ALKYNE CYCLOADDITION REACTIONS

A thesis presented by

Indrani Paramasivam

in partial fulfilment for

the degree of

Doctor of Philosophy

of the

University of London

Hofmann Laboratory,

Department of Chemistry,

Imperial College of Science, Technology and Medicine,

London, SW7 2AY.

May 1990

TO

Mum, Dad, Murali, Sumathi and Shiamala

with all my love

forever

OMM

KADKA KASARADA KATRAWEY

KATRAPIN NIDKA ATHAKU THAHA

— VALUVAR

(One should put into practice whatever one learns, only then can one be said to be an accomplished scholar).

Abstract

This thesis is presented in eight chapters. Chap. One is a brief introductory review on the cycloaddition reactions of dimethyl acetylenedicarboxylate (DMAD), and Chap. Three is a review of the similar reactions of the highly electron-deficient alkyne, hex-3-yne-2,5-dione (diacetylacetylene) (DAA). An improved synthesis and the self-condensation reactions of hex-3-yne-2,5-dione are described in Chap. Four; the oligomers formed as a result of self-condensation of DAA are characterised, and their chemistry studied, and they are compared with those derived from DMAD. Cycloaddition reactions of DAA with various dienes are discussed in Chap. Five; these reactions include a simple synthesis of *o*-diacetylbenzene *via* Diels-Alder reaction of DAA with 1-acetoxy-1,3-butadiene.

Chap. Two is a review of the literature claims for the preparation of norborna-2,5-dien-7-ones. The comparative stabilities of the related norbornen-7-one and norbornan-7-one systems are also discussed. Chap. Six describes the attempted isolation of norborna-2,5-dien-7-one derivatives and the isolation and characterisation of an unusually stable derivative, 9,14-diphenyl-9,14-dihydro-dibenz[*a*,*c*]anthracene-9,14-methanone. X-ray diffraction data show that the bridged-carbonyl group is protected by the phenyl groups on C_9 and C_{14}.

The synthesis of new 2-arylidene-1,3-dithioles, including the formation of mono- and bis-1,3-dithioles, are discussed in Chap. Seven.

Experimental results are presented in Chap. Eight.

Acknowledgements

I thank the following people for their help during my stay at Imperial College. Dr D.J.Willams, Ms A.M.Z.Slawin (for X-ray cyrstallography); Mr J.N.Bilton, Mr G.Tucker, and Dr J.Challis (for mass spectrometry); Mr R.N. Sheppard, Ms S.Thompson (for high field n.m.r); Mr K.I.Jones (for elemental analysis); Mr P.Sulsh (for technical advice and assistance); Prof. C.J.Moody (for helpful discussions); Ms D.Pappoe (for advice on administrative matters); Dr P.J. Dunn (for showing me the ropes at the begining) and the Hofmannites (both the Westenders and the Eastenders) for providing the necessary "intellectual" climate in the lab. I thank Xiao-Lan with whom I enjoyed working as I have never done before.

I also thank the The British High Commissioners Awards Committee for a year's financial support. I thank my friend Ambi, her husband, her parents and family for their understanding, and for patiently putting up with me for the past year.

My heartfelt thanks go to my parents , my brother and my sisters for their boundless encouragement and support and for the love showered on me throughout, and for their selfless financial support which they willingly provided.

Mostly I thank my supervisor, Prof. C.W.Rees, F.R.S., for his guidance, encouragement and advice throughout and also for putting up with my notorious hand writing.

Indrani Paramasivam

May 1990

Contents

Tables, Schemes and Figures

CHAPTER ONE

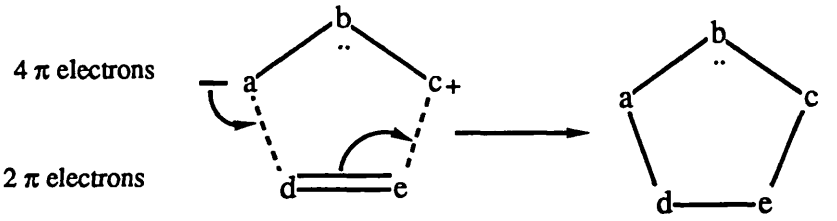
Review of the Reactions of Dimethyl Acetylenedicarboxylate

1 Introduction

1.1 Alkyne Cycloadditions

In spite of the enormous amount of work devoted to cycloaddition reactions, there is still scope for much more research to be carried out on them. Cycloadditions are ring-closure reactions where the number of σ bonds increases at the expense of the π bonds; the reactants combine in such a way that σ bonds are formed but not broken and where no fragments of the molecules are eliminated.

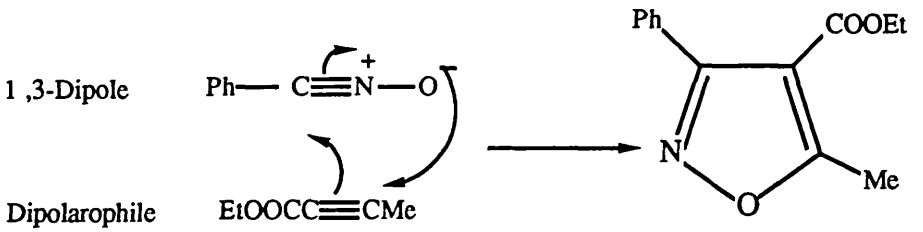
Cycloadditions can be classified according to the ring size of the cycloadduct. For example, Diels-Alder reactions are [4+2]cycloadditions, since the two reactants contribute four and two atoms, respectively, to the cycloadduct. One can also classify cycloaddition reactions according to the number of electrons involved. The Diels-Alder reaction now becomes a [4 π+2 π] process. In this example the number of atoms is the same as the number of electrons in each component, but this is not always so. For instance, in 1,3-dipolar cycloaddition the 1,3-dipole has four π electrons distributed over three atoms. Thus according to the first classification it is a [3+2] cycloaddition, and according to the second a [4π+2π] cycloaddition:[1]



The term cycloaddition is not only limited to concerted reactions but applies also to reactions that occur in a stepwise manner, *via* intermediates, but so far many more concerted cycloadditions have been reported. In this review only the cycloaddition reactions of the electron-deficient alkyne, dimethyl acetylenedicarboxylate, will be considered; the review is not comprehensive but examples have been chosen to illustrate the range of the known reactions.

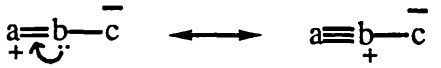
1.2 1,3-Dipolar Cycloadditions

1,3-Dipolar cycloaddition reactions are an invaluable tool for the synthetic chemist since they provide an excellent route to various five-membered heterocyclic compounds. There are two components, namely the 1,3-dipole and the dipolarophile which undergo cycloaddition to give a five- membered cyclic system, as in the example shown:

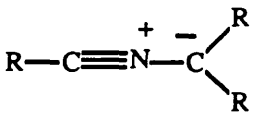


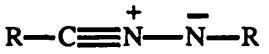
CYCLOADDUCT

Some 1,3-dipolar systems can be written with triple bonds (b = N).

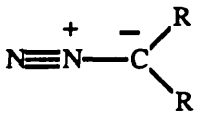


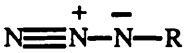
Examples are :

nitrile ylides 

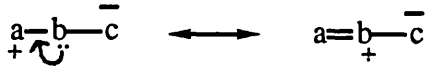
nitrilimines 

nitrile oxides 

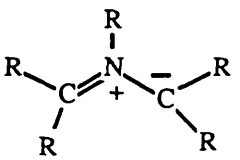
diazoalkanes 

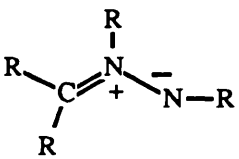
and azides 

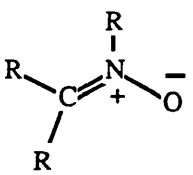
Certain 1,3-dipolar system have no such triple bonds (b = N , O , S).

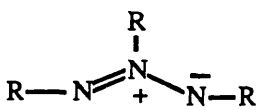


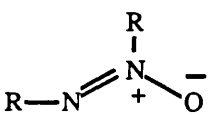
Examples are :

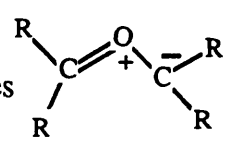
azomethine ylides 

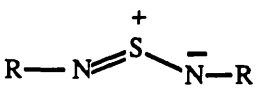
azomethine imines 

nitrones 

azimines 

azoxy compounds 

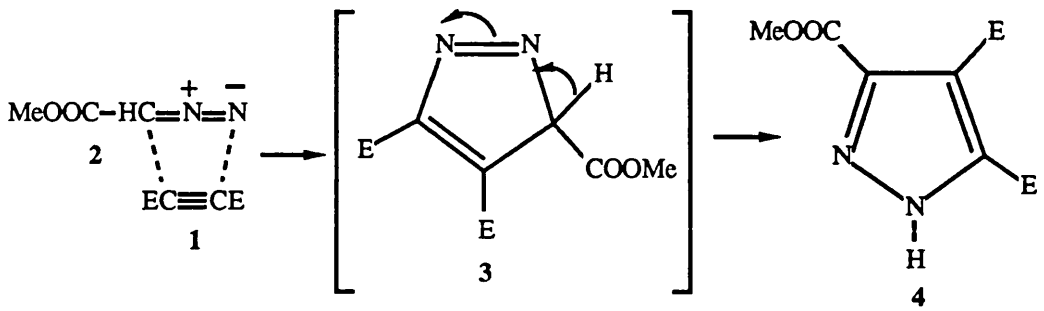
carbonyl ylides 

and sulphur diimides 

The reactions of some of these 1,3-dipoles with dimethyl acetylenedicarboxylate (DMAD) will now be considered in more detail.

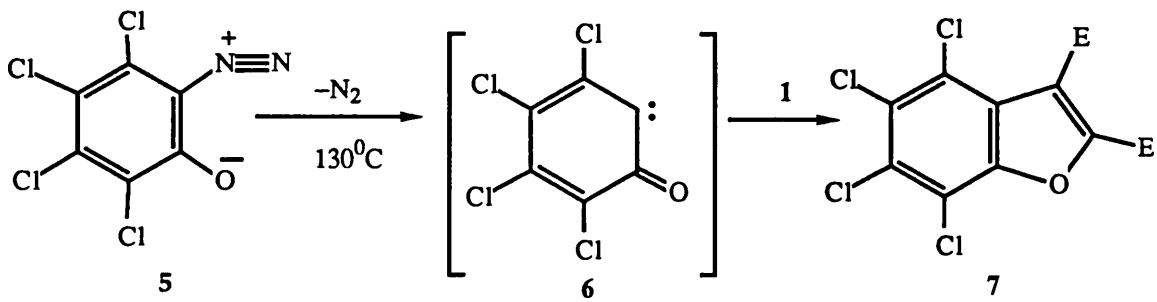
1.2.1 Diazo Compounds

The first cycloaddition of a diazo compound with DMAD (**1**) was carried out exactly a century ago by Buchner.[2] He subjected DMAD to cycloaddition with methyl diazoacetate (**2**). The product that he obtained was trimethyl 1H-pyrazole-3,4,5-tricarboxylate (**4**), which resulted from aromatisation of the initially formed 3H-pyrazole (**3**).

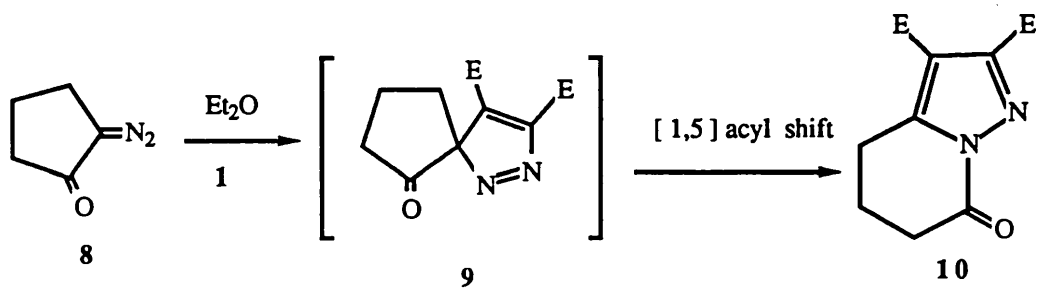


Where E = COOMe

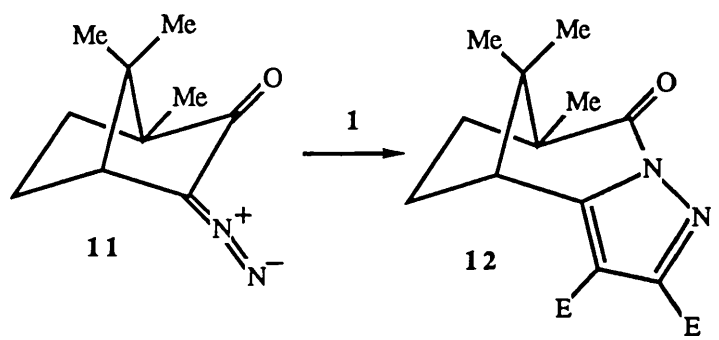
At 130°C, 3,4,5,6-tetrachlorobenzene-2-diazo-1-oxide (**5**) underwent 1,3-dipolar cycloaddition with DMAD (**1**) to form dimethyl 4,5,6,7-tetrachlorobenzo[*b*]furan-2,3-dicarboxylate (**7**) in 48% yield.[3] It is believed that the ketocarbene (**6**), generated when 3,4,5,6-tetrachlorobenzene-2-diazo-1-oxide (**5**) was heated, is the actual species which adds to the triple bond of DMAD to form the product (**7**).



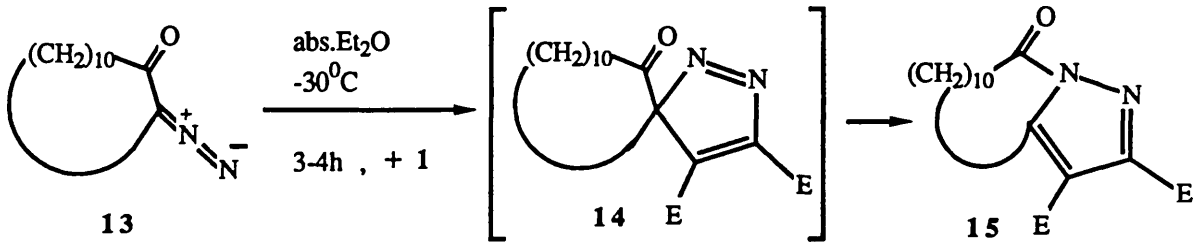
The initial cycloadduct, 3H-pyrazole (**9**), formed as a result of reaction between 2-diazocyclopentanone (**8**) and DMAD (**1**), underwent an [1,5] acyl shift to nitrogen to form dimethyl 4,5-dihydro-7(6H)-oxopyrazolo[1,5-*a*]pyridine-2,3-dicarboxylate (**10**) (86%).[4]



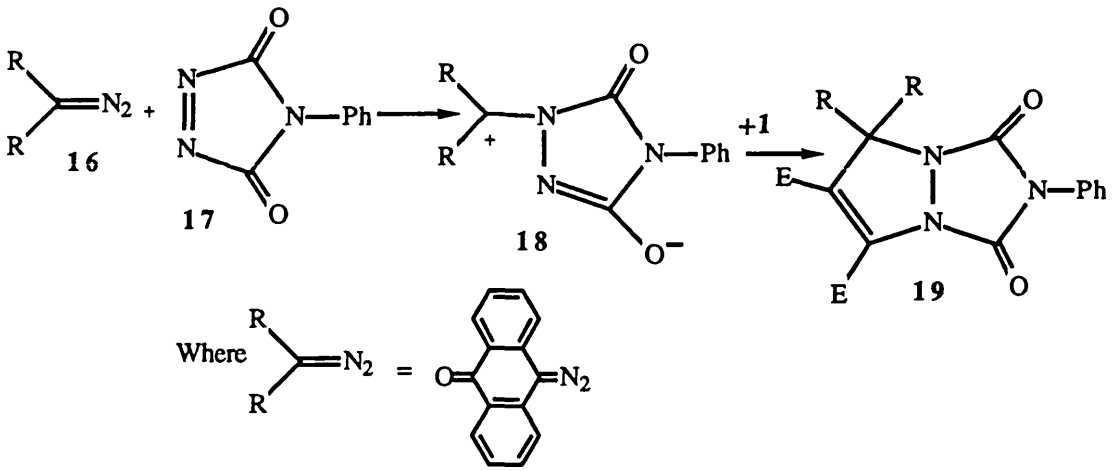
Even bicyclic diazo compounds such as diazocamphor (**11**) undergo 1,3-dipolar cycloaddition; in refluxing benzene cycloaddition of (**11**) with DMAD (**1**) was followed by a [1,5] acyl shift to afford (**12**) in 73% yield.[5]



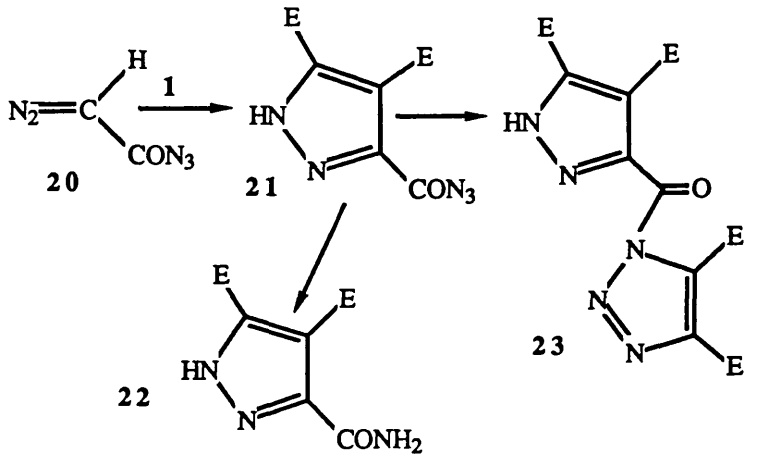
2-Diazocyclododecanone (**13**) underwent a similar cycloaddition and rearranged to give the bicyclic product (**15**) in 89% yield.[6]



The diazoquinone (**16**) reacts with the triazolindione (**17**) and the resultant product eliminates nitrogen readily to form a 1,3-dipole (**18**) which is trapped by DMAD (**1**) to form the spiropyrazoline (**19**) as the cycloaddition product (65%).[7]

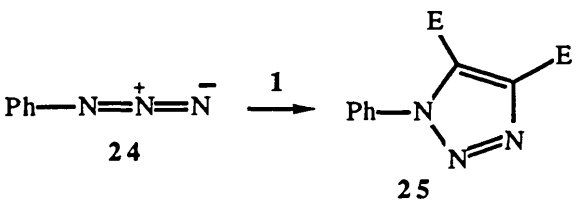


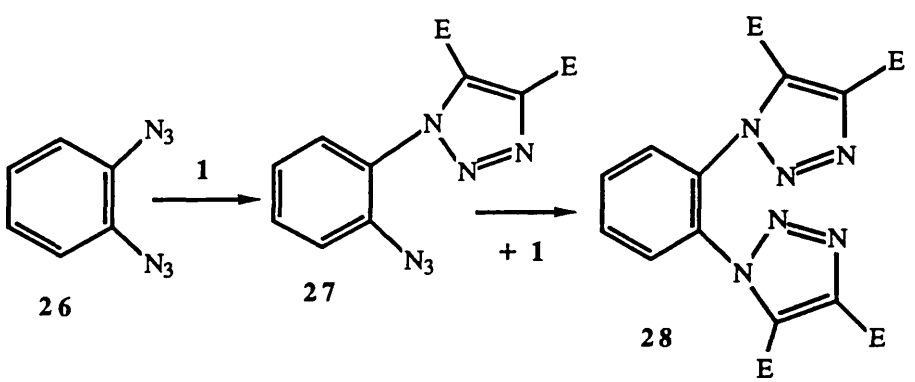
The highly functionalised pyrazole (**21**) (88%) was obtained by DMAD (**1**) undergoing cycloaddition with the diazo group present in diazoacetyl azide (**20**).[8] Pyrazole (**21**) is an interesting synthetic intermediate since it could be converted into a range of compounds, e.g. (**22**) and (**23**) by modification of the substituents and by cycloaddition of the acyl azide.



1.2.2 Azides

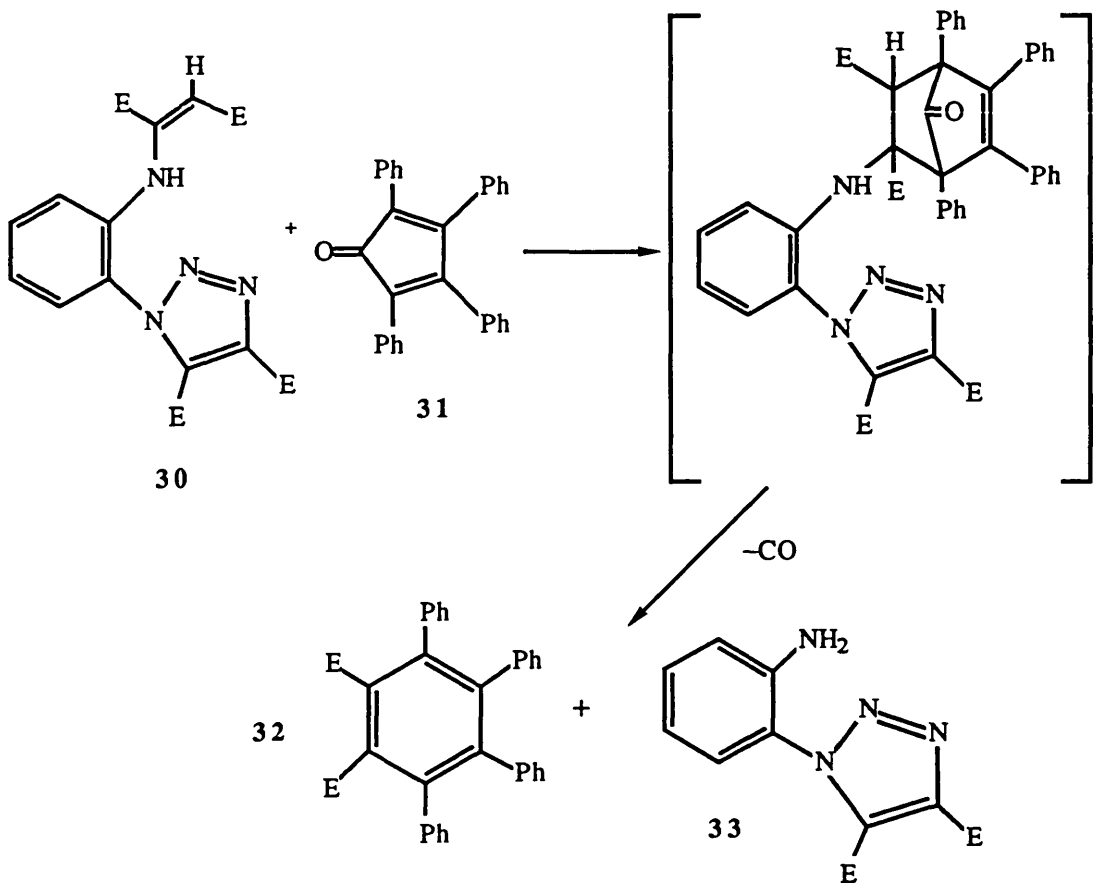
Slightly less than a century ago Michael synthesised dimethyl 1-phenyltriazole-4,5-dicarboxylate (**25**) when he cycloadded phenyl azide (**24**) to DMAD (**1**),[9] thus uncovering a facile route to substituted triazoles, which has since been used very widely.[10]





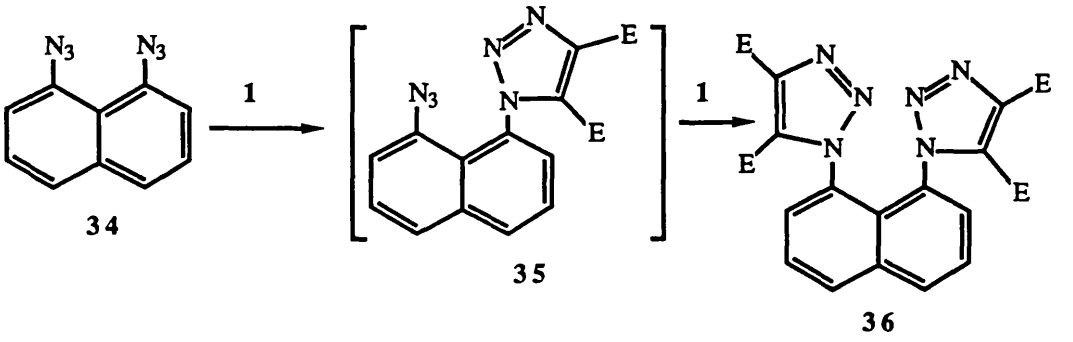
o-Diazidobenzene (**26**) underwent 1,3-dipolar cycloaddition twice with DMAD (**1**) to afford the bis-triazole (**28**) (65%).[11] None of the intermediate monoadduct (**27**) was reported to have been isolated.

Interestingly, *o*-azidoaniline (**29**) was found to undergo not only the normal cycloaddition but also Michael addition to give the anilinofumarate (**30**) in 43% yield.[11] Not much was said about this enamine (**30**) by the authors, though it could prove to be a useful synthetic intermediate; for example when treated with tetracyclone (**31**),[12] compounds (**32**) and (**33**) could be formed.



1,8-Diazidonaphthalene (**34**) underwent cycloaddition twice with DMAD (**1**) in a similar manner to 1,2-diazidobenzene; it gave the bis-adduct (**36**) in 89% yield when treated with DMAD (**1**) at room temperature for 14

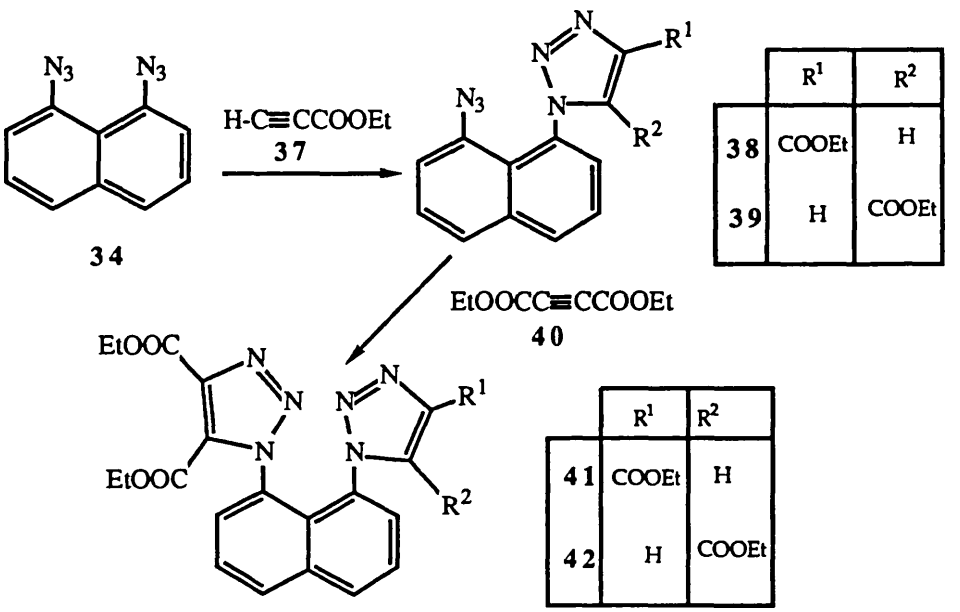
days.[13] The intermediacy of the monoadduct (**35**) was postulated but it was not isolated.



34 **35** **36**

However when 1,8-diazidonaphthalene (**34**) was treated with ethyl propiolate (**37**) for 24 h at room temperature, it afforded the intermediate monoadducts (**38**) and (**39**) in 48% and 17% yield respectively.[13]

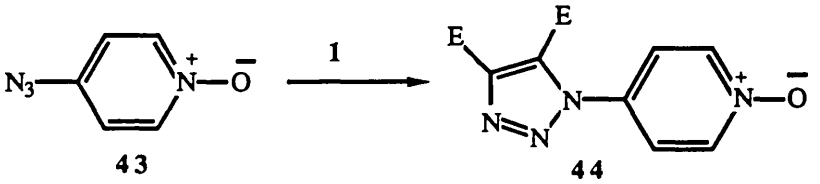
These were then individually treated with excess of diethyl acetylenedicarboxylate (**40**) at room temperture for 14 days to afford the bis-adducts (**41**) and (**42**) in 68% and 61% yield respectively.[13] No parallel set of experiments were carried out with DMAD itself.



	R^1	R^2
38	COOEt	H
39	H	COOEt

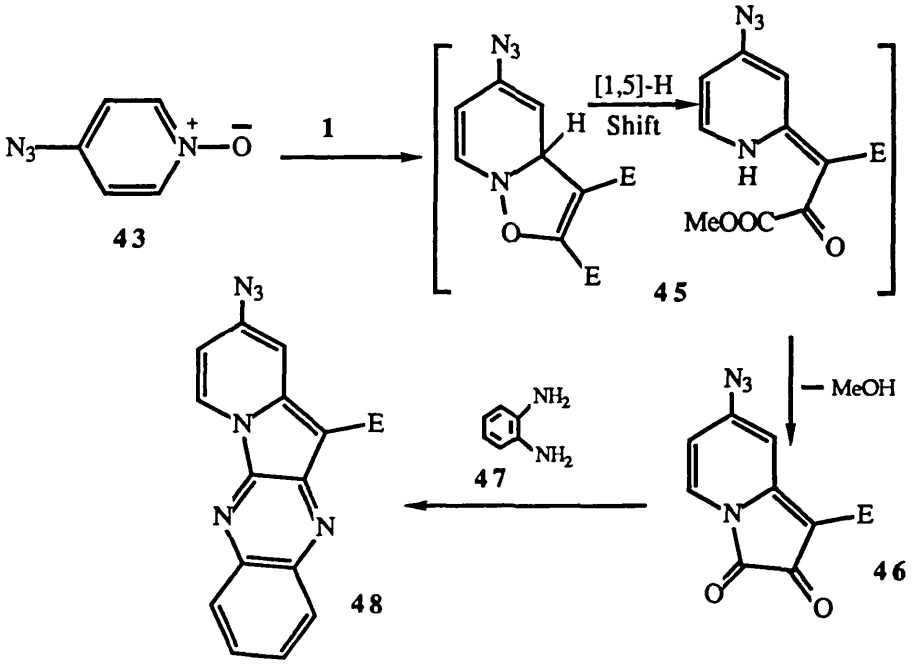
	R^1	R^2
41	COOEt	H
42	H	COOEt

Depending on the nature of the solvent employed, it was observed that 4-azidopyridine 1-oxide (**43**) underwent 1,3-dipolar cycloaddition with DMAD either at the azido group or the ring.[14] When 4-azidopyridine 1-oxide (**43**) was heated at 80°C with DMAD in benzene, the sole product isolated in 7% yield was the 1,2,3-triazole (**44**).When 4-azido-pyridine 1-oxide (**43**) and DMAD were stirred overnight in methanol 7-azido -2,3-dioxo-pyrazolo[2,1-*a*]pyridine (**46**) was obtained in 5% yield.



43 **44**

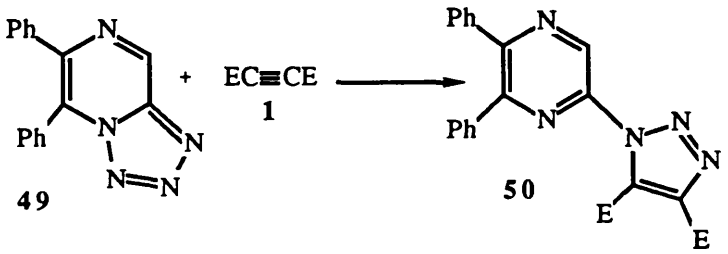
Methyl 7-azido-2,3-dioxopyrazole[2,1-a]pyridine-4-carboxylate (**46**) is the result of 1,3-dipolar cycloaddition of DMAD to the pyridine-N-oxide ring, followed by a [1,5]-H shift and elimination of methanol. This reaction is considered to be worthy of reinvestigation, especially in view of the very low yields of the products isolated.



43 **45** **47** **46** **48**

Compound (**46**) could form tetracyclic compound (**48**) if treated with *o*-phenylene diamine (**47**). This could undergo further reactions, for example 1,3-cycloaddition with alkynes.

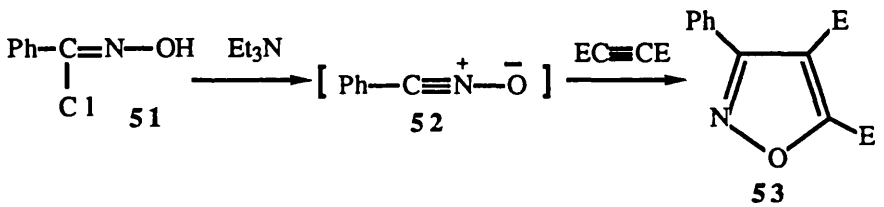
6,7-Diphenyltetrazolo[1,5-*a*]pyrazine (**49**) underwent reaction with DMAD when heated at 70°C in chloroform for 15 h to give the simple product of cycloaddition (**50**) (15%) to the open azido form of (**49**).[15]



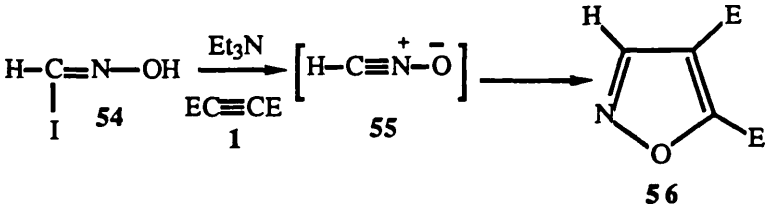
1.2.3 Nitrile Oxides

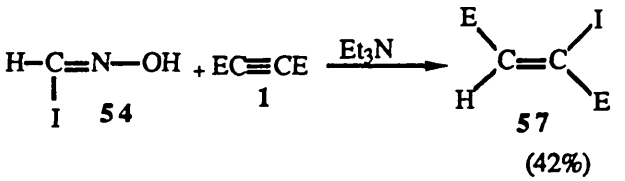
One of the most important routes leading to the formation of isoxazoles is the 1,3-dipolar cycloaddition of alkynes to nitrile oxides. Since this reaction has been extensively reviewed[16] it will not be treated in detail here.

Benzonitrile oxide (**52**) generated *in situ*, reacts with DMAD (**1**) to form the isoxazole (**53**) (72%).[17]

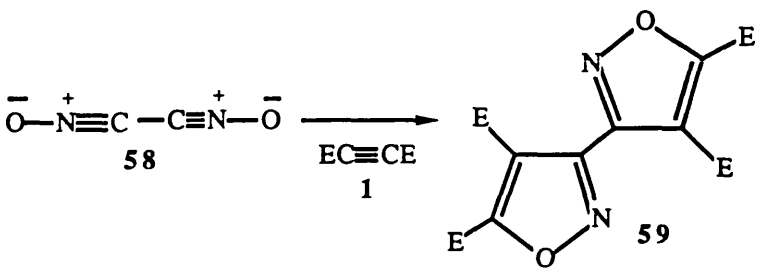


DMAD undergoes an analogous reaction with the nitrile oxide (**55**) to afford the isoxazole (**56**) (33%). The authors have also observed that the nature of the product formed in this reaction depends on the order of addition of the reactants, to give either isoxazole (**56**) or the vinyl iodide (**57**).[18]

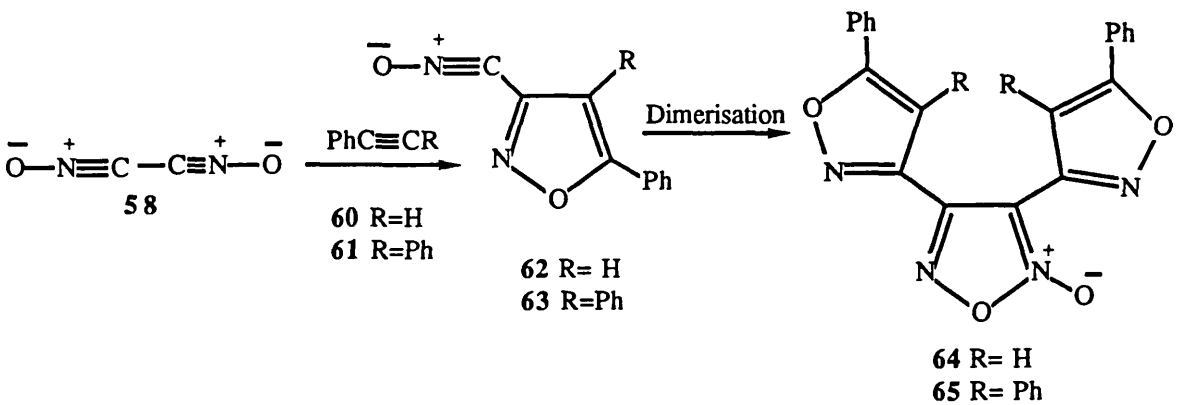




Oxalonitrile bis-N-oxide (**58**) underwent cycloaddition readily with DMAD to afford the bis-adduct (**59**).[19]

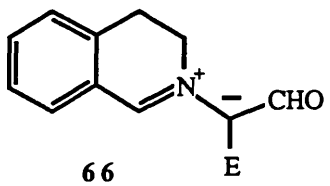


It was also observed that both phenylacetylene (**60**) and diphenylacetylene (**61**) underwent 1,3-dipolar cycloaddition with oxalonitrile bis-N-oxide (**58**). The cycloadducts (**62**) and (**63**) thus formed then underwent dimerization to afford the furoxans (**64**) and (**65**).[19] This type of reaction was not observed with DMAD.

