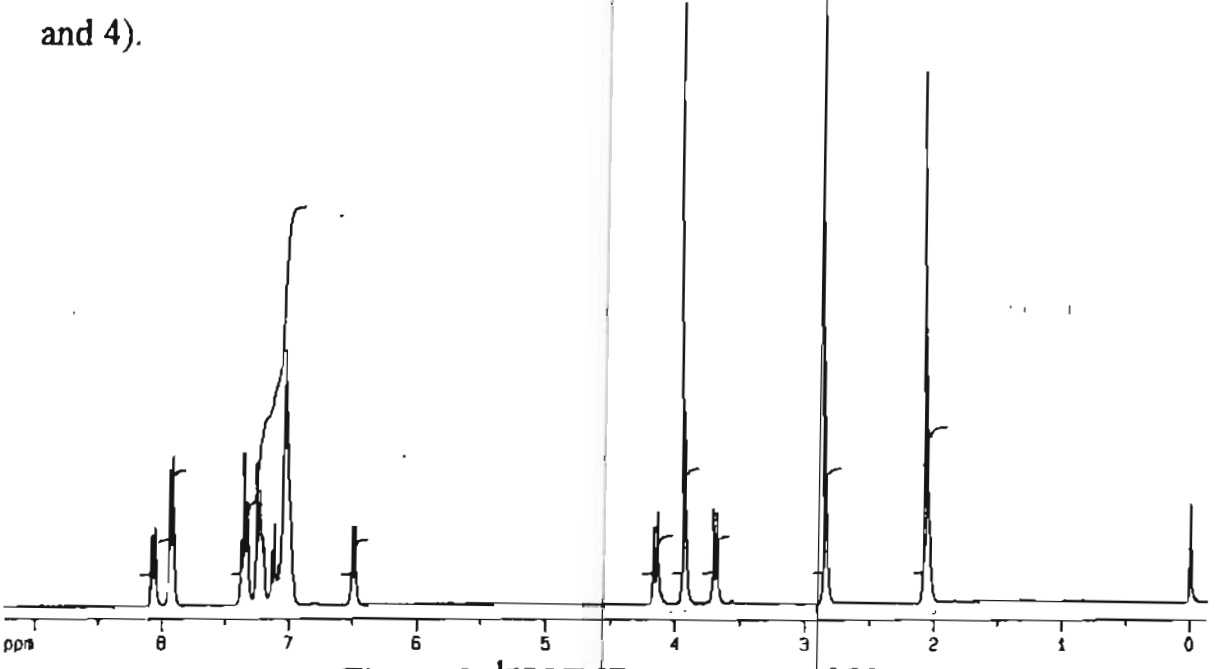



**Figure 2. $^1H$ NMR spectrum of 22**

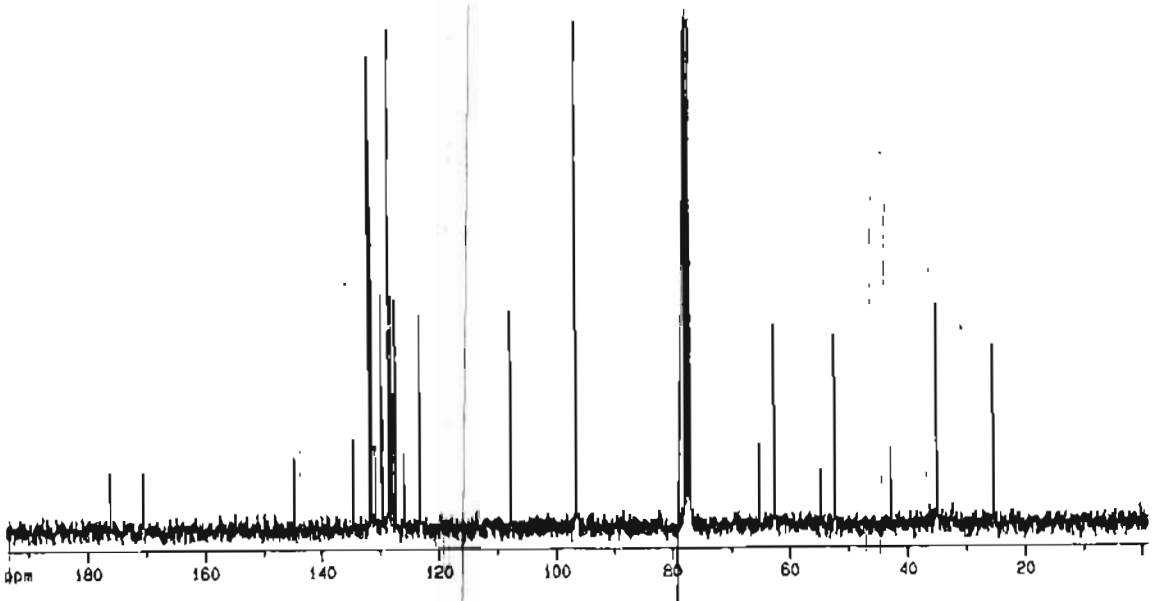



**Figure 3. $^{13}C$ NMR spectrum of 22**

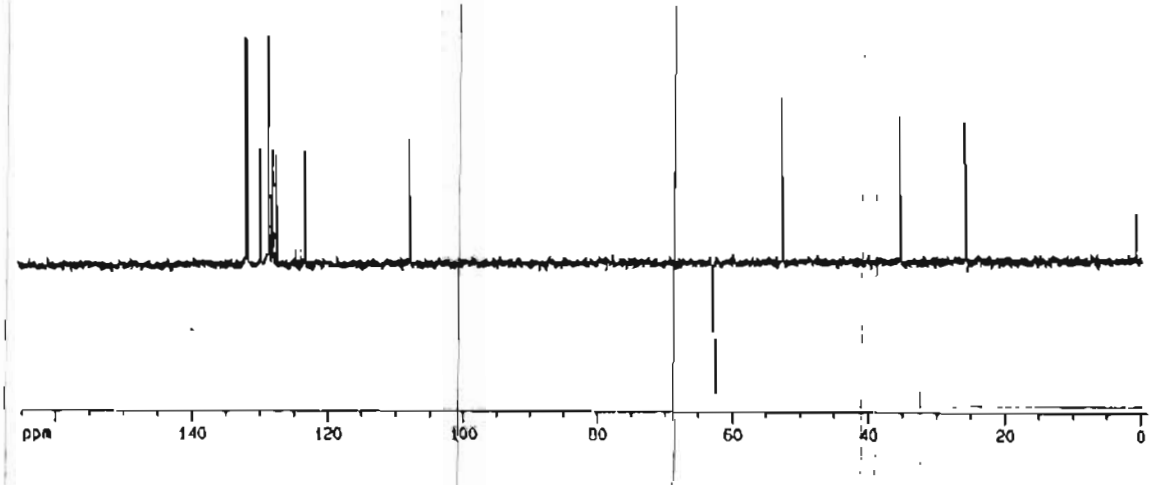



**Figure 4. DEPT-135 spectrum of 22**

Ultimately the structure was confirmed unequivocally by single crystal X-ray analysis of **22** (Figure 5).

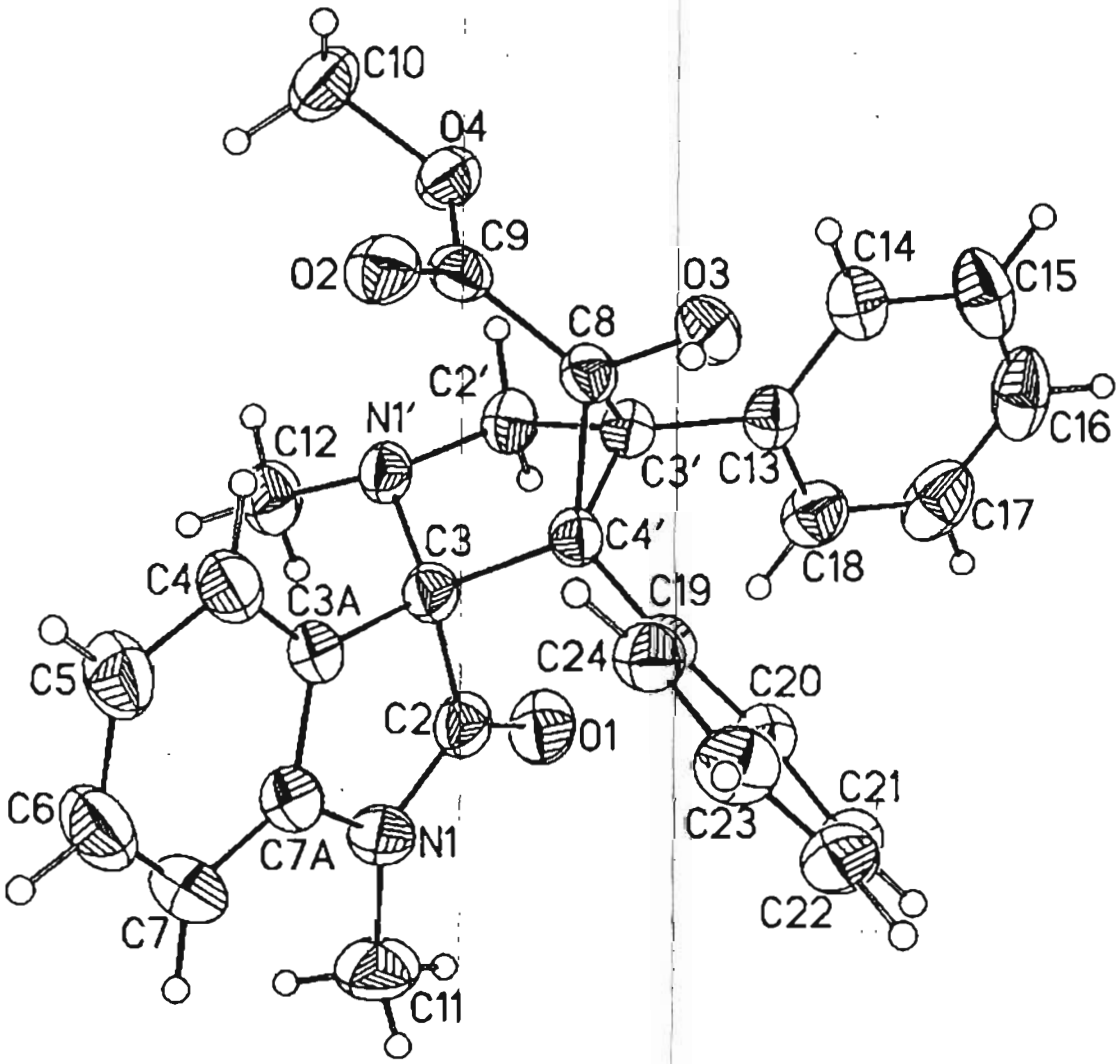
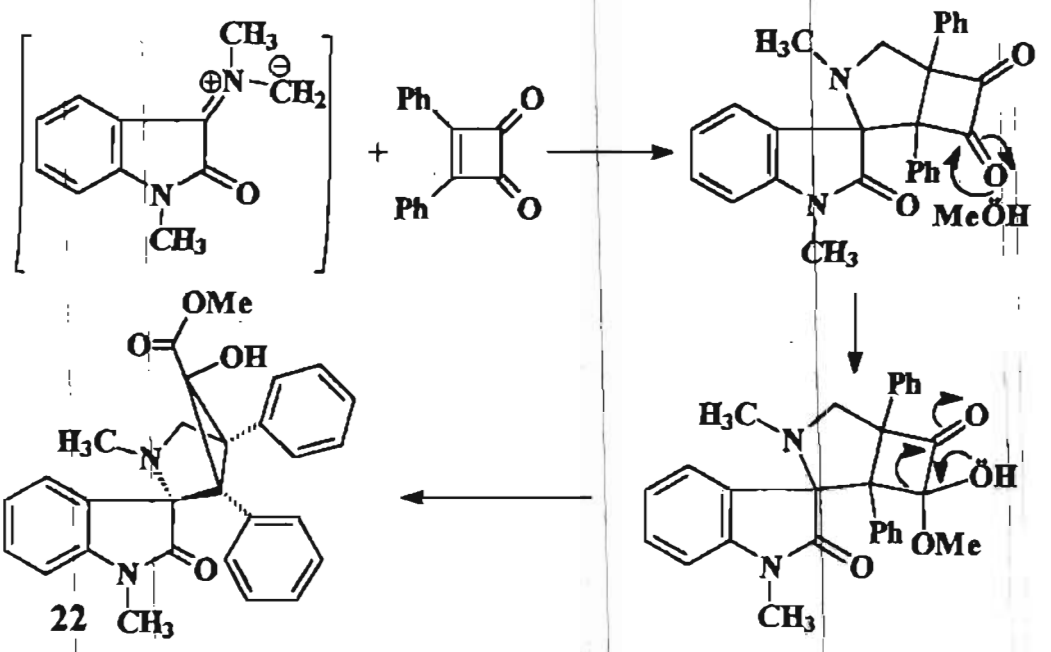



**Figure 5. X-ray crystal structure of 22**

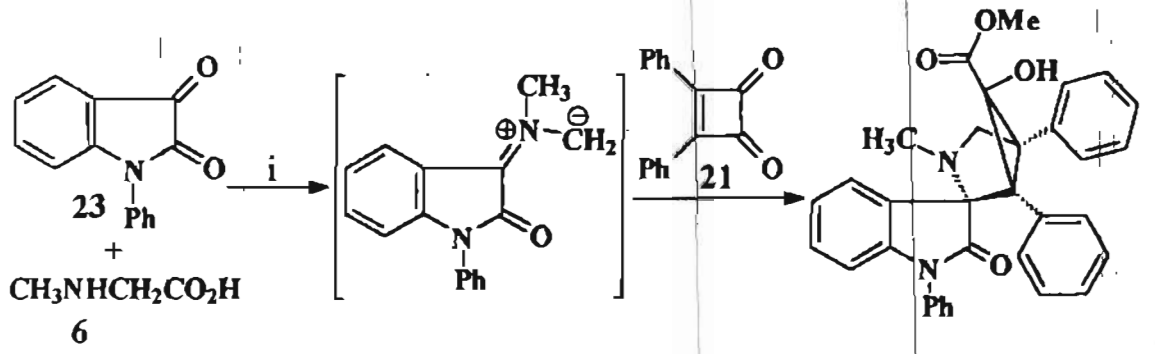
Regarding the mechanism of formation of the product **22**, a rationalization as outlined in Scheme 8 may be invoked. It is reasonable to assume that the cycloaddition proceeds by the initial attack of azomethine ylide preferentially on the carbon-carbon double bond of 3,4-diphenylcyclobutene-1,2-dione leading to a cyclobutane derivative which then undergoes rearrangement.[27]



**Scheme 8**

Similar reactivity was observed with other substituted isatins also. The results are discussed below.

Trapping of the azomethine ylide **24**, generated by the decarboxylative condensation of 1-phenylisatin **23** and sarcosine with 3,4-diphenylcyclobutene-1,2-dione **21** in MeOH:$H_2O$ system at 90 °C afforded a colorless solid product **25** in 38% yield (Scheme 9). Yield based on recovered cyclobutenedione was 53%.

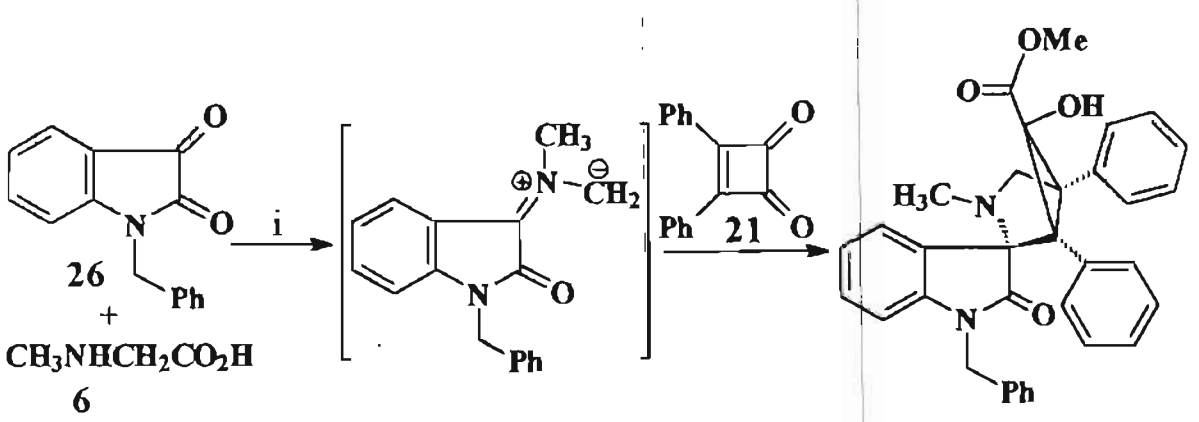


**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 9**

The structure of the product was established from its spectral data. The IR spectrum of **25** showed the -OH stretching at 3455 $cm^{-1}$. A broad band was observed at 1715 $cm^{-1}$ in the IR spectrum due to overlapping of the ester and lactam carbonyls. In the $^1H$ NMR spectrum, the methoxy protons appeared as a sharp singlet at δ 3.96 and the $-NCH_3$ protons were visible as a singlet at δ 2.23. The hydroxyl proton was discernible as a singlet δ 2.17 (exchangeable with $D_2O$). In the $^{13}C$ NMR spectrum, the lactam and ester carbonyl signals were visible at δ 175.38 and 170.21 respectively. The characteristic spiro carbon signal was discernible at δ 77.98. All the other signals were in agreement with the assigned structure.

The reaction of 1-benzylisatin[25] **26**, sarcosine and 3,4-diphenylcyclobutene-1,2-dione also proceeded in a similar fashion affording a colorless solid product **28** in 48% isolated yield. Yield based on recovered cyclobutenedione was 65% (Scheme 10).



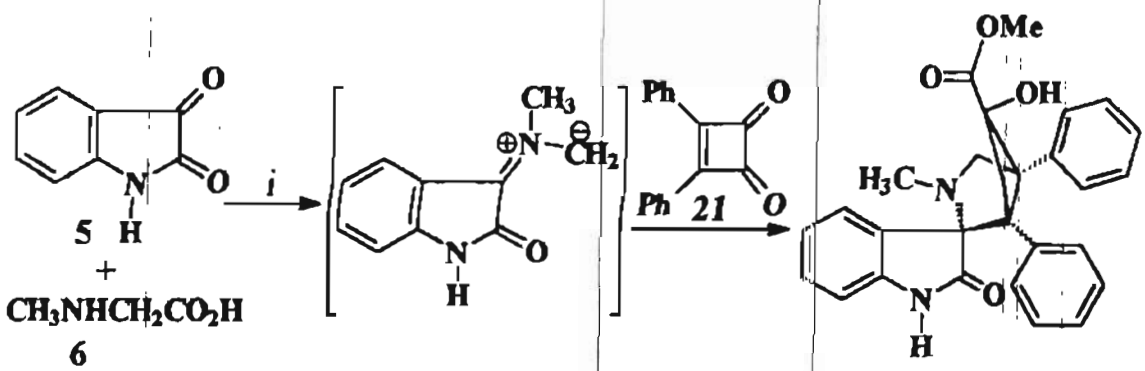

**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 10**

The characterization of the product was done by the usual spectral methods. The IR spectrum of **28** showed the -OH stretching as a broad band

at 3425 $cm^{-1}$ and the lactam and the ester carbonyls at 1689 and 1732 $cm^{-1}$ respectively. In the $^1H$ NMR spectrum, the -OH proton appeared as a sharp singlet at δ 2.16 (exchangeable with $D_2O$). The benzylic protons resonated as doublets at δ 5.00 (1H, $J$ = 16 Hz) and 4.36 (1H, $J$ = 16 Hz). In the $^{13}C$ NMR, the lactam and ester carbonyls resonated at δ 175.57 and 170.54 respectively; **28** gave satisfactory high resolution mass also.

Similarly, the azomethine ylide **7** generated *in situ* from isatin and sarcosine under the above reaction conditions underwent facile cycloaddition with 3,4-diphenylcyclobutene-1,2-dione to afford the spiropyrrolidine derivative **29** in 49% yield (Scheme 11). Yield based on recovered dione **21** was 57%.