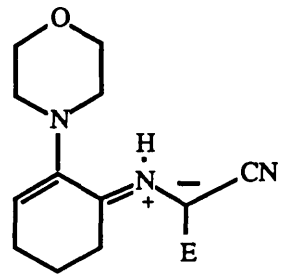


1.2.4 Azomethine Ylides

3-Pyrrolines can be synthesised by the addition of azomethine ylides to the triple bond of alkynes. Azomethine ylides are usually unstable and are generated *in situ*. Azomethine ylides (**66**) and (**67**) have been isolated.[20]

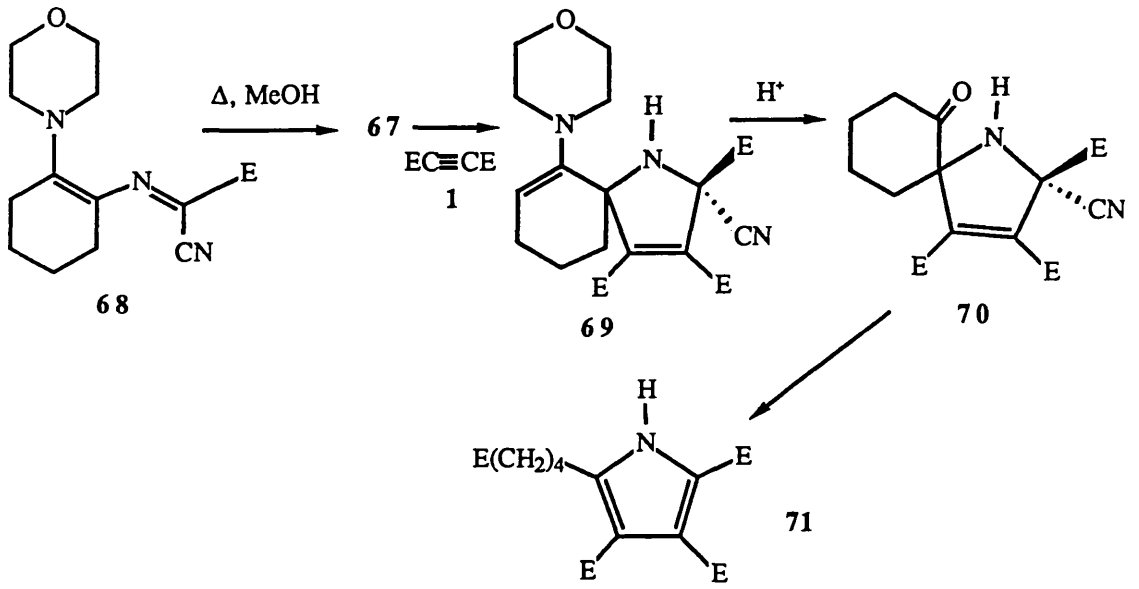


66

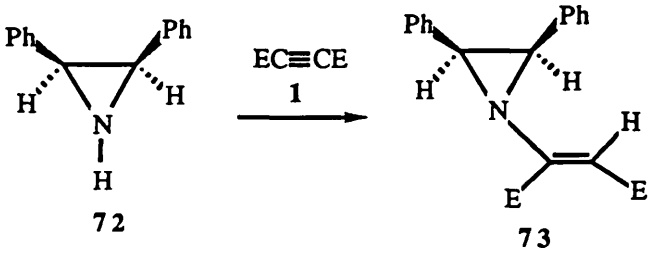


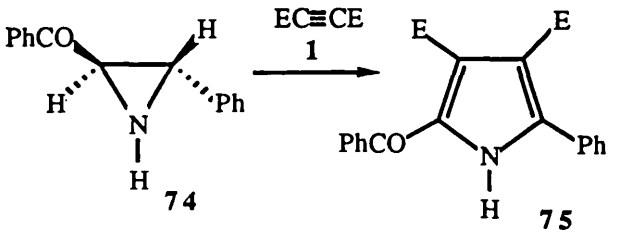
67

The imine (**68**) rearranged thermally when refluxed in methanol, to afford the azomethine ylide (**67**) which underwent 1,3-dipolar cycloaddition with DMAD to afford the spiropyrroline (**69**) (92%). On hydrolysis this affords the spiropyrroline (**70**) (83%), which gave methyl tri(methoxycarbonyl)-pyrrole-2-butyrate (**71**) (89%) on refluxing in methanol with phosphoric acid.[21] The formation of compound (**71**) is believed to proceed by the elimination of HCN from (**70**) followed by [1,5]acyl shift and the cleavage of the amide bond.

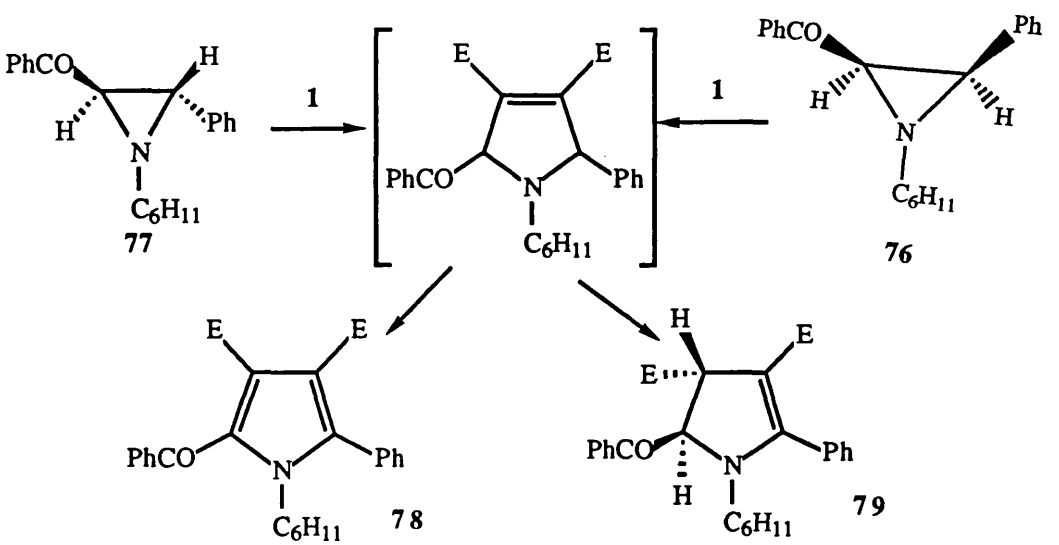


DMAD (**1**) reacts with *cis*-2,3-diphenylaziridine (**72**) to form dimethyl 2-[1-(2,3-diphenylaziridinyl)]-maleate (**73**) (85%) but with *trans*-2-phenyl-3-benzoylaziridine (**74**), pyrrole (**75**) was obtained in 80% yield.[22]

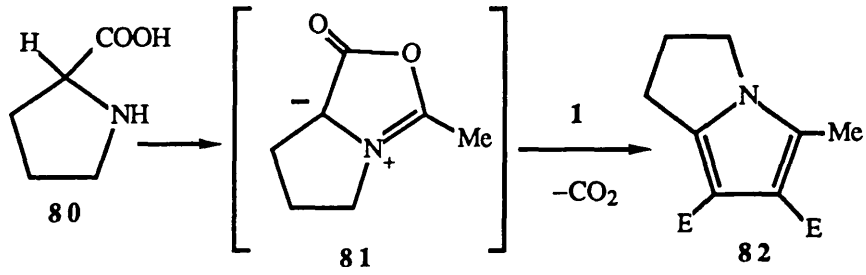




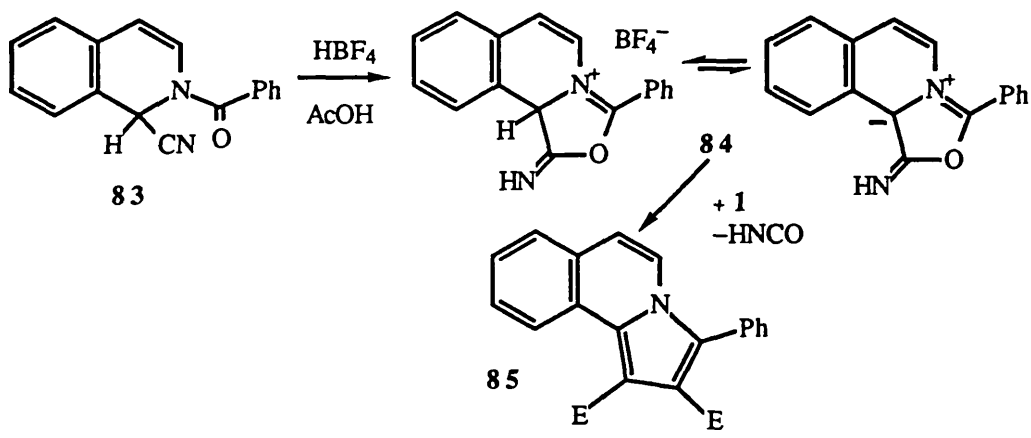
DMAD (**1**) reacts with *cis* and *trans* aziridine (**76**) and (**77**) to form pyrrole (**78**) and pyrroline (**79**). On heating with selenium dioxide at 200°C, pyrroline (**79**) is converted into pyrrole (**78**).[22]



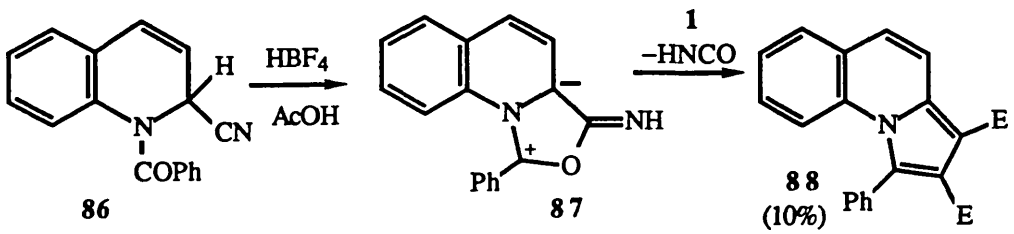
Oxazolium-5-olates (**81**), otherwise known as "münchnones," behave as masked azomethine ylides. Their synthetic potential is exemplified by the formation of (**82**) in 76% yield when proline (**80**) is heated with DMAD (**1**) and acetic anhydride at 130°C; presumably the oxazolium-5-olate (**81**) is the intermediate.[23]



The Reissert salt (**84**) generated *in situ* from 2-benzoyl-1,2-dihydro-isoquinaldonitrile (**83**) reacts with DMAD (**1**) to form the isoquinoline (**85**) in 90% yield.[24]



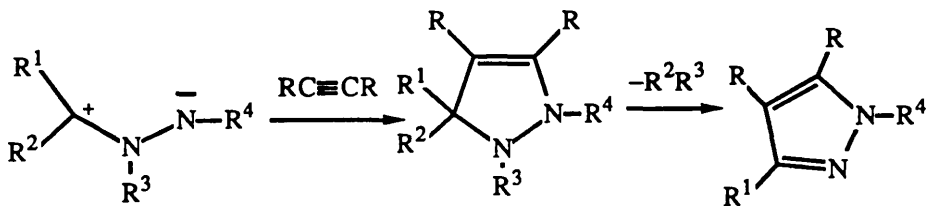
Quinoline Reissert compounds underwent 1,3-dipolar cycloaddition less satisfactorily than the isoquinolines. This was illustrated when the quinalonitrile (**86**) was treated as above, to give the quinoline (**88**) in poor yield.[24]



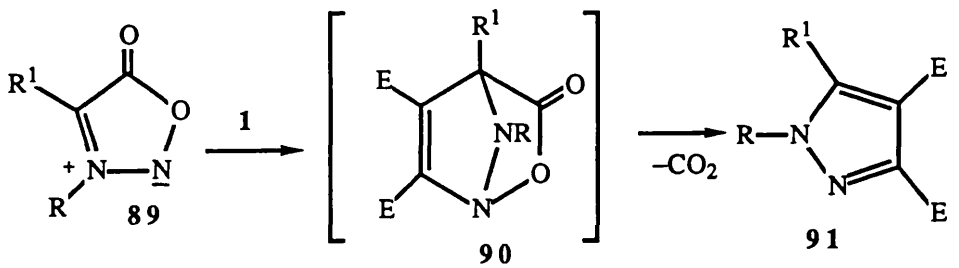
86 87 88 (10%)

1.2.5 Azomethine Imines

Alkynes react with azomethine imines to give 3-pyrazolines which usually undergo spontaneous aromatisation to pyrazoles.



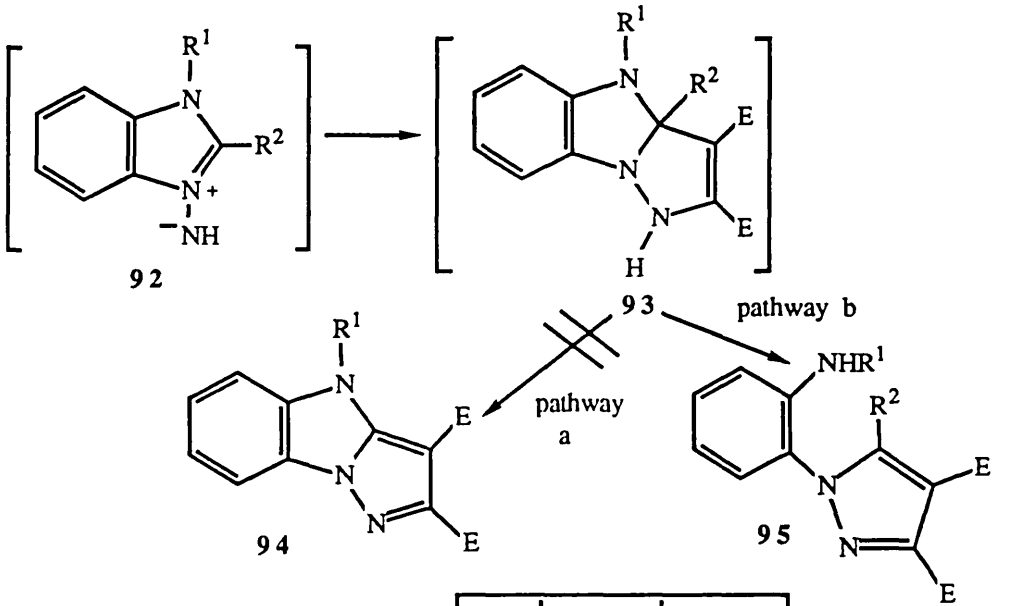
Sydnones (**89**) are azo imines which react with DMAD (**1**) to afford pyrazoles and carbon dioxide.[25]



89 90 91

R	R^1	Yield of **91**
Ph	H	92%
$PhCH_2$	H	93%
Ph	Me	100%

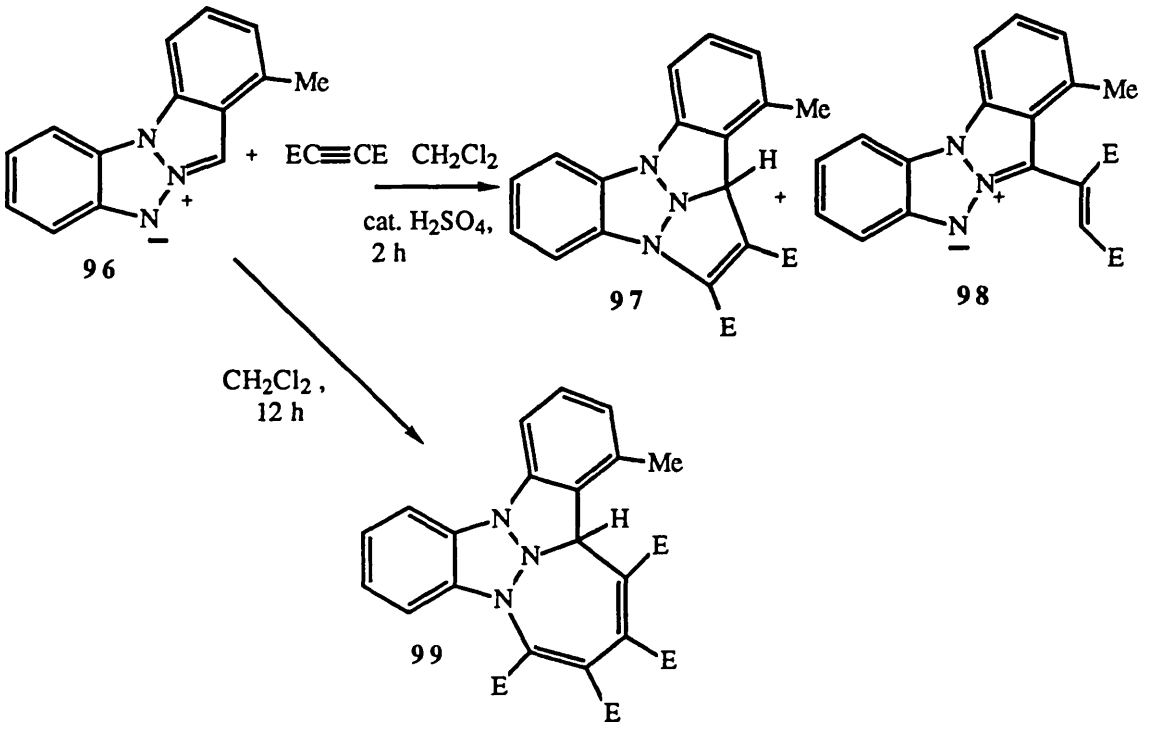
1-Alkylbenzimidazolium-3-imines (**92**) reacts with DMAD (**1**) to form the primary cycloadducts (**93**); these lead to the formation of the ring opened pyrazole (**95**) (pathway b), rather than formation of pyrazolo[1,5-*a*]benzimidazole derivative (**94**) by pathway a. The driving force for the ring opening reaction, pathway b, was considered to be the relief in strain of the [6.5.5] fused ring system.[26]



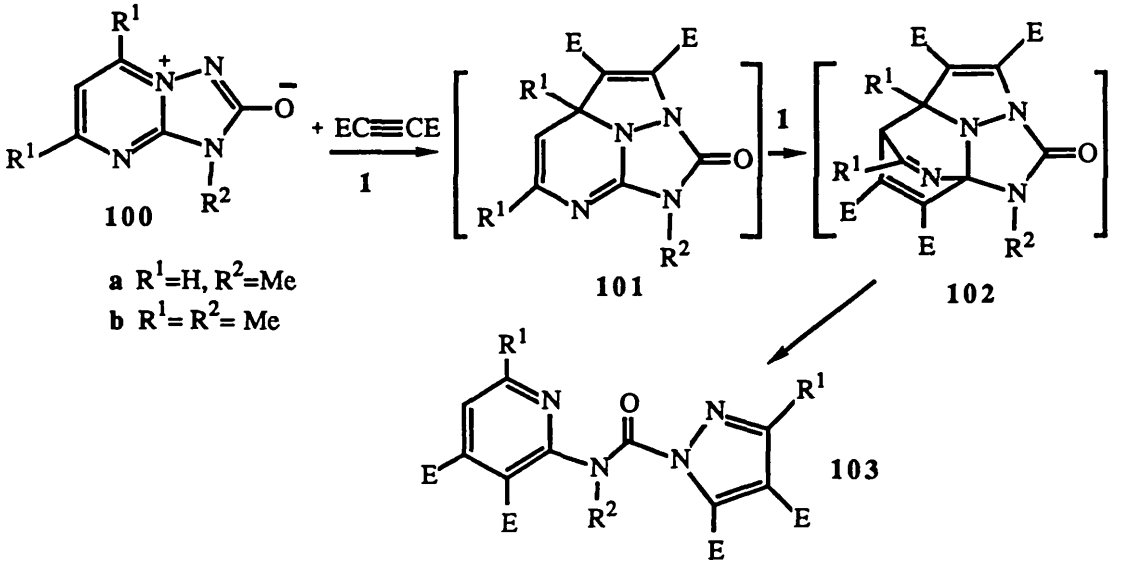
R^1	R^2	Yield %
Me	H	57%
Et	H	33%
Me	Me	28%
Et	Me	28%

Similarly, 8-methyldibenzo-[1,3*a*,6*a*]-triazapentalene (**96**) reacts with DMAD (**1**) to give cycloaddition products.[27] The nature of the cycloadduct depends on the experimental conditions. Here the dibenzotriazapentalene system appears to behave partly as a cyclic azomethine imine, to give the expected

adduct (**97**) in 60% yield. Another product was also isolated and this was claimed to be (**98**) (32%) formed as a result of a Michael addition reaction of (**96**) to DMAD. This product is worthy of reinvestigation. Compound (**96**) reacts with DMAD in refluxing dichloromethane for 12 h to form a 1:2-adduct (**99**) (60%), whose structure was not confirmed by the authors.



[1,2,4]Triazolo[1,5-*a*]pyrimidinium-2-olates (**100**) react with DMAD in refluxing xylene for 24 h to give rise to pyridine derivatives (**103**). The 3-methyl derivative (**100a**) underwent a 1,3-dipolar cycloaddition with DMAD to form the cycloadduct (**101a**) which underwent a hetero Diels-Alder reaction with DMAD, followed by fragmentation of the pyrimidine and triazole rings of the adduct to afford the carboxamide (**103a**) in 62% yield.[28]



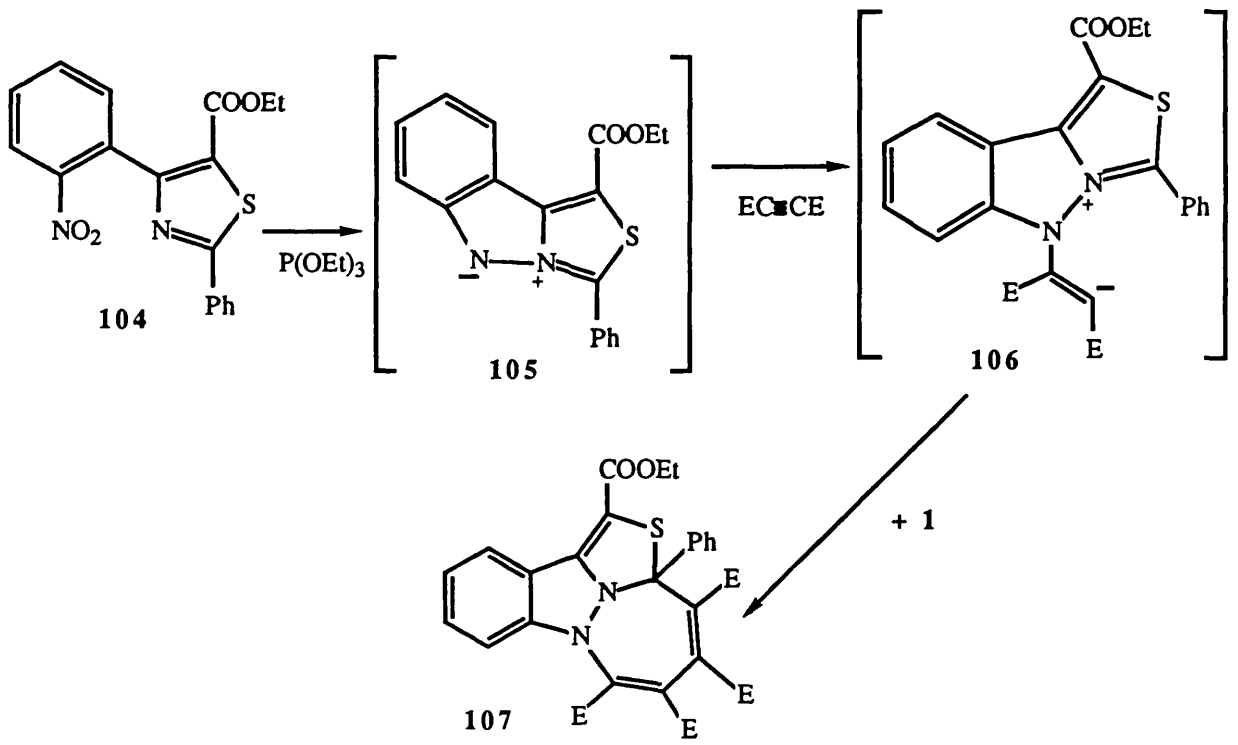
100

a R^1=H, R^2=Me
b R^1= R^2= Me

101 **102** **103**

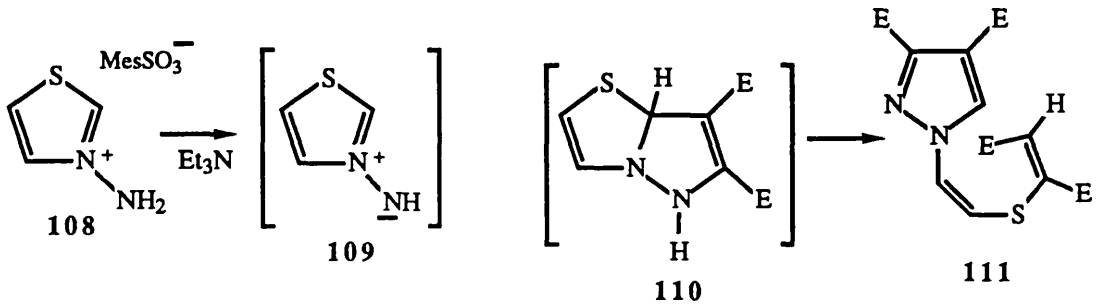
The trimethyl derivative (**100b**) underwent an entirely similar sequence of reactions when treated with DMAD.

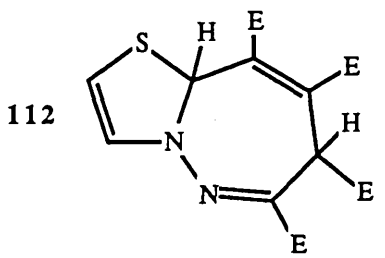
Reductive cyclisation of the thiazole (**104**) gave the azomethine imine (**105**) which underwent cycloaddition with DMAD to afford the 1:2-adduct, dihydroindazole (**107**), in 82% yield.[29]

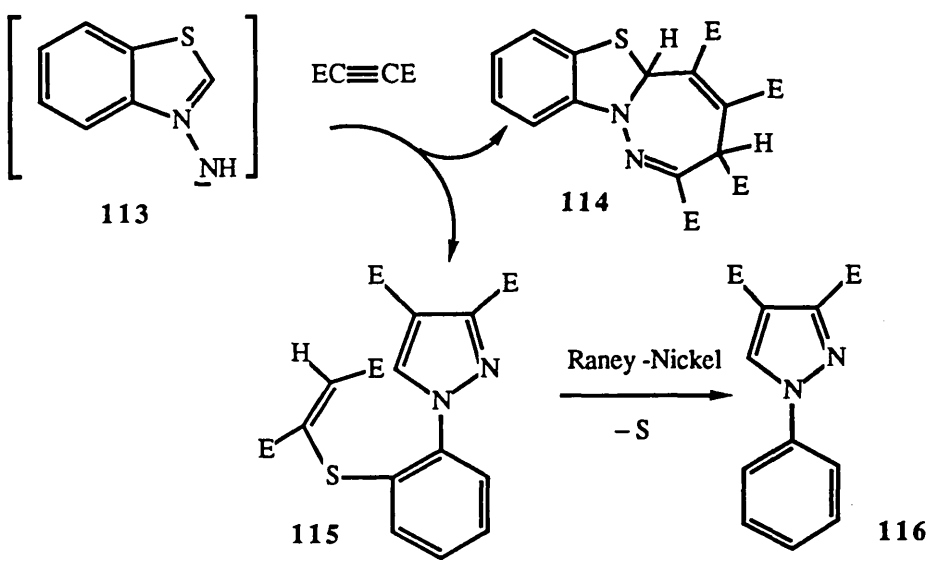


104 **105** **106** **107**

N-Iminothiazolium ylide (**109**), generated *in situ* by the action of triethylamine on 3-aminothiazolium mesitylsulphonate (**108**), reacted with DMAD to form the pyrazole (**111**) and not the diazepine (**112**).[30,31]





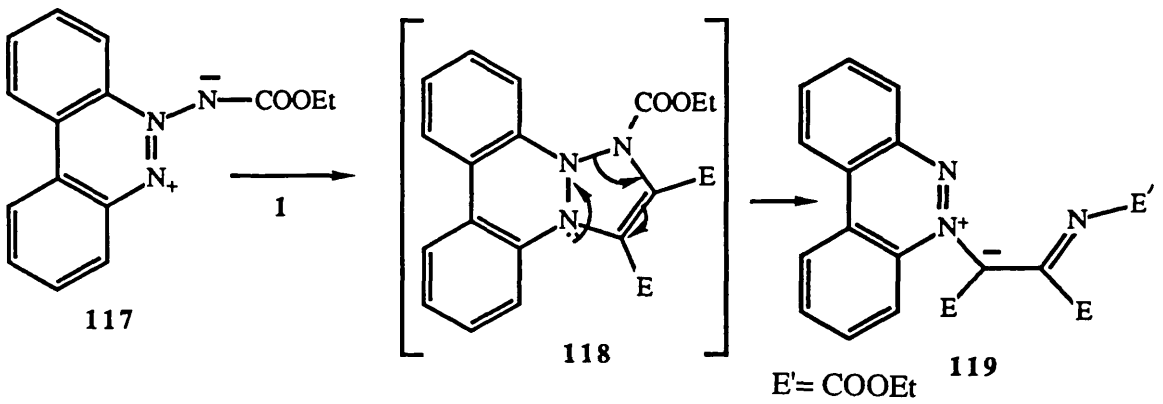


DMAD is said to undergo an analogous reaction with the azomethine

imine (**113**), generated similarly, to form the diazepine (**114**).[31,32] Based on the work of Potts just cited, the structure of the product (**114**) must be questionable, and a more likely structure, by analogy, would be (**115**). This could be investigated by desulphurisation of (**115**), which would presumably give the N-phenyl compound (**116**).

1.2.6 Azimines and Azoxy Compounds

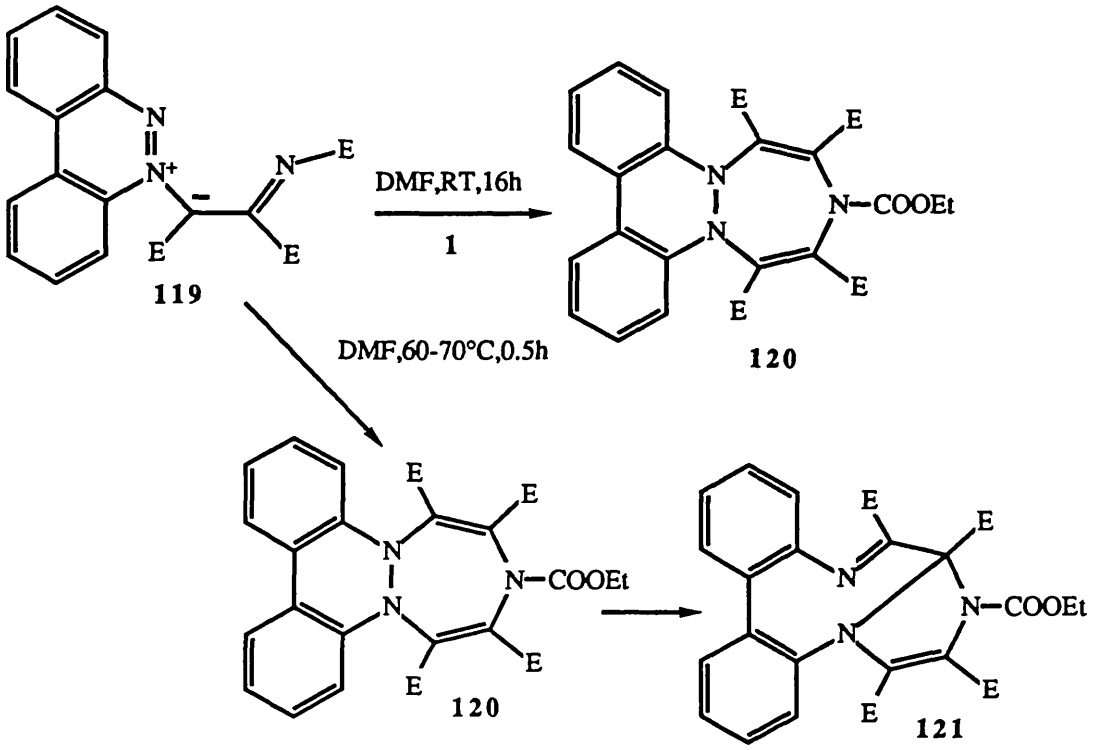
These potential 1,3-dipoles have as yet been much less investigated. 1,3-Dipolar cycloaddition reactions of azimines are less well known, probably because azimines have not been known for very long (since 1970), and the initial 1,3-dipolar adducts of azimines have three saturated contiguous nitrogen atoms and the instability of this type of species could lead to various secondary reactions.



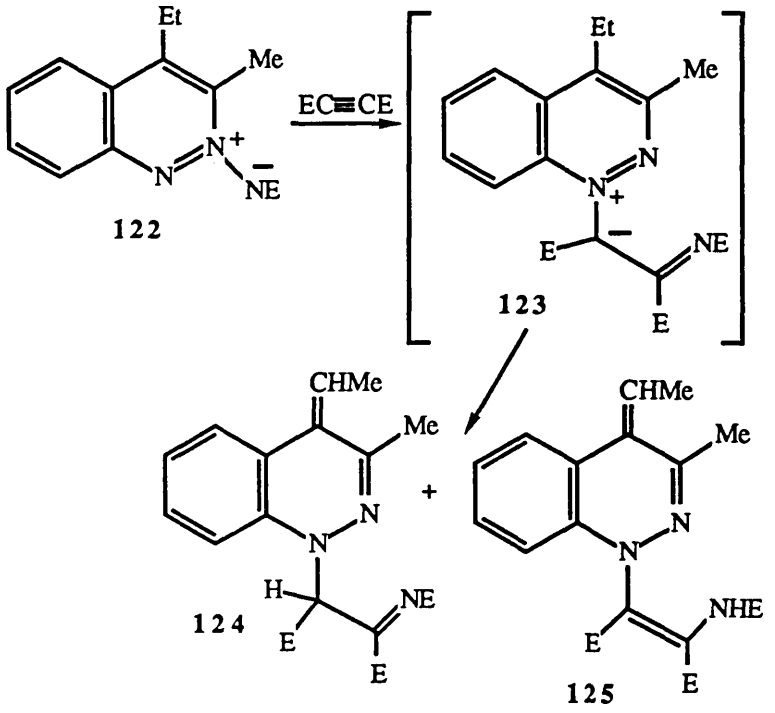
117 118 119

Benzo[*c*]cinnolinium N-ethoxycarbonylimide (**117**) gave the product (**119**) (90%) when treated with DMAD (**1**); the DMAD has become inserted into the N-N bond. The most probable intermediate here is the 1,3-dipolar cycloadduct (**118**) which has undergone electrocyclic ring opening due to the weak nitrogen-nitrogen bond.[33] The product (**119**), an extended 1,3-dipole, undergoes further reaction with DMAD, reacting as a 1,5-dipole.

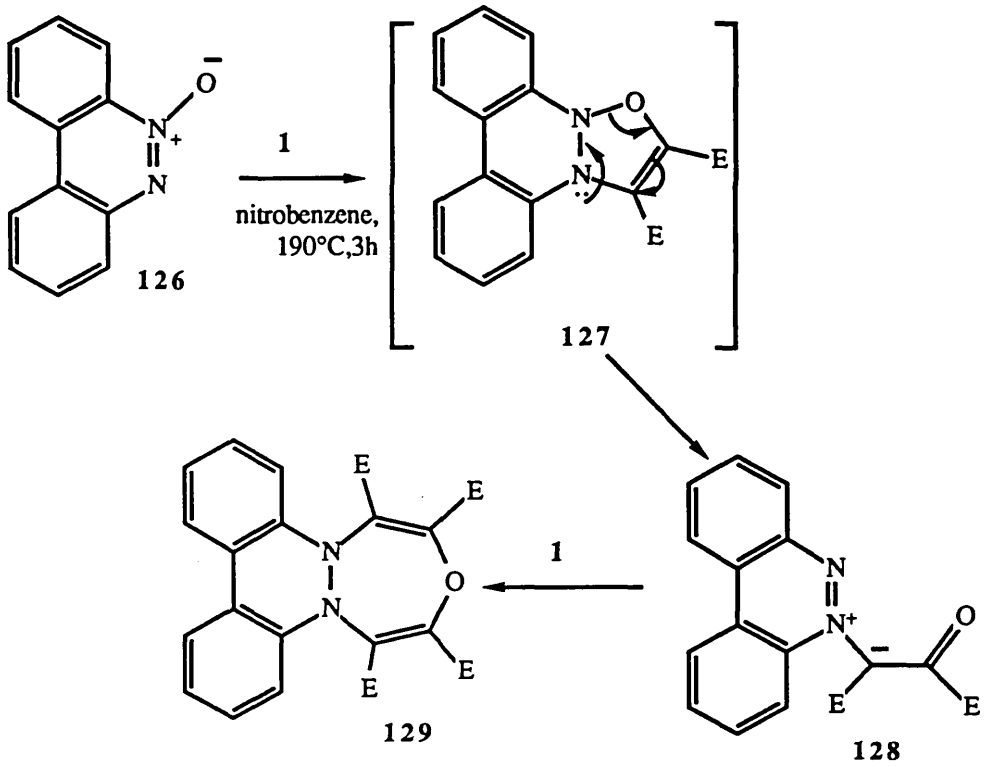
Depending on the experimental conditions either the triazepine (**120**)



(47%) or the diazocine (**121**) (67%) was formed.[34] Compound (**121**) is said to be formed as a result of compound (**120**) undergoing rearrangement *via* the highly stabilised diradical formed by homolysis of the N-N bond.