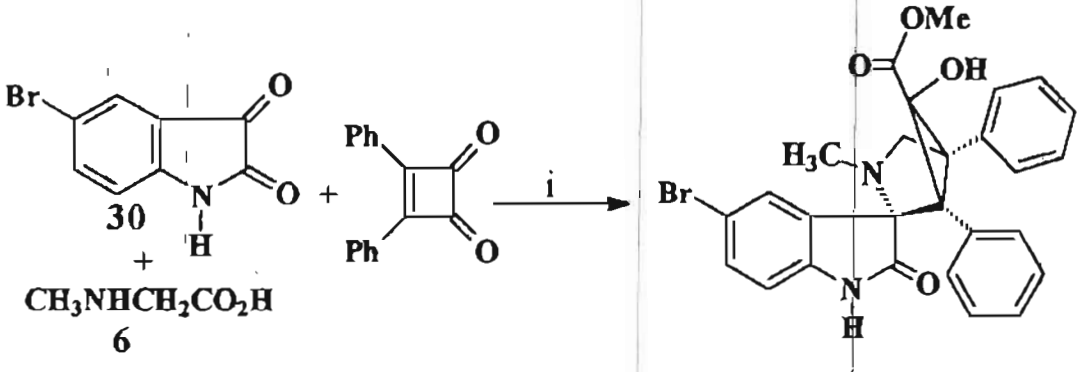

**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 11**

The structure of the product **29** was established from the spectral data. The IR spectrum of **29** showed the -OH stretching at 3431 $cm^{-1}$. In the $^1H$ NMR spectrum, the -NH proton resonated as a sharp singlet at δ 8.36 while the -OH proton was seen as a singlet at δ 2.60 (exchangeable with $D_2O$). The methoxy and methyl protons appeared as singlets at δ 3.90 and 2.03 respectively. In the $^{13}C$ NMR spectrum, the lactam carbonyl was discernible

at δ 178.25 while the ester carbonyl appeared at δ 170.59. From the DEPT-135 spectrum, the presence of one methylene moiety was easily discernible. The signals due to the four quaternary carbons were absent in the DEPT-135 spectrum.

Similar reactivity was shown by 5-bromoisatin **30**, sarcosine and 3,4-diphenylcyclobutene-1,2-dione. The major product isolated was the colorless solid spiropyrrolidine derivative **31** in 31% yield (Scheme 12). Yield based on recovered cyclobutenedione was 41%.




**21** **31** (31%)

**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 12**

As usual, the structure of the product was ascertained from its spectral data. The stretching bands characteristic to -OH and -NH were observed at 3555 and 3299 $cm^{-1}$ respectively in the IR spectrum. A broad band was observed at 1721 $cm^{-1}$ in the IR spectrum, due to the overlapping of the ester and lactam carbonyls. In the $^1H$ NMR spectrum, the -NH proton resonated at δ 8.17 as a broad singlet and the -OH proton as a sharp singlet at δ 2.44; both disappeared on $D_2O$ exchange. In the $^{13}C$ NMR spectrum, the lactam and the ester carbonyls resonated at δ 178.08 and 170.48 respectively. All the other signals were in good agreement with the assigned structure.

## 3.2.2 Theoretical Calculations

In order to explain the observed regioselectivity in the above reactions, we have carried out some theoretical calculations using PC SPARTAN Graphical Interface Package for Molecular Mechanics and Molecular Orbital Models. The correlation diagram for the reaction of 3,4-diphenylcyclobutene-1,2-dione **21** with the azomethine ylide **20** is provided as an illustrative example in Figure 6.

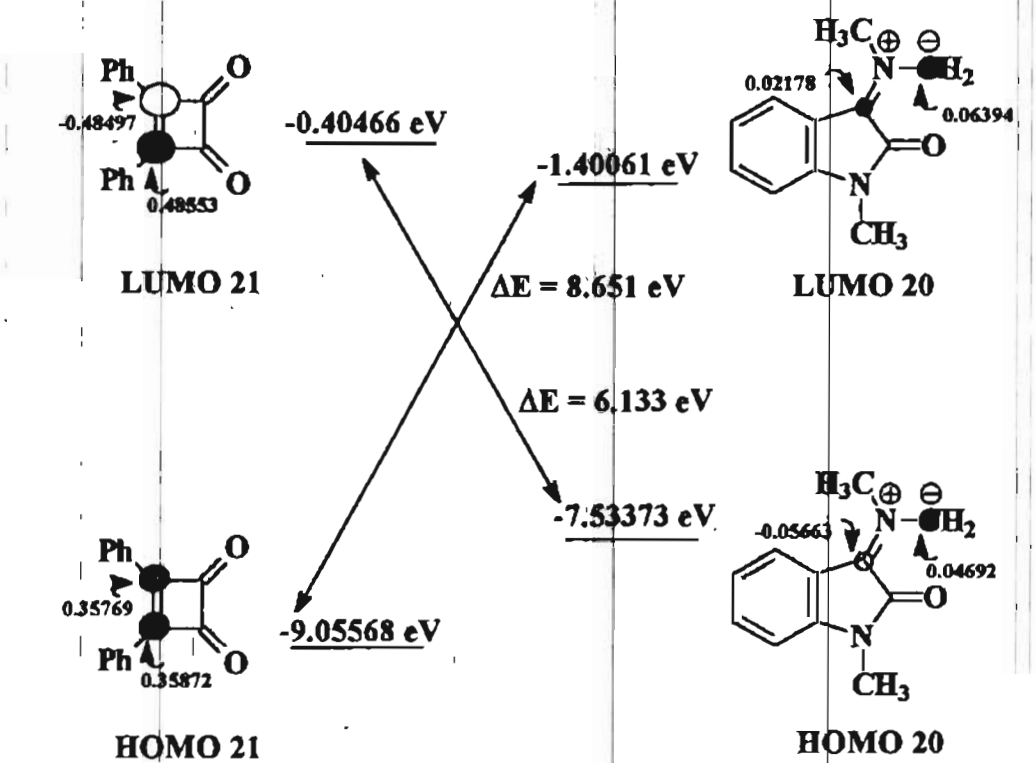


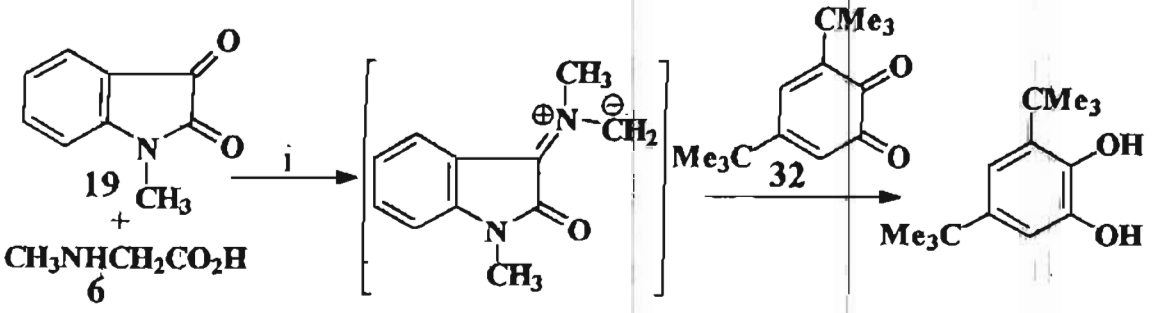

**Figure 6.** Molecular orbital correlation diagrams of 3,4-diphenylcyclobutene-1,2-dione **21** and the azomethine ylide **20**.

From the correlation diagram in Figure 6, it is clear that the reaction of 3,4-diphenylcyclobutene-1,2-dione **21** with the azomethine ylide **20** is controlled by HOMO of the dipole ie, a type I reaction according to Sustmann's classification.[3] It is found that HOMO(**21**)-LUMO(**20**)

interaction is unimportant due to large energy gap while HOMO(**20**)-LUMO(**21**) interaction is favorable.

### 3.2.3 Attempted Cycloaddition Reactions of Isatin-Derived Azomethine Ylide with 1,2-Benzoquinones

As a part of our continuing interest in probing the dipolarophilic profile of 1,2-benzoquinones,[23,24] we carried out some work on their reaction with azomethine ylide generated *in situ* from isatin and sarcosine. Attempts to trap the azomethine ylide **20** with 3,5-di-*tert*-butyl-1,2-benzoquinone **32** and 4-*tert*-butyl-1,2-benzoquinone failed to give any cycloadduct under the reaction conditions. In both cases, the quinones were converted to the corresponding catechols. An illustrative example is shown below (Scheme 13).



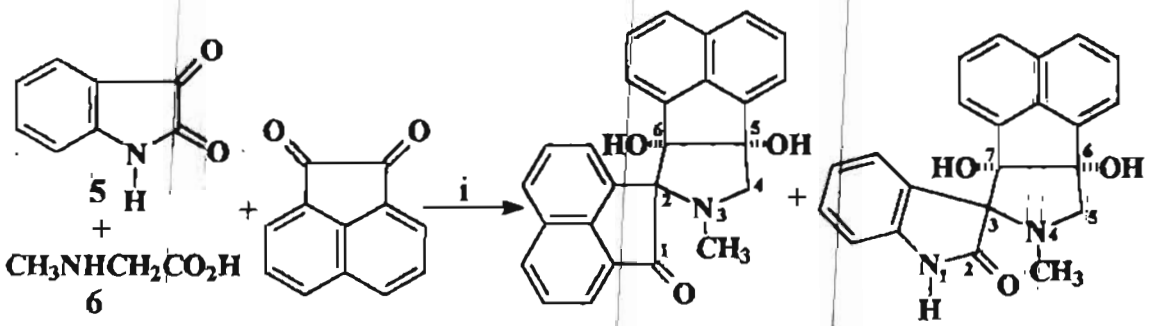

**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 13**

Presumably, the genesis of the catechol involves electron transfer between the ylide and the quinone.

### 3.2.4 Cycloaddition Reactions of Azomethine Ylides with Acenaphthenequinone

Subsequent to the investigations described, we focused our attention on the reaction of isatin with sarcosine and acenaphthenequinone. Interestingly, the reaction proceeded smoothly to afford a mixture of two products. These were separated by silica gel column chromatography and characterized by spectral analysis as the cycloadducts **35** (52%) and **36** (30%) (Scheme 14).




**34** **35** (52%) **36** (30%)

**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 14**

The IR spectrum of **35** showed stretching bands characteristic to hydroxyl and carbonyl groups at 3499, 3455 and 1710 $cm^{-1}$ respectively. In the $^1H$ NMR spectrum, the methylene protons on C-4 appeared as two doublets at δ 4.21 (1H, $J$ = 9.9 Hz) and 3.77 (1H, $J$ = 10.0 Hz). The two -OH protons resonated as sharp singlets at δ 3.57 and 3.36 (exchangeable with $D_2O$). The $-NCH_3$ protons appeared as a singlet at δ 2.01 (Figure 7). In the $^{13}C$ NMR spectrum, the signal due to the carbonyl group was discernible at δ 209.92. The three quaternary carbons appeared at δ 91.51, 86.96 and 81.31. The methylene carbon C-4 resonated at δ 66.95 while the methyl

carbon at δ 35.18. From the DEPT-135 spectrum, the presence of one methylene moiety was easily discernible (Figures 8 and 9).