The cinnoline 2-imide (**122**) underwent a 1,3-cycloaddition with DMAD to form the imine (**124**) (22%) and enamine (**125**) (60%). Their formation is explained by the ring opening of the initial azimine cycloadduct (**123**) followed by hydrogen migration from the 4-ethyl group.[35]

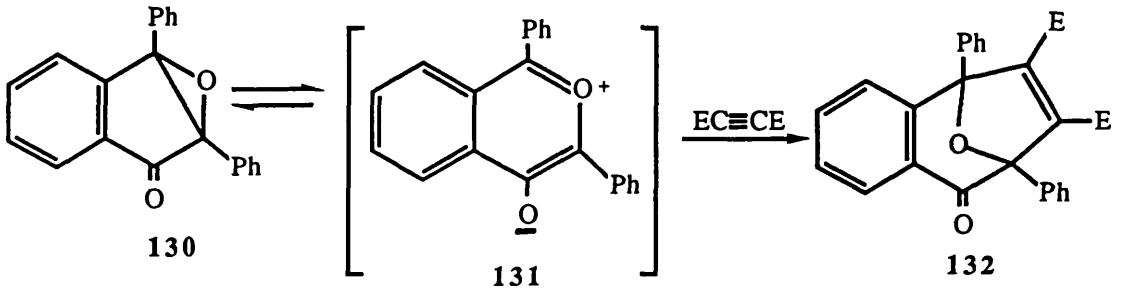


The azoxy structure of benzo[*c*]cinnoline N-oxide (**126**) is much less reactive as a 1,3-dipole. It required heating in nitrobenzene at 190°C for reaction to occur with DMAD. The cycloaddition was followed by electrocyclic ring opening to form the azomethine imine (**128**) in very low yield (2%); yield attributed to side reactions occurring under the vigorous cycloaddition conditions.[36]

The azomethine imine (**128**) could also have undergone a 1,5-dipolar cycloaddition with DMAD (**1**) to form compound (**129**), but this was not reported by the authors.

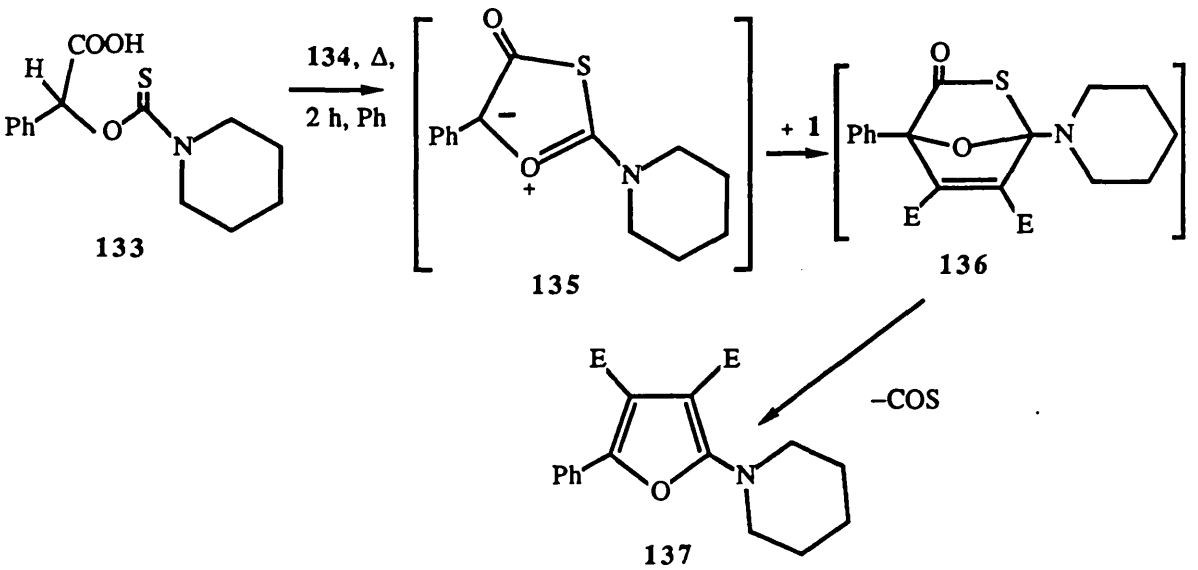
1.2.7 Carbonyl Ylides

Carbonyl ylides are much less stable and are generated *in situ*. The treatment of 2,3-diphenylindenone oxide (**130**) with DMAD afforded the cycloadduct (**132**). This strongly suggests the probability of 1,3-diphenyl-2-benzopyrylium-4-oxide (**131**) being formed in equilibrium with (**130**) and reacting with DMAD as a 1,3-dipole.[37] This is an example of an acylcarbonyl ylide undergoing 1,3-dipolar cycloaddition.

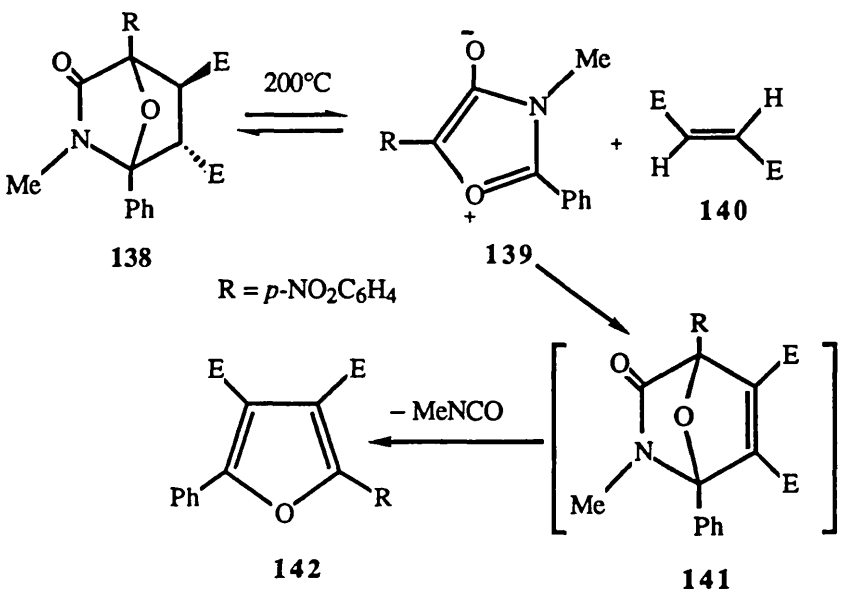


Mesoionic, 6π arenes, 1,3-oxathiolylium-4-olates, for example (**135**), are prepared *in situ* from thiocarbonyloxyacetic acids and can be trapped by [3+2] cycloaddition which then leads to the formation of substituted furans.

For example, carboxylic acid (**133**) was treated with dicyclohexylcarbodi-imide (**134**) in refluxing benzene for 2h to give the 1,3-oxathiolylium-4-olates (**135**) which is a carbonyl ylide and adds to DMAD (**1**) to form the cycloadduct (**136**) which loses COS to form the furan (**137**) (67%).[38]

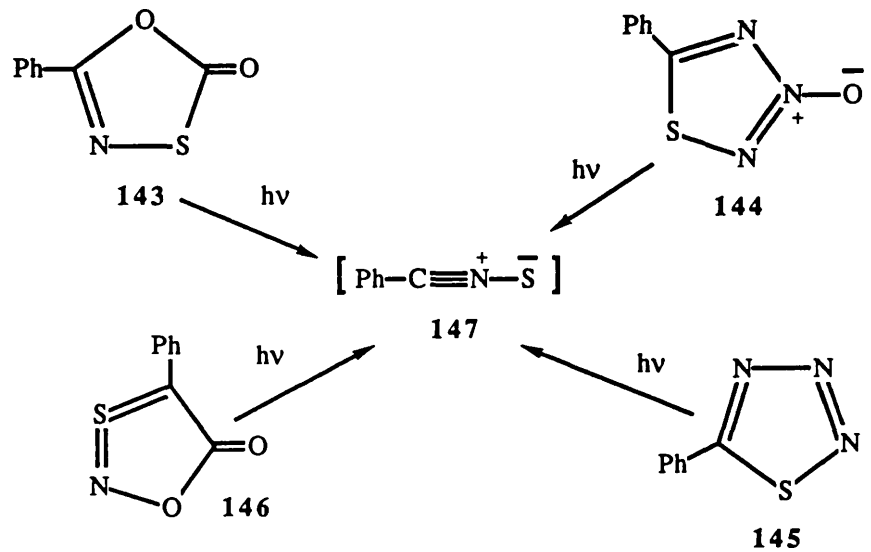


The bicyclic compound (**138**) is in thermal equilibrium with the mesoionic carbonyl ylide (**139**) and dimethyl fumarate (**140**), its dissociation being favoured by high temperatures. The carbonyl ylide (**139**) so generated is trapped by DMAD (**1**) to form (**141**) which undergoes a retro Diels-Alder reaction to form the substituted furan (**142**) quantitatively.[39]

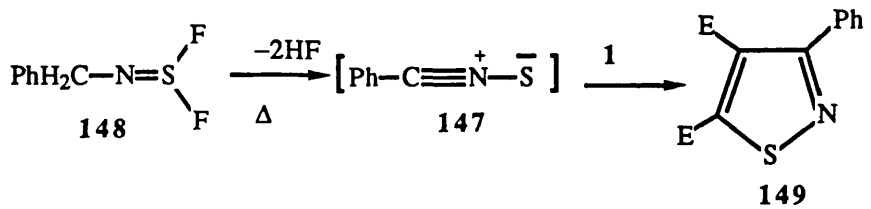


1.2.8 Some Sulphur Containing 1,3-Dipoles

One common sulphur containing 1,3-dipole is the nitrile sulphide, R-C≡N$^+$S$^-$. These can be generated as shown.[40,41,42]

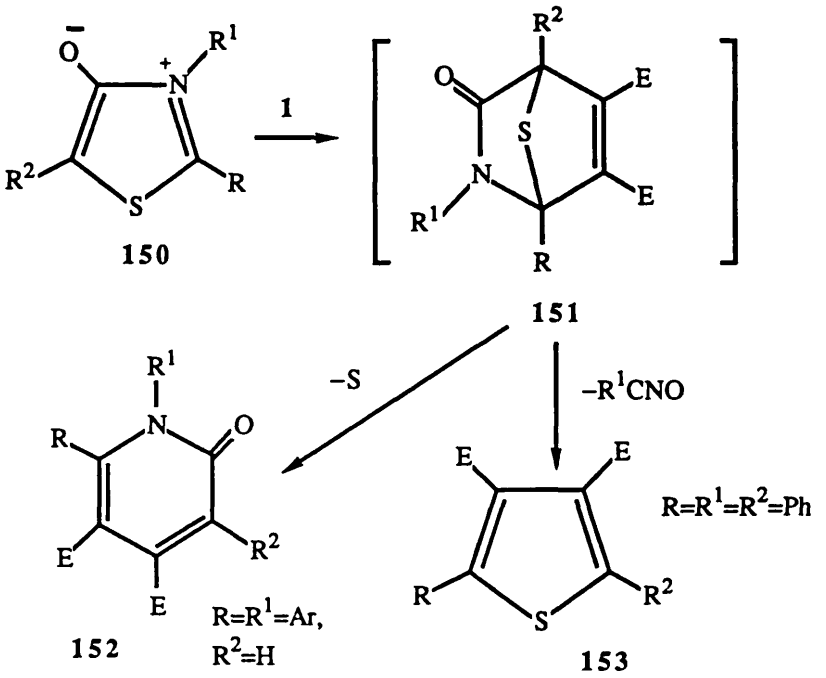


Dimethyl 3-phenylisothiazole-4,5-dicarboxylate (**149**) was obtained as the result of a 1,3-dipolar cycloaddition between DMAD (**1**) and benzonitrile-N-sulphide (**147**). The highly reactive benzonitrile-N-sulphide (**147**) was generated *in situ* by subjecting N-benzyliminosulphurdifluoride (**148**) to thermolysis at elevated temperature.[43]

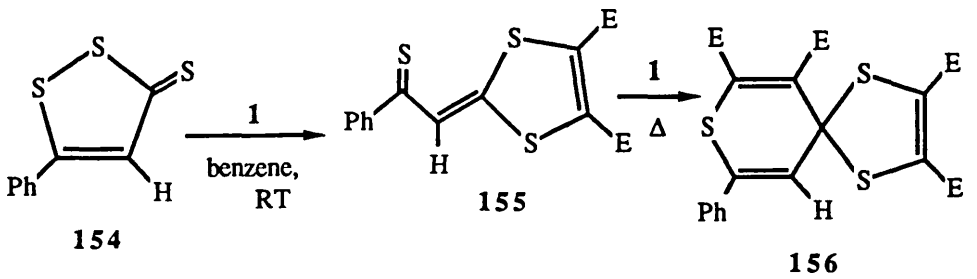


The addition of substituted anhydro-4-hydroxy-thiazolium hydroxides (**150**) to DMAD (**1**) led to unstable adducts (**151**) which rearranged differently

according to the nature of the substituents, as shown.[44,45]

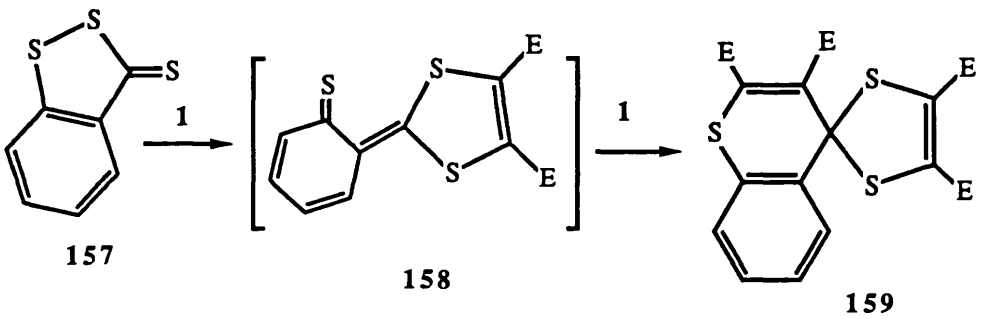


5-Phenyl-1,2-dithiole-3-thione (**154**) reacts with DMAD (**1**) to form dimethyl 2-thiophenacylidene-1,3-dithiole-4,5-dicarboxylate (**155**) (43%) and tetramethyl 6-phenylthiopyran-4-spiro-2'-(1,3-dithiole)-2,3,4',5'-tetracarboxylate (**156**) (44%). Compound (**156**) is obtained in 93% yield when dimethyl 2-thiophenacylidene-1,3-dithiole-4,5-dicarboxylate (**155**) in refluxing benzene is treated with DMAD (**1**).[46]



DMAD (**1**) adds across the 1,3-related S atoms and it reacts with the

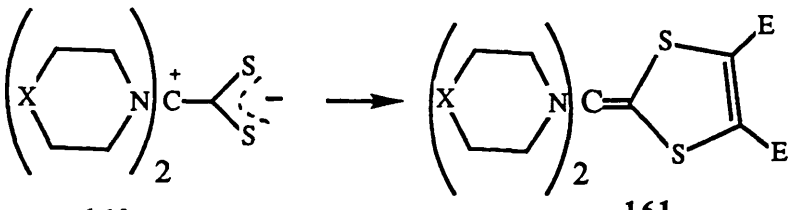
intermediate in a Diels-Alder fashion. 1,2-Benzodithiole-3-thione (**157**) reacts with DMAD (**1**) to form the analogous spiro compound (**159**) almost quantitatively.[46] In this example the 1:1 adduct (**158**) was not isolated, presumably because of its much greater reactivity.



157 **158** **159**

1.2.9 Related 1,3-Dipolar Cycloadditions

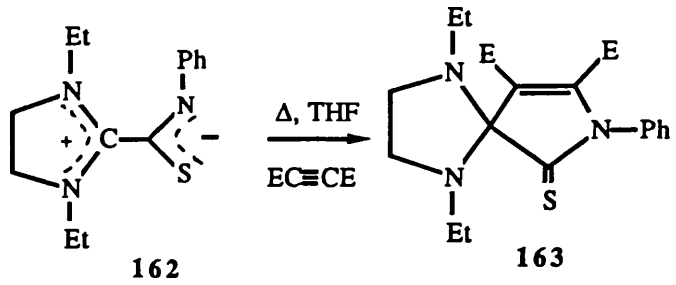
N,N'-bis-3-Oxapentamethyleneformamidiniumdithiocarboxylate (**160a**) and N,N'-bis-pentamethyleneformamidiniumthiocarboxylate (**160b**) underwent a kind of 1,3-dipolar cycloaddition with DMAD (**1**) to form 2-(dimorpholinomethylen)-1,3-dithiole-4,5-dicarboxylate (**161a**) and 2-(dipiperidinomethylen)-1,3-dithiole-4,5-dicarboxylate (**161b**) in (96%) and (92%) respectively.[47]



160 **161**

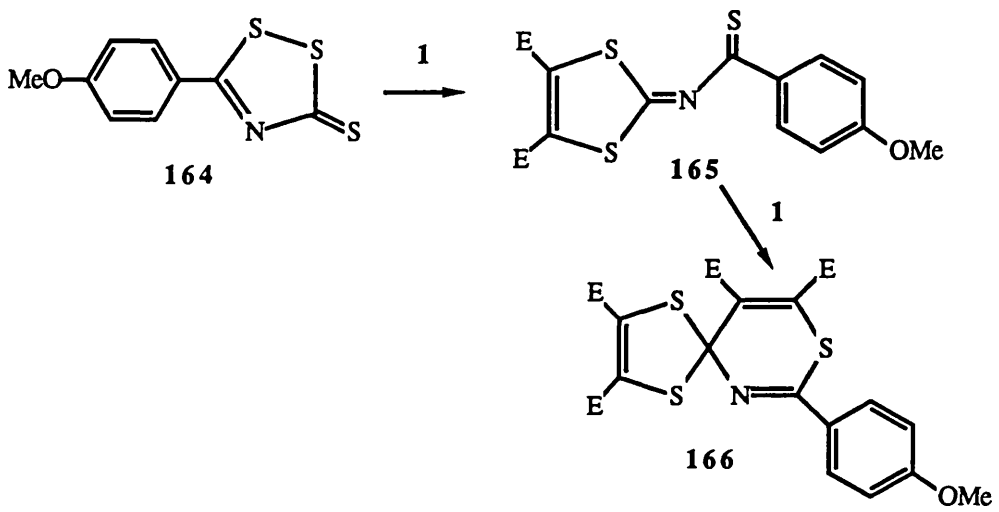
160a, 161a X= O
160b, 161b X= CH_2

Mercapto-N-arylformimidoylimidazolium (**162**) readily underwent a similar type of 1,3-cycloaddition in refluxing THF with DMAD (**1**) to form the unsaturated spiroheterocyclic system (**163**) in 79% yield.[48]



162 163

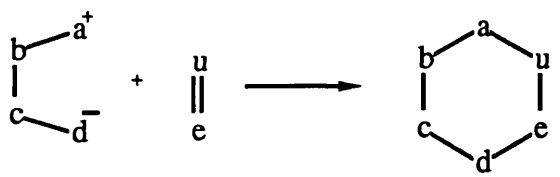
Similarly DMAD reacts with (**164**) to form (**165**) (79%) which in turn is converted into (**166**) by a Diels-Alder reaction of DMAD.[49]



164 165 166

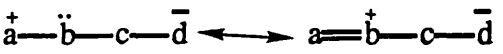
1.3 1,4-Dipolar Cycloadditions

The name 1,4-dipolar cycloaddition was coined in 1965 for a molecule a-b-c-d where 'a' is electron deficient and 'd' has at least one free electron pair.[50] The 1,4-dipole reacts with dipolarophiles to form a 6-membered ring.



1,4-Dipoles with an electron sextet undergo internal or external octet

stabilisation; internal stabilisation occurs if 'b' has a free electron pair.

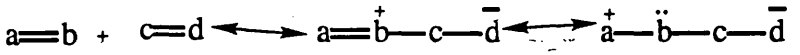


Huisgen[50] noted that 1,4-dipoles and their cycloadditions are not as similar to those of 1,3-dipoles as first appears. In contrast to the 1,3-dipoles, the electrophilic and nucleophilic centres in the 1,4-dipoles are localised and this causes definite mechanistic differences.

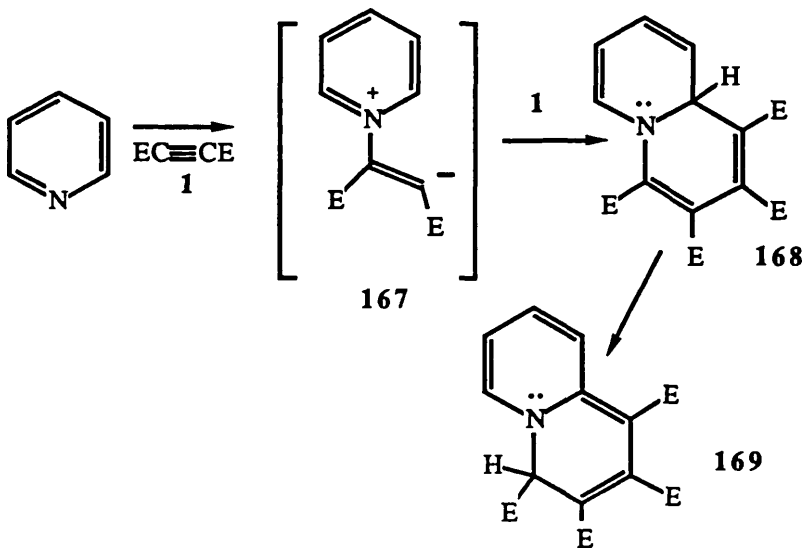
Since 1,4-dipoles cannot rearrange into mesomeric sextet forms, no double bond can form between 'b' and 'c'. A double bond here would make 1,4-dipoles like a 1,3-diene which would undergo Diels-Alder reactions.

1,4-Dipolar addition is different from the cyclic electron flow of the Diels-Alder reaction. Electrons cannot migrate in a cyclic manner if 'c' is a tetrahedral centre.

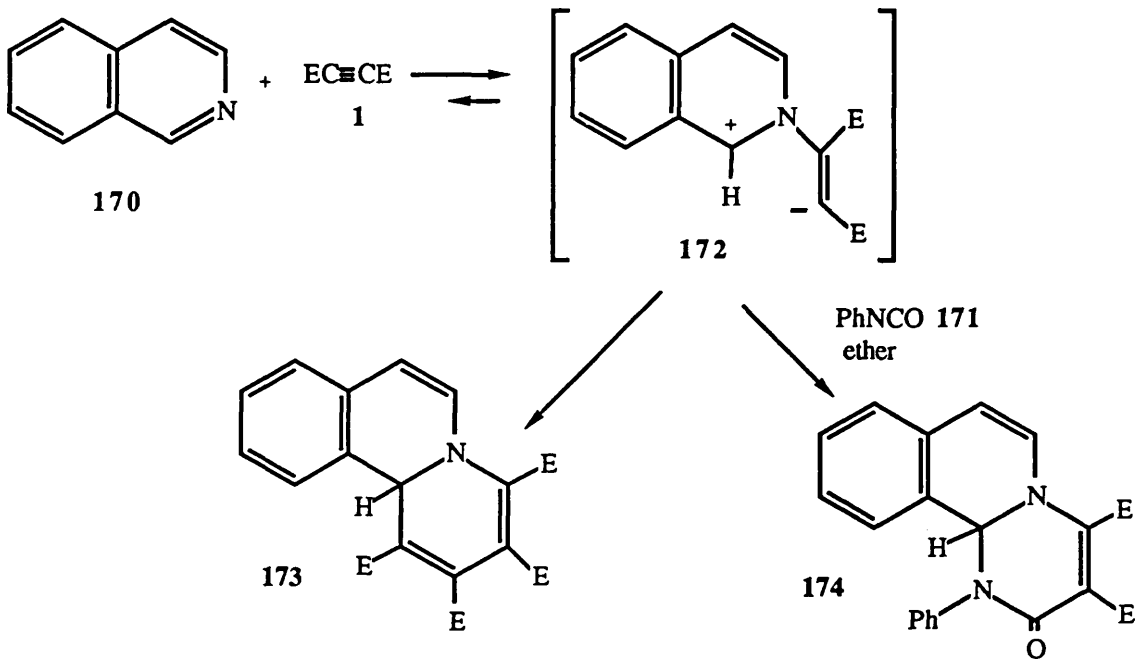
Most of the known examples which are classified as 1,4-dipolar compounds have not been isolated, but are generated *in situ* from a nucleophile a=b and an electrophile c=d.



DMAD reacts with pyridine to form tetramethyl 9*a*H-benzo[*a*]pyridine-1,2,3,4,-tetracarboxylate (**168**). This tetra-ester underwent a [1,5] sigmatropic shift rapidly to form the 4H-isomer (**169**). The stability of compound (**169**) was attributed to delocalisation of the nitrogen lone pair of electrons into the ester groups.[51]



Phenylisocyanate (**171**) does not react with isoquinoline (**170**), but it reacts with the 1,4-dipole formed by the addition of DMAD (**1**) to the mixture.[52]

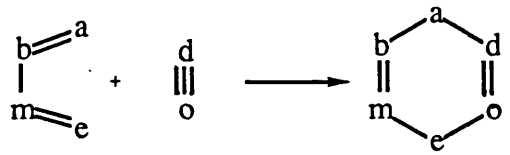


Isoquinoline (**170**) reacts with DMAD (**1**) to form tetramethyl 11*b*H-benzo[*a*]quinoline-1,2,3,4-tetracarboxylate (**173**) in the absence of phenylisocyanate (**171**) but in its presence the 1,4-dipole is intercepted to form dimethyl 2-oxo-1-phenyl-1,11*b*-dihydro-2H-pyrimido[2,1-*a*]isoquinoline-3,4-

dicarboxylate (**174**) 46% yield.

1.4 Diels-Alder Reactions

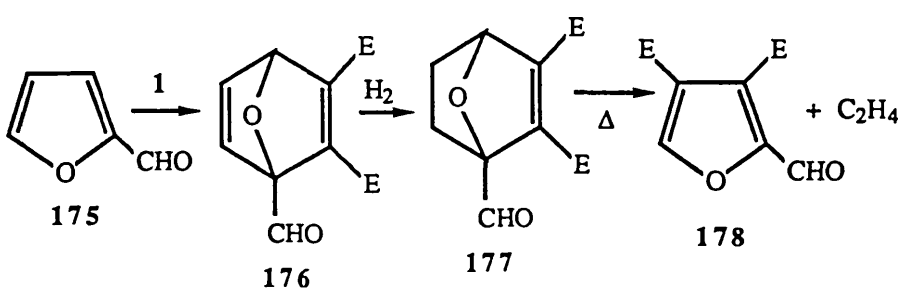
Activated triple bonds are good dienophiles which react readily with dienes. The general diene synthesis may then be represented as follows:[50]



This reaction has formed the basis of very many useful ring syntheses, and some of those involving DMAD will be described here.

1.4.1 Synthesis of Substituted Furans

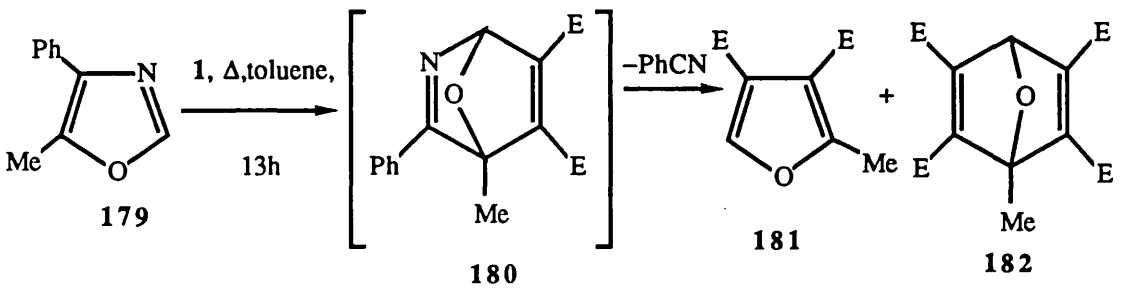
Furfural (**175**) underwent Diels-Alder reaction with DMAD (**1**). The initial cycloadduct (**176**) was subjected to hydrogenation, followed by pyrolysis to afford dimethyl 2-formylfuran-3,4-dicarboxylate (**178**) in poor yield, accompanied by the evolution of ethylene.[53] Compound (**178**) is formed as the result of the bicyclic compound (**177**) undergoing a retro Diels-Alder (Alder-Rickert) reaction on heating.



175 **176** **177** **178**

A more convenient synthesis of substituted furans is the cycloaddition of DMAD (**1**) to oxazoles.

5-Methyl-4-phenyl oxazole (**179**) reacts with DMAD (**1**) to form the cycloadduct (**180**) which undergoes retro Diels-Alder reaction to form benzonitrile and dimethyl furan-3,4-dicarboxylate (**181**) (69%). Tetramethyl 1-methyl-7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3,5,6-tetracarboxylate (**182**) was also obtained in 10% yield as a result of compound (**181**) undergoing further Diels-Alder reaction with the DMAD.[54]

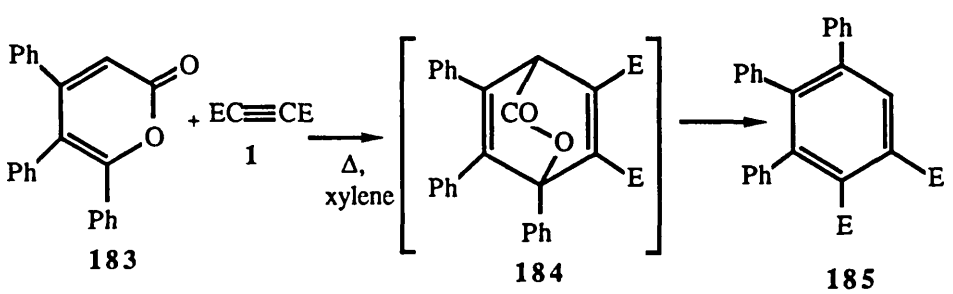


179 **180** **181** **182**

1.4.2 Synthesis of Substituted Benzenes

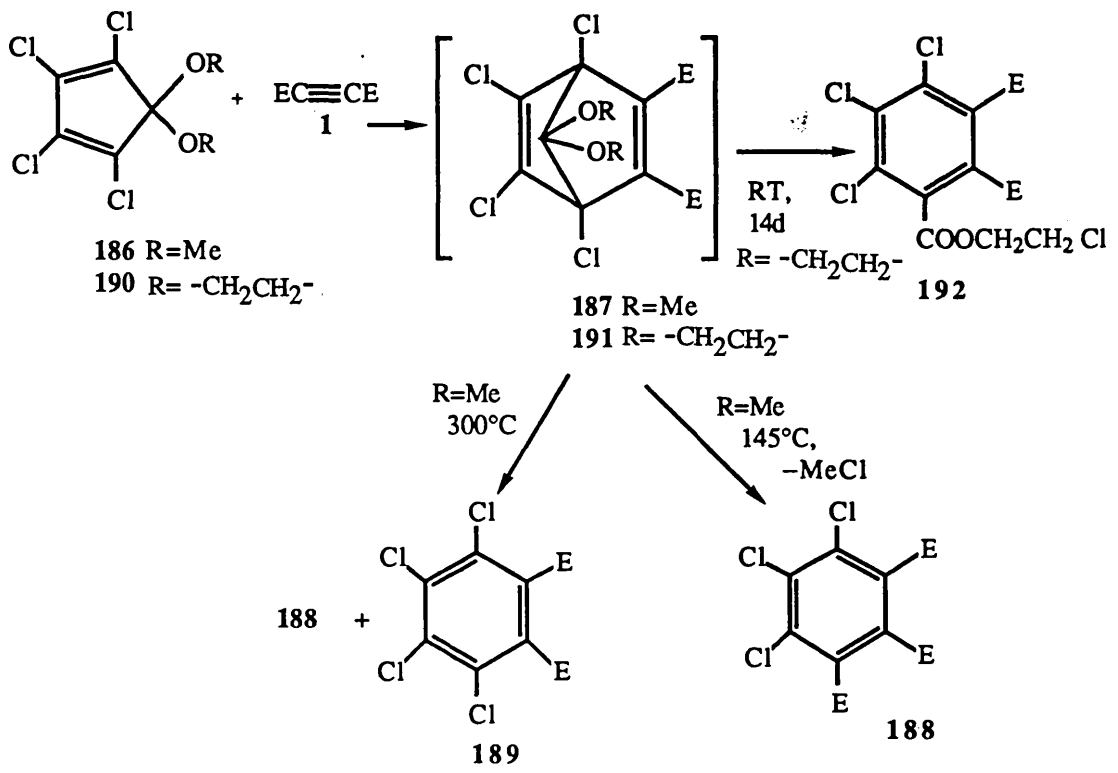
Aromatic rings are made available by the Diels-Alder reaction of DMAD (**1**) with cyclic dienes, followed by subsequent elimination of stable molecules.

Dimethyl 3,4,5-triphenylphthalate (**185**) is formed when DMAD is refluxed in xylene with 4,5,6-triphenylpyrone (**183**), by the loss of carbon dioxide from the initial cycloadduct (**184**).[55]



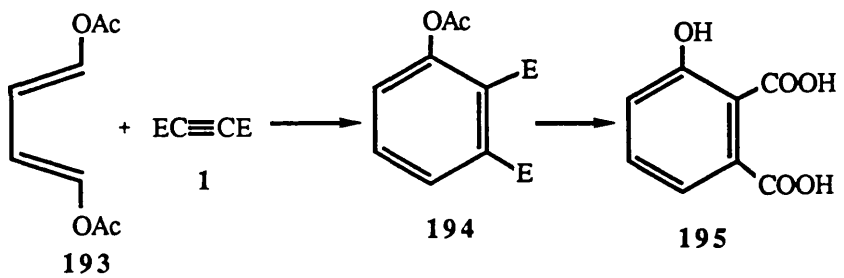
183 **184** **185**

DMAD underwent a Diels-Alder reaction with the dimethyl ketal (**186**). Various substituted benzenes were obtained by varying the experimental conditions, as shown.[56] DMAD also reacted with the ethylene ketal (**190**) to form the benzene derivative (**192**) in 88% yield.[56]



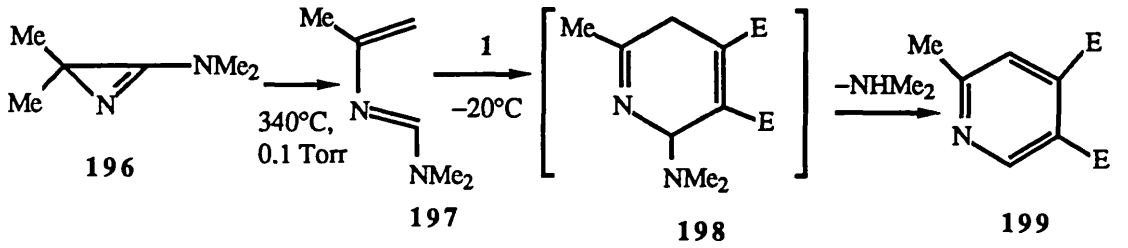
Ratio of **188** : **189** = 4:1

3-Hydroxyphthalic acid (**195**) was prepared by hydrolysis of the Diels-Alder adduct dimethyl 3-acetoxybenzene-1,2-dicarboxylate (**194**), obtained when DMAD is treated with *trans,trans*-1,4-diacetoxybutadiene (**193**).[57]



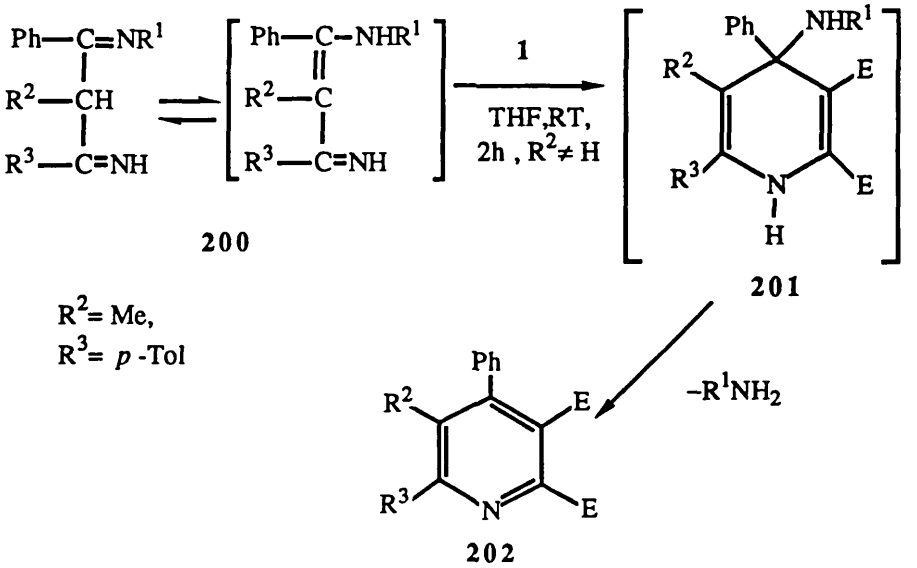
1.4.3 Synthesis of Substituted Pyridines

1-Dimethylamino-3-methyl-2-azabutadiene (**197**) obtained by thermal isomerisation of 2-dimethylamino-3,3-dimethyl-1-azirine (**196**), underwent facile cycloaddition to DMAD (**1**) followed by loss of dimethylamine to afford dimethyl 2-methylpyridine-4,5-dicarboxylate (**199**) (47%).[58]



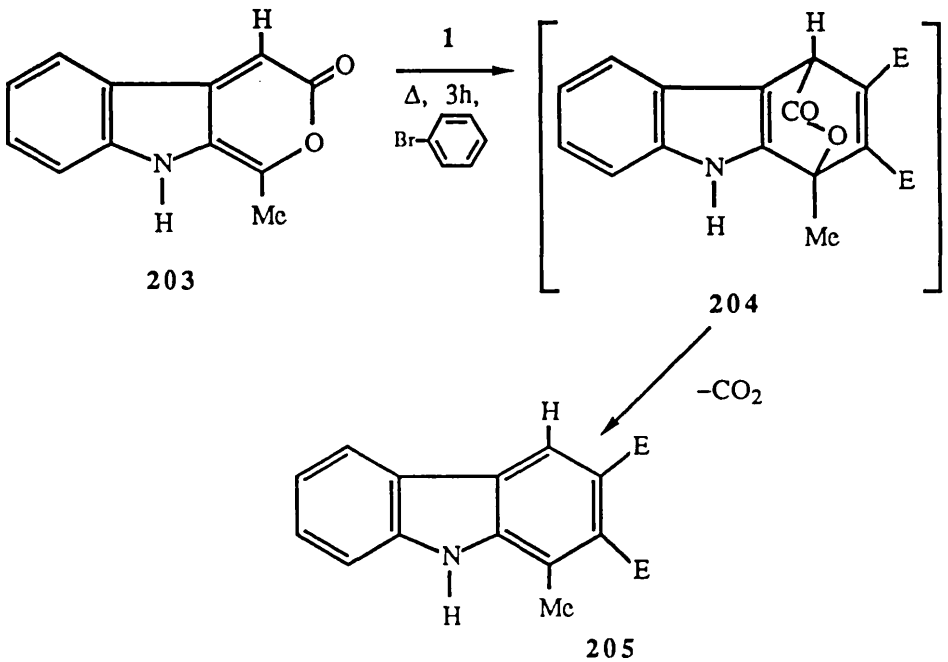
The synthesis of pyridines by the addition of bis-imines to DMAD (**1**) proceeds in the same fashion, where the alkyne reacts with the tautomeric azadiene form.