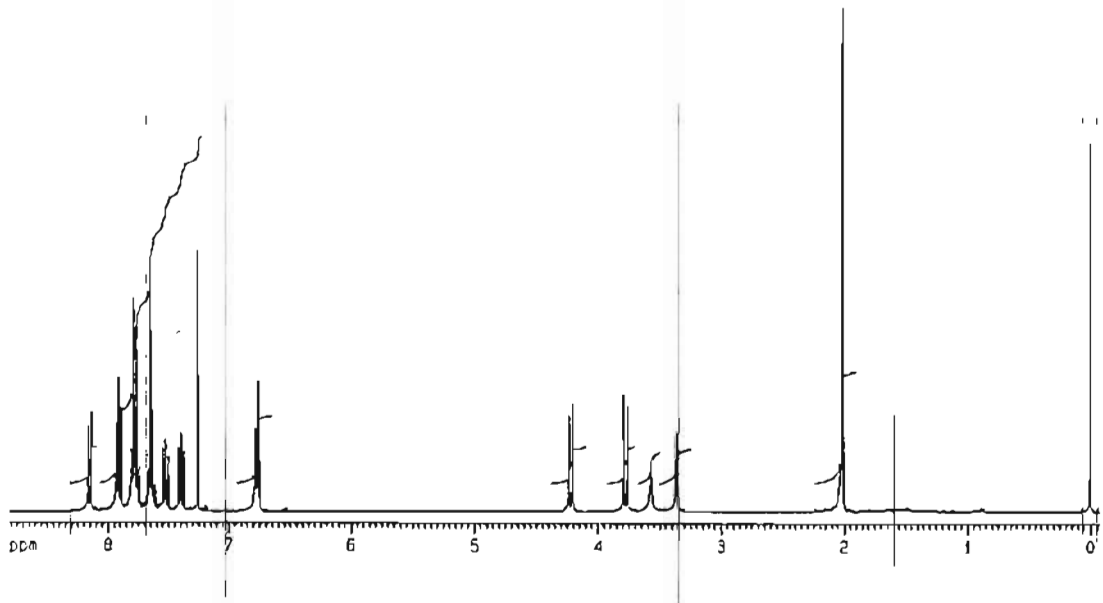



**Figure 7. $^{1}$H NMR spectrum of 35**

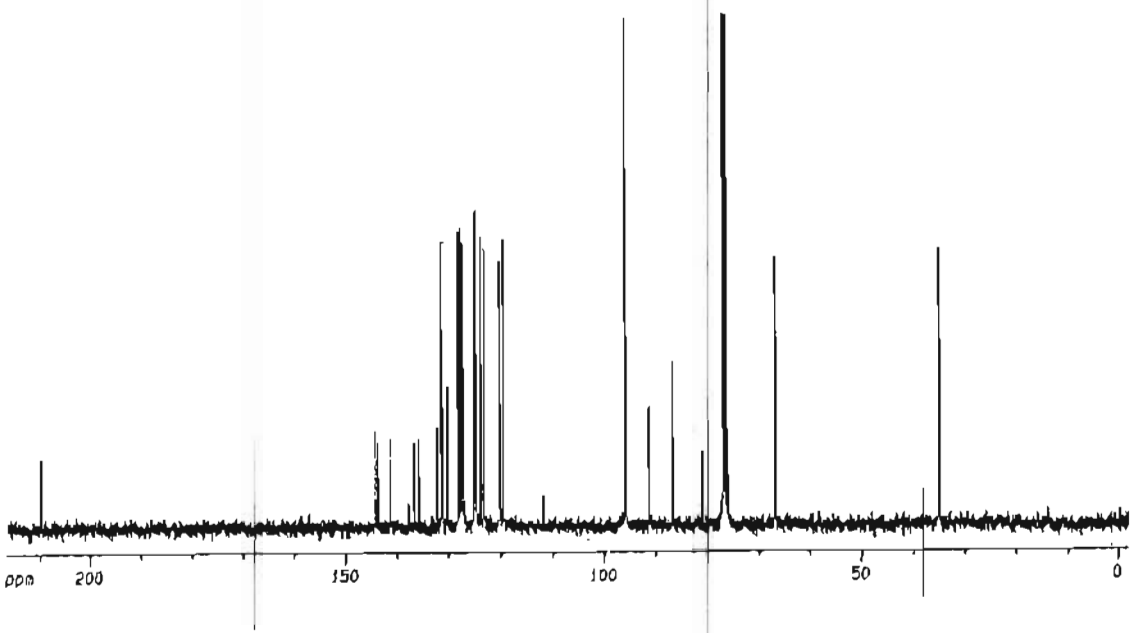



**Figure 8. $^{13}$C NMR spectrum of 35**

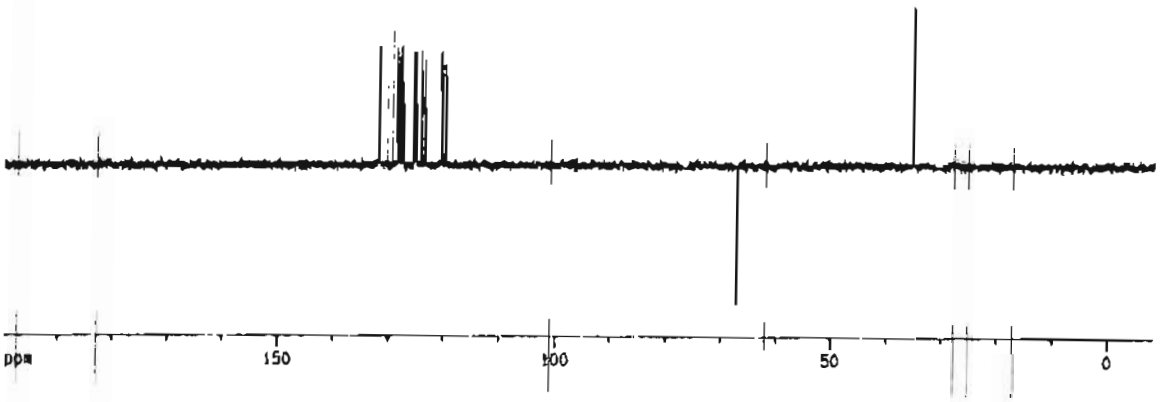



**Figure 9. DEPT-135 NMR spectrum of 35**

Finally the structure assigned was confirmed unequivocally by single crystal X-ray structure determination of **35** (Figure 10).

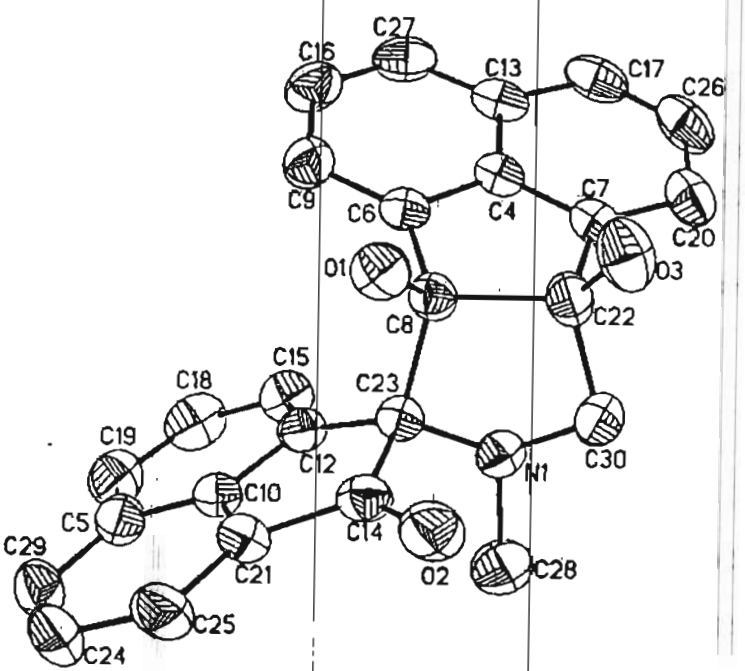
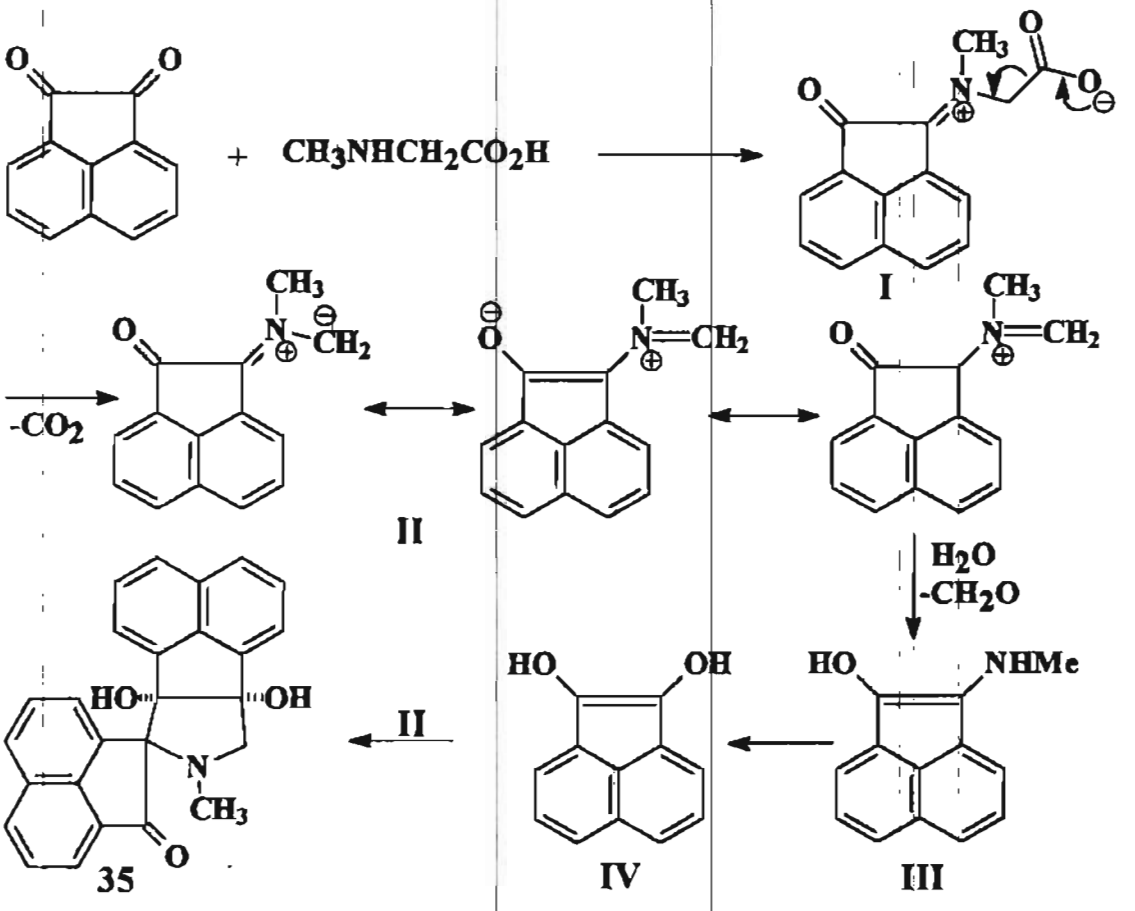



**Figure 10. X-ray crystal structure of 35**

A mechanistic rationalization as outlined in Scheme 15 may be invoked for the formation of the product **35**.[28,29] It is conceivable that the reaction of sarcosine with acenaphthenequinone leads to the formation of **I**. Decarboxylative transamination of **I** produces the aza-allylic species **II**, which undergoes further transformation leading to the enediol **IV**; the latter undergoes cycloaddition to the dipole **II** to afford the spirocompound **35**.