3-Imino-1-cyclohexylimino-1-phenyl-2-methyl-3-(4-methylphenyl)propane (**200**) underwent Diels-Alder reaction with DMAD (**1**). This is followed by the loss of amine to form the substituted pyridine (**202**).[59,60]

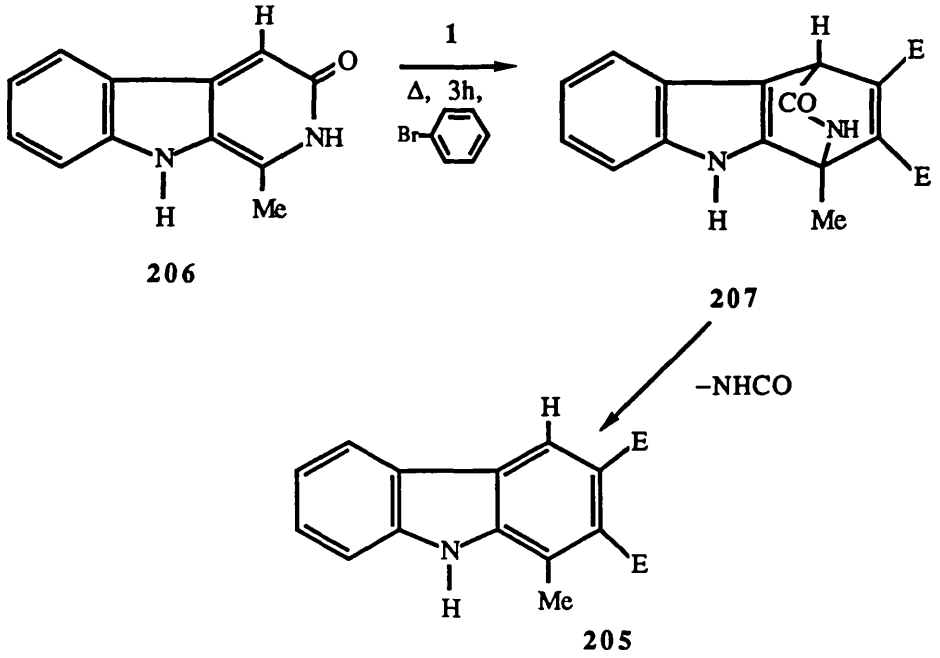


1.4.4 Synthesis of Substituted Carbazoles

1-Methylpyrano[3,4-*b*]indol-3-one (**203**) underwent Diels-Alder reaction when refluxed for 3h in bromobenzene with DMAD (**1**) to afford dimethyl 1-methyl-9H-carbazole-2,3-dicarboxylate (**205**) (81%). The initially formed cycloadduct (**204**) was not isolated as it spontaneously aromatises to form (**205**) with evolution of carbon dioxide.[61]



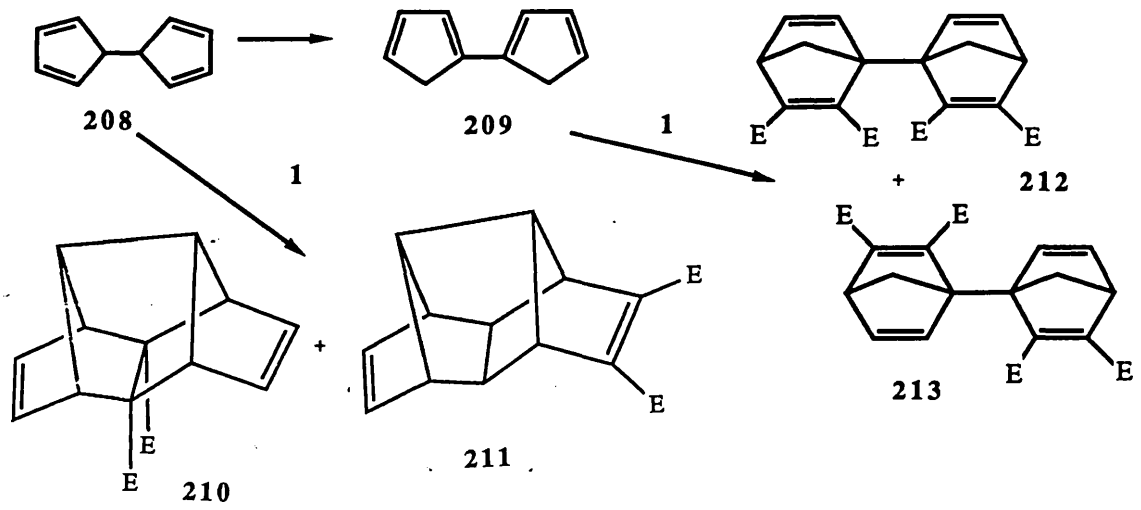
1-Methylpyrido[3,4-*b*]indol-3-one (**206**) reacts with DMAD (**1**) in refluxing bromobenzene to form dimethyl 1-methyl-3-oxo-2,3,4,9-tetrahydro-1H-1,4-ethenopyrido[3,4-*b*]indole-10,11-dicarboxylate (**207**) (7%) and dimethyl-9H-carbazole-2,3-dicarboxylate (**205**) (46%). Here the more stable initial cycloadduct (**207**) was isolated in low yields.[62]



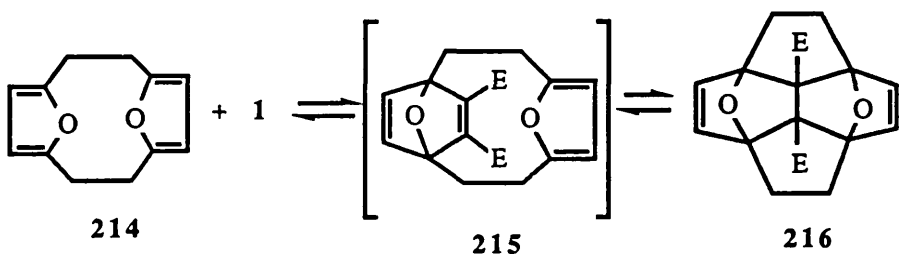
1.4.5 Domino Diels-Alder Reactions

Another development in the Diels-Alder reaction is the "Domino" Diels-Alder reaction. In these, one Diels-Alder reaction triggers off another within the molecule.

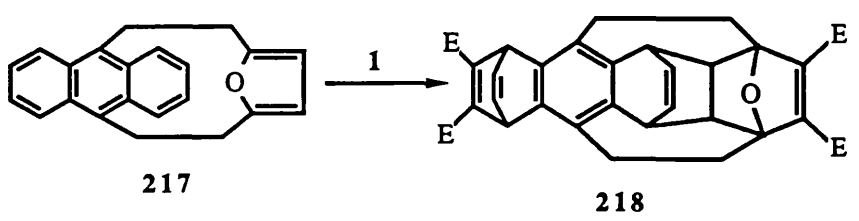
When DMAD (**1**) was added to 9,10-dihydrofulvalene (**208**) in THF at −78°C, four products (**210-213**) were obtained. 9,10-Dihydrofulvalene (**208**) can rearrange before undergoing Diels-Alder reaction with DMAD (**1**). The rearranged product (**209**) itself is capable of undergoing Diels-Alder with DMAD. This accounts for the formation of the major and the minor products. Compounds (**210**) and (**211**) were obtained in 58% and 41% yield respectively, and compounds (**212**) and (**213**) were obtained as a mixture in 4% yield.[63]



Another example of Domino Diels-Alder reaction is the reaction that occurred between [2.2]furanophane (**214**) and DMAD (**1**). The resultant cycloadduct (**215**) underwent a [2+4] cycloaddition to form the product (**216**) (71%).[64] When compound (**216**) was heated at a higher temperature, it underwent a retro Diels-Alder reaction to give furanophane (**214**).



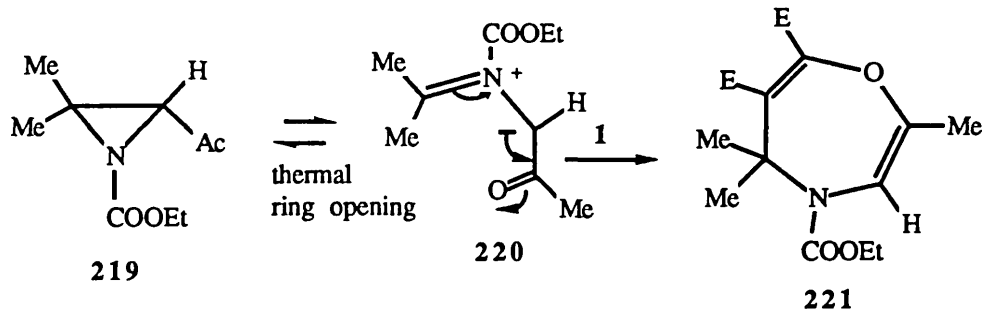
When [2.2](9,10)anthraceno(2,5)-furanophane (**217**) was reacted with DMAD it afforded the Domino Diels-Alder adduct (**218**) in 36% yield.[65]



1.5.0 Higher Order Cycloadditions

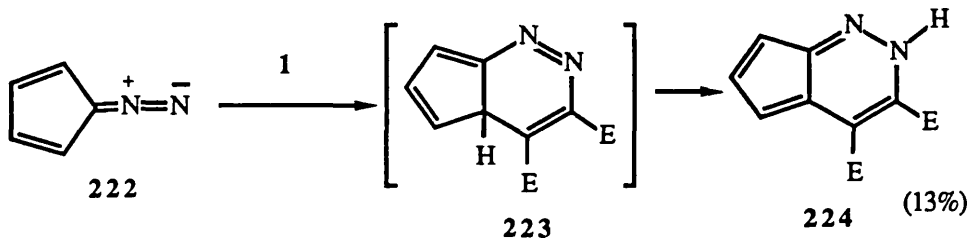
We have seen many examples of 1,3-dipolar reactions, and examples of 1,4-dipolar reactions. In principle, any 1,3-dipole which is conjugated with further unsaturated centres, could undergo higher order (1, n)-cycloaddition and several of these are now known.[66]

Aziridine (**219**) reacted with DMAD (**1**) to form oxazepine (**221**) (89%). The proposed mechanism involves a 1,5-cycloaddition of DMAD to the intermediate acyl azomethine ylide (**220**).[67]



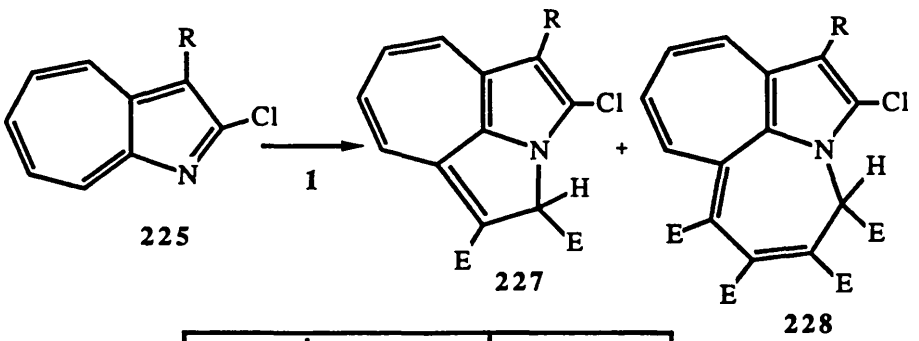
219 **220** **221**

A 1,7-dipolar cycloaddition reaction between diazocyclopentadiene (**222**) and DMAD (**1**), followed by H-tautomerism, gave the fused pyridazine (**224**).[68]



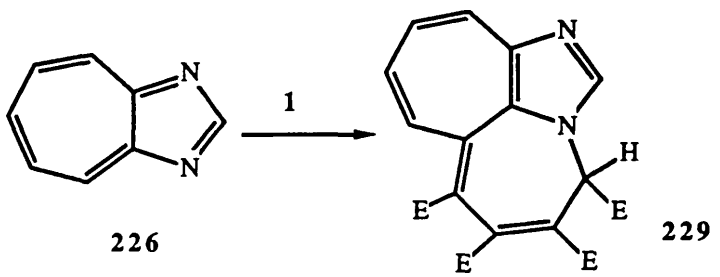
222 **223** **224** (13%)

The tricyclic ring systems (**227**), (**228**) and (**229**) were obtained in low to moderate yields when DMAD (**1**) was treated with the mono-aza (**225**) and diaza-azulenes (**226**) respectively.[69]



225 227 228

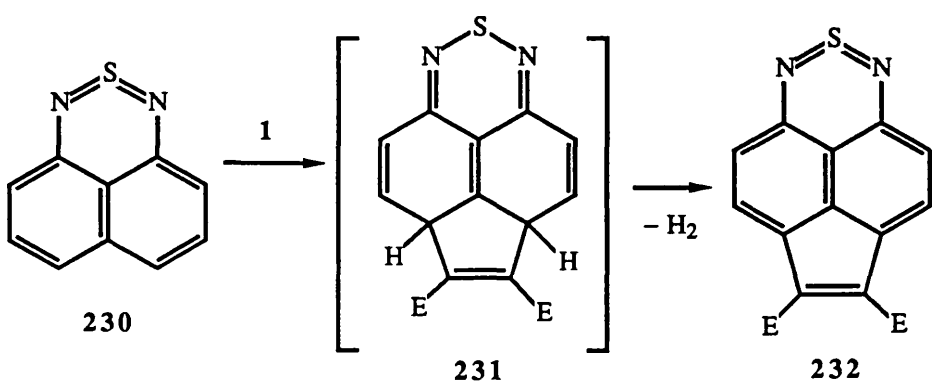
R	Yield of 227	Yield of 228
COOEt	14 %	2 %
H	30 %	14 %



226 229

These reactions were considered as 1,8-dipolar cycloadditions.

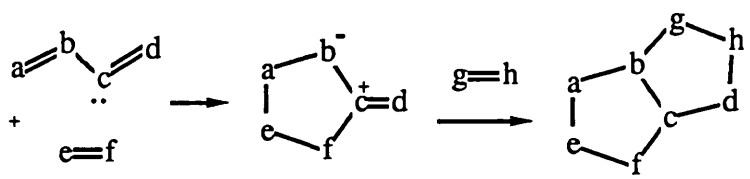
The expected 1,3-dipolar cycloaddition between DMAD (**1**) and the naphthothiadiazine (**230**) did not occur; instead the product (**232**) was isolated in low yield (6%). Compound (**230**) was considered to have undergone a 1,11-dipolar cycloaddition to form the initial cycloadduct (**231**) which underwent aromatisation to the isolated product (**232**).[34]



230 231 232

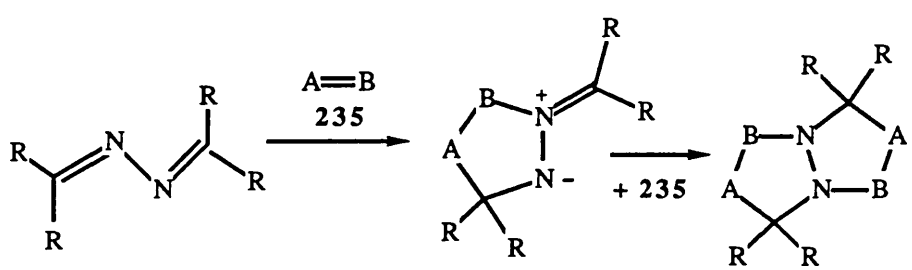
1.6 Crisscross Additions

A 1,3-diene with no formal charges can have at centre 'c' an unshared electron pair. Rotation of the b-c bond through 90° until the σ plane of the double bond c=d is perpendicular to the a-b-c plane gives rise to an allyl anion type system. During cycloaddition to e=f there is charge migration which transfers electronic charge from 'a' and 'c' to centre 'b'. Thereby creating a 1, 3-dipole b-c-d (**233**) as a 1:1 adduct which can undergo further cycloaddition with dipolarophile g=h that is either identical to or different from e=f.[70]



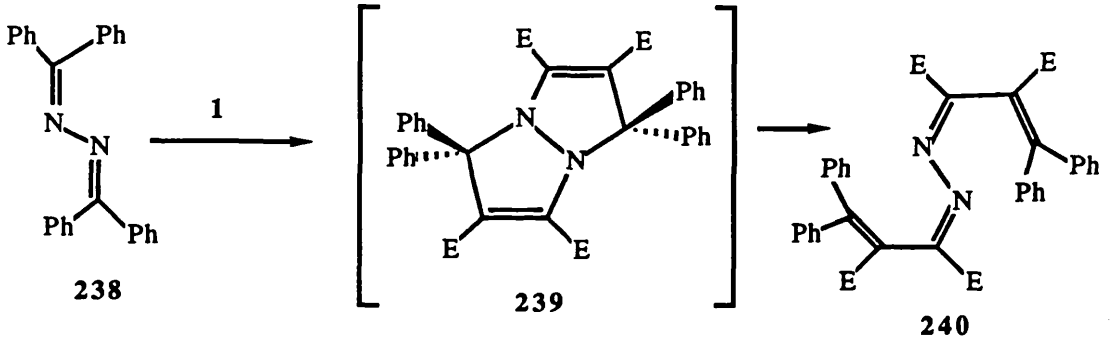
233

The "crisscross" reaction or the (1,3-2,4)-addition was first described in 1917.[71a] Azomethine imine (**236**) was postulated as the key intermediate in these crisscross reactions.[71b]



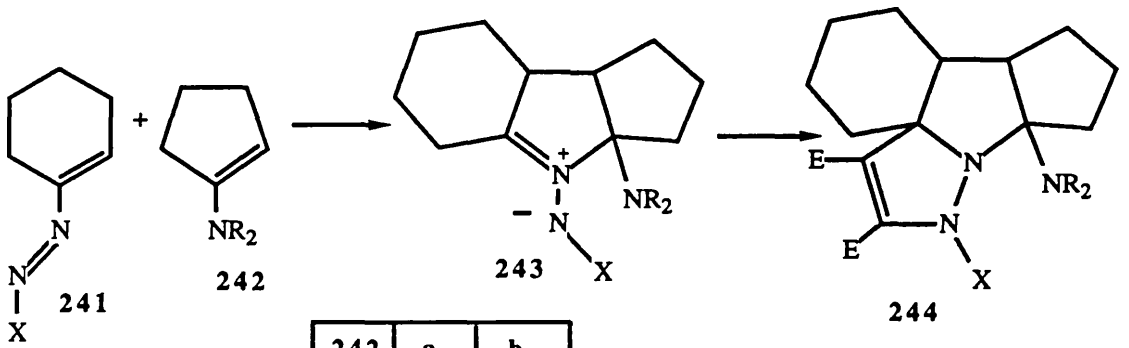
234 **236** **237**

For example, benzophenone azine (**238**) in refluxing acetonitrile underwent addition to DMAD (**1**) to form the conjugated azine (**240**) in 82% yield *via* the crisscross adduct (**239**) which had undergone electrocyclic ring opening twice to form (**240**).[72]



238 239 240

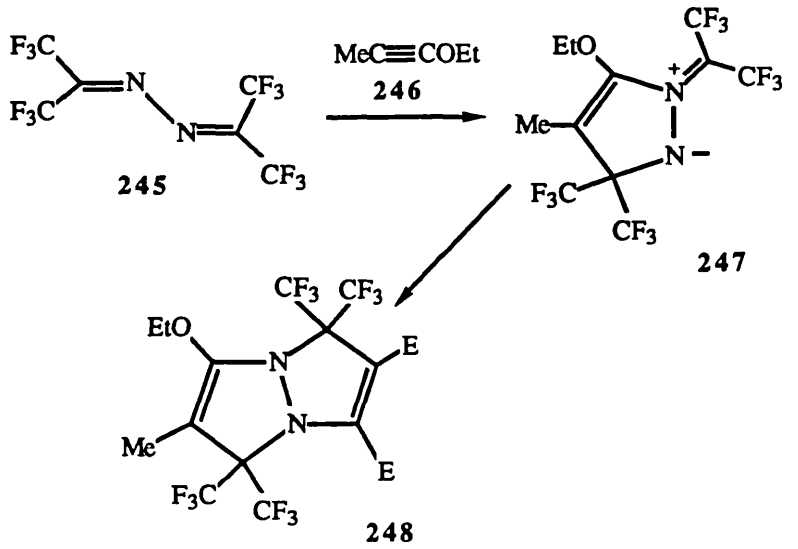
Azo alkenes react with enamines to form azomethine imines which undergo the crisscross reaction.[73] An example which illustrates this is the reaction between the azo compound (**241**) and enamine (**242**). The labile but isolable azomethine imine (**243**) reacts with DMAD (**1**) to form the crisscross cycloadducts (**244**) in good yield.[73]



241	X
a	COO^tBu
b	Tosyl

242	a	b
NR_2	O, N	N

Hexafluoroacetone azine (**245**) reacts with 1-ethoxypropyne (**246**) to form the azomethine imine (**247**) which undergoes reaction with DMAD (**1**) to the crisscross cycloadduct (**248**) (52%).[74]



1.7 Summary

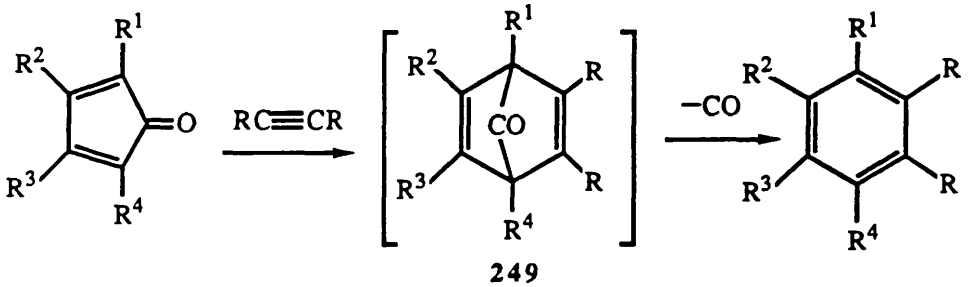
Cycloaddition reactions of the important electron-deficient alkyne, dimethyl acetylenedicarboxylate (**1**), to various selected systems have been briefly reviewed. The cycloaddition reactions of DMAD (**1**) to 1,3-dipoles, 1,4-dipoles, and dienes are seen to provide a wide range of synthetically useful processes.

CHAPTER TWO

Norbornadien-7-ones

2.1 Introduction

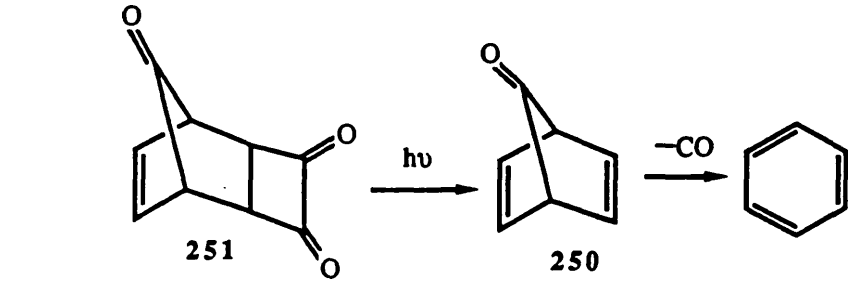
The chemistry of bicyclo[2.2.1]hept-2,5-dien-7-ones was briefly reviewed in 1967 by Yankelevich.[75] The bicyclo[2.2.2]hept-2,5-dien-7-ones, obtained as a result of Diels-Alder reactions between cyclopentadienones and alkynes, are usually unstable and the product undergoes extrusion of carbon monoxide to form an aromatic product. The decarbonylation of (**249**) to give a substituted benzene is an example of a cheletropic reaction which is predicted to occur by a disrotatory mode if fragmentation follows a linear path.[76]

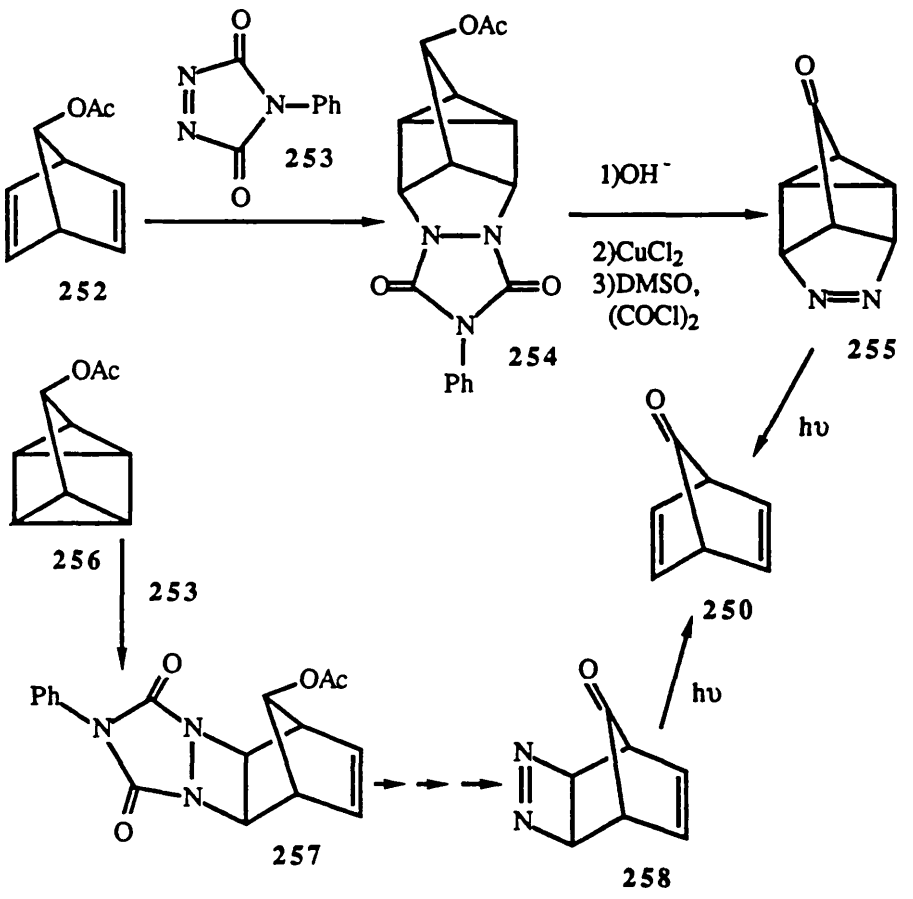


249

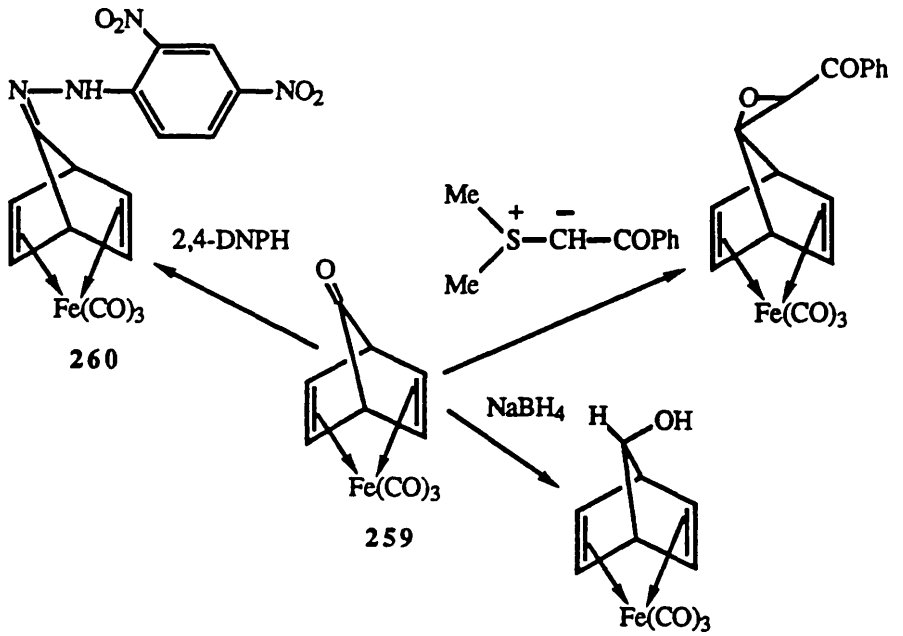
Chemists have been trying to isolate these initial Diels-Alder adducts for the past fifty years. Many have reported the isolation of the adducts, but their results were later found to be incorrect. Many have tried and failed to isolate the parent norbornadien-7-one (**250**). It has been reported recently that norbornadien-7-one (**250**), formed by photolysis of (**251**), can be isolated in an argon matrix at −81°C.[77] Compound (**252**) when treated with N-phenyltriazolinedione (**253**) gave the adduct (**254**) which was converted into the azo compound (**255**). Compound (**255**) on photolysis gave norbornadien-7-one (**250**). Compound (**250**)

was also prepared in an analogous sequence starting from compound (256).[78]

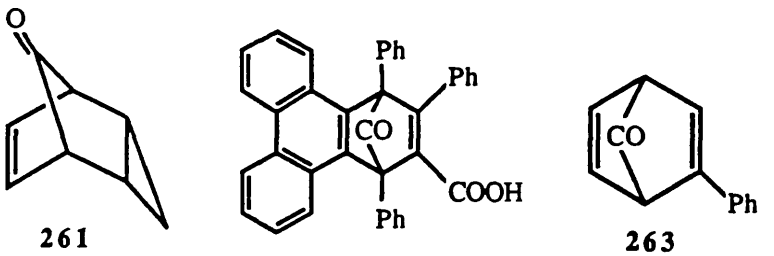




The iron tricarbonyl complex (**259**) of norbornadien-7-one was synthesised and characterised. It is stable below 0°C and the carbonyl group behaves as a normal ketone;[79] some of its reactions are illustrated.

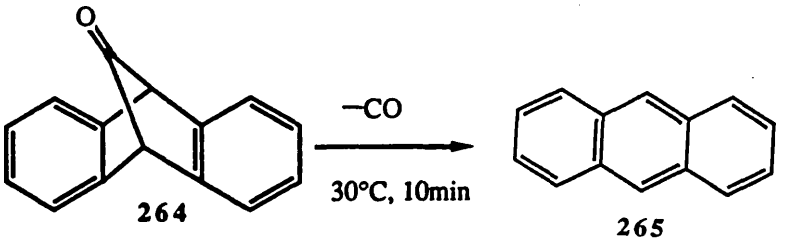


Compound (**261**), with one of the destabilising double bonds replaced by a cyclopropane ring, was isolable. It had a half-life of 10 min at 30°C.[80] It is definitely more stable than the parent norbornadien-7-one (**250**) and the iron tricarbonyl complexed norbornadien-7-one (**259**).



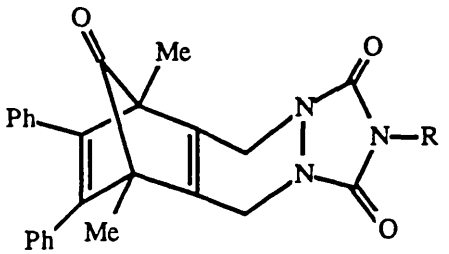
Compounds (**262**) and (**263**) were two of the earliest bridged adducts claimed to have been isolated, but these were later found to be incorrect.

The first authentic bridged adduct to be isolated was 2,3,5,6-dibenzonorbornadien-7-one (**264**), but this was not fully characterised as it extruded carbon monoxide very readily to afford anthracene (**265**).[81] Recently mono- and di-nitro derivatives of compound (**264**) have been synthesised and isolated and found to be somewhat more stable than (**264**) itself.[82]

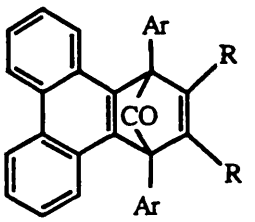


264 265

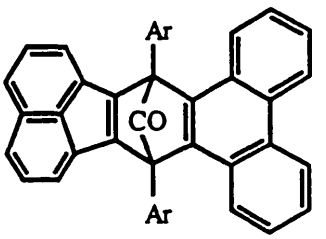
Another bridged adduct (**266**) was characterised but found to be stable only below –40°C.[83]



266 R=*p*-MeC_6H_4

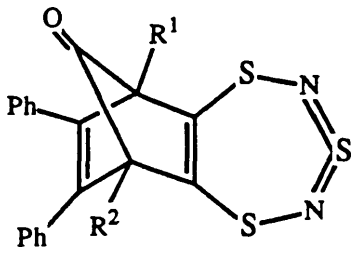


267a R=R=Ph,
b R,R =-CH=CH-CH=CH-



268

The isolation of compounds (**267**) and (**268**) has been claimed but whether these compounds were actually isolated is highly questionable, in view of experimental inconsistencies in the papers[84-86] (see Chap.6 for discussion of this work).

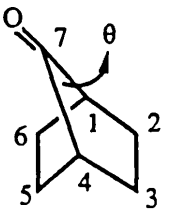


269 $R^1 = R^2 =$ Me
270 $R^1 = R^2 =$ Et
271 $R^1 =$ Ph, $R^2 =$ Me

However, compounds (**269**), (**270**) and (**271**) have very recently been isolated, fully characterised, and found to be stable at room temperature.[87]

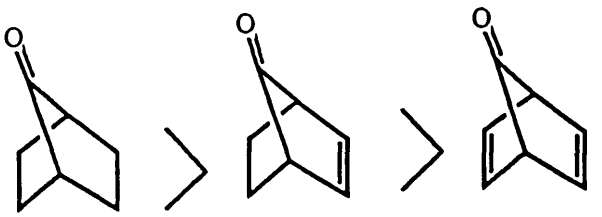
2.2 Stability

The instability of norbornadien-7-one (**250**) has been greatly debated in the literature. It was found to have a similar framework to norbornan-7-one (**272**) and the C_1-C_7-C_4 angle, θ, is *ca.* 96-97° in both cases.[75]



272

Norbornan-7-one (**272**) is stable even though it is a strained ketone. Introduction of a double bond changes the stability and norbornen-7-one (**273**) lies in between compounds (**250**) and (**272**) as far as stability is concerned.[88]



272 **273** **250**

Ready thermal and photochemical decarbonylation of compound (**273**) supports the fact that compound (**273**) is less stable than (**272**).

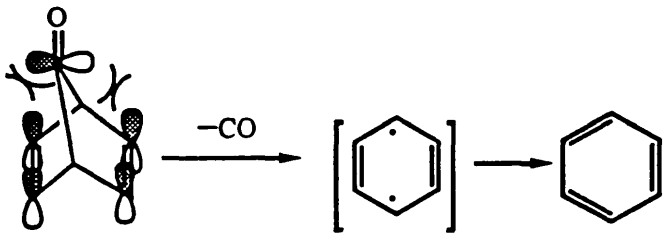
Factors invoked in order to rationalise the ready decarbonylation of compounds (**250**) and (**273**) are:

a) relief of strain

b) stabilisation of excited intermediates

c) formation of thermodynamically stable products

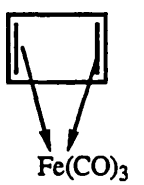
and d) repulsive interaction of the π-orbitals of the olefinic bonds and the carbonyl bond.



250

The mono-ene (**273**) is more stable than diene (**250**) because in the former this repulsive interaction is partly overcome by the bending of the bridged carbonyl towards the saturated C_5-C_6 bond; in the case of the latter this is not possible.

Unstable organic molecules with π electrons can sometimes be stabilised and isolated as ligands on a transition metal into the system. A classic example is the stable cyclobutadiene-iron tricarbonyl complex (**274**).



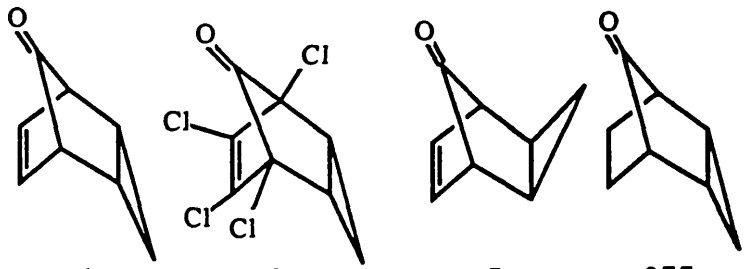
274

Tricarbonyl(norbornadien-7-one)iron (**259**) was found to be more stable than norbornadien-7-one (**250**). This is attributed to the fact that the electron density on the olefinic bonds is reduced due to the "forward-backward" π bonding postulated for transition metal complexes. Reduction in electron density on the olefinic bonds means reduction in the unfavourable π cloud interaction

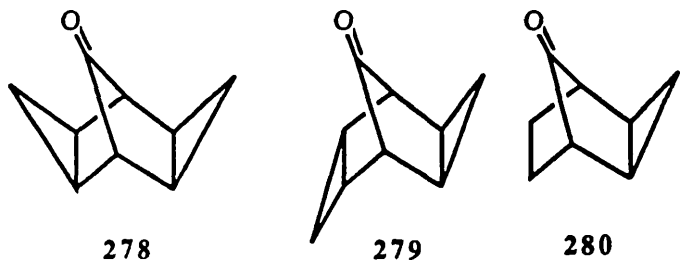
and this in turn means that complex (**259**) is rendered much more stable than the uncomplexed compound (**250**).[79]

The stability of complex (**259**) might also be due to other factors. Concerted loss of carbon monoxide from the norbornadienones is allowed by disrotatory transformation, but the analogous transformation might be not possible for compound (**259**) as a result of metal-olefin bonding.[79]

The decarbonylation of a series of cyclopropane fused norbornanes has been studied.[89]



261 **275** **276** **277**

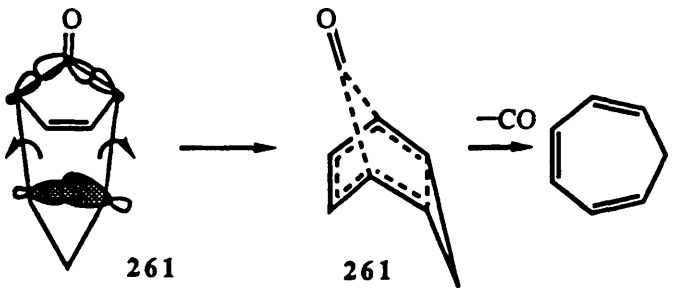


278 **279** **280**

The ease of decarbonylation of these, and related compounds was found to decrease in the order:

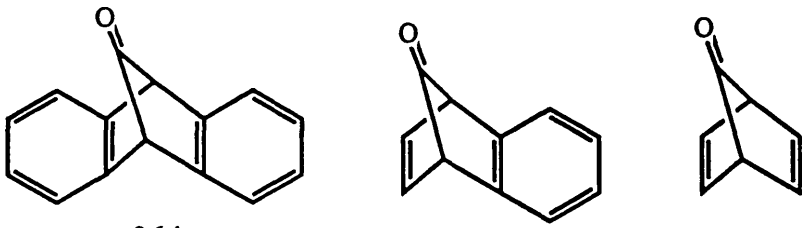
(261) > (275) > (273) > (276) > (277) > (279) > (280), (272), (278)

The decarbonylation of the endo isomer (**261**) proceeds *via* a concerted mechanism involving participation of the $C_{(2)}$-$C_{(4)}$ cyclopropane bond while the exo isomer (**276**) decarbonylates *via* a non-concerted mechanism involving no stabilisation of the transition state by the cyclopropane bond.[89]



261 261

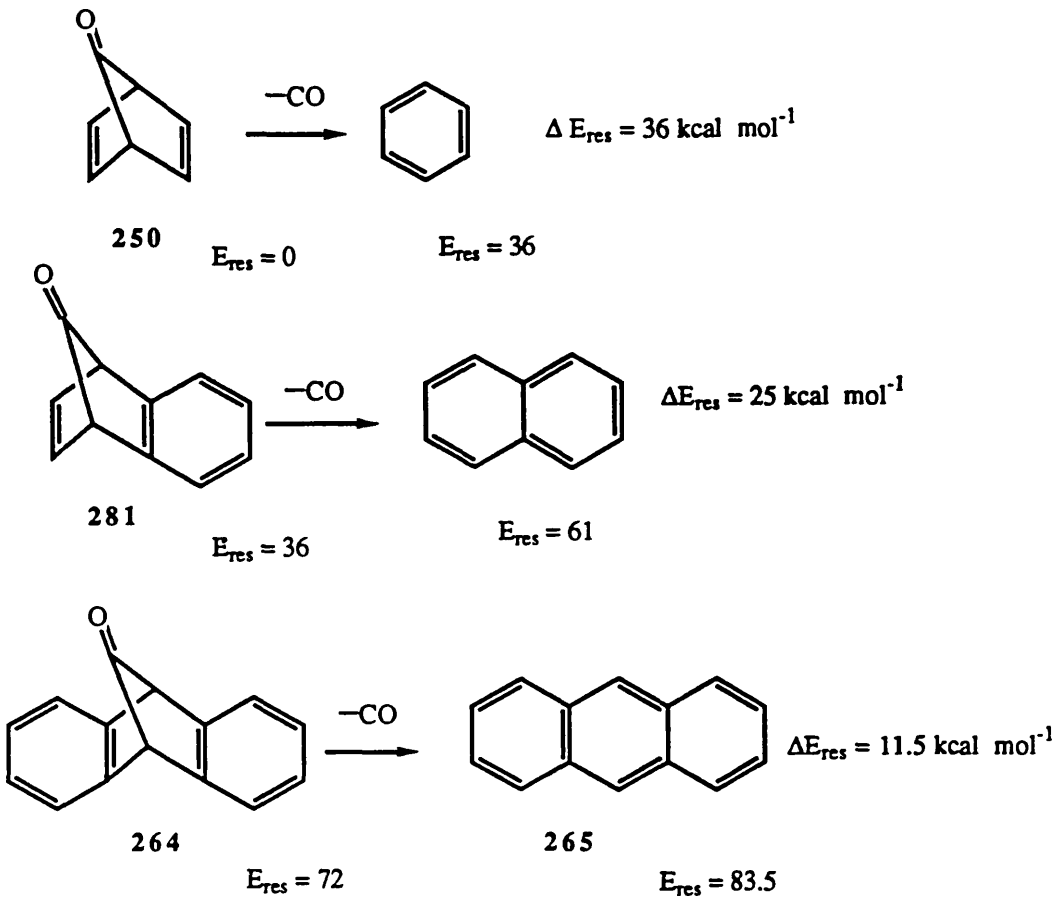
In the endo ketone (**261**) the orbitals forming the cyclopropane bent bond between C_2 and C_4 are ideally situated for interaction and subsequent π-bond formation with the developing π orbitals at C_1 and C_5. The geometry of the cyclopropane ring in exo ketones does not allow overlap of C_2-C_4 bond orbitals with the developing π-orbitals thus here only the C_6-C_7 π bond is involved in the decarbonylation.[90]



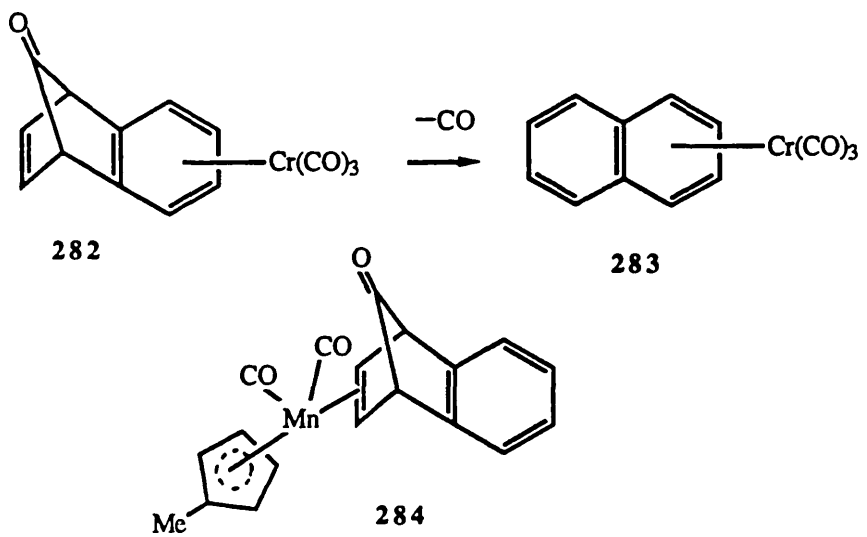
264 281 250

In the norbornadienone (**250**), benzonorbornadienone (**281**) and dibenzonorbornadienone (**264**) series, the order of decreasing stability is (**264**) > (**281**) > (**250**). Their stability is attributed to the total bond order of the π-bonds on either side of the carbonyl group which is in the order (**264**) < (**281**) < (**250**).

Another important factor that has to be taken into consideration is the gain in resonance energy on decarbonylation of the ketone. This is in the order (**264**) < (**281**) < (**250**). The gain in resonance energy must be reflected in the energy of the transition state for decarbonylation and hence in the activation energy for the reaction. Approximate values are shown below.[76]



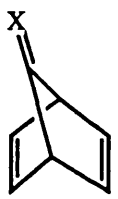
It is thus not surprising that norbornadien-7-one (**250**) is the least stable.



As attempts to isolate benzonorbornadienone (**281**) failed, synthesis of the

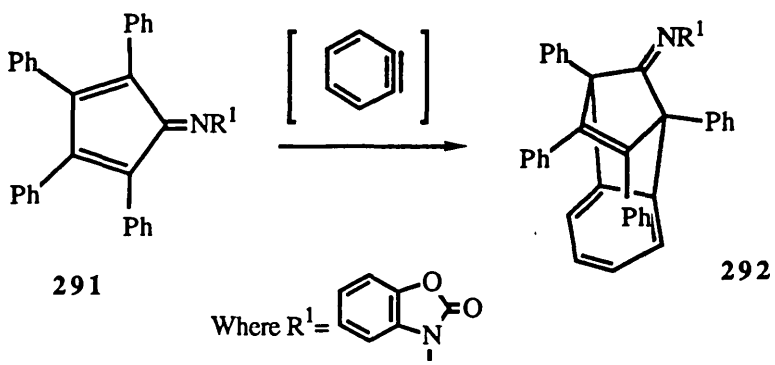
complexed ketone (**282**) and its endo isomer were attempted.[76] The exo- and endo-tricarbonyl(benzonorbornadienone)chromium (**282**) and (**283**) could not be isolated, indicating that there still is considerable driving force for decarbonylation to form compound (**283**). This is said to be due to the participation of the olefinic π-bond. Clearly the electron density on the olefinic π-bond has to be reduced still further to enable compound (**281**) to be isolated, and this is supported by the isolation of the manganese complex (**284**).[91]

It is interesting to note that compounds (**285**), (**286**) and (**287**) are also unstable and have never been isolated, whereas compounds (**288**), (**289**) and (**290**) undergo extrusion reactions only at elevated temperatures.[92,93]



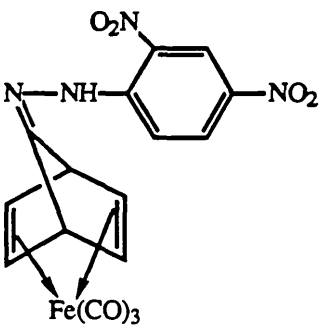
285 X = NOMe
286 X = NPh
287 X = NCN
288 X = $C(SiMe_3)_2$
289 X = $=CH_2$
290 X = cyclopropyl

It would be interesting to see if compounds (**285**), (**286**) and (**287**) are stable if complexed to a transition metal. The benzonorbornadienone hydrazone (**292**) was isolated and found to be completely stable at room temperature.[94] The cheletropic elimination from compound (**292**) is sluggish and this was attributed to the non-colinearity of R^1, N and the bridging carbon. Stabilisation of



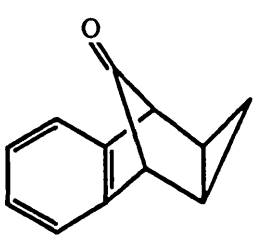
the incipient carbene as an isocyanide is maximum when R^1, N and C_7 have a linear geometry.[94]

One example of a complexed norbornadienone hydrazone is compound (**260**).[79] This was formed only under special conditions, since it was destroyed under the usual conditions employed for hydrazone formation.[79]

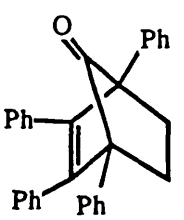


260

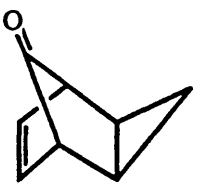
Tetraphenylnorbornenone (**294**) undergoes decarbonylation seven times slower than exo ketone (**276**) and compound (**293**) undergoes decarbonylation only above 400°C.[90] Thus the stability of these compounds decreases in the order: (**293**) > (**294**) > (**276**).



293

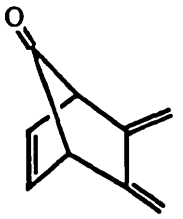


294



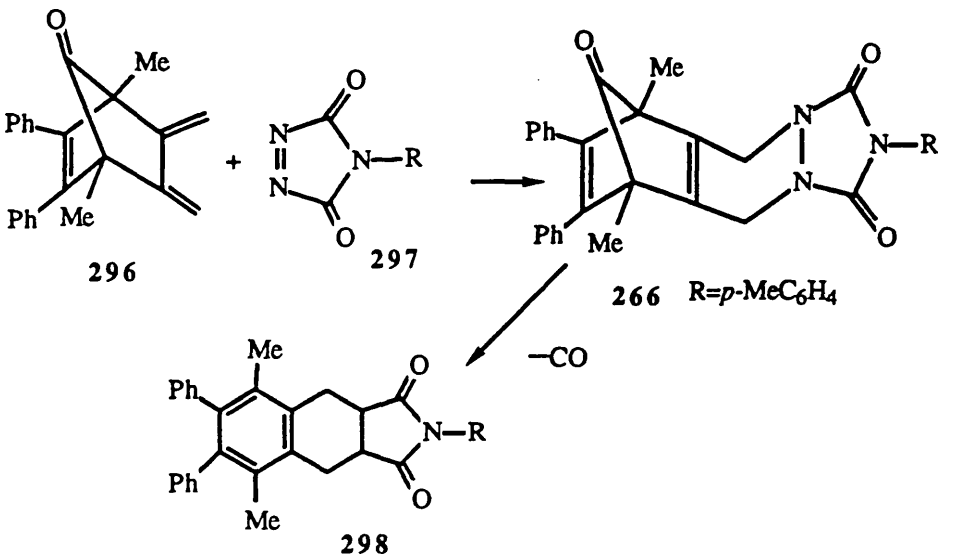
276

Compound (**295**) is stable but has been little investigated.[95] It would be interesting to compare its stability with the norbornadienones already discussed; it would be expected to be more stable than most of them.

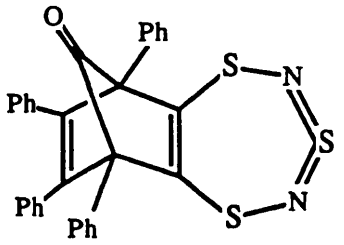


295

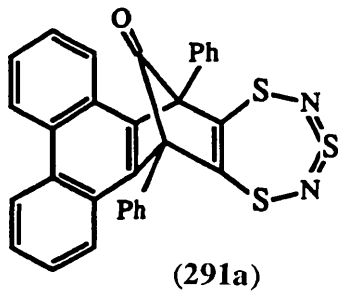
When the diene (296) was treated with the N-*p*-tolyltriazolinedione (297), it gave the bridged Diels-Alder adduct (266) which could be isolated but underwent decarbonylation readily at room temperature.[83]



The heterocyclic compounds (269-271) were found to be stable, but they exhibited a reverse in stability trend (269 > 270 > 271) compared to that shown by the carbocyclic norbornadienone systems discussed above. It is possible that the sulphur atoms α to the norbornadienone framework play a major role in this reversal of stability. The related compounds (290a) and (291a) could not, however, be isolated.



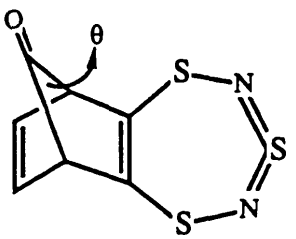
(290a)



(291a)

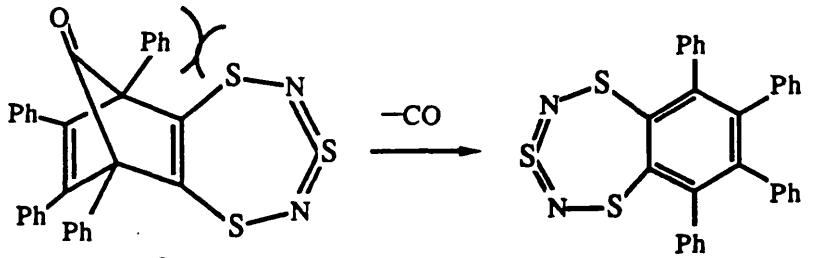
By analogy, compounds (290a) and (291a) should be somewhere between norbornadienone (**250**) and benzonorbornadienone (**281**) in stability, thus accounting for their instability. Therefore, the overall stability trend could be as follows: (**269**), (**270**), (**271**) > (**264**) >(290a), (291a), (**281**) > (**250**).

Another factor which might correlate with the stability of these norbornadienone derivatives in the C–CO–C bond angle, θ.



The olefinic π bond interaction with the carbonyl π bond is not severe in compounds (**269-271**) and (290a) as the ketone is flanked on one side only by an olefinic bond, and an aromatic ring on the other side. This explains why compound (290a) and (291a) should be more stable than compound (**250**). Since compounds (290a) and (291a) are not stable some other factor is also playing a role here.

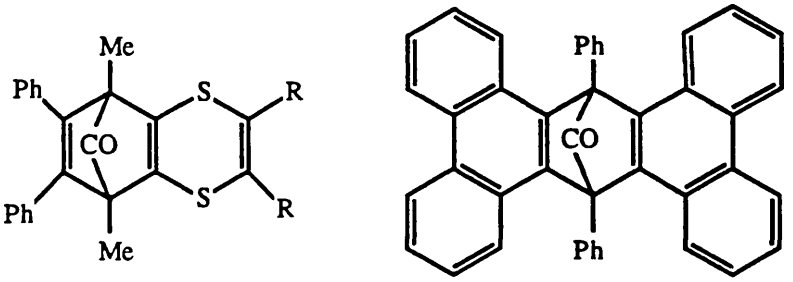
Compound (290a) should have a boat conformation and would thus give rise to steric hindrance between the phenyl groups at the bridge-head carbon atoms and the sulphur atoms of the trithiadiazepine ring. This could be a destabilising effect which favours decarbonylation to the aromatic compound (292a).



(290a) (292a)

Similarly the phenanthrene derivative (291a) would have a boat conformation which is unfavourable because here not only is there steric hindrance between sulphur and the phenyl group but also between the phenanthrene ring and the trithiadiazepine ring.

Compounds (**269-271**) are more stable because there is less steric hindrance between the substituents (Me, Me; Et, Et; Me, Ph) on bridge-head carbon atoms and the sulphur atoms of trithiadiazepine.



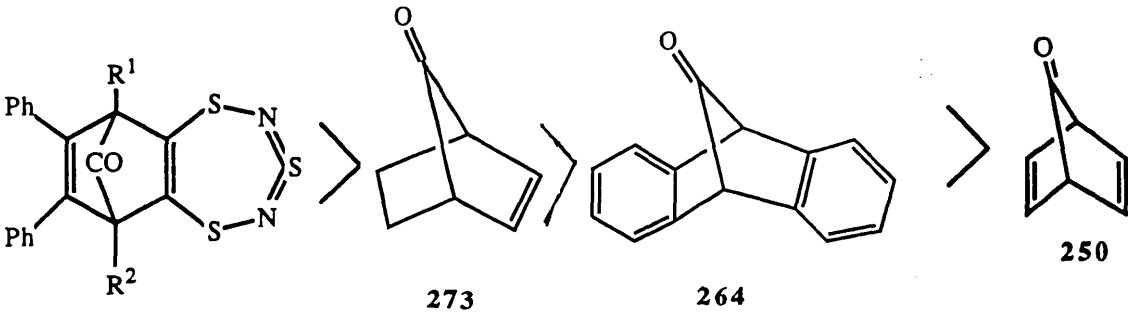
(293a) (294a)

It would be interesting to prepare and study the stability of compounds like (293a) and (294a). Compound (294a) could be stable enough for isolation since in the present work a mono-phenanthrene analogue (**267**) has been isolated and found to be stable (see Chap.6).

2.3 Summary

The ease with which carbon monoxide is extruded from norbornadien-7-

one derivatives depends mainly upon the nature of the double bonds. Normally extrusion occurs under the conditions of Diels-Alder reaction used to prepare the norbornadien-7-one and the initial bridged cyclo-adducts cannot be isolated.[96] Very few authenticated bridged carbonyl compounds of this type have been isolated, and norbornadien-7-one (**250**) itself has not been fully characterised. We have tried to explain the relative stabilities of the various norbornadien-7-one derivatives in terms of their structures, and a resonable trend in stability, shown below, of norbornadienones and related compounds, is observed.



273 **264** **250**

269 $R^1=R^2=Me$
270 $R^1=R^2=Et$
271 $R^1=Ph, R^2=Me$

CHAPTER THREE

Review of the Reactions of Hex-3-yne-2,5-dione

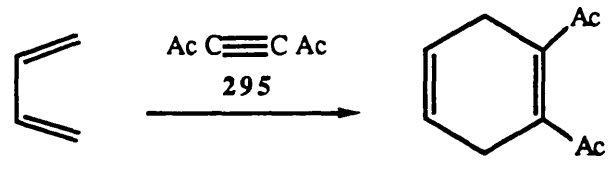
3.1 Introduction

Although much work had been carried out on the reactions of dimethyl acetylenedicarboxylate (**1**), surprisingly little work had been carried out on the similarly electron-deficient alkyne, hex-3-yne-2,5-dione (**295**), otherwise known as diacetylacetylene (DAA). The preparation of DAA is considered in Chap.4.

1 **295** Where E = COOMe

3.2 Attempted Formation of 1,2-Diacetylcyclohexa-1,4-diene

Hex-3-yne-2,5-dione (**295**), first synthesised in 1961, was heated with butadiene (**296**) in an autoclave at 100°C for 12 h.[97] As the vapours of the reaction were reported to cause nausea, headache and eczema, the reaction mixture was not analysed and it still remains to be seen if the Diels-Alder product, 1,2-diacetylcyclohexa-1,4-diene (**297**), was ever formed.

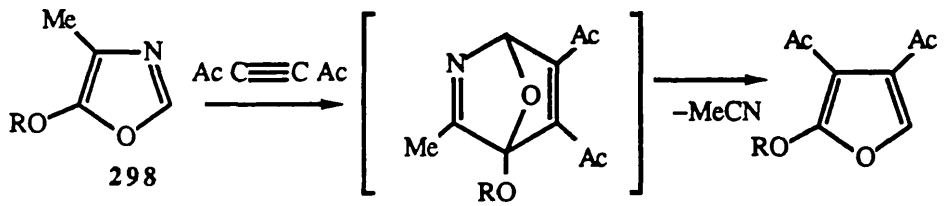


296 **297**

3.3 Formation of Furans

Alkoxy substituted oxazoles undergo Diels-Alder reaction with alkynes and the resultant adducts undergo the Alder-Rickert reaction to give substituted furans.[98]

5-Alkoxyoxazoles (**298a**) and (**298b**) underwent a Diels-Alder reaction with hex-3-yne-2,5-dione (**295**) to give 2-alkoxy-3,4-diacetylfurans (**300a**) (65%) and (**300b**) (68%).[99]



298

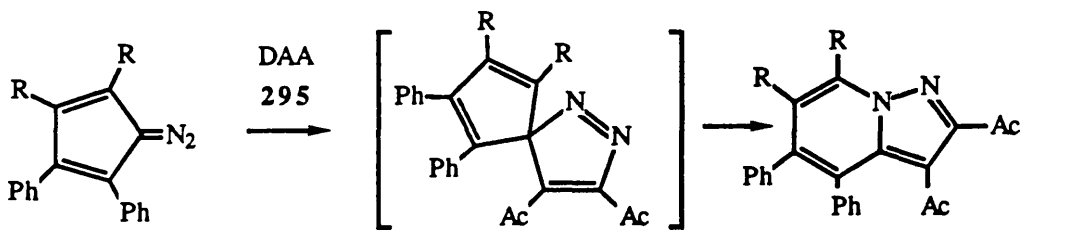
a R=C_3H_7 ,
b R=C_4H_9

299

300

3.4 Formation of Azaindolizines

The nature of the products formed as a result of cycloaddition between alkynes and diazocyclopentadienes depends mainly on the substituents present on the diazocyclopentadienes.[100]



301 R,R = CH=CH–CH=CH
304 R = Ph

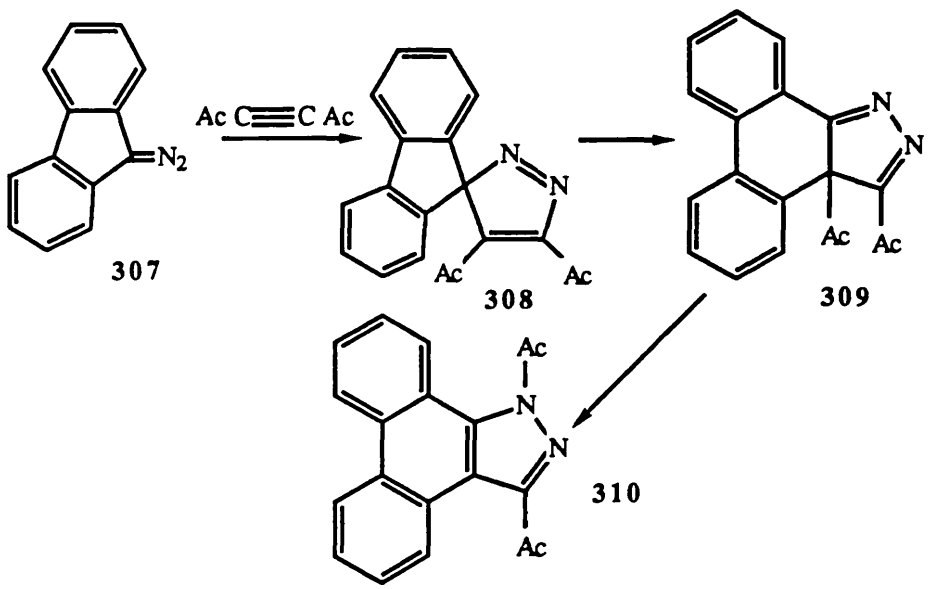
302 R,R= CH=CH–CH=CH
305 R = Ph

303 R,R = CH=CH–CH=CH
306 R = Ph

Azaindolizines (**303**) (75%) and (**306**) (67%) were obtained when hex-3-

yne-2,5-dione (**295**) reacted with diazocyclopentadienes (**301**) and (**304**). None of the diazaspiro compounds (**302**) and (**305**) were isolated as they readily undergo [1,5] sigmatropic shift to form the respective azaindolizines.[100]

Diazofluorene (**307**) underwent cycloaddition with hex-3-yne-2,5-dione (**295**) to give 3,4-diacetyl-6,7,8,9-dibenzo-1,2-diazaspiro[4.4]nona-1,3,6,8-tetraene (**308**) (82%) which, when refluxed in acetic acid, undergoes the van Alphen rearrangement to give indazole (**310**) in 80% yield.[100]

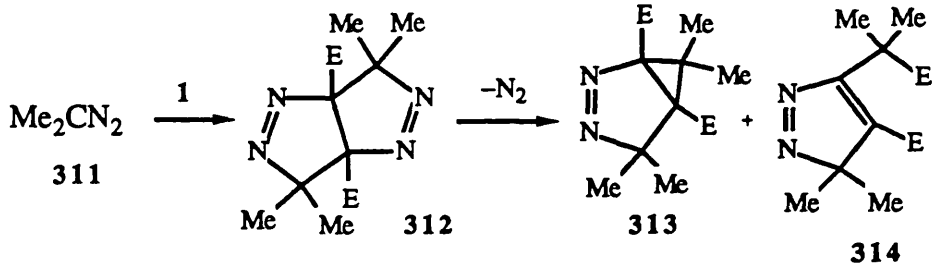


307 308 309 310

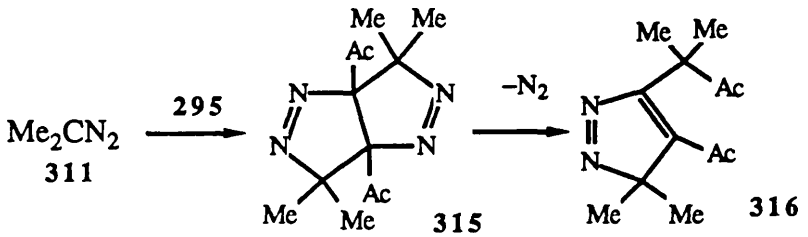
Dimethyl acetylenedicarboxylate (**1**) behaves similarly when treated with substituted diazocyclopentadienes.[100]

3.5 Formation of Pyrazolines

Dimethyl acetylenedicarboxylate (**1**) reacts with excess of dimethyldiazomethane (**311**), to give the 1:2-adduct (**312**) which on heating at 110°C in *o*-dichlorobenzene evolves nitrogen to give pyrazolines (**313**) (65%) and (**314**) (35%).[101]



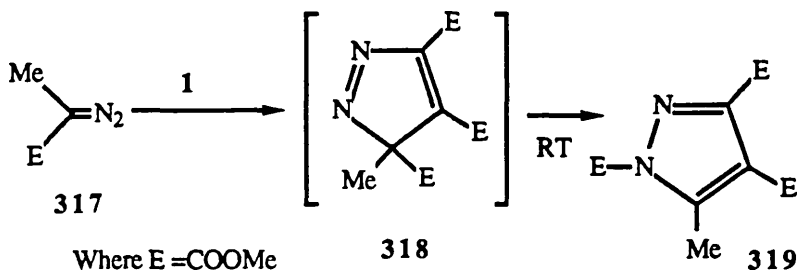
With excess of dimethyldiazomethane (**311**) hex-3-yne-2,5-dione (**295**) gives the analogous adduct (**315**) (in approximately 60%) which on heating at 90°C extrudes nitrogen readily to give rearranged pyrazoline (**316**) in 75%.[101]



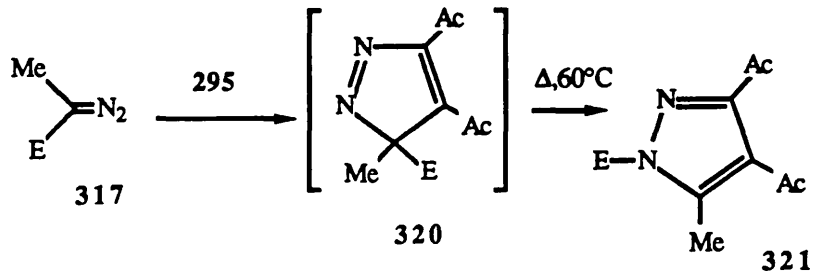
Compounds (**314**) and (**316**) are the result of a [1,2] shift of the ester and acetyl groups, respectively.[101] The bis adduct (**315**) is less stable than the bis adduct (**312**).

3.6 Formation of N-Substituted Pyrazoles

Dimethyl acetylenedicarboxylate (**1**) reacts with diazoester (**317**) to give 3-methoxycarbonyl-3H-pyrazole (**318**) which undergoes a spontaneous [1,5] methoxycarbonyl shift to give the aromatic pyrazole (**319**).[102]



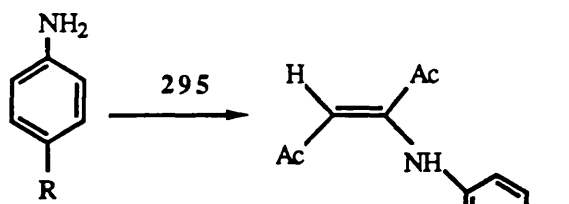
When diazoester (**317**) was treated with hex-3-yne-2,5-dione (**295**) it gave the analogous pyrazole (**321**) *via* pyrazolenine (**320**). The pyrazolenine (**318**) is now less stable than pyrazolenine (**320**).[102]



317 320 321

3.7 Formation of Enamines

Hex-3-yne-2,5-dione (**295**) is found to be much more reactive than dimethyl acetylenedicarboxylate (**1**) towards Michael addition of aniline (**322**) and 4-nitroaniline (**323**). The *trans* products, 3-anilinohex-3-ene-2,5-dione (**324**) and 3-(4-nitroanilino)hex-3-ene-2,5-dione (**325**), were obtained in (76%) and (62%) respectively.[103]



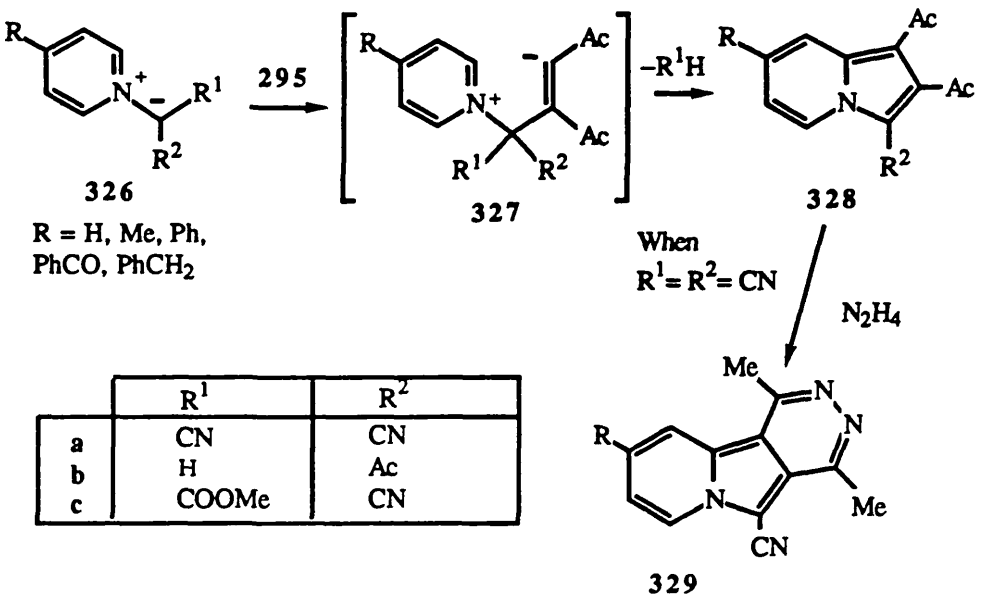
322 R= H
323 R= NO_2

324 R= H
325 R= NO_2

3.8 Formation of Indolizines

Pyridinium methylides (**326**) combine with hex-3-yne-2,5-dione (**295**) to give dihydroindolizines (**327**), which aromatise to indolizines (**328**), though all in

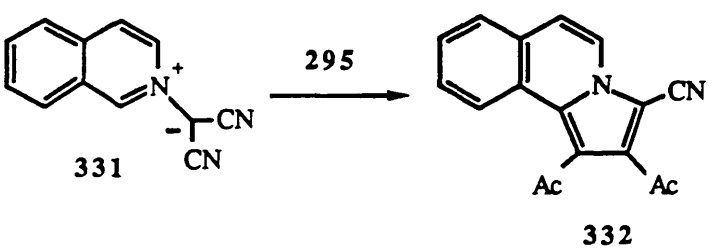
very low yield (5-10%). The heterocyclic ylide (**326b**) was reacted with various



	R^1	R^2
a	CN	CN
b	H	Ac
c	COOMe	CN

alkynes and the reactivity of the alkynes towards the ylide (**326b**) decreased in the order hex-3-yne-2,5-dione (**295**), dimethyl acetylenedicarboxylate (**1**), but-3-yne-2-one and methyl propiolate, as would be expected. No indolizine was observed with hex-3-yne-5-ol-2-one (**330**).[103] This work has been extended to ring substituted derivatives of ylide (**326**), which gives similar products but in considerably higher yields.[104]

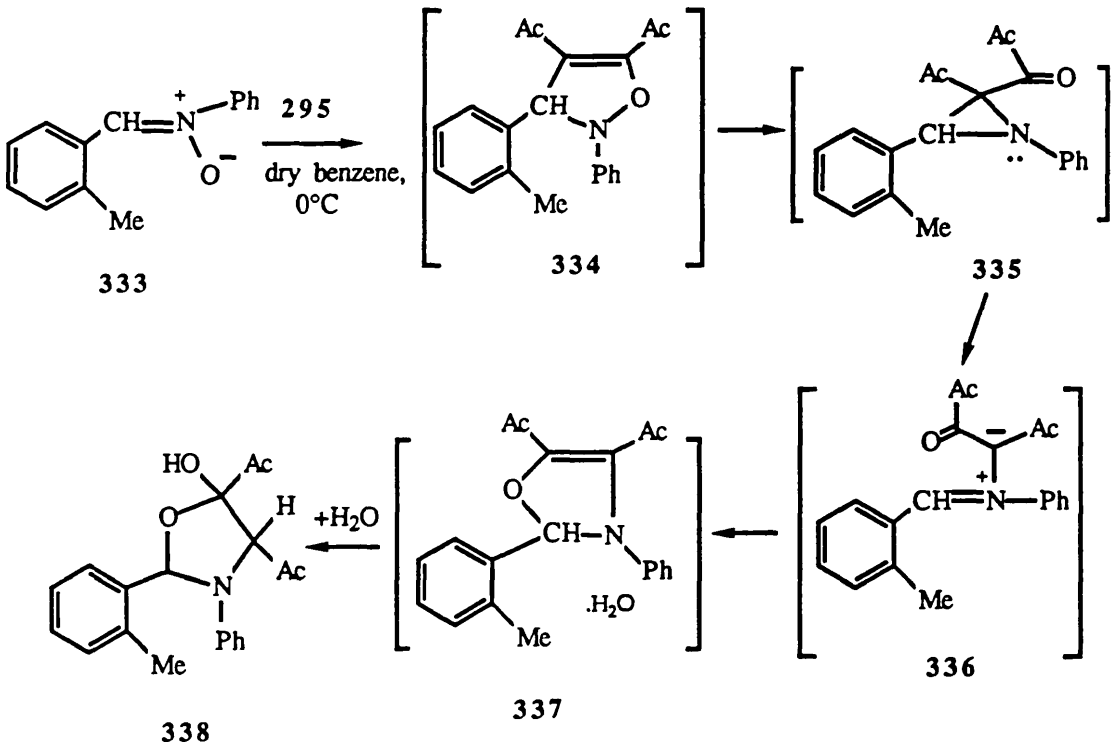
The ylide (**331**) reacts similarly with hex-3-yne-2,5-dione (**295**) to form the indolizine (**332**) in 7% yield.[103]



3.9 Formation of an Oxadiazolidine

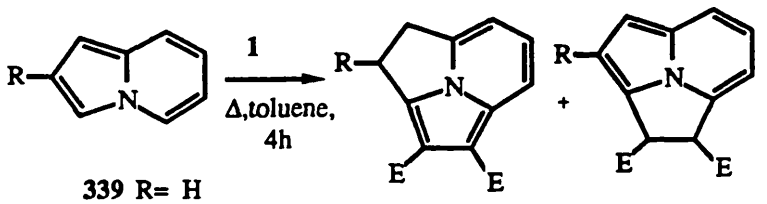
C-(2-Methylphenyl)-N-phenyl nitrone (**333**) reacts with hex-3-yne-2,5-dione (**295**) to give the oxadiazolidine (**338**) (59%), which is thought to be formed as a result of rearrangement of the initial adduct (**334**).[105]

More work is needed on this interesting reaction, to confirm the structure of the product and to explore the reaction pathway.



3.10 Formation of Michael Adducts from Indolizines

The reactions of indolizines with the electron-deficient alkynes, dimethyl acetylenedicarboxylate (**1**) and hex-3-yne-2,5-dione (**295**), were studied recently.[106] It was found that while DMAD (**1**) underwent cycloaddition , hex-3-yne-2,5-dione (**295**) underwent Michael addition.