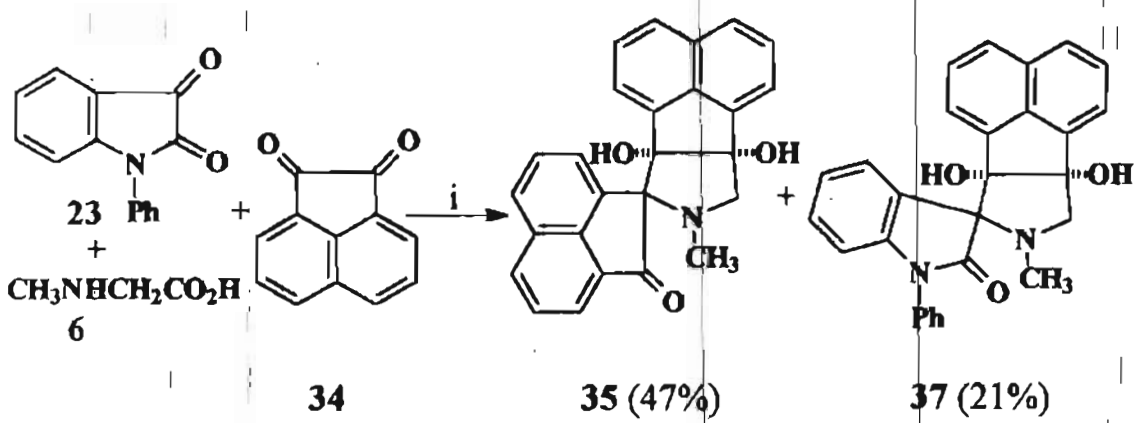

**Scheme 15**

The structure of the product **36** was ascertained from the spectral data. The bands characteristic to -OH and -NH were observed at 3363 and 3176 $cm^{-1}$ respectively. A strong absorption at 1689 $cm^{-1}$ was assigned to the carbonyl group. In the $^1H$ NMR spectrum, the -NH proton resonated at δ 10.13 as a sharp singlet and the two -OH protons appeared as sharp

*singlets at δ 5.06 and 5.00 (exchangeable with $D_2O$). The two methylene* protons on C-5 appeared as doublets at δ 4.13 (1H, $J$ = 9.2 Hz) and 3.52 (1H, $J$ = 9.2 Hz). In the $^{13}C$ NMR spectrum, the lactam carbonyl resonance was seen at δ 178.14. The signals at δ 64.81 and 34.40 were assigned to the methylene and methyl carbons respectively. All the other signals were comparable to those of **35**.

The reaction took a similar course with other substituted isatins also. The results are discussed below.

The reaction of 1-phenylisatin **23**, sarcosine and acenaphthenequinone **34** in MeOH:$H_2O$ at 90 °C proceeded smoothly to afford a mixture of products **35** (47%) and **37** (21%) (Scheme 16).



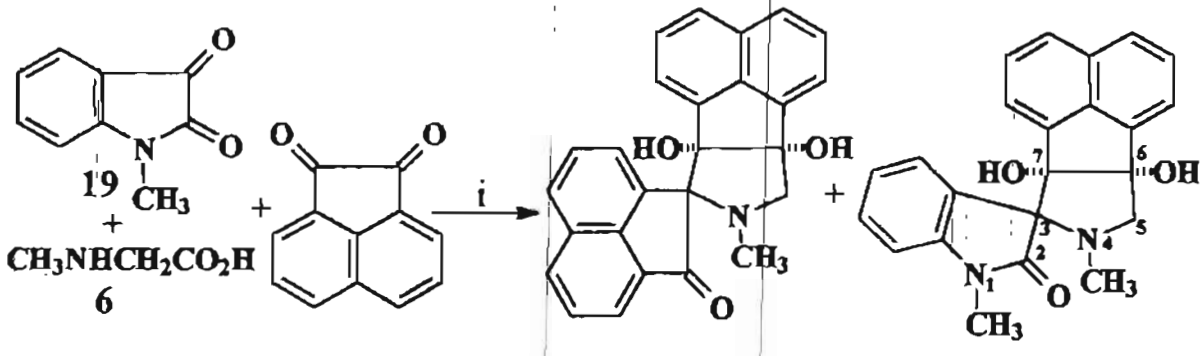

**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 16**

The structures of the products were established on the basis of their spectral data. The IR spectrum of **37** showed bands characteristic to hydroxyl and carbonyl groups at 3488 and 1695 $cm^{-1}$ respectively. In the $^1H$ NMR spectrum, the two -OH protons resonated as sharp singlets at δ 5.27 and 5.14 (exchangeable with $D_2O$). The $-NCH_3$ protons appeared as a singlet at δ 2.07. In the $^{13}C$ NMR spectrum, the signal due to the lactam carbonyl

was visible at δ 174.69. The methylene carbon was discernible at δ 64.14 and the methyl carbon at δ 33.75. All the other signals were in agreement with the proposed structure.

Similar reactivity pattern was observed in the multicomponent reaction between 1-methylisatin **19**, sarcosine and acenaphthenequinone. The reaction proceeded smoothly and afforded the products **35** (56%) and **38** (31%) (Scheme 17).




**34** **35** (56%) **38** (31%)

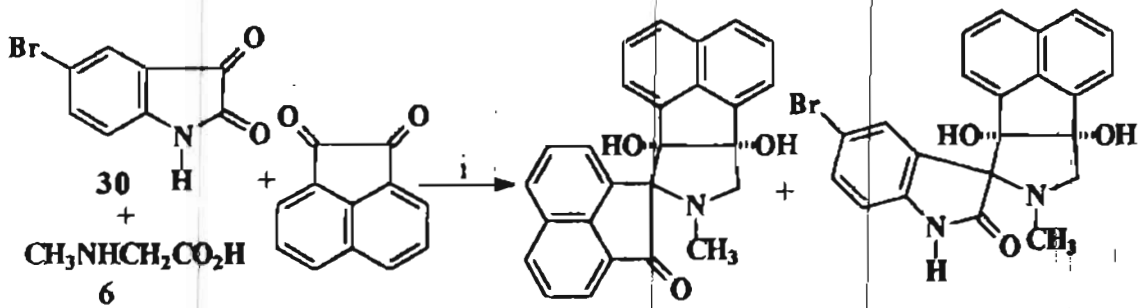
**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 17**

The products were characterized on the basis of spectral data. The IR spectrum of **38** showed a broad band at 3438 $cm^{-1}$ characteristic for -OH group; the carbonyl absorption was seen at 1686 $cm^{-1}$. In the $^1H$ NMR spectrum, the two -OH protons were discernible at δ 4.01 and 3.68 (exchangeable with $D_2O$) as sharp singlets. The two C-5 protons appeared as separate doublets at δ 4.04 (1H, $J$ = 9.9 Hz) and 3.62 (1H, $J$ = 9.9 Hz). The protons of the N-1 methyl group resonated at δ 3.23 while that of N-4 methyl group resonated at δ 1.92. In the $^{13}C$ NMR spectrum, the lactam carbonyl C-2 appeared at δ 177.86. The signal at δ 78.27 was assigned to the

spiro carbon C-3. All the other signals were in agreement with the assigned structure.

The multicomponent reaction between 5-bromoisatin **30**, sarcosine and acenaphthenequinone proceeded smoothly to afford a mixture of products **35** (55%) and **39** (20%) (Scheme 18).



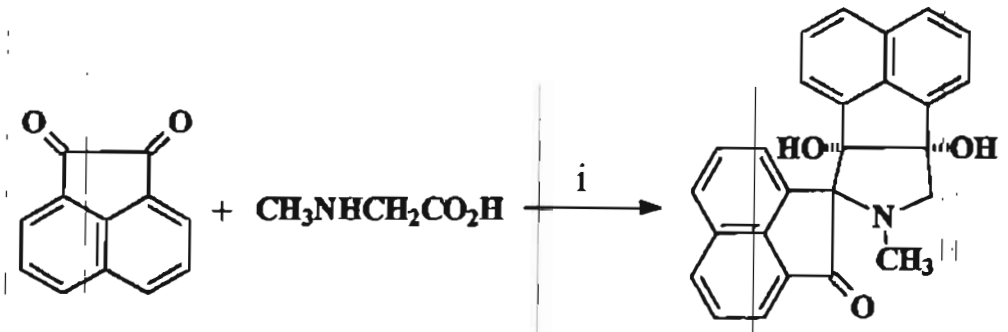

**34** **35** (55%) **39** (20%)

**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 18**

The products were characterized on the basis of spectral data. The IR spectrum of **39** showed strong bands at 3363 and 1696 $cm^{-1}$ characteristic for hydroxyl and carbonyl groups respectively. In the $^1H$ NMR spectrum, the two -OH protons resonated as sharp singlets at δ 5.23 and 5.12 (exchangeable with $D_2O$). The signal due to the $-NCH_3$ proton was discernible at δ 1.98 as a sharp singlet. In the $^{13}C$ NMR spectrum, the lactam carbonyl resonated at δ 176.39. All the other signals were in agreement with the assigned structure.

In order to verify the origin of cycloadduct **35**, we carried out a reaction of sarcosine and excess acenaphthenequinone in MeOH:$H_2O$ at 90 °C. As expected, the blank reaction also gave the cycloadduct **35** in 72% yield (Scheme 19).