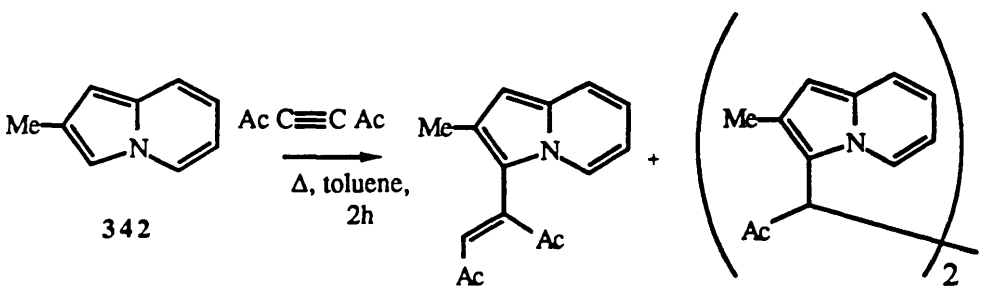
339 R= H
342 R= Me
344 R= Ph

340 R= H

341 R= H
343 R= Me
345 R= Ph

Dimethyl acetylenedicarboxylate (**1**) reacts with indolizine (**339**) to give 3,4-dihydropyrrolo[2,1,5-*cd*]indolizine (**340**) and 1,2-dihydropyrrolo[2,1,5-*cd*] indolizine (**341**) in 10% and 18% yield respectively.[106]

Similarly, with 2-methylindolizine (**342**) and 2-phenylindolizine (**344**), DMAD gave 1,2-dihydropyrrolo[2,1,5-*cd*]indolizines (**343**) (43%) and (**345**) (18%).



342

346

347

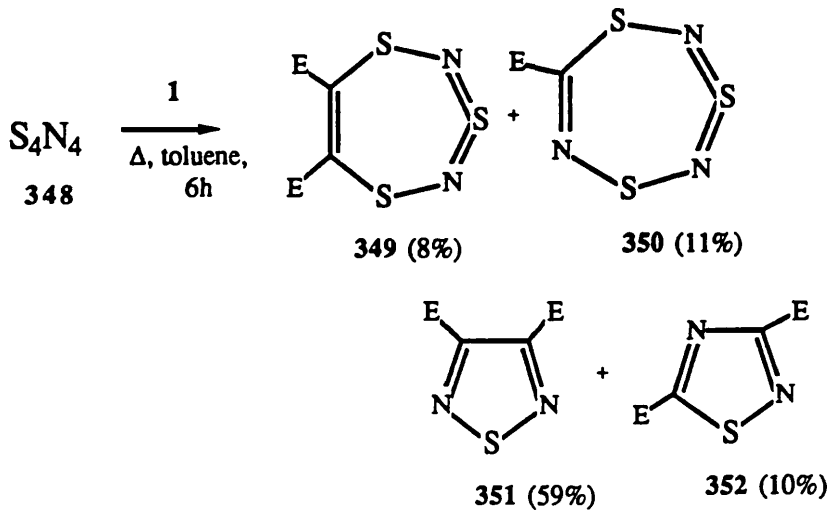
2-Methylindolizine (**342**) reacts with hex-3-yne-2,5-dione (**295**) to give 3,4-bis(2'-methyl-3'-indolizinyl)-2,5-hexandione (**347**) (8%) and 3-(2'-methyl-3'-indolizinyl)-3-hexen-2,5-dione (**346**) (6%).[106]

This reaction is important since it illustrates a difference in the behaviour of the two alkynes (**1**) and (**295**).

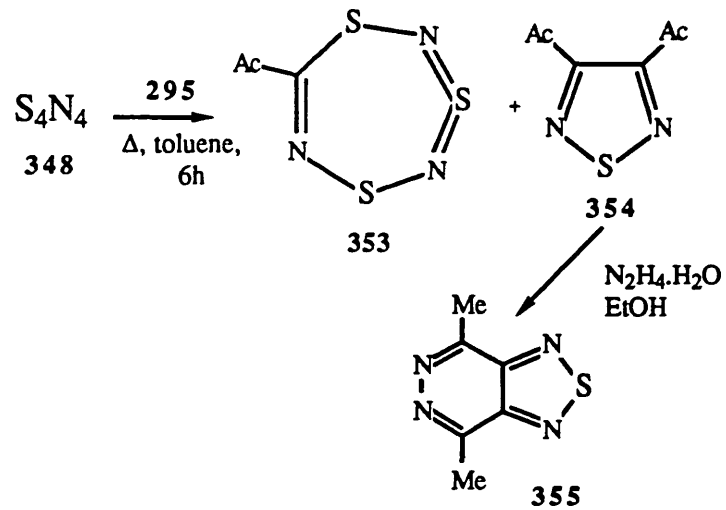
3.11 Formation of Various S-N Heterocyclic Systems

Dimethyl acetylenedicarboxylate (**1**) reacts with tetrasulphur tetranitride

(**348**) to give the various heterocyclic products shown.[107]



Two analogous products, trithiatriazepine (**353**) (29%) and thiadiazole (**354**) (7%), were isolated when hex-3-yne-2,5-dione (**295**) reacts with tetrasulphur tetranitride (**348**). Thiadiazole (**354**) was converted into pyridazine (**355**) (96%) when treated with hydrazine hydrate.[108]



3.12 Summary

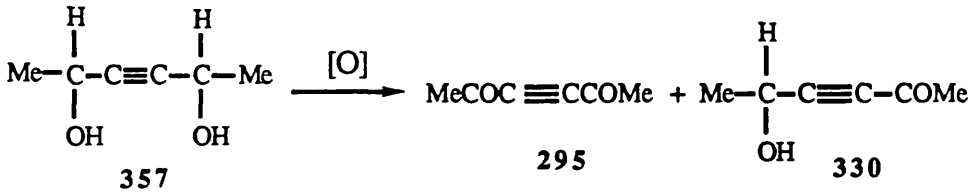
From the little work done in the literature on hex-3-yne-2,5-dione (**295**), it is clear that hex-3-yne-2,5-dione (**295**) is a highly reactive electron-deficient alkyne which behaves in a broadly similar way to dimethyl acetylenedicarboxylate (**1**), but with subtle differences.

CHAPTER FOUR

Chemistry of Hex-3-yne-2,5-dione

4.1 Preparation

Hex-3-yne-2,5-dione (diacetylacetylene, DAA) (**295**), a highly electron-deficient alkyne, was first synthesised in 1961 by Jones oxidation of hex-3-yne-2,5-diol (**357**)[97] (see Table 1 for further details).



As the yield of pure hex-3-yne-2,5-dione (**295**) was poor, its preparation was slightly modified.[103] Further modification increased the yield of hex-3-yne-2,5-dione (**295**).[108]

TABLE 1 Oxidation of hex-3-yne-2,5-diol (**357**)

	YIELD OF		REF
	295	**330**	
CrO_3,aq.H_2SO_4,acetone,–10°C	15%	11%	97
CrO_3,aq.H_2SO_4,acetone,–5°C	11%	41%	103
$Na_2Cr_2O_7$,aq.H_2SO_4,C_6H_6,40°C	30%	15%	108
$Na_2Cr_2O_7$,aq.H_2SO_4,CH_2Cl_2, 40°C,1.5h	60%	0%	Present work

We found that two-phase oxidation of hex-3-yne-2,5-diol (**357**) afforded

hex-3-yne-2,5-dione (**295**) exclusively, in 60% yield. This is by far the best and least cumbersome method available for the preparation of hex-3-yne-2,5-dione (**295**).

The yield of hex-3-yne-2,5-dione (**295**) depends on:

a) the oxidising agent,

b) concentration of the oxidising agent,

c) rate of addition of the oxidising agent,

d) rate of agitation,

e) the solvent used

and f) the temperature of the reaction.

If any one of the six factors is not optimum, the yield of hex-3-yne-2,5-dione (**295**) is very much reduced.

When pyridinium dichromate (PDC) was the oxidising agent, no hex-3-yne-2,5-dione (**295**) was observed. Barium manganate or manganese dioxide as the oxidising agent resulted in an increase of the yield of hex-3-yne-5-ol-2-one (**330**) and a decrease in the yield of hex-3-yne-2,5-dione (**295**).

From our study, we conclude that the best oxidising agent here is acidified aqueous sodium dichromate (60%). It was also observed that with acidified aqueous chromium trioxide (11%), the yield of the oxidised product (**295**) was lower.

The yield of hex-3-yne-2,5-dione (**295**) was greater in dichloromethane (60%) than in benzene (30%). The yield drops sharply when the reaction temperature is below 40°C (boiling DCM).

One good feature of our oxidation is the absence of hex-3-yne-5-ol-2-one (**330**). Because of this, the distillation of the oxidation product after aqueous work-up is not required.

4.2 Properties

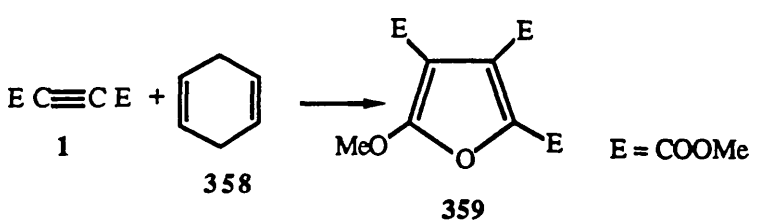
Hex-3-yne-2,5-dione (**295**) is a highly unstable pale yellow oil, b.p 26-38°C at 0.1mmHg.[97] It is normally stored at −12°C in high dilution in DCM. Even at this temperature and dilution, it slowly decomposes and can be kept for a period of only about three weeks. Hex-3-yne-2,5-dione (**295**) is a lachrymator.

4.3

A comparative study of the cycloadditions of hex-3-yne-2,5-dione (**295**) and dimethyl acetylenedicarboxylate (**1**) will be dealt with in Chap.5. In this section we will deal with a) the thermolysis of DAA (**295**) and compare it with that of DMAD (**1**) and b) the self-condensation reactions of DAA.

4.4 Thermolysis of Dimethyl Acetylenedicarboxylate

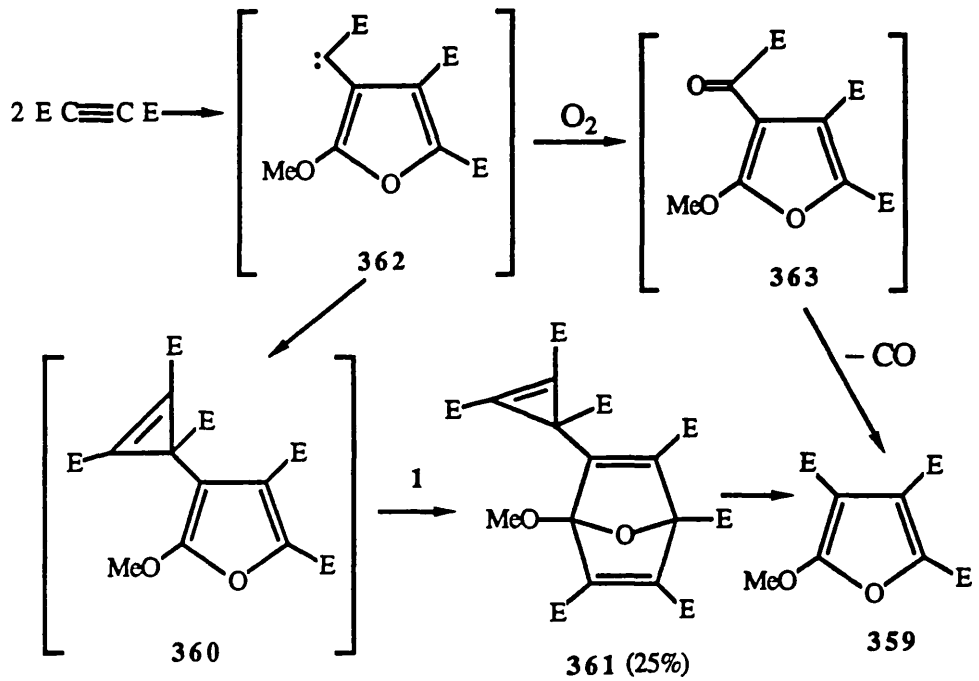
When 1,4-cyclohexadiene (**358**) was treated with DMAD,[109] the furan (**359**) was formed as a minor product, in addition to the cycloadduct.



When a parallel experiment was carried out in the absence of the diene, it was found that the furan (**359**) was again formed, thus ruling out the mechanism involving hexadiene (**358**) proposed by previous authors.[110]

Various oligomerised products were obtained when dimethyl acetylene-dicarboxylate (**1**) was subjected to thermolysis.[111] When the reaction temperature

was maintained at or below 80°C, the tetramer (**361**) was obtained. At higher temperatures compound (**359**), formally a dimer minus carbon, was the product. The trimer (**360**) was never isolated, as it underwent Diels-Alder reaction readily with DMAD to give (**361**). The tetramer (**361**) underwent a retro Diels-Alder reaction to form compound (**359**) at higher temperatures.[112]



Scheme 1

This mechanism accounts for the formation of the tetramer (**361**) and furan (**359**) unlike an earlier one where the authors had invoked the formation of α-carbonyl ester (**363**) which they said afforded furan (**359**) accompanied by elimination of carbon monoxide.[110,111]

According to the authors, DMAD underwent dimerisation to form the carbene (**362**) which reacted with oxygen to afford the α-carbonyl ester (**363**), which eliminated carbon monoxide spontaneously to give furan (**359**). The yield of furan (**359**) is said to fluctuate depending on the pyrolytic conditions.[110,111,113] Since (**359**) can be formed very reasonably without

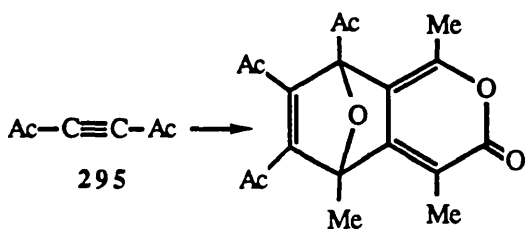
involving oxygen, as shown in Scheme 1, their proposal needs further verification.

4.5 Thermolysis of Hex-3-yne-2,5-dione

When we carried out a comparative study of cycloaddition reactions of DMAD and DAA (see Chap.5), we found that with DAA, besides the expected cycloadducts, we also obtained various other products which were the result of DAA reacting with itself.

It has long been known that DMAD, when left standing at room temperature, undergoes very slow oligomerisation. It takes approximately a year for a (3%) conversion into the tetramer (**361**).[112] But it takes only **minutes** for DAA to undergo oligomerisation under analogous condition. A solution of DAA in dichloromethane also oligomerises, but more slowly over a period of 33 days at room temperature. Thus, it is clear that DAA undergoes oligomerisation much more rapidly than DMAD. This might be due to the greater electron withdrawing effect of the acetyl group over the ester group making the triple bond in DAA more electron-deficient.

When DAA was heated in various solvents it afforded several products. These were isolated and identified by X-ray crystallography. When DAA was heated, as shown in Table 2, the major product always proved to be, $C_{18}H_{18}O_6$, 6,7,8-triacetyl-5,8-dihydro-1,4,5-trimethyl-5,8-epoxy-2-benzopyran-3-one (**364**).



364

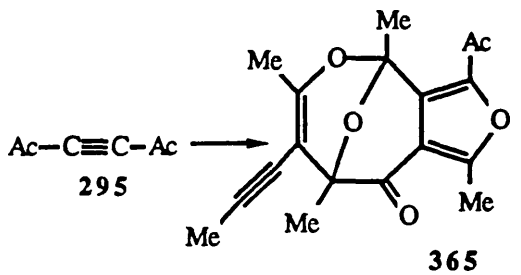
The X-ray structure of 6,7,8-triacetyl-5,8-dihydro-1,4,5-trimethyl-5,8-epoxy-2-benzopyran-3-one (**364**) is as shown in Fig.1 (see page 84).

TABLE 2

The conversion of DAA (**295**) into 6,7,8-triacetyl-5,8-dihydro-1,4,5-trimethyl-5,8-epoxy-2-benzopyran-3-one (**364**)

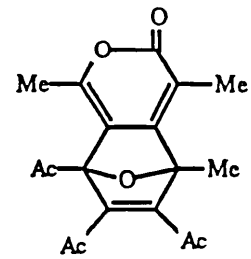
Solvent at reflux	Reaction time (h)	% Yield of **364**
Benzene (80°C)	72	43
Dioxane (101°C)	17	35
Toluene (110°C)	21	21
Xylene (140°C)	7	63
Xylene (140°C)	21	26

The benzopyran-3-one (**364**) is a trimer of DAA (**295**). Another, much more minor, product that was obtained also proved to be a trimer of DAA; this is 3-acetyl-1,4,6,8-tetramethyl-7-prop-1-ynyl-4,8-epoxy-4H-furo[3,4-*c*]oxocin-9(8H)-one (**365**) in 8% yield.



365

Compound (**365**) was almost always detected by t.l.c and it was observed that higher temperatures favoured its formation. It was isolated in an attempted cycloaddition of S_4N_4 to DAA (Table 3).



364

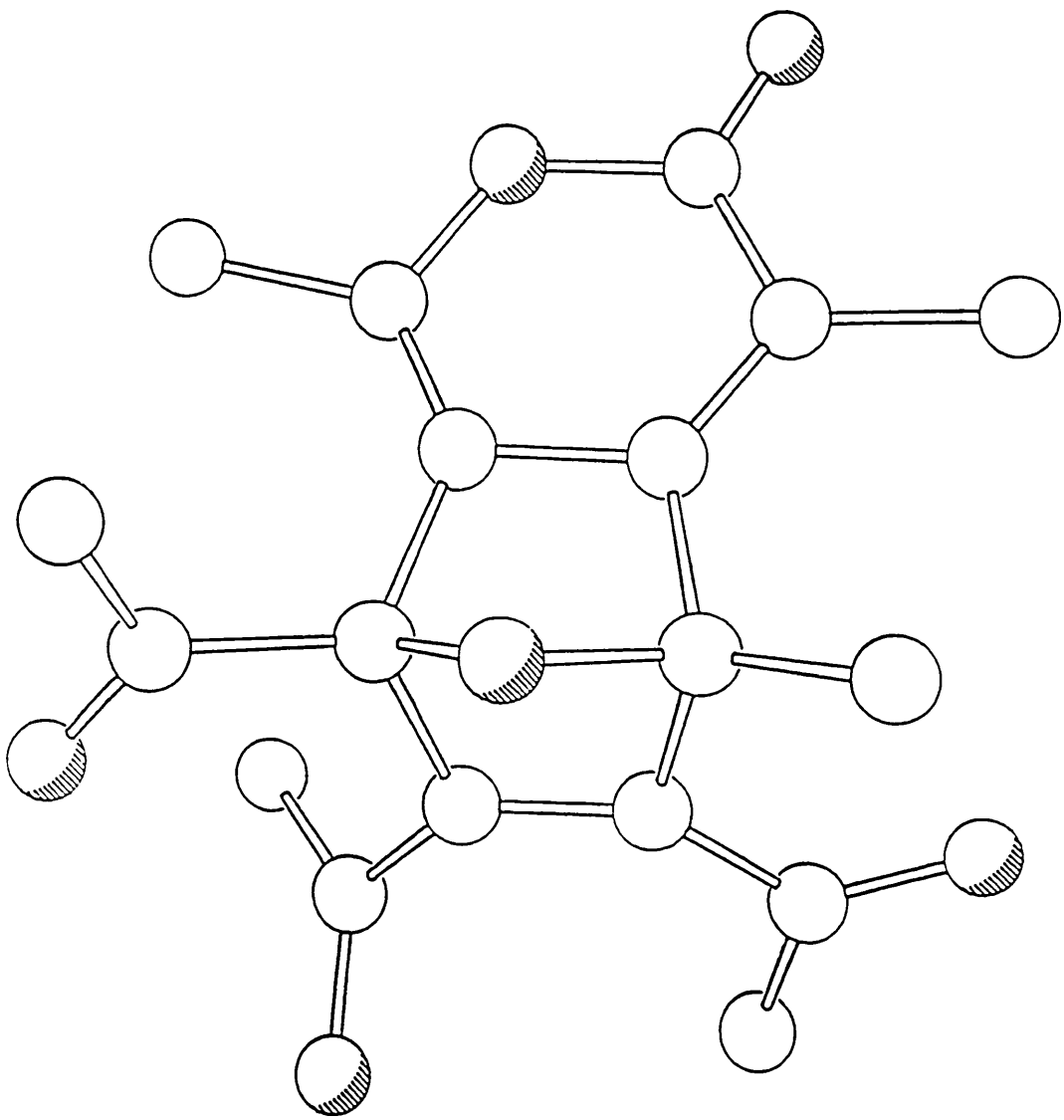
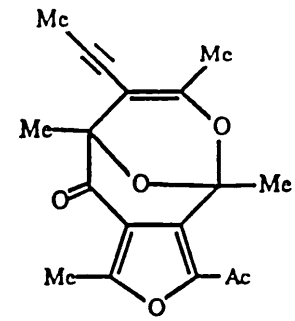


Fig.1 6,7,8-Triacetyl-5,8-dihydro-1,4,5-trimethyl-5,8-epoxy-2-benzopyran-3-one (364)



365

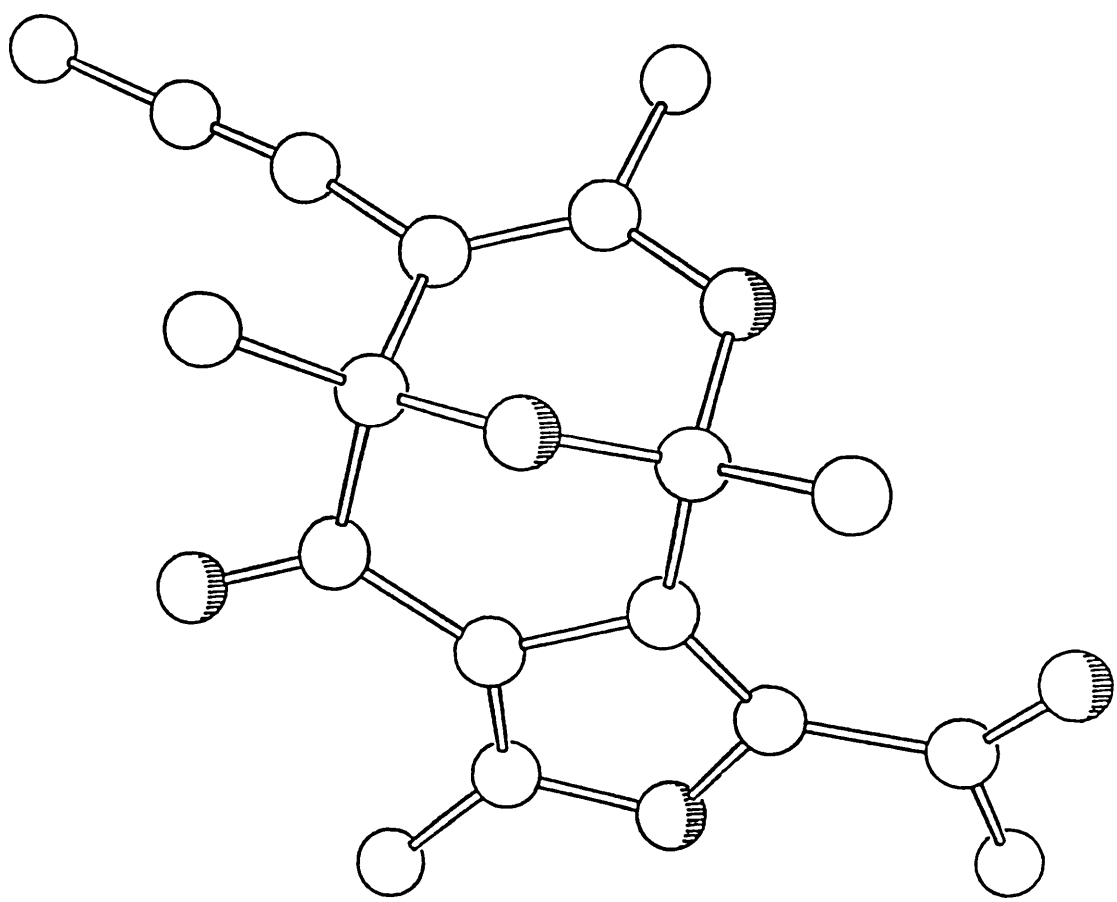
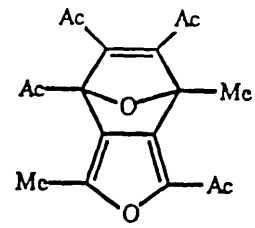


Fig.2 3-Acetyl-1,4,6,8-tetramethyl-7-prop-1-ynyl-4,8-epoxy-4H-furo[3,4-*c*]oxocin-9(8H)-one (365)



366

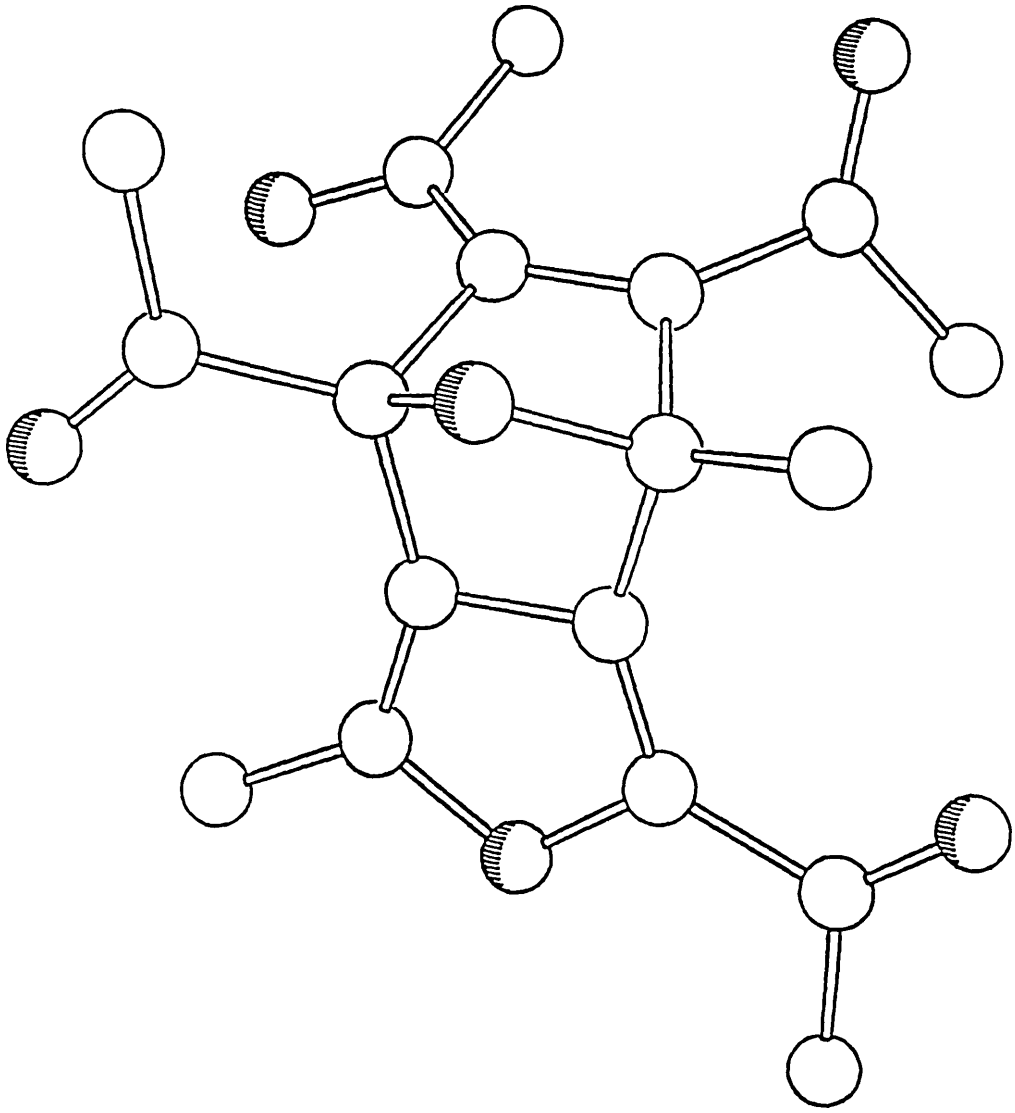
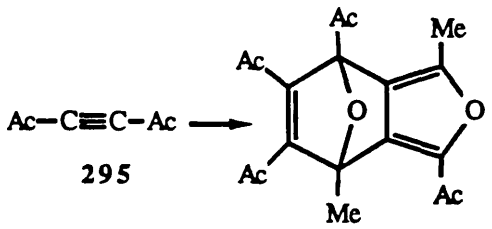


Fig.3 1,4,5,6-Tetra-acetyl-4,7-dihydro-3,7-dimethyl-4,7-epoxy-2-benzofuran (366)

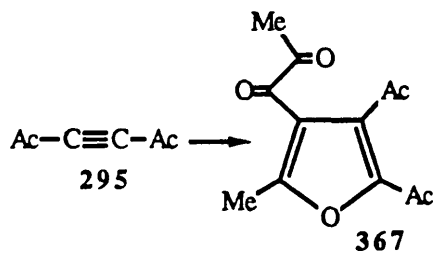
Besides this, yet another minor trimer of DAA was isolated (4.5%), which proved to be 1,4,5,6-tetra-acetyl-4,7-dihydro-3,7-dimethyl-4,7-epoxy-2-benzofuran (**366**) (see Table 3).



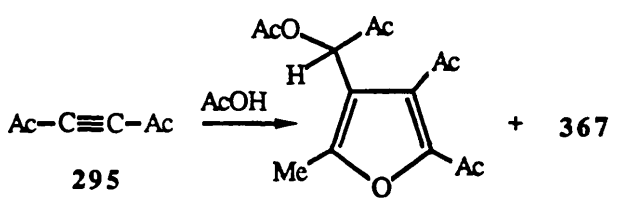
366

The X-ray structures of compounds (**365**) and (**366**) are as shown in Fig. 2 and Fig. 3 respectively (see page 85 & 86).

Dimeric structures were also formed when DAA (**295**) was subjected to thermolysis. Thus 4,5-diacetyl-2-methyl-3-(1,2-dioxopropyl)-furan (**367**) was obtained, its formation being favoured at lower temperatures (see Table 3). Furan (**367**) has an i.r. carbonyl stretch at 1717 cm^{-1}, characteristic of 1,2-diketo groups.



367



368

When DAA was heated in either glacial acetic acid or aqueous acetic acid, another dimeric product (50%) was obtained. This is believed to be 4,5-

diacetyl-3-(1-acetoxy-2-oxopropyl)–2-methyl-furan (**368**) (see Table 3).

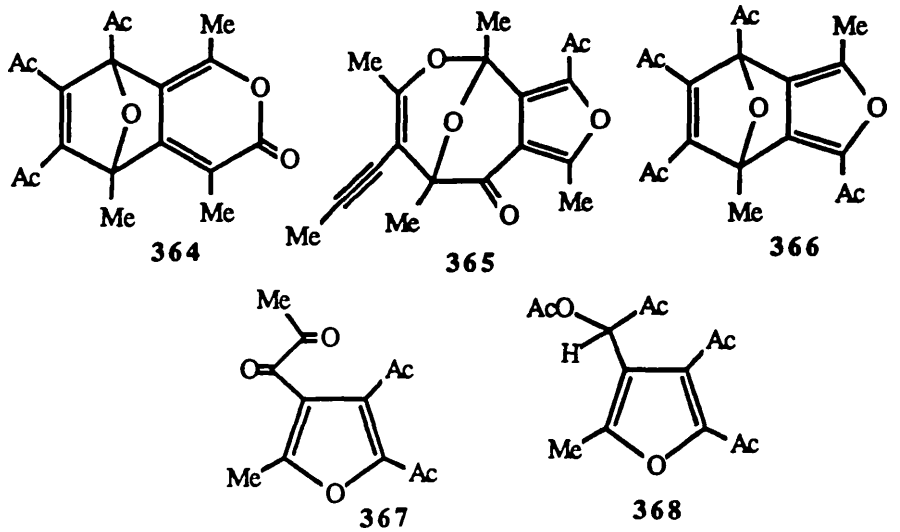


TABLE 3

Conversion of DAA into Oligomeric Compounds (**364-368**)

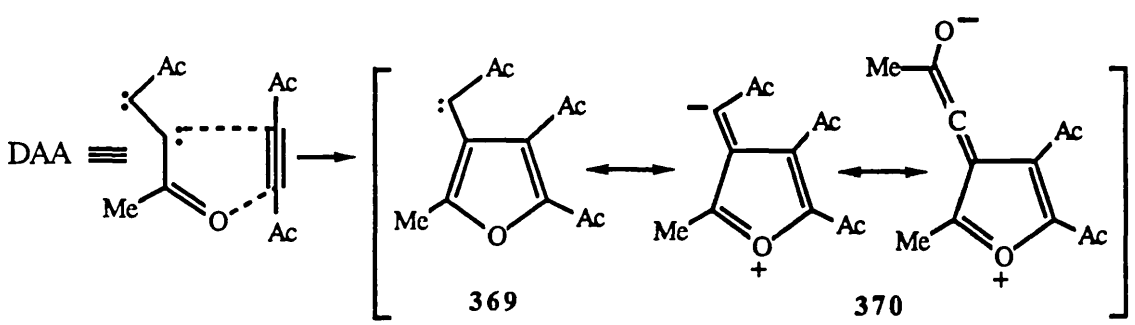
Reaction Conditions	Yield in %				
	364	**365**	**366**	**367**	**368**
CH_2Cl_2 , RT, 33 days	40	–	–	9	–
Acetic acid, 17h, Δ	Trace	–	–	2	50
Acetic acid- H_2O,11h,Δ	Trace	–	–	2	46
Acetic acid-H_2O-Dioxane, 23h, Δ	–	–	–	2	Trace
H_2O-Dioxane, 4h, Δ	–	–	–	3	–
H_2O, 2.5h, Δ	–	–	–	1	–
H_2O-Dioxane-10% Na_2CO_3,7h,Δ	–	–	–	1	–
Benzene, 21h, Δ	35	Trace	Trace	13	–
Iodobenzene-benzene, 45h, Δ	55	Trace	4	5	–
Acetic acid, dark, RT, 59 days	7	–	Trace	6	11
S_4N_4, Benzene,31h, Δ	Trace	8	Trace	Trace	–

The 1,2-diketone (**367**) was also obtained in about (2%) when DAA (**295**) was heated in glacial acetic acid.

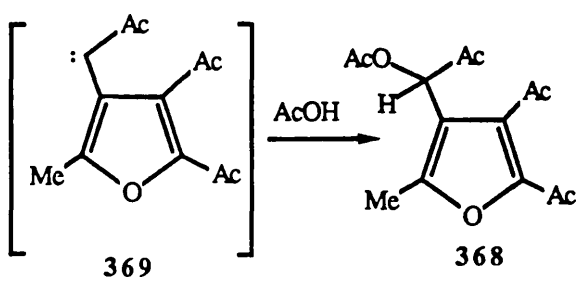
Besides the compounds which were isolated and characterised, many more products could be detected by t.l.c but could not be isolated in a pure form.

4.6 Mechanistic Proposals

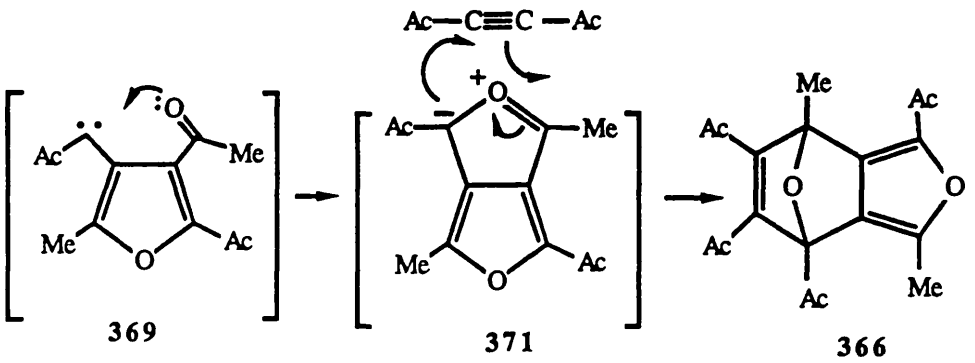
The mechanisms we propose for the formation of these oligomers of DAA (**295**) involve the initial dimerisation of DAA to form the transient carbene (**369**), which is considered to be the key intermediate. It can be envisaged as resulting from a type of 1,3-dipolar cycloaddition reaction of one molecule of DAA (written as a bis-carbene) to another, as shown. The carbene could be stabilised by electron release from the furan ring (**370**).



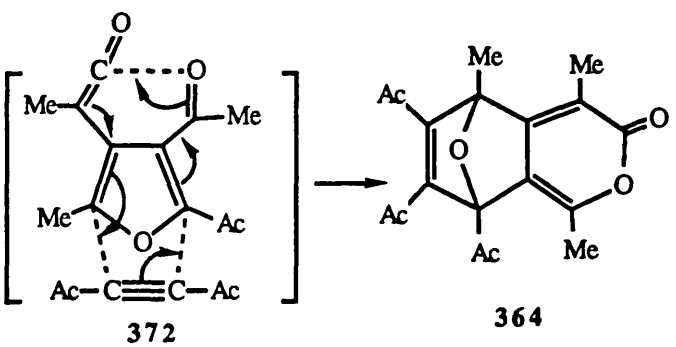
Carbene (**369**) is a highly reactive species which could be rapidly trapped by glacial acetic acid to form the keto-ester (**368**), one of the isolated products.



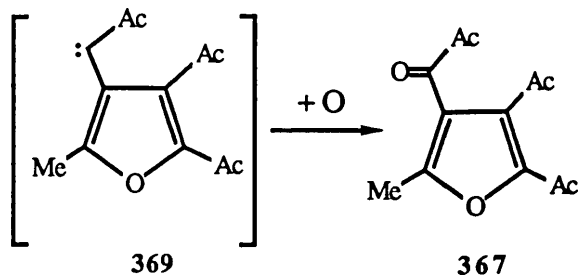
Carbene (**369**) could also cyclise to form the carbonyl ylide (**371**) which could then undergo a 1,3-dipolar cycloaddition to another molecule of DAA to form the benzo[*c*]furan (**366**).



Carbene (**369**) could also undergo Wolff-rearrangement to form the ketene (**372**) which could then react further with DAA, as shown, to form benzo[*c*]pyran-3-one (**364**), the major product of DAA oligomerisation.



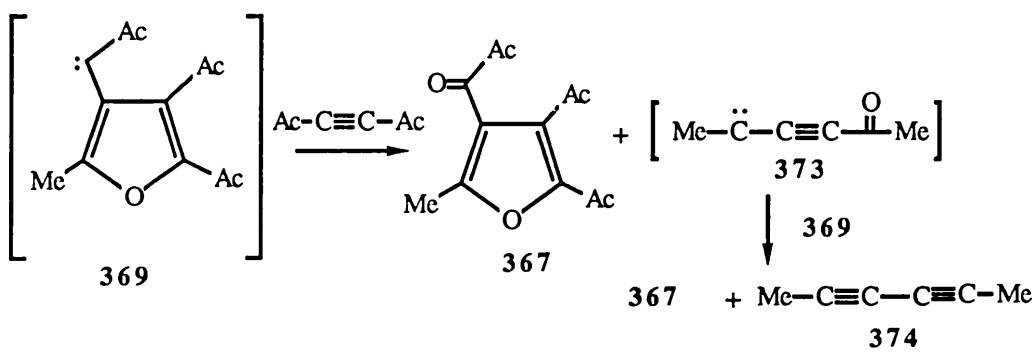
1,2-Diketone (**367**) is formally an oxidation product of carbene (**369**), and could be formed if (**369**) were to abstract an oxygen atom. It is highly unlikely that carbene (**369**) abstracted oxygen from air or water in the solvent as there was no apparent change in the yield of furan (**367**) when the reaction was carried out with air bubbling through the reaction mixture, or when water was added to it. No increase in yield of furan (**367**) was observed when DAA was



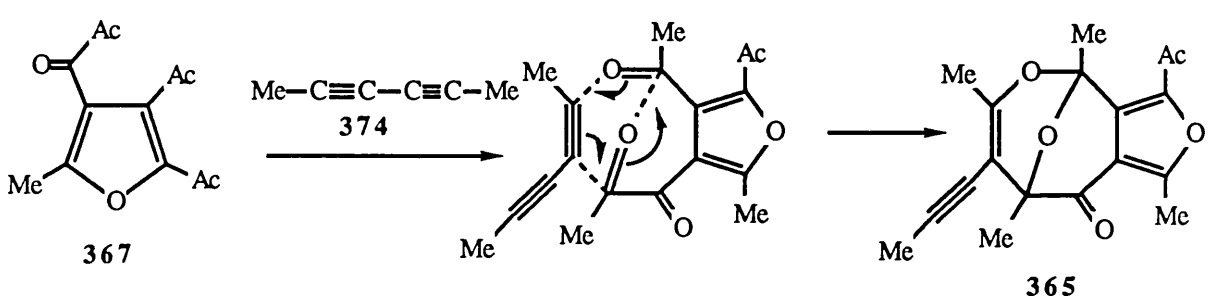
369 367

treated with propylene oxide as a possible source of an oxygen atom.

Another possibility is that the carbene (**369**) abstracts oxygen from more DAA to form a new carbene (**373**) and the 1,2-diketone (**367**); if both oxygen atoms of DAA are abstracted, hexa-2,4-diyne (**374**) would result.

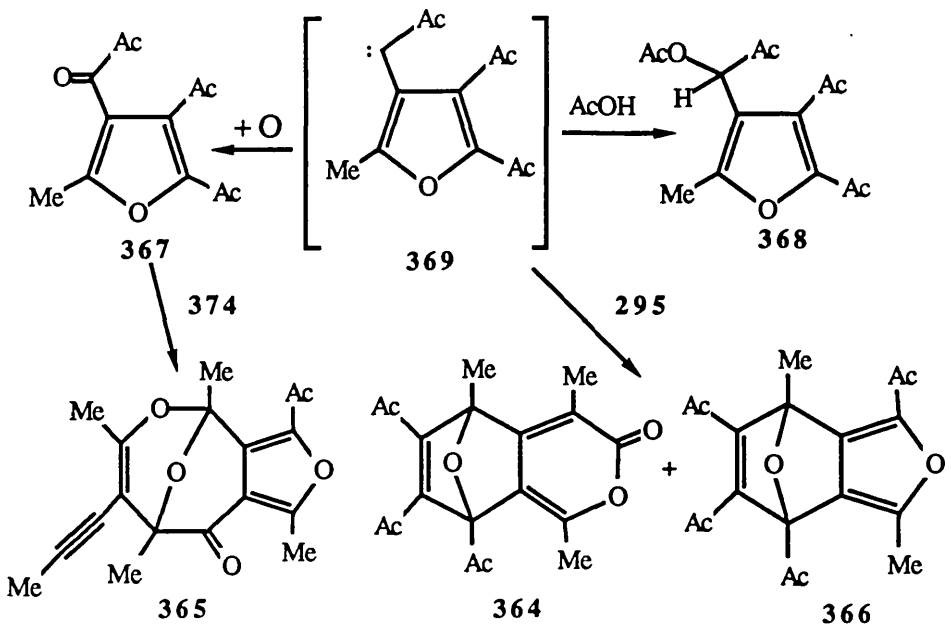


Finally, compound (**365**) is formally the result of furan (**367**) undergoing a cycloaddition reaction with hexa-2,4-diyne (**374**), as shown; but there is as yet no evidence to support this proposal.



367 365

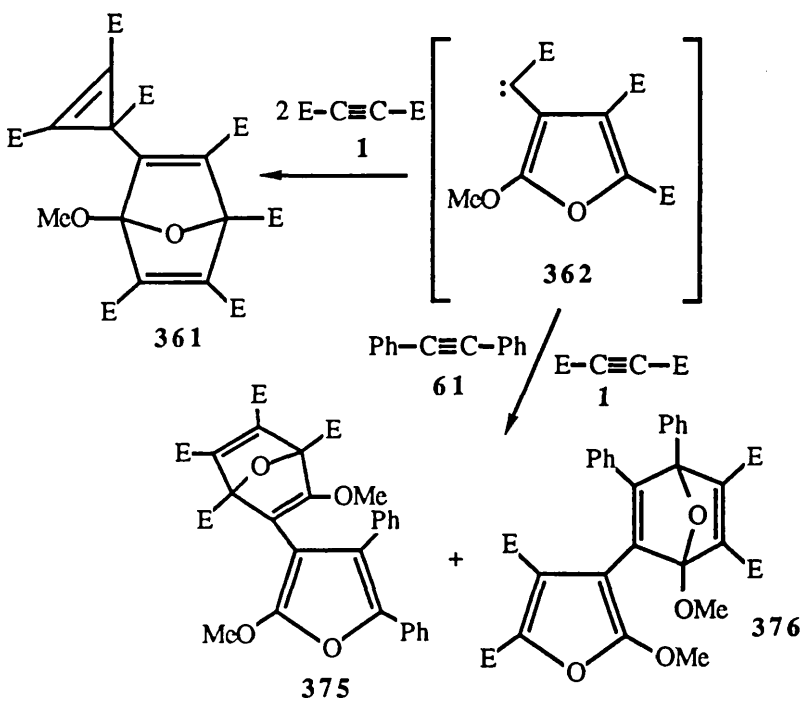
The formation of these five products from DAA is summarised below (Scheme 2).



Scheme 2

4.7 Comparative Study

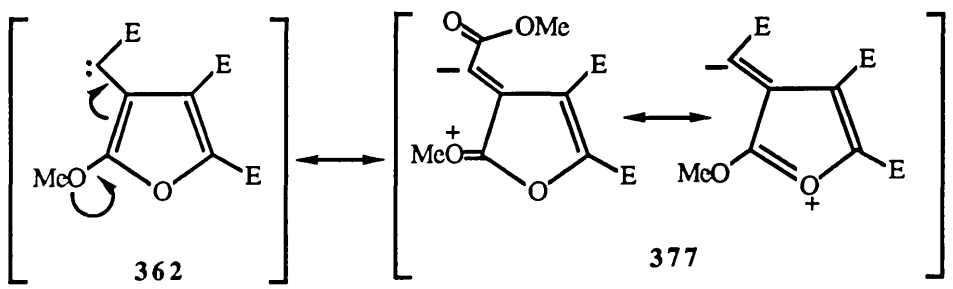
Thus from the literature and from our work, it seems likely that both DMAD (**1**) and DAA (**295**) dimerise to form highly reactive carbene intermediates.



The DMAD-derived carbene (**362**) has been trapped with DMAD (**1**) in the presence and absence of diphenylacetylene (**61**).[111] Tetramers (**361**), (**375**), (**376**) were obtained.

In our DAA-acetic acid reaction, the DAA-derived carbene (**369**) is trapped by acetic acid or by more DAA.

Unlike the DMAD-derived carbene (**362**), the DAA-derived carbene (**369**) could not be trapped either by DMAD (**1**) or diphenyacetylene (**61**). Nor could it be trapped by diphenyl disulphide or sulphur. The DMAD-derived carbene (**362**)



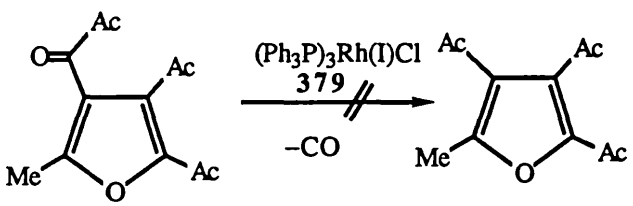
and the DAA-derived carbene (**369**) are both stabilised by the ring oxygen, as shown in (**377**) and (**378**), but (**362**) has extra stabilisation from the methoxy group (see **377**). Because of this stabilisation, the DMAD-derived carbene (**362**) is less reactive than the DAA-derived carbene (**369**) and is longer lived. This could explain why the DMAD-derived carbene is trapped more readily than its DAA counterpart (**369**).

4.8 Chemistry of DAA Oligomers

Since the oligomerisation of DAA had given us some interesting and quite complex stuctures, we decided to investigate some of their chemistry.

4.8.1 Attempted decarbonylation of 1,2-diketone (367)

When 1,2-diketone (**367**) was treated with Wilkinson's catalyst (**379**) in benzene, none of the decarbonylated product, 3,4,5-triacetyl-2-methylfuran (**380**), was obtained. Infact furan (**367**) was recovered quantitatively.

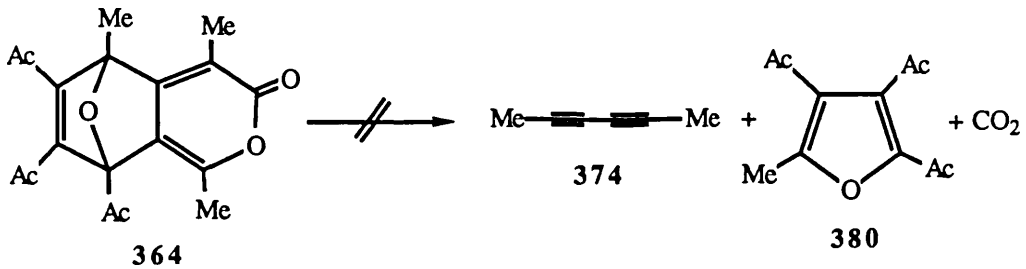


367 **380**

Interestingly, the analogous intermediate from the DMAD reaction, the α-carbonyl ester (**363**) (see page 81), was never isolated.

4.8.2 Attempted pyrolysis and Diels-Alder reaction of benzo[*c*]-pyran-3-one (364)

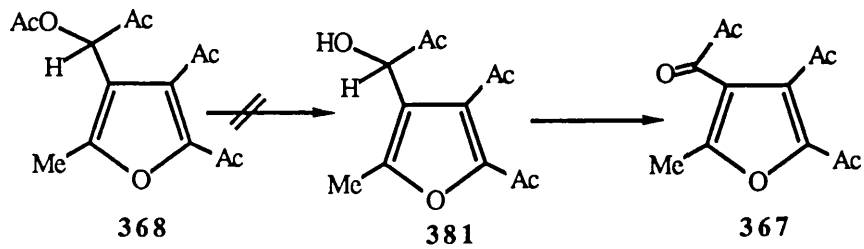
From an inspection of the structure of the DAA trimer, benzo[*c*]pyran-3-one (**364**), it seemed possible that on pyrolysis it could fragment to give carbon dioxide, hexa-2,4-diyne (**374**), and 3,4,5-triacetyl-2-methylfuran (**380**). However compound (**364**) proved to be very stable and it was unchanged on heating to 280°C.



Similarly compound (**364**) might have undergone a Diels-Alder reaction across the α-pyrone ring, but when treated with either DMAD (**1**) or diphenyl-acetylene (**61**) at 110°C there was no reaction.

4.8.3 Attempted hydrolysis of furan-ester (368)

We wished to hydrolyse the furan-ester (**368**) in order to obtain the corresponding alcohol (**381**) which in turn we hoped to oxidise to the known 1,2-diketone (**367**).



However, when furan (**368**) was subjected to hydrolysis under a wide range of conditions (aq.HCl, methanolic Et_3N, NaOH, MeCOONa, $NaHCO_3$) it decomposed extensively and it proved impossible to isolate any pure reaction products. Nevertheless the product, (**367**), of hydrolysis and oxidation was detected as a minor product in some reactions.

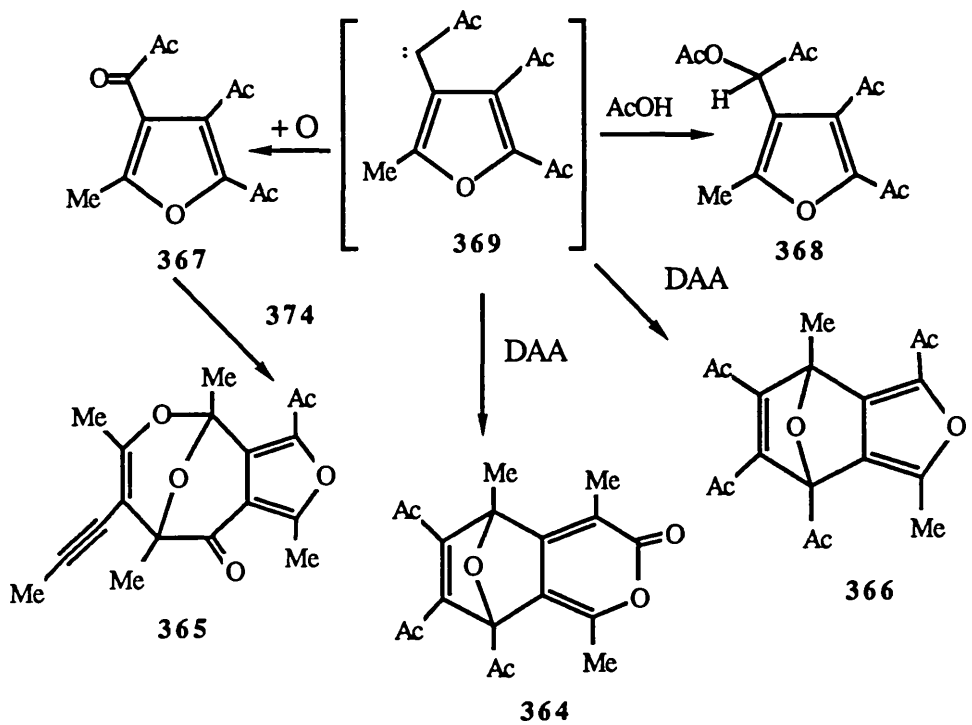
4.9 Summary

There is not much work done in the literature on the electron-deficient

alkyne, hex-3-yne-2,5-dione (**295**) which was first prepared in 1961. We have improved the yield of DAA (**295**) from (10%) to (60%) and also have excluded the distillation step in the isolation of DAA.

DAA behaves in a similar manner as DMAD but is more reactive, particularly towards self-condensation. On standing for a few **minutes** at room temperature, or on heating, DAA rapidly gives a range of oligomers, whose structures were determined by X-ray crystallography.

Formation of these products is believed to involve a reactive carbene intermediate (**369**) as shown below in Scheme 2.



Scheme 2

CHAPTER FIVE

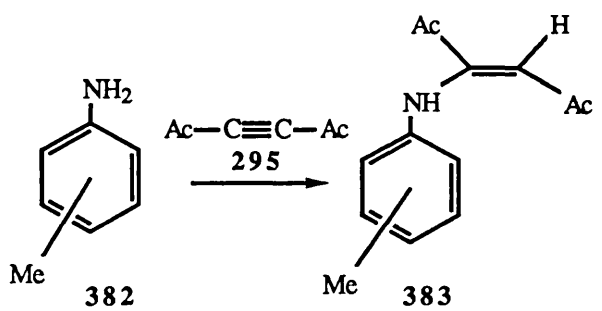
Further Chemistry of Hex-3-yne-2,5-dione

5.1 Introduction

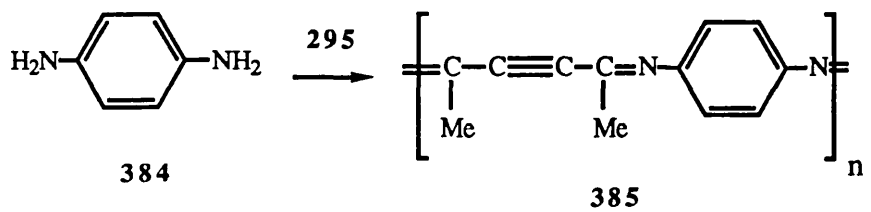
As only very little chemistry of hex-3-yne-2,5-dione (DAA) (**295**) had been reported, (see Chap.3) we decided to investigate some nucleophilic additions and cycloadditions of DAA.

5.2 Nucleophilic Additions to Hex-3-yne-2,5-dione (DAA)

Hex-3-yne-2,5-dione (diacetylacetylene) (DAA) (**295**) was found to undergo addition reactions with aniline and 4-nitroaniline to afford *trans*-addition



	Yield of **383**
o -	58%
m -	16%
p -	57%



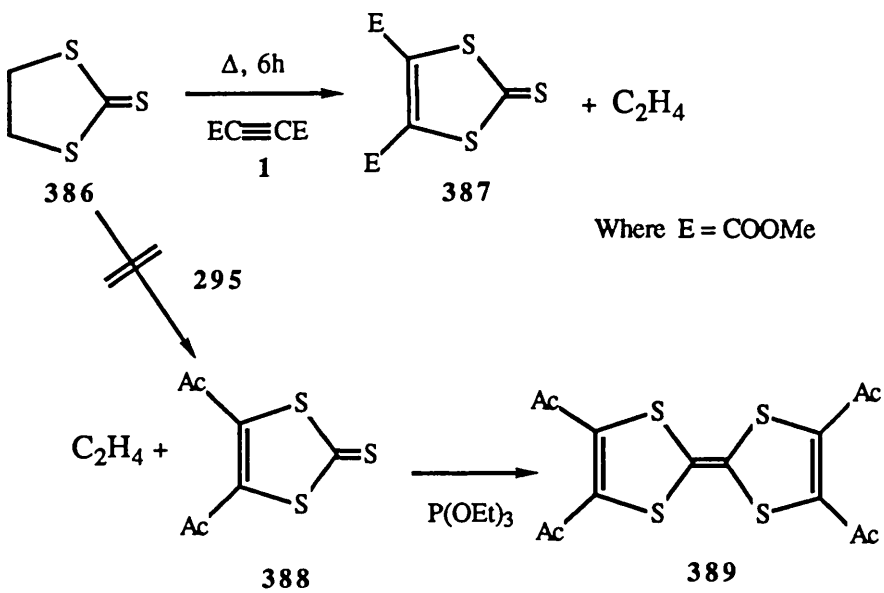
384 **385**

products[103] (see Chap.3). We treated hex-3-yne-2,5-dione (**295**) with *o*-, *m*- ,and *p*-toluidine (**382**) at room temperature in dry benzene. The corresponding enamines (**383a**), (**383b**), and (**383c**) were formed as oils in the case of *o*- and *m*-toluidine and as a stable crystalline solid in the case of *p*-toluidine, in moderate yields. They are the result of nucleophilic addition of the amine to the activated triple bond of DAA. It should be noted that, in contrast with these reactions, DAA has been reported to undergo carbonyl condensation reactions with *p*-phenylenediamine (**384**) to form polymers (**385**).[114]

We also treated DAA with 1,8-diaminonaphthalene, thiobenzamide and dimethyldisilazane, but in each case the reaction was complex, no pure products could be isolated, and there was no indication of the formation of simple addition products; these unpromising reactions were not investigated further.

5.3 Cycloaddition Reactions of DAA

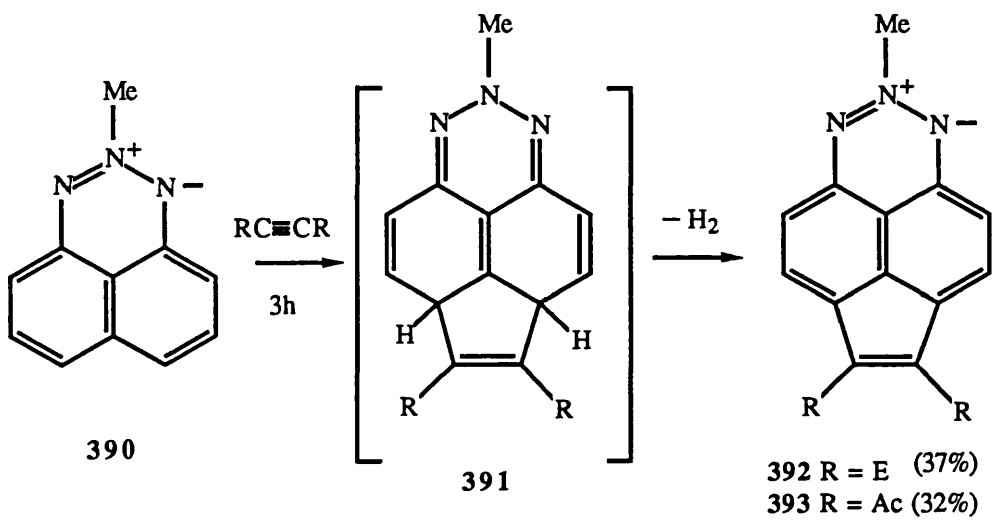
We decided to carry out selected cycloaddition reactions of DAA for comparison with those of DMAD (**1**) (see Chap.1).



When ethylene trithiocarbonate (**386**) was refluxed in toluene with DMAD, the cycloadduct (**387**) was reported to be formed in 56% yield.[115] When we repeated the experiment in refluxing toluene, the expected product (**387**), formed as a result of a 1,3-polar cycloaddition across the sulphur atoms, was obtained in the same yield.

Under exactly analogous conditions DAA gave a complex reaction mixture, making purification impossible. This was also observed when the DAA reaction was carried out in refluxing benzene. Compound (**388**) would have been of interest to us as we had hoped to convert it into tetra-acetyltetrathiafulvalene (**389**) (see Chap.7).

Treatment of the naphthotriazine (**390**) with DMAD (**1**) in boiling *o*-dichlorobenzene has been reported in the literature.[34] The cycloadduct (**392**) (37%) is formed as a result of a 1,11-cycloaddition and dehydrogenation. We repeated the reaction and obtained the same product in the same yield.



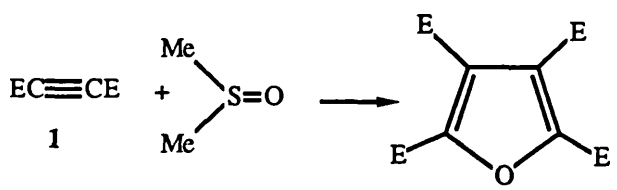
390 **391**

392 R = E (37%)
393 R = Ac (32%)

Reaction of triazine (**390**) with DAA under the same conditions resulted only in the recovery of the starting triazine. We repeated the reaction but varied the (boiling) solvent from propionitrile, DMF, benzene, toluene, xylene and *o*-dichlorobenzene. At the higher temperatures a reaction seemed to occur but the

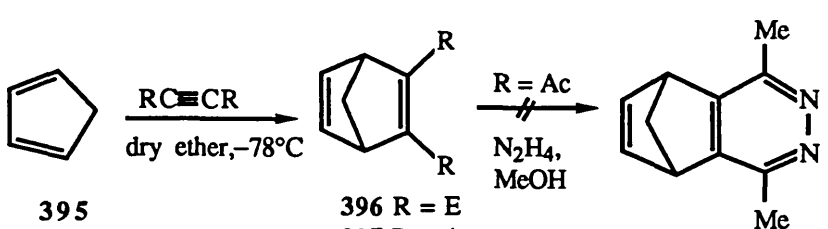
yield was very low. But when we carried out the reaction in the much more polar solvent dimethylsulphoxide (DMSO) at 80°C the triazine (**390**) underwent the desired cycloaddition to form the new cycloadduct (**393**) in 32% yield. We also obtained two very minor unidentified products, together with cycloadduct (**393**). It was reported in the literature,[34] and also observed by us, that two analogous minor unidentified products were formed in the DMAD reaction.

In view of the great improvement in the yield of (**393**) in DMSO, we repeated the reaction of triazine (**390**) with DMAD in the same solvent at 80°C; surprisingly this resulted in the complete recovery of triazine (**390**). This is presumably because DMAD reacts spontaneously with the solvent DMSO to form the tetrasubstituted furan (**394**).[116] The reaction of DMAD with DMSO was confirmed in a blank experiment, and DAA was also found to react with DMSO, though more slowly and to give a complex mixture. These reactions provide another indication of the subtle differences in the nature of DAA and DMAD.



394

The reactive cyclic diene, freshly cracked cyclopentadiene (**395**), undergoes



395

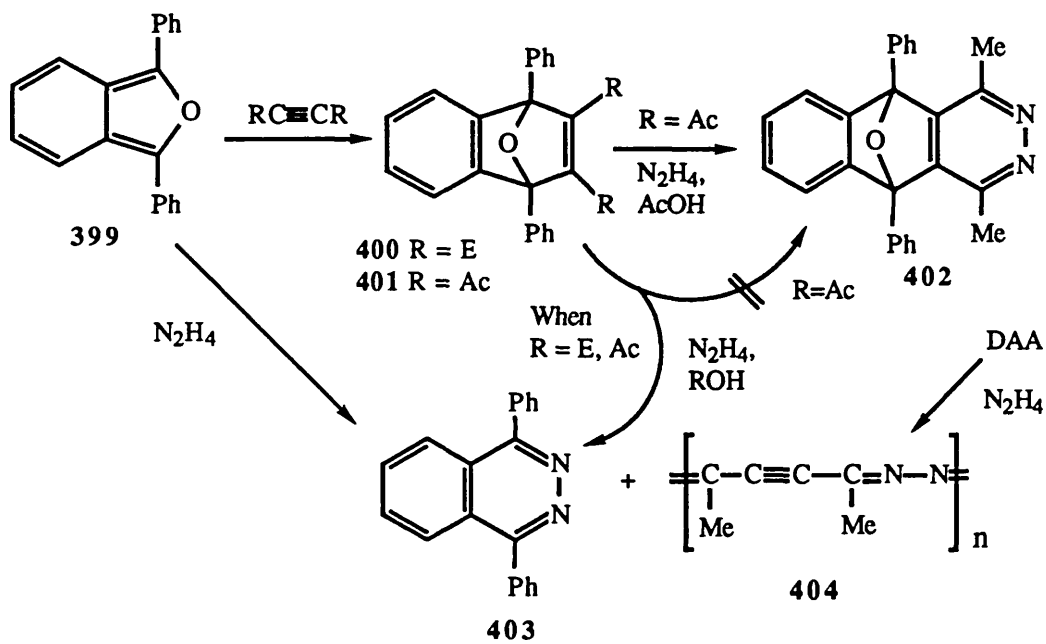
396 R = E
397 R = Ac

398

Where E = COOMe

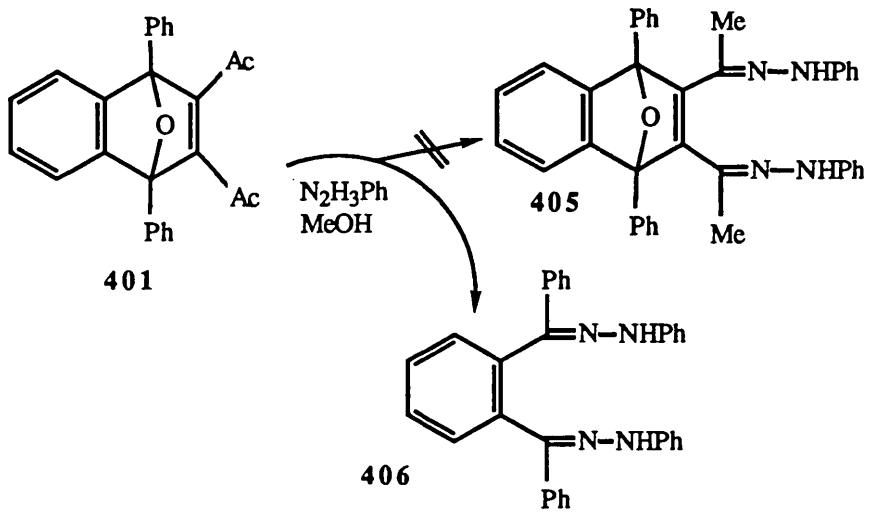
a Diels-Alder reaction with DMAD to form dimethyl bicyclo[2.2.2]hept-2,5-diene-2,3-dicarboxylate (**396**).[117] We carried out this reaction in dry ether at –78°C and obtained 43% yield of the cycloadduct (**396**). We found that under the same conditions, DAA (**295**) afforded 2,3-diacetylbicyclo[2.2.1]hept-2,5-diene (**397**) in 56% yield. When we treated compound (**397**) with hydrazine hydrate none of the desired hydrazone (**398**) was obtained; no reaction occurred. Subsequent observations suggest that acetic acid would have been a much better solvent for this reaction.

Treatment of 2,5-diphenylisobenzofuran (**399**) with DMAD gave the Diels-Alder adduct (**400**) in 90% yield (lit.[118] 98%). Under the same conditions, DAA afforded the analogous cycloadduct, 2,3-diacetyl-1,4-diphenyl-1,4-epoxy-1,4-dihydronaphthalene (**401**), in a similar high yield (88%).



Conversion of compound (**401**) into its hydrazone (**402**) proved unexpectedly difficult. We found that when hydrazine was added to a methanolic or ethanolic solution of compound (**401**) it resulted in the formation of 1,4-diphenylphthalazine (**403**) and not the expected compound (**402**).

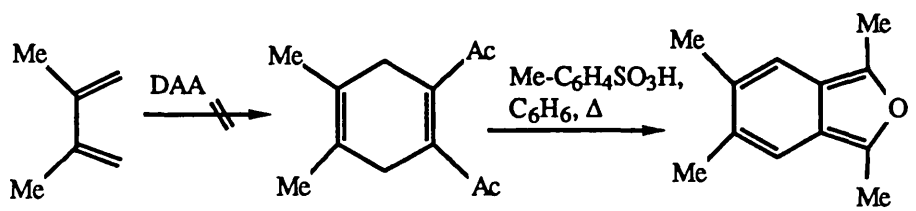
In agreement with this, the DMAD adduct (**400**) and isobenzofuran (**399**) also form compound (**403**) when treated with hydrazine in methanol. The structure of (**403**) was established by direct comparison with an authentic specimen.[119] Compound (**403**) is believed to be formed as a result of the cycloadducts (**400**) and (**401**) undergoing retro-Diels-Alder reactions to reform the isobenzofuran (**399**) which then reacts with hydrazine. Compound (**401**) was found to undergo a retro-Diels-Alder reaction in methanol or ethanol in the absence of hydrazine, but not in chloroform. It was found that DAA formed polymers, as reported in literature,[114] with hydrazine hydrate. Isobenzofuran (**399**) was observed to be formed and to be converted on standing into phthalazine (**403**), when 7-oxabenzonorbornadiene (**401**) in methanolic solution was treated with hydrazine, together with the polymeric products of DAA (**404**) (t.l.c).



However, when 7-oxabenzonorbornadiene (**401**) was dissolved in acetic acid, and hydrazine was added to this solution, the desired pyridazine (**402**) was formed as a stable crystalline compound in good yield (73%). When cycloadduct (**401**) was treated with phenylhydrazine it did not afford the standard condensation product (**405**), but rather compound (**406**) was obtained (not fully

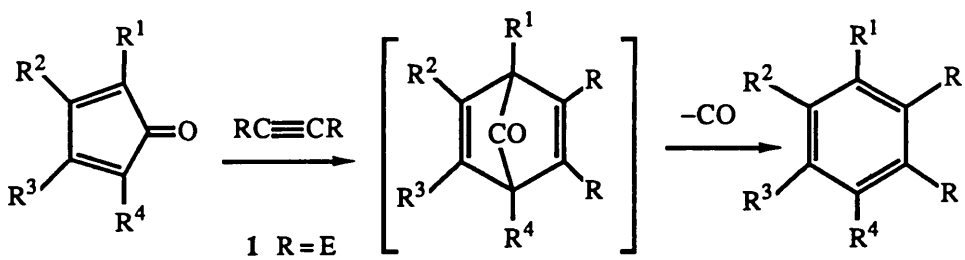
characterised). Again this could have resulted from a retro-Diels-Alder reaction of the compound (**401**) to give (**399**) and reaction of this with phenylhydrazine, and oxidation to give compound (**406**).

When 2,3-dimethyl-1,3-butadiene (**407**) was treated with DAA (**295**) in refluxing toluene, none of the expected cycloadduct (**408**) was obtained; DAA had undergone preferential oligomerisation (see Chap.4). Compound (**408**) would have been of interest to us as a useful starting material for further transformation such as cyclodehydration to the isobenzofuran (**409**).



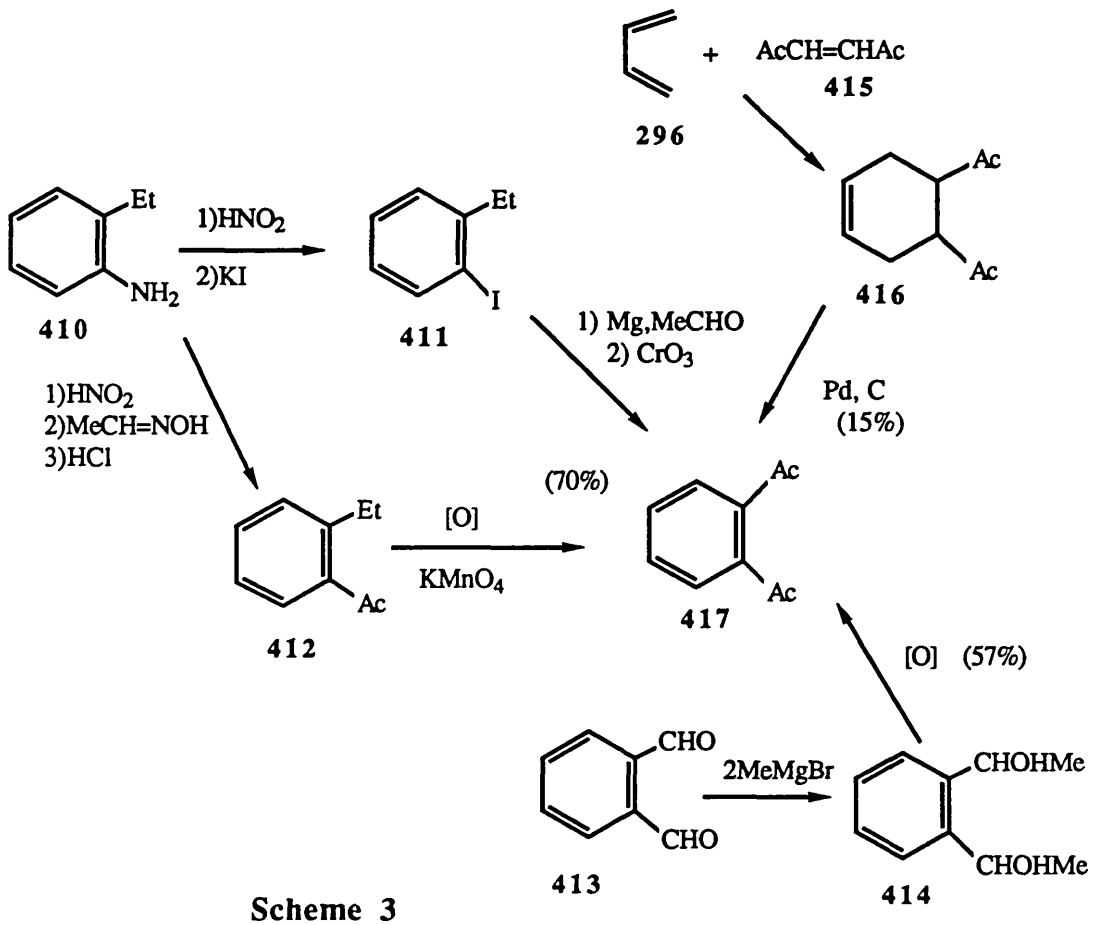
407 **408** **409**

When DMAD (**1**) and DAA (**295**) were treated with various substituted cyclopentadienones, substituted benzenes were obtained; these reactions are described in Chap.6.



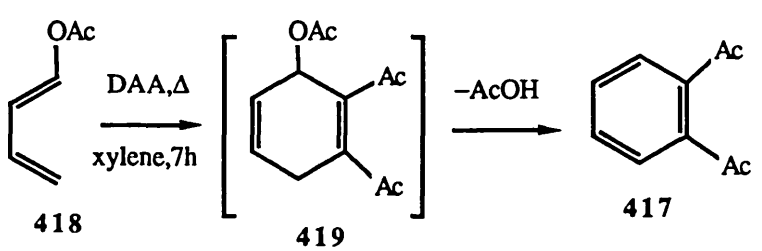
o-Diacetylbenzene (**417**) is an interesting compound which should be readily available from DAA by an appropriate cycloaddition reaction. It has been used to detect amino acids, and could possibly be of forensic use since a trace of compound (**417**) stains the fingers, the colour turns from pink to purple within minutes and remains purple for at least a week. Compound (**417**) has

been prepared as shown in Scheme 3.[97,120]



Scheme 3

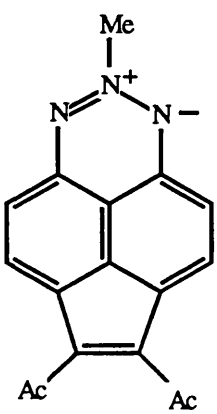
We first treated 1-acetoxy-1,3-butadiene (**418**) with DMAD which gave dimethyl phthalate which on subsequent hydrolysis[57] afforded phthalic acid.