**34** **6** **35** (72%)

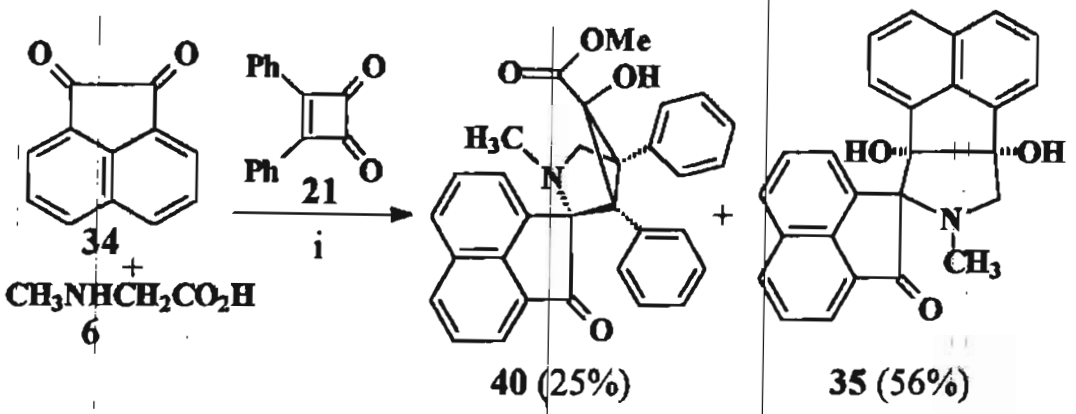
**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 19**

The product was purified by silica gel column chromatography and characterized by spectral analysis. The spectra obtained were identical to those of **35**, isolated in earlier experiments.

## 3.2.5 Cycloaddition Reaction of Acenaphthenequinone-Derived Azomethine Ylide and 3,4-Diphenylcyclobutene-1,2-dione

From the above experiments, it is clear that an azomethine ylide is generated by the reaction between acenaphthenequinone and sarcosine. Therefore we performed an experiment with a view to trap this azomethine ylide, (generated *in situ*) with 3,4-diphenylcyclobutene-1,2-dione. The reaction afforded a yellow solid product **40** in 25% isolated yield together with 56% of the cycloadduct **35** (Scheme 20). Yield of the cycloadduct **40** based on recovered dione **21** was 38%. The products were purified by silica gel column chromatography and characterized by spectral analysis.




**i. MeOH:$H_2O$ (3:1), 90 °C, 24 h**

**Scheme 20**

The IR spectrum of **40** showed the -OH stretching at 3550 $cm^{-1}$ and two sharp bands at 1771 and 1716 $cm^{-1}$ assignable to the ester and the keto carbonyls respectively. In the $^1H$ NMR spectrum, the -OH proton was discernible at δ 2.17 as a sharp singlet (exchangeable with $D_2O$). In the $^{13}C$ NMR spectrum, the ester and aryl carbonyl signals were observed at δ 170.35 and 207.86. The characteristic spiro carbon signal was discernible at δ 80.73. All the other signals were in agreement with the assigned structure.

In conclusion, we have encountered facile dipolar cycloaddition reactions of 3,4-diphenylcylobutene-1,2-dione with the azomethine ylides derived from isatins yielding novel spiro[pyrrolidine-2,3'-oxindole]derivatives which may be amenable to a number of useful synthetic transformations. It is worthy of note that the spiro[pyrrolidinyl-oxindole]ring system is a recurring structural motif in a number of natural products with remarkable biological activity. Novel spiropyrrolidine derivatives are also formed in a mechanistically intriguing reaction involving isatins, sarcosine and acenaphthenequinone.

## 3.3 EXPERIMENTAL DETAILS

General information about the experiments is given in section **2.4** (Chapter 2).

**Typical Experimental Procedure**

The general procedure for the synthesis of spiro pyrrolidines/oxindoles is exemplified by the synthesis of **22**.

***Methyl 1',2'-dihydro-6-hydroxy-1',3-dimethyl-2'-oxo-1,5-diphenyl spiro[3-azabicyclo[3.1.0]hexane-2,3'-[3H]indole]-6-carboxylate (22)***

To a solution of 1-methylisatin **19** (0.206 g, 1.28 mmol) in methanol (6 mL) was added sarcosine **6** (0.228 g, 2.56 mmol) in distilled water (2 mL) and the mixture stirred at 90 °C for 5 min. This was followed by the addition of 3,4-diphenylcyclobutene-1,2-dione **21** (0.200 g, 0.85 mmol). The reaction mixture was allowed to stir at 90 °C for 24 h. The reaction mixture was diluted with water (30 mL) and extracted with dichloromethane (3 x 20 mL). The combined extract was washed with brine solution (10 mL) and dried over anhydrous sodium sulfate. The solvent was removed and the residue was chromatographed on a silica gel column. The unreacted cyclobutenedione **21** (0.031 g) was eluted using hexane-ethyl acetate (95:5) mixture. The cycloadduct **22** was separated using 10% ethyl acetate in hexane as eluent (0.226 g, 58%; yield based on recovered cyclobutenedione was 69%).

Colorless crystals; recrystallized from methanol-dichloromethane.

mp : 238-240 °C.

IR (KBr) $\nu_{max}$ : 3562, 3063, 2969, 1728, 1702, 1617, 1499, 1347, 1256, 1114, 762, 711 $cm^{-1}$.

$^1$H NMR : δ 8.07-7.01 (m, 13H), 6.49 (d, 1H, *J* = 7.5 Hz), 4.15 (d, 1H, *J* = 8.7 Hz), 3.93 (s, 3H), 3.69 (d, 1H, *J* = 8.7 Hz), 2.85 (s, 3H), 2.08 (s, 1H), 2.06 (s, 3H).

$^{13}$C NMR : δ 175.84, 170.31, 144.53, 134.35, 131.59, 131.22, 130.61, 129.46, 128.31, 128.21, 127.82, 127.67, 127.15, 125.72, 122.91, 107.46, 77.92, 65.03, 62.42, 54.59, 52.16, 42.74, 34.85, 25.33.

**Crystal data for 22**: $C_{28}H_{26}N_2O_4$. M. 454.51, monoclinic, space group $P2_1/n$, unit cell dimensions a = 11.8530 (2) Å, b = 15.1826 (2) Å, c = 13.1144 (2) Å, α = 90 °, β = 100.321(1)°, γ = 90°, R indices (all data) R1 = 0.0725, wR2 = 0.1055, volume, Z = 2321.87 (6) Å$^3$, 4. D calc = 1.300 Mg/m$^3$, absorption coefficient = 0.087 mm$^{-1}$, T = 213(2) K, λ = 0.71073 Å, 37247 reflections measured, 4744 unique [$R_{(int)}$ = 0.06] which were used in all calculations.

***Methyl 1',2'-dihydro-6-hydroxy-1'-phenyl-3-methyl-2'-oxo-1,5-diphenyl spiro[3-azabicyclo[3.1.0]hexane-2,3'-[3H]indole]-6-carboxylate (25)***

To a solution of 1-phenylisatin **23** (0.286 g, 1.28 mmol) in methanol (6 mL) was added sarcosine **6** (0.228 g, 2.56 mmol) in water (2 mL). After stirring the reaction mixture at 90 °C for 5 min, 3,4-diphenylcyclobutene-1,2-dione **21** (0.200 g, 0.85 mmol) was added and the mixture stirred at 90 °C overnight. Aqueous work up of the reaction mixture followed by silica gel column chromatography of the residue (hexane-ethyl acetate, 95:5) gave 0.058 g of unreacted cyclobutenedione. Elution with 10% ethyl acetate in hexane afforded the cycloadduct **25** (0.166 g, 38%; yield based on recovered cyclobutenedione was 53%).

Colorless crystals; recrystallized from methanol-dichloromethane.

mp : 174-176 °C.

IR (KBr) $\nu_{max}$ : 3455, 3062, 2956, 1715, 1610, 1498, 1369, 1268, 754, 699 $cm^{-1}$.

$^1H$ NMR : δ 8.07-6.35 (m, 19H), 4.19 (d, 1H, $J$ = 8.7 Hz), 3.96 (s, 3H), 3.75 (d, 1H, $J$ = 8.7 Hz), 2.23 (s, 3H), 2.17 (s, 1H).

$^{13}C$ NMR : δ 175.38, 170.21, 144.64, 134.12, 133.96, 131.56, 131.32, 130.62, 129.52, 129.30, 128.37, 128.16, 128.08, 127.83, 127.69, 127.06, 126.85, 125.33, 123.17, 108.71, 77.98, 65.06, 62.60, 55.03, 53.30, 52.12, 42.77, 34.84.

HRMS Calcd for $C_{33}H_{28}N_2O_4$: 516.206662. Found: 516.204908.

***Methyl 1',2'-dihydro-6-hydroxy-1'-(phenylmethyl)-3-methyl-2'-oxo-1,5-diphenyl spiro[3-azabicyclo[3.1.0]hexane-2,3'-[3H]indole]-6-carboxylate (28)***

A mixture of 1-benzylisatin **26** (0.303 g, 1.28 mmol) in methanol (6 mL) and sarcosine **6** (0.228 g, 2.56 mmol) in water (2 mL) was stirred at 90 °C for 5 min. This was then followed by the addition of 3,4-diphenylcyclobutene-1,2-dione **21** (0.200 g, 0.85 mmol) and the reaction mixture was allowed to stir at 90 °C overnight. Work up and purification as described in the general procedure afforded 0.051 g of unreacted cyclobutenedione and the cycloadduct **28** (0.218 g, 48%; yield based on recovered cyclobutenedione was 65%).

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 164-166 °C.

IR (KBr) $\nu_{max}$ : 3425, 3052, 1732, 1689, 1458, 1178, 998, 730 $cm^{-1}$.

$^1$H NMR : δ 8.15-6.28 (m, 19H), 5.00 (d, 1H, $J$ = 16 Hz), 4.36 (d, 1H, $J$ = 16 Hz), 4.16 (d, 1H, $J$ = 8.7 Hz), 3.93 (s, 3H), 3.71 (d, 1H, $J$ = 8.7 Hz), 2.16 (s, 1H), 2.08 (s, 3H).

$^{13}$C NMR : δ 175.57, 170.54, 143.75, 135.07, 134.40, 131.64, 131.42, 130.94, 129.48, 128.72, 128.65, 128.17, 127.81, 127.14, 126.32, 125.80, 123.02, 108.86, 77.62, 65.08, 62.40, 54.33, 52.19, 42.95, 42.54, 34.76.

HRMS Calcd for $C_{34}H_{30}N_2O_4$: 530.222621. Found: 530.220558.

***Methyl 1',2'-dihydro-6-hydroxy-3-methyl-2'-oxo-1,5-diphenyl spiro[3-azabicyclo[3.1.0]hexane-2,3'-[3H]indole]-6-carboxylate (29)***

A mixture of isatin **5** (0.188 g, 1.28 mmol) in methanol (6 mL) and sarcosine (0.228 g, 2.56 mmol) in water (2 mL) was allowed to stir at 90 °C for 5 min. Then 3,4-diphenylcyclobutene-1,2-dione **21** (0.200 g, 0.85 mmol) was added to it and the reaction mixture was allowed to stir at 90 °C for 24 h. The reaction mixture after work up and purification according to the general experimental procedure afforded unreacted cyclobutenedione (0.028 g) and the cycloadduct **29** (0.184 g, 49%; yield based on recovered cyclobutenedione was 57%).

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 106-108 °C.

IR (KBr) $\nu_{max}$ : 3431, 3176, 3058, 1683, 1458, 1328, 1222, 1029, 823, 736 cm$^{-1}$.

$^1$H NMR : δ 8.36 (s, 1H), 8.09-6.89 (m, 13H), 6.53 (d, 1H, $J$ = 7.3 Hz), 4.06 (d, 1H, $J$ = 8.6 Hz), 3.90

(s, 3H), 3.66 (d, 1H, $J$ = 8.8 Hz), 2.60 (s, 1H), 2.03 (s, 3H).

$^{13}$C NMR : δ 178.25, 170.59, 141.87, 134.43, 131.56, 131.39, 130.69, 129.74, 129.53, 128.40, 128.18, 127.78, 127.16, 126.35, 122.99, 109.56, 78.13, 65.17, 62.12, 54.20, 52.25, 42.39, 34.80.

***Methyl 1',2'-dihydro-6-hydroxy-5'-bromo-3-methyl-2'-oxo-1,5-diphenyl spiro[3-azabicyclo[3.1.0]hexane-2,3'-[3H]indole]-6-carboxylate (31)***

To a solution of 5-bromoisatin **30** (0.289 g, 1.28 mmol) in methanol (6 mL) was added sarcosine **6** (0.228 g, 2.56 mmol) in water (2 mL). After stirring the reaction mixture at 90 °C for 5 min, 3,4-diphenylcyclobutene-1,2-dione **21** (0.200 g, 0.85 mmol) was added. The reaction mixture was stirred for 24 h at 90 °C and worked up as usual. The residue on purification afforded 0.048 g of unreacted cyclobutenedione and 0.138 g of the cycloadduct **31** (31%; yield based on recovered cyclobutenedione was 41%). Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 233-235 °C.

IR (KBr) $\nu_{max}$ : 3555, 3299, 2935, 1721, 1627, 1479, 1337, 1263, 778, 717 cm$^{-1}$.

$^{1}$H NMR : δ 8.17 (br s, 1H), 8.10-6.88 (m, 12H), 6.53 (d, 1H, $J$ = 7.3 Hz) 4.06 (d, 1H, $J$ = 8.8 Hz), 3.90 (s, 3H), 3.66 (d, 1H, $J$ = 8.8 Hz), 2.44 (s, 1H), 2.03 (s, 3H).

$^{13}$C NMR : δ 178.08, 170.48, 141.82, 134.40, 131.53, 131.35, 130.66, 129.72, 129.49, 128.75, 128.51, 128.38, 128.16, 127.76, 127.13, 126.32, 122.95, 109.45, 78.07, 65.13, 62.11, 54.18, 52.19, 42.42, 34.77.

HRMS Calcd for $C_{27}H_{23}N_2O_4Br$: 518.084340. Found: 518.084119.

***(5aS,8aR)-5a,7,8,8a-Tetrahydro-5a,8a-dihydroxy-7-methyl spiro[6H-acenaphtho[1,2-c]pyrrole-6,1'(2'H)-acenaphthylen]-2'-one (35)***

To a mixture of isatin **5** (0.220 g, 1.5 mmol) in methanol (6 mL) and sarcosine **6** (0.267 g, 3 mmol) in water (2 mL) at 90 °C was added acenaphthenequinone **34** (0.182 g, 1 mmol) and the reaction mixture was allowed to stir at 90 °C overnight. After completion of the reaction, the reaction mixture was processed as described above. Column chromatography of the residue on silica gel using hexane-ethyl acetate (90:10) mixture afforded 0.103 g of the cycloadduct **35** (52%).

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 175-177 °C.

IR (KBr) $\nu_{max}$ : 3499, 3455, 2962, 1710, 1493, 1343, 1182, 1114, 835, 783 $cm^{-1}$.

$^1H$ NMR : δ 8.16-7.36 (m, 10H), 6.76 (t, 2H, $J$ = 6.4 Hz), 4.21 (d, 1H, $J$ = 9.9 Hz), 3.77 (d, 1H, $J$ = 10.0 Hz), 3.57 (s, 1H), 3.36 (s, 1H), 2.01 (s, 3H).

$^{13}C$ NMR : δ 209.92, 144.42, 143.84, 141.53, 136.95, 136.09, 132.43, 131.61, 130.56, 130.49, 128.38, 127.95, 127.57, 127.24, 125.34, 125.05, 124.97, 124.05, 123.37, 120.33, 119.61, 91.51, 86.96, 81.31, 66.95, 35.18.

HRMS Calcd for $C_{26}H_{19}N_1O$: 393.133604. Found: 393.132471.

Further elution of the column using hexane-ethyl acetate (80:20) afforded **36** (0.107 g, 30%).

***Cycloadduct 36***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 222-224 °C.

IR (KBr) $\nu_{max}$ : 3363, 3176, 1689, 1620, 1465, 786, 736 $cm^{-1}$.

$^1H$ NMR (DMSO-$d_6$) : δ 10.13 (s, 1H), 7.76-6.72 (m, 9H), 6.10 (d, 1H, $J$ = 7.2 Hz), 5.06 (s, 1H), 5.00 (s, 1H), 4.13 (d, 1H, $J$ = 9.2 Hz), 3.52 (d, 1H, $J$ = 9.2 Hz), 1.98 (s, 3H).

$^{13}C$ NMR (DMSO-$d_6$) : δ 178.14, 145.31, 143.00, 141.22, 136.16, 129.24, 127.98, 127.30, 126.64, 126.20, 125.60, 123.80, 123.35, 122.84, 119.42, 118.41, 108.61, 89.97, 85.04, 77.60, 64.81, 34.40.

***Cycloadducts 35 and 37***

To a mixture of 1-Phenylisatin **23** (0.275 g, 1.23 mmol) in methanol (6 mL) and sarcosine **6** (0.220 g, 2.47 mmol) in water (2 mL) at 90 °C was added acenaphthenequinone **34** (0.150 g, 0.82 mmol) and the reaction mixture allowed to stir at 90 °C for 24 h. The usual work up and purification of the product by silica gel column chromatography afforded the cycloadduct **35** (0.077 g, 47%).

Further elution of the column using hexane-ethyl acetate (80:20) afforded **37** (0.074 g, 21%).

***Cycloadduct 37***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 188-190 °C.

IR (KBr) $\nu_{max}$ : 3488, 3046, 1695, 1602, 1496, 1465, 1359, 1216, 1122, 780, 761 $cm^{-1}$.

$^1$H NMR (DMSO-$d_6$) : δ 8.59-6.70 (m, 14H), 6.11 (d, 1H, $J$ = 7.0 Hz), 5.27 (s, 1H), 5.14 (s, 1H), 4.20 (d, 1H, $J$ = 9.1 Hz), 3.57 (d, 1H, $J$ = 9.1 Hz), 2.07 (s, 3H).

$^{13}$C NMR (DMSO-$d_6$) : δ 174.69, 144.97, 143.63, 140.65, 134.12, 133.05, 131.54, 130.23, 127.89, 127.60, 126.23, 126.02, 125.62, 125.29, 123.37, 122.39, 119.90, 117.94, 117.27, 107.18, 90.30, 89.91, 84.32, 64.14, 33.75.

***Cycloadducts 35 and 38***

To a mixture of 1-methylisatin **19** (0.241 g, 1.5 mmol) in methanol (6 mL) and sarcosine **6** (0.267 g, 3 mmol) in water (2 mL) at 90 °C was added acenaphthenequinone **34** (0.182 g, 1 mmol) and the reaction mixture was allowed to stir at 90 °C for 24 h. After completion of the reaction, the reaction mixture was processed as described in the general procedure. Purification of the residue by chromatography on silica gel (hexane-ethyl acetate, 90:10) afforded the cycloadduct **35** (0.110 g) in 56% yield.

Further elution of the column using hexane-ethyl acetate (80:20) afforded **38** (0.116 g, 31%).

***Cycloadduct 38***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 189-191 °C.

IR (KBr) $\nu_{max}$ : 3438, 3058, 1686, 1461, 1376, 1112, 776, 752 cm$^{-1}$.

$^1$H NMR : δ 7.77-6.85 (m, 9H), 6.52 (d, 1H, $J$ = 7.2 Hz), 4.04 (d, 1H, $J$ = 9.9 Hz), 4.01 (s, 1H), 3.68 (s, 1H), 3.62 (d, 1H, $J$ = 9.9 Hz), 3.23 (s, 3H), 1.92 (s, 3H).

$^{13}$C NMR : δ 177.86, 145.33, 144.36, 141.02, 136.99, 130.58, 129.39, 128.30, 127.58, 127.29, 125.31, 124.87,

123.54, 121.71, 119.47, 108.04, 90.02, 86.65, 78.27, 66.67, 35.27, 25.64.

***Cycloadducts 35 and 39***

To a mixture of 5-bromoisatin **30** (0.339 g, 1.5 mmol) in methanol (6 mL) and sarcosine **6** (0.267 g, 3 mmol) in water (2 mL) at 90 °C was added acenaphthenequinone **34** (0.182 g, 1 mmol) and the reaction mixture was allowed to stir at 90 °C overnight. After completion of the reaction, the reaction mixture was processed as described above and the residue was subjected to column chromatography to obtain the cycloadduct **35** (0.108 g, 55%).

Further elution of the column using hexane-ethyl acetate (70:30) afforded **39** (0.087 g, 20%).

***Cycloadduct 39***

Colorless crystals; recrystallized from hexane-ethyl acetate.

mp : 208-210 °C.

IR (KBr) $\nu_{max}$ : 3363, 3164, 1696, 1622, 1468, 1115, 785 $cm^{-1}$.

$^1H$ NMR : δ 10.36 (s, 1H), 7.97-6.67 (m, 8H), 5.92 (s, 1H), 5.23 (s, 1H), 5.12 (s, 1H), 4.12 (d, 1H, $J$ = 9.0 Hz), 3.48 (d, 1H, $J$ = 9.1 Hz), 1.98 (s, 3H).

$^{13}C$ NMR : δ 176.39, 144.84, 141.54, 140.48, 135.37, 129.83, 128.79, 128.46, 126.63, 125.29, 123.32, 122.73, 122.02, 117.82, 110.80, 109.36, 108.88, 89.91, 89.42, 84.16, 63.61, 33.74.

***Cycloadducts 35 and 40***

To a mixture of acenaphthenequinone **34** (0.175 g, 0.96 mmol) in methanol (6 mL) and sarcosine **6** (0.114 g, 1.28 mmol) in water (2 mL) at 90 °C was added 3,4-diphenylcyclobutene-1,2-dione **21** (0.150 g, 0.64 mmol) and the reaction mixture was stirred for 24 h at this temperature according to the general procedure. The reaction mixture after work up and purification afforded unreacted cyclobutenedione **21** (0.052 g), the cycloadducts **40** (0.075 g, 25%) and **35** (0.105 g, 56%). Yield of the cycloadduct **40** based on recovered cyclobutenedione was 38%.

***Methyl 6'-hydroxy-3'-methyl-2-oxo-1',5'-diphenyl spiro[acenaphthylene-1-(2H),2'-[3]azabicyclo[3.1.0]hexane]-6'-carboxylate (40)***

Yellow crystals; recrystallized from hexane-ethyl acetate.

mp : 180-182 °C.

IR (KBr) $\nu_{max}$ : 3550, 2946, 1771, 1716, 1431, 1255, 1102, 1014, 790, 709 $cm^{-1}$.

$^1H$ NMR : δ 8.43-6.79 (m, 16H), 4.21 (d, 1H, $J$ = 8.8 Hz), 3.95 (s, 3H), 3.77 (d, 1H, $J$ = 8.8 Hz), 2.17 (s, 1H), 2.03 (s, 3H).

$^{13}C$ NMR : δ 207.86, 170.35, 143.13, 136.04, 134.35, 131.41, 131.06, 130.56, 130.12, 128.80, 128.43, 128.39, 128.03, 127.36, 127.31, 126.92, 126.32, 125.09, 124.64, 119.63, 80.73, 65.25, 62.62, 54.51, 51.95, 42.85, 34.48.

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# SUMMARY

The thesis entitled "**NOVEL DIPOLAR CYCLOADDITION REACTIONS OF 1,2-DIONES AND RELATED CHEMISTRY**" embodies the results of extensive investigations carried out to gain some insight into the reactivity of various 1,2-diones with different dipolar species, especially carbonyl ylides.

A general introduction to the cycloaddition chemistry of 1,2-diones with special emphasis on dipolar cycloadditions of 1,2-benzoquinones, isatins and cyclobutenediones are presented in Chapter 1. A definition of the present research problem has also been incorporated.

The second chapter deals with the results of a detailed investigation of the cycloaddition reactions of 1,2-diones such as 1,2-benzoquinones, acenaphthenequinone and isatins with a number of carbonyl ylides. The regio and stereochemistry of the products were confirmed by single crystal X-ray analysis. It has been shown that carbonyl ylides undergo facile cycloaddition with 1,2-diones thus offering an efficient method for the synthesis of novel spiro oxabicyclic derivatives. In all cases, the cycloaddition is highly regio and stereoselective. Interestingly in the case of 1,2-benzoquinones, the ylide preferentially adds to the more electron deficient of the two carbonyls of each quinone. In the case of 3-methoxy-4,6-bis(1,1-diphenylmethyl)-1,2-benzoquinone and 1,2-naphthoquinone, mixtures of regioisomers are obtained. The reaction of carbonyl ylide with acenaphthenequinone proceeded in a highly stereoselective fashion. With isatins also the reaction is regio and stereoselective and afforded novel spiro oxindole derivatives in good yields. Interestingly the cycloadducts obtained by the reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone with the carbonyl ylides undergo facile

photochemical rearrangement. Preliminary investigation has revealed that 1,4-naphthoquinone undergoes cycloaddition to carbonyl ylide preferentially at the C=C bond.

The third chapter contains the results of investigations aimed at studying the reactivity of azomethine ylides towards 1,2-diones. In this work we have observed facile dipolar cycloaddition reactions of 3,4-diphenylcylobutene-1,2-dione with the azomethine ylides derived from isatins, yielding novel spiro[pyrrolidine-2,3'-oxindole]derivatives which may be amenable to a number of useful synthetic transformations. It is worthy of note that the spiro[pyrrolidinyl-oxindole]ring system is a recurring structural motif in a number of natural products with remarkable biological activity. Novel spiropyrrolidine derivatives are also formed by the reaction of isatins, sarcosine and acenaphthenequinone.

In conclusion, we have uncovered some novel reactivity patterns of 1,2-diones such as 1,2-benzoquinones, isatins and cyclobutenediones towards various dipolar species. In the process, facile synthesis of a variety of interesting heterocyclic compounds has been achieved. It is conceivable that further explorations in the area of dipolar cycloaddition to 1,2-diones will be rewarding both from the synthetic and mechanistic standpoints.

# LIST OF PUBLICATIONS

a) **Articles in journals**

1. Diels-Alder reactions of a 6-arenyl fulvene with dienes and dienophiles and related chemistry. Nair, V.; Nair, A. G.; Radhakrishnan, K. V.; **Sheela, K. C.**; Rath, N. P. *Tetrahedron* **1997**, *53*, 17361.
2. Novel 1,3-dipolar cycloaddition reactions of carbonyl ylide with *o*-quinones. Nair, V.; **Sheela, K. C.**; Radhakrishnan, K. V.; Rath, N. P. *Tetrahedron Lett.* **1998**, *39*, 5627.
3. Novel cycloaddition reactions of *o*-benzoquinones and related chemistry. Nair, V.; Kumar, S.; Nair, A. G.; Anilkumar, G.; Radhakrishnan, K. V.; Nair, J. S.; Maliakal, D.; **Sheela, K. C.**; Mathew, B.; Treesa, P. M.; Vinod, A. U.; Prabhakaran, J.; Sheeba, V.; Thomas, A. *Proc. Indian Acad. Sci. (Chem. Sci.)* **1998**, *110*, 507.
4. Cycloaddition reactions of carbonyl ylides to [60] fullerene: synthesis of novel $C_{60}$ derivatives. Nair, V.; Sethumadhavan, D.; **Sheela, K. C.**; Eigendorf, G. K. *Tetrahedron Lett.* **1999**, *40*, 5087.
5. 1,3-Dipolar cycloadditions of *o*-benzoquinones: An overview. Nair, V.; Radhakrishnan, K. V.; **Sheela, K. C.** *Res. Chem. Intermed* **1999**, *24*, 877.
6. 1,3-Dipolar cycloaddition reactions of nitrile-N-oxides with 1,2-benzoquinones. Nair, V.; Radhakrishnan, K. V.; **Sheela, K. C.**; Rath, N. P. *Tetrahedron* **1999**, *55*, 14199.
7. Novel heterocyclic construction *via* dipolar cycloadditions to 1,2-dicarbonyl compounds. Nair, V.; **Sheela, K. C.**; Vinod, A. U.; Nair, J. S.; Radhakrishnan, K. V.; Rajesh, C.; Treesa, P. M. *J. Heterocycl. Chem.* **2000**, *37*, 0000.
8. Cycloaddition of carbonyl ylides to isatins: synthesis of novel spiro oxindole derivatives. Nair, V.; **Sheela, K. C.**; Sethumadhavan, D.; Bindu, S.; Rath, N. P.; Eigendorf, G. K. (Communicated to J. Org. Chem.).
9. Dipolar cycloaddition reactions of isatin-derived azomethine ylides with 3,4-diphenylcyclobutene-1,2-dione: synthesis of novel spiro[pyrrolidine-2,3'-oxindole]derivatives. Nair, V.; **Sheela, K. C.**; Rath, N. P. (communicated).

10. Novel dipolar cycloaddition reactions of azomethine ylides with acenaphthenequinone. Nair, V.; **Sheela, K. C.**; Rath, N. P. (to be communicated).
11. Dipolar cycloaddition reactions of carbonyl ylides with 1,2-diones and photochemical rearrangement of the cycloadducts. Nair, V.; **Sheela, K. C.**; Rath, N. P.(to be communicated).

**b) Published contributions to academic conferences**

1. Novel cycloaddition chemistry of *o*-benzoquinones. Nair, J. S.; Radhakrishnan, K. V.; Maliakal, D.; Treesa, P. M.; Vinod, A. U.; Mathew, B.; **Sheela, K. C.**; Nair, V. National Symposium on Emerging Trends in Organic Chemistry; Trivandrum, November **1996**, Poster # P-21.
2. Diels-Alder reactions of *o*-benzoquinones with 6-vinyl fulvenes: An easy entry into extensively conjugated benzofulvenes. Nair, A. G.; Radhakrishnan, K. V.; **Sheela, K. C.**; Nair, V. National Symposium on Emerging Trends in Organic Chemistry; Trivandrum, November **1996**, Poster # P-23.
3. Uncommon cycloaddition reactions of *o*-benzoquinones leading to novel heterocyclic construction. Radhakrishnan, K. V.; **Sheela, K. C.**; Anilkumar, G.; Mathew, B.; Nair, V. 16th International Conference on Heterocyclic Chemistry; Bozeman, U.S.A., August **1997**, Poster # PO II, 181.
4. Novel 1,3-dipolar cycloaddition reactions of carbonyl ylides with 1,2-diones. **Sheela, K. C.**; Radhakrishnan, K. V.; Bindu, S.; Nair, V. National Symposium in Chemistry; Bangalore, January **1999**, Poster # PSI-56.
5. Novel dipolar cycloaddition reactions of 1,2-diones and related chemistry. **Sheela, K. C.**; Sethumadhavan, D.; Bindu, S.; Nair, V. National Symposium in Chemistry; Hyderabad, January **2000**, Poster # P-19.
6. Novel cycloaddition reactions of carbonyl ylides to [60] fullerene. Sethumadhavan, D.; **Sheela, K. C.**; Nair, V. National Symposium in Chemistry; Hyderabad, January **2000**, Poster # P-20.
7. Novel heterocyclic construction *via* dipolar cycloadditions to 1,2-dicarbonyl compounds. Nair, V.; **Sheela, K. C.**; Vinod, A. U.; Rajesh, C.; Nair, J. S. International Symposium on Trends in Medicinal Chemistry and Biocatalysis; Delhi, January **2000**, IL-47.