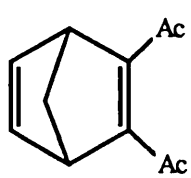
Under analogous conditions, DAA gave *o*-diacetylbenzene (**417**) in good yield (57%), together with a very minor red product which was not characterised. We could thus synthesise *o*-diacetylbenzene in one step from readily available starting materials, and this is probably the shortest method available for its synthesis.

5.4 Summary

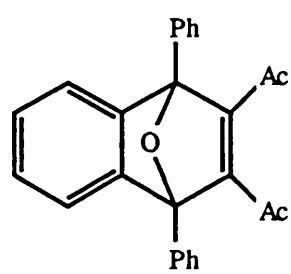
We have shown that DAA forms 1:1–adducts with aromatic amines, conjugated dienes, 1, 3-dipoles and related compounds. The aromatic amines add to the triple bond to form enamines. The other reactants give cycloadducts, such as (**393**), (**397**), and (**401**).



393



397



401

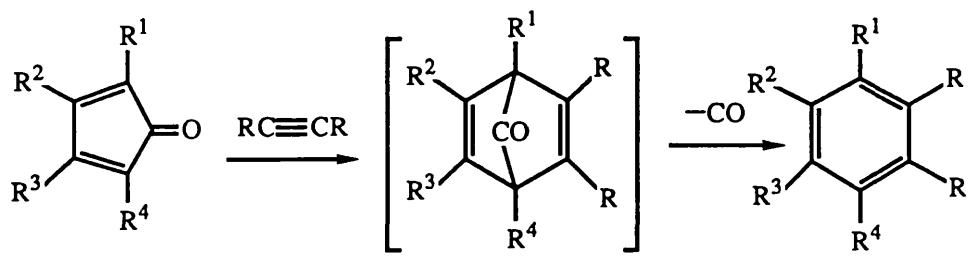
Cycloaddition of 1-acetoxy-1,3-butadiene (**418**) to DAA provides a ready one-step synthesis of *o*-diacetylbenzene in good yield. DAA is found to be rather less reactive than DMAD in these cycloaddition reactions, and nearly all DAA reactions are complicated by its strong tendency to undergo self-condensation (see Chap.4).

CHAPTER SIX

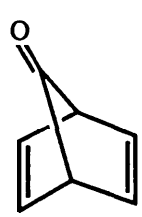
Substituted Norbornadien-7-ones

6.1 Introduction

Chemists have for many years tried to isolate the initial Diels-Alder adduct (**249**) formed when an alkyne is treated with a cyclopentadienone. Almost all of their attempts proved fruitless; though many claims have been recorded in the literature, these claims were later shown to be wrong.[75] The product of this reaction was usually the decarbonylated aromatic system. Recently, a number of these rather elusive norbornadien-7-one systems have been reported to have been either detected or isolated at very low temperatures, and this work was discussed in Chap.2.



249

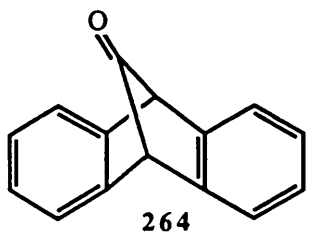


250

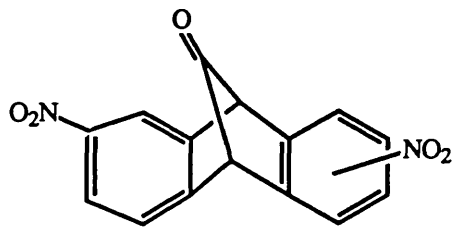
The most elusive was the parent norbornadien-7-one (**250**), which was

detected in an argon matrix at −81°C.[77] The reasons why these norbornadien-7-ones are highly unstable was discussed briefly in Chap.2.

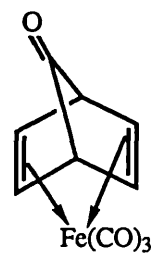
Some of the norbornadien-7-one systems isolated are as follows:[79,81-83,87]



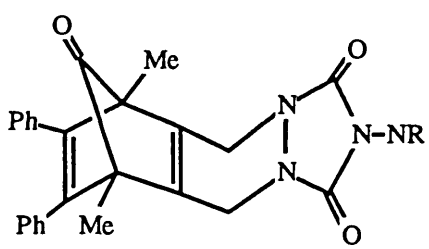
264



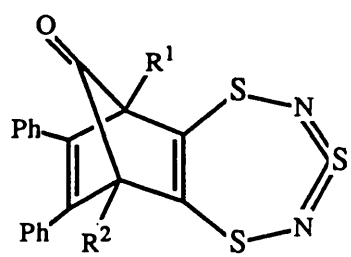
264a



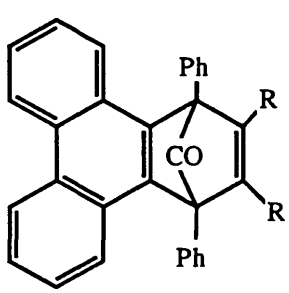
259



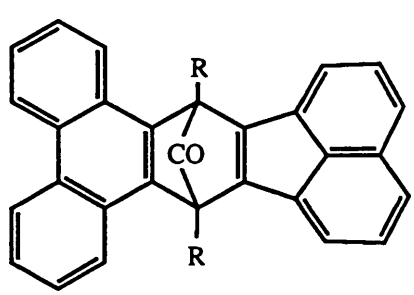
266 R=*p*-MeC_6H_4



269 $R^1 = R^2 = Me$
270 $R^1 = R^2 = Et$
271 $R^1 = Ph, R^2 = Me$



267 a R = Ph
267 b R,R = −CH=CH−CH=CH−

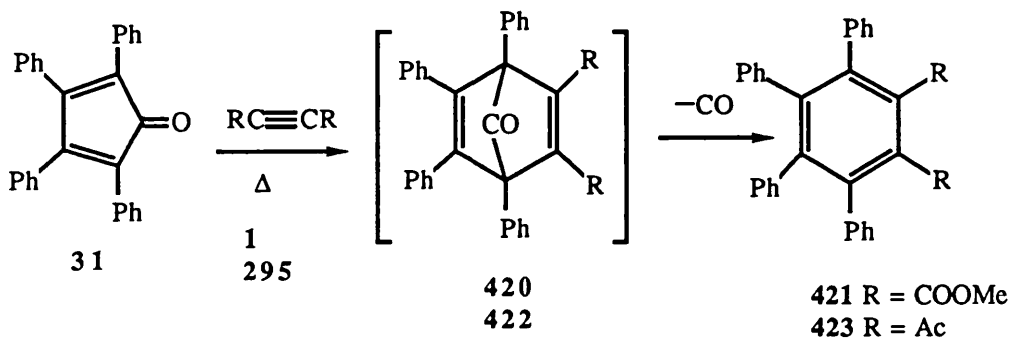


268 a R = Ph
b R = C_6H_4-OMe-*p*

Mondal, Bandyopadhyay and Bhattacharya claimed to have isolated compounds (**267**) and (**268**).[84-86] A close study of their paper and the papers published previously by the same authors on this subject indicated certain inconsistencies and irregularities e.g. in melting points and micro-analytical data. We therefore decided to repeat, and modify, some of these reactions (see Sec.6.4).

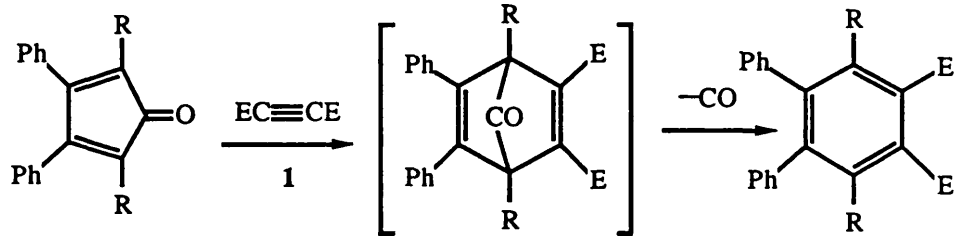
6.2 Attempted Synthesis of Substituted Norbornadien-7-ones from Electron-Deficient Alkynes, DMAD (Literature Work) and DAA (Present Work)

It is well documented that when DMAD (**1**) reacts with tetracyclone (**31**) the substituted benzene (**421**) is the product.[121] We repeated this and obtained the aromatic product, dimethyl 3,4,5,6-tetraphenylphthalate (**421**) (58%).



We also carried out the reaction of hex-3-yne-2,5-dione (DAA) (**295**) with tetracyclone (**31**) in the hope of obtaining the initial Diels-Alder adduct (**422**); but we obtained the aromatised product, 1,2-diacetyl-3,4,5,6-tetraphenylbenzene (**423**), in low yield (18%) because of the accompanying oligomerisation of DAA (see Chap.4).

Treatment of 2,5-dimethyl-3,4-diphenylcyclopentadienone (**424**) with DMAD (**1**) again afforded only the aromatised product (**426**) (67%). Under



424 R = Me
427 R = Et

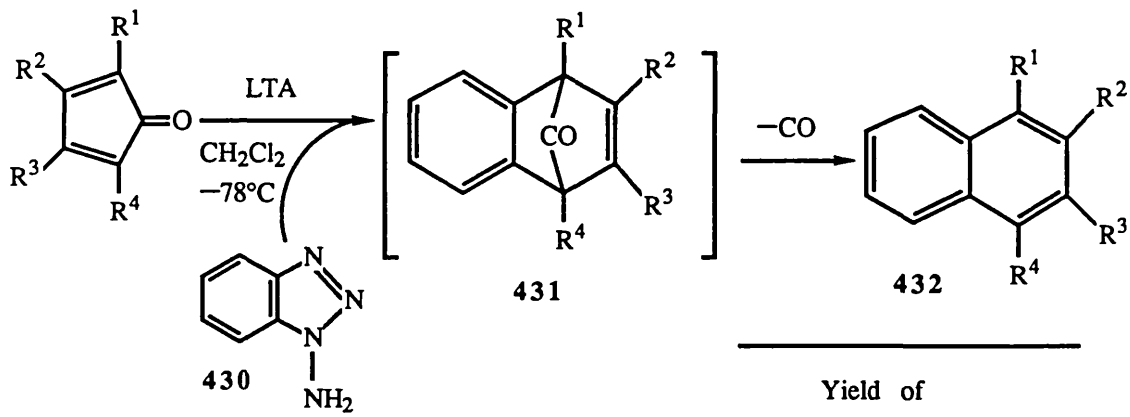
425 R = Me
428 R = Et

426 R = Me
429 R = Et

Where E = COOMe

analogous conditions, DAA (**295**) gave a complex mixture which could not be purified. With 2,5-diethyl-3,4-diphenylcyclopentadienone (**427**), again none of the elusive norbornadien-7-one (**428**) was detected. DAA (**295**), when refluxed in acetonitrile with cyclopentadienone (**427**), gave a complex mixture which resisted many attempts at separation. However no indication for the presence of the bridged carbonyl compound could be obtained from mass spectra of various reaction product fractions, but there was some indication of the presence of the 1,2-diacetylbenzene.

6.3 Attempted Synthesis of Substituted Benzonorbornadien-7-ones



430

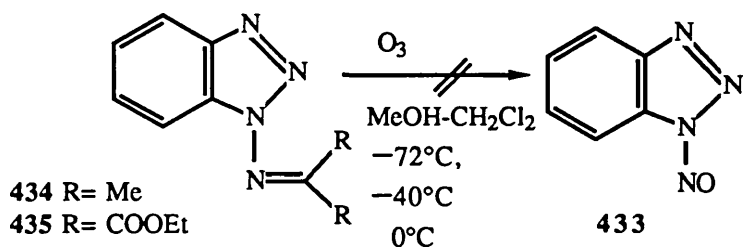
431

432

				Yield of	
R^1	R^2	R^3	R^4	**431**	**432**
Ph	Ph	Ph	Ph	—	93%
Me	Ph	Ph	Ph	—	88%
Et	Ph	Ph	Et	—	62%

It is reported that substituted naphthalenes were obtained when cyclopentadienones were subjected to Diels-Alder reaction with benzyne, generated from diazotised anthranilic acid.[122] We repeated this reaction with a few modifications. We generated benzyne by oxidation of 1-aminobenzotriazole (**430**) with lead tetra-acetate (LTA) and we conducted the experiments at –78°C, in the hope of obtaining the substituted benzonorbornadien-7-one system under these very mild conditions. However, we isolated only the fully aromatised products in the high yields shown above.

Compared to the initial Diels-Alder adducts already mentioned, the adducts (**431**) formed here should have been more stable. The carbonyl group can bend towards the aromatic ring and the π-electron repulsion between the olefinic bond and lone pair on the carbonyl group is thus reduced slightly in case of adducts (**431**) (see Chap.2).



434 R= Me
435 R= COOEt

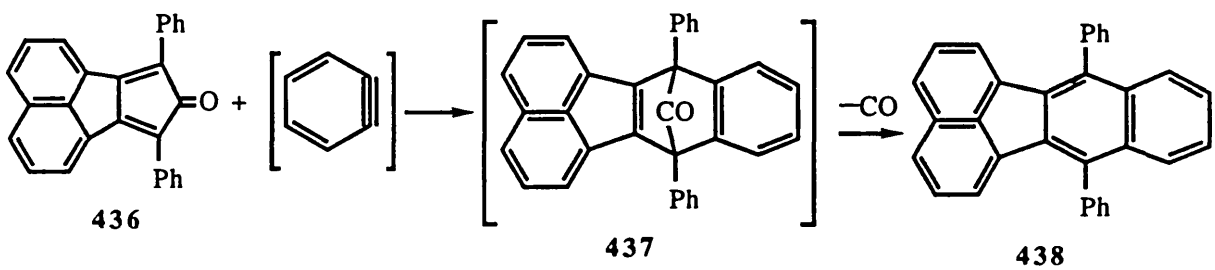
433

1-Aminobenzotriazole (**430**) is an excellent precursor of benzyne as it can be used down to very low temperatures. Another benzyne precursor which was of interest to us is 1-nitrosobenzotriazole (**433**). This has been prepared in unstated yield by treating benzotriazole with nitrosyl chloride and pyridine in ether, but has been used very little to give benzyne.[123] We decided to attempt its preparation by an alternative route based on the oxidative cleavage of an imine bond.[124] We treated 1-aminobenzotriazole (**430**) with acetone to form the imine (**434**) in 82% yield. This imine was subjected to ozonolysis over a range of temperatures but it did not afford the desired nitroso compound (**433**), nor 1-

nitrobenzotriazole. We subjected compound (**435**) to ozonolysis under analogous conditions but neither the desired nitroso compound (**433**) nor the 1-nitrobenzotriazole was observed.

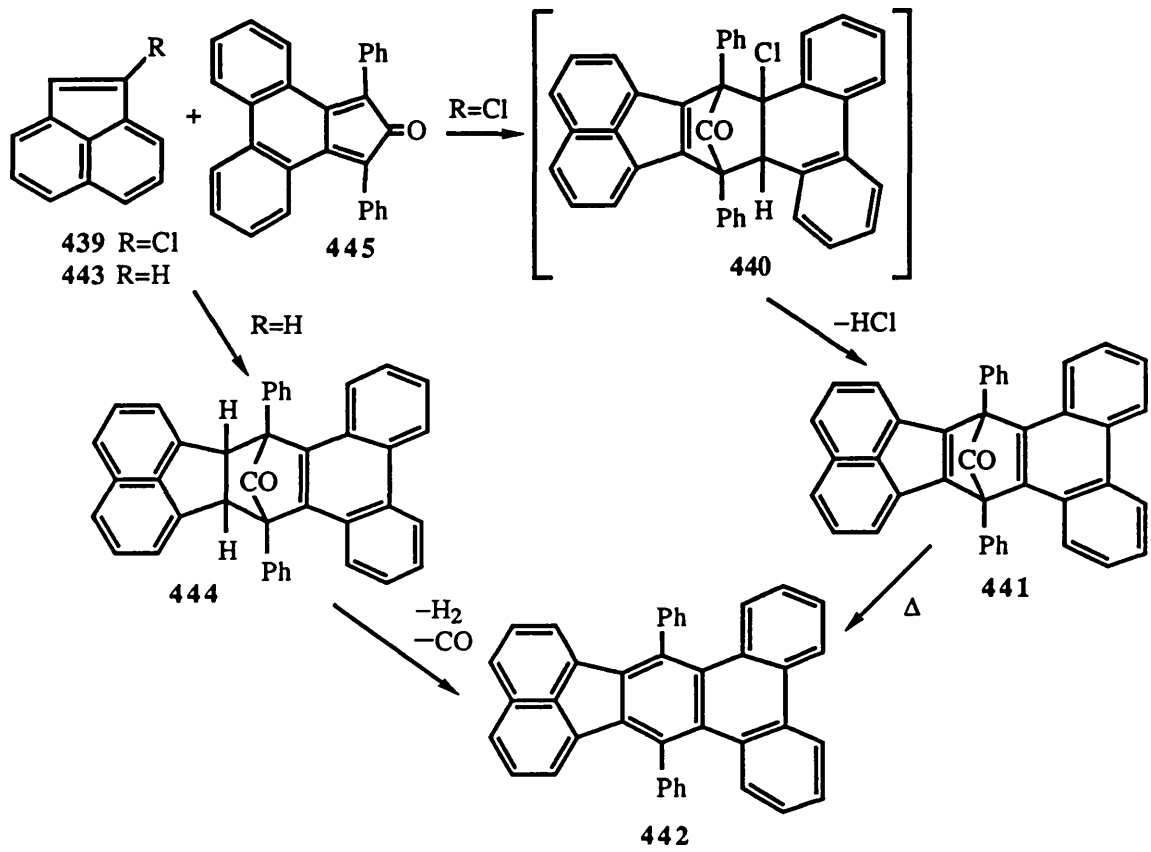
6.4 Synthesis of 9,14-Diphenyl-9,14-dihydrodibenz[*a*,*c*]anthracene-9,14-methanone (267b)

We next decided to repeat the questionable literature reactions mentioned in Sec. 6.1. In 1972 the authors, Mondal, Bandyopadhyay and Bhattacharya had carried out a Diels-Alder reaction between acecyclone (**436**) and benzyne and obtained benz[*k*]fluoranthene (**438**), m.p. 268°C.[84] When they repeated this experiment in 1983, compound (**438**) was again claimed to be the product but now with m.p. 246-248°C.[85]



The same authors studied the reaction between 1-chloroacenaphthylene (**439**), and phencyclone (**445**) in boiling toluene (110°C) and claimed the isolation of the norbornadienone derivative (**441**), m.p. 260°C. Compound (**441**) was said to be stable but to undergo decarbonylation to give the aromatised product (**442**) on further heating in toluene. Compound (**442**) was formed when acenaphthylene (**443**) is heated with phencyclone (**445**) boiling toluene. The dihydro compound (**444**) was then isolated and on treatment with ethanolic potassium hydroxide gave compound (**442**).[82] The reaction temperature (110°C) is high for compound (**441**) to be stable since norbornadienones are notoriously

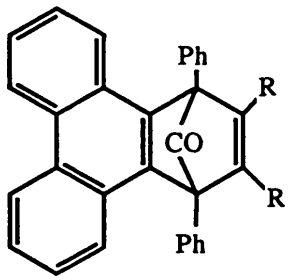
unstable at elevated temperatures. The i.r. absorption of the carbonyl groups of compound "(**441**)" and (**444**) were **both** claimed to be 1785cm.$^{-1}$ The authors might have actually isolated compound (**440**) and not (**441**).



Besides this, irregularities in the micro-analytical data, melting points, and experimental data all make this work less than convincing.

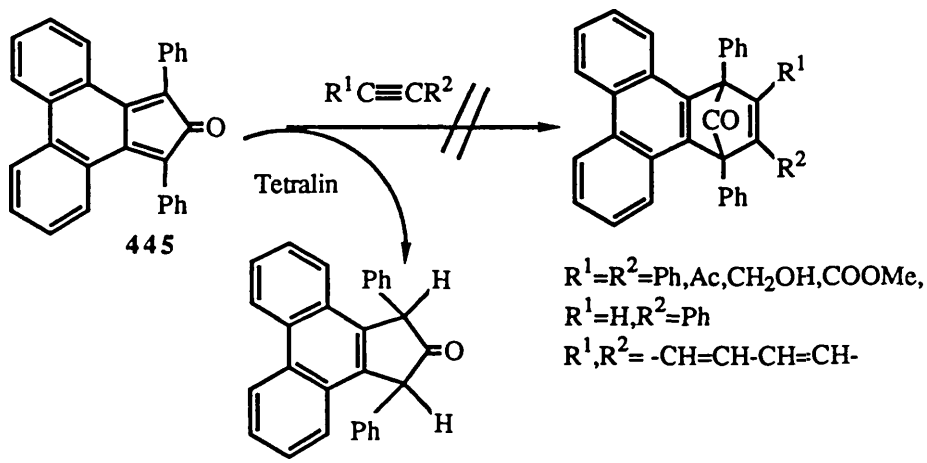
Further work carried out by the same authors claimed the isolation of compound (**267a**), m.p. 300°C and (**267b**), m.p. 270°C.[86]

We decided to repeat the reaction between phencyclone (**445**) and diphenylacetylene in refluxing tetralin as described in the paper,[86] and found the product obtained had a m.p. 314°C. We gradually brought the reaction temperature down from 207°C to room temperature and found that phencyclone was consumed in tetralin even at room temperature. We carried out similar reactions of phencyclone in tetralin at room temperature with various other



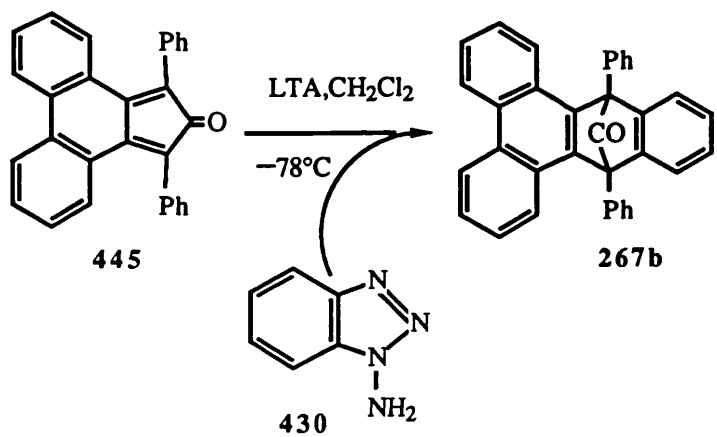
267 a R = Ph
267 b R,R = –CH=CH–CH=CH–

alkynes like DMAD (**1**), DAA (**295**), phenylacetylene and butyn-1,4-diol. The dark green colour of phencyclone was slowly discharged over about 24 h.

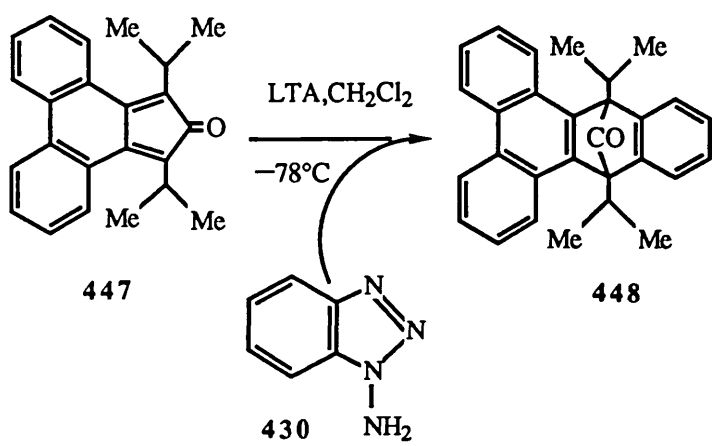


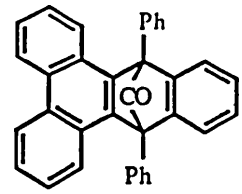
Careful study indicated that the product, m.p. 314°C, formed in all these experiments was the same. It is thus highly unlikely that phencyclone and the alkynes had undergone Diels-Alder reactions, and this was proved not to have occurred when some of the alkynes were quantitatively recovered. It had already been reported that when phencyclone (**445**) was heated in tetralin or decalin the 1,4-dihydro compound was obtained.[125] This was verified by carrying out a blank experiment, and all the above products were identical with the dihydro compound (**446**) and this is what the Indian authors had isolated, not the Diels-Alder adducts (**267a**) and (**267b**) claimed.

We then repeated the reaction of phencyclone (**445**) with benzyne but with a slight modification. We used 1-aminobenzotriazole (**430**) as the benzyne



precursor instead of diazotised anthranilic acid, and now we did obtain a good yield (67%) of the initial Diels-Alder adduct (**267b**). The i.r. absorption of the carbonyl group is 1805cm^{-1}, the ^{13}C nmr signal for the carbonyl carbon is at 195 ppm [*cf.* 194ppm for the parent norbornadienone (**250**)], M^+ is at 458, and the X-ray structure of compound (**267b**) is as shown in Fig.4 (see page 115).





267b

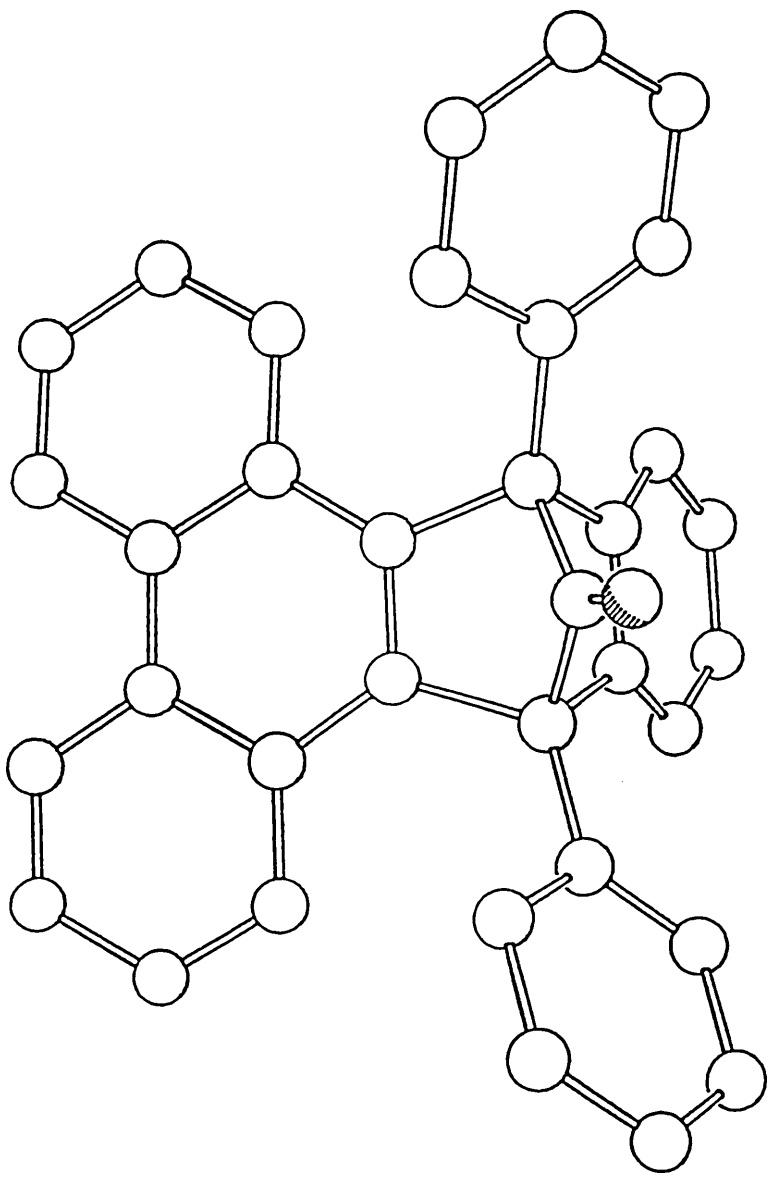
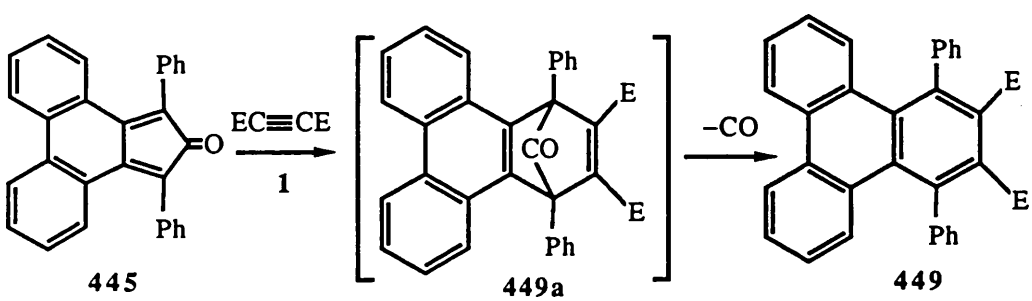


Fig.4 9,14-Diphenyl-9,14-dihydrodibenz[*a*,*c*]anthracene-9,14-methanone (267b)

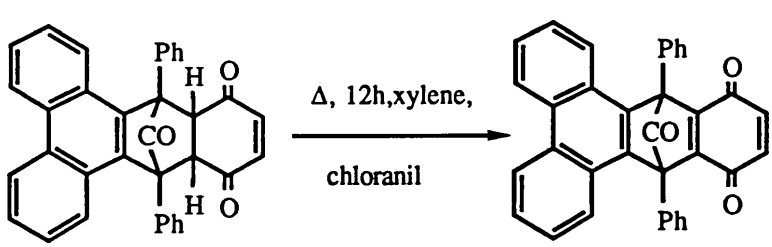
In a preliminary experiment we treated the di-isopropyl compound (**447**),[126] analogous to phencyclone, with benzyne in the hope of isolating compound (**448**) analogous to compound (**267b**). There is a signal in the ^{13}C nmr of the resultant product at 194 ppm, an i.r. absorption at 1797cm^{-1} and an M^+ at 390 which agree well with the presence of the bridged-carbonyl group, which is very promising. Unfortunately, this reaction was carried out on a very small scale and further work is required to characterise compound (**448**) fully.

Treatment of phencyclone with DMAD (**1**) gave only the aromatised product (**449**),[127] and we confirmed this result, under various conditions.

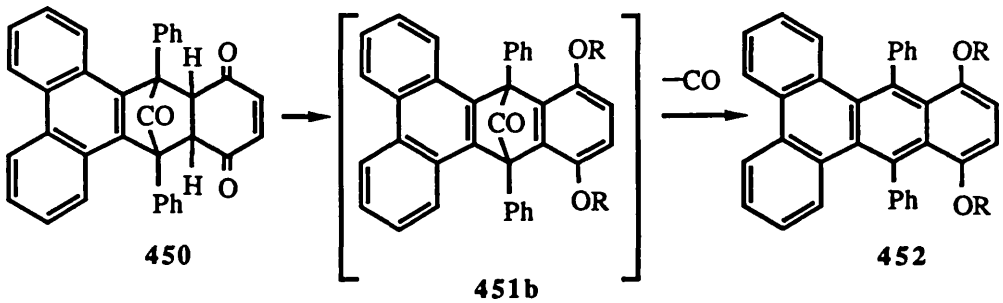


445 **449a** **449**

Formation of the bridge-head compound (**451a**) has been claimed[127a] but the melting point of the starting material (**450**) (195°C) was very different from that reported later (272°C)[127] and with our own work (270°C). Besides this, under the experimental conditions used (boiling xylene), it is most unlikely that the bridge-head compound would survive.



450 **451a**

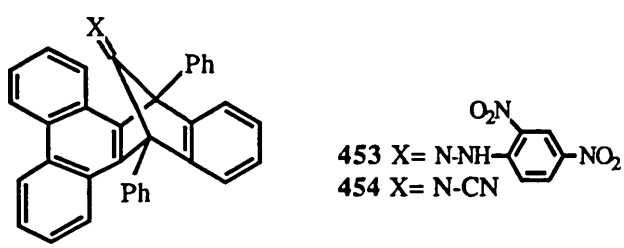


Finally we attempted to convert the dihydro compound (**450**),[127] into a fully aromatic bridged-carbonyl compound (**451b**) by oxidation (sulphur,chloranil, DDQ), enolisation (Et_3N, KO^{t}Bu, DBU), and trapping of the enol form (Ac_2O-pyridine, AcOH-H_2SO_4). However we gained no evidence for the presence of the bridged-carbonyl compound (**451b**).

6.5 Attempted Chemistry of 9,14-Diphenyl-9,14-dihydrodibenz-[*a*,*c*]anthracene-9,14-methanone (267b)

In view of the rarity of authentic norbornadien-7-ones, we decided to explore the chemistry of the authentic example (**267b**).

We treated compound (**267b**) with 2,4-dinitrophenylhydrazine (DNP) in the hope of forming the hydrazone (**453**) but surprisingly quantitative recovery



of compound (**267b**) was observed. We treated compound (**267b**) with bis(trimethylsilyl)carbodiimide[128] in the hope of forming compound (**454**) which, along with compound (**453**), should be relatively stable (see Chap.2).

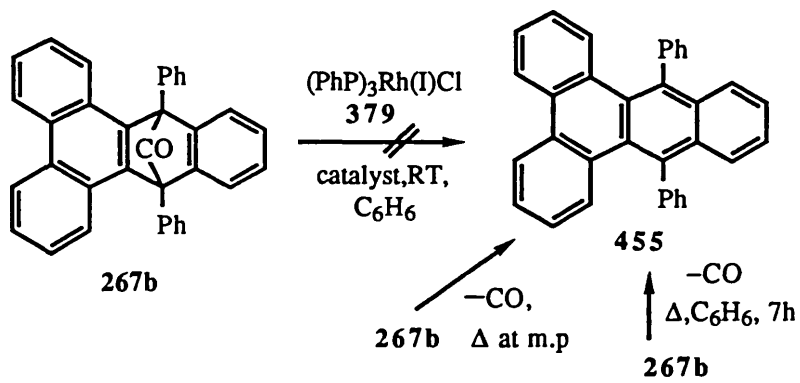
Unfortunately no reaction occurred. Compound (**267b**) also resists reduction with

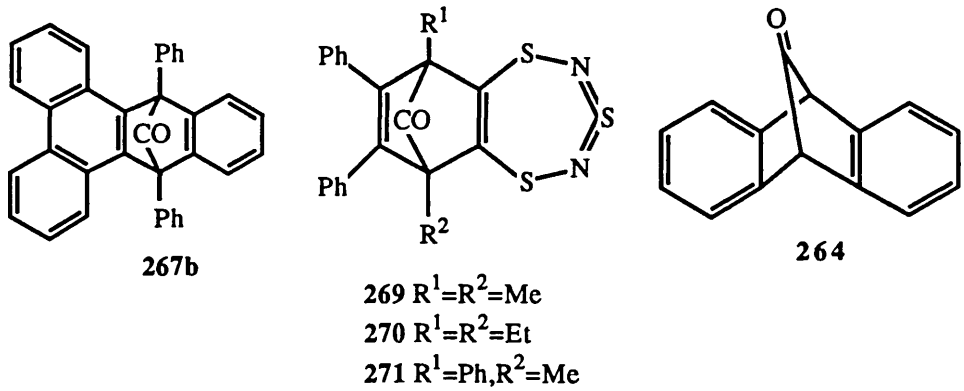
sodium borohydride.

We were initially surprised by this inertness of (**267b**) but on examination of the X-ray structure of compound (**267b**) (see page 115), we found that the angle of approach of the nucleophile is blocked and the carbonyl group is sterically protected by both the phenyl groups.

Compound (**267b**) on heating at its melting point (163-167°C), evolved carbon monoxide (which was detected by change in colour of a drop of blood) to give the aromatised product (**455**), m.p. 276°C, identical with the authentic compound.[86]

Treatment of compound (**267b**) with Wilkinson's catalyst in benzene at room temperature did not result in decarbonylation. On heating in boiling benzene (80°C) over a period of 7h it gave the aromatic product (**455**), which could be obtained under the same conditions in the absence of Wilkinson's catalyst.





269 $R^1=R^2=Me$
270 $R^1=R^2=Et$
271 $R^1=Ph, R^2=Me$

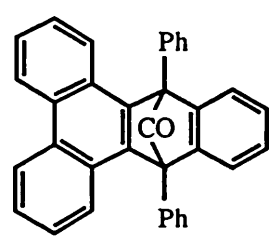
Compound (**267b**) is completely stable at room temperature unlike the simpler dibenzo derivative (**264**). We assume that the enhanced stability of compound (**267b**) must be associated with the presence of the phenyl groups since in other respects it is very similar to compound (**264**).

Compound (**267b**) seems to be even more stable than compounds (**269-271**) (see Chap.2), which decarbonylate readily in refluxing acetonitirile (8 min), whilst compound (**267b**) underwent decarbonylation in refluxing benzene (7 h) rather slowly.

6.6 Summary

Diels-Alder reactions of cyclopentadienones with alkynes normally afford the fully aromatised products; the initial norbornadien-7-one adducts have so far been very elusive.

We have tried to isolate these norbornadien-7-ones but have been unsuccessful in the case of norbornadien-7-ones and benzonorbornadien-7-ones. However, we have successfully isolated and characterised compound (**267b**), and disproved earlier claims of its isolation.



267b

Compound (**267b**) is stable at room temperature and decarbonylates only slowly (over 7h) in refluxing benzene. The rate of decarbonylation is not increased by the presence of Wilkinson's catalyst. The bridged-carbonyl compound (**267b**) does not react with carbonyl reagents, presumably because of

severe steric congestion of the carbonyl group.

Our work suggests that it may be possible to isolate other elusive fused norbornadien-7-ones and to study their interesting chemistry.

CHAPTER SEVEN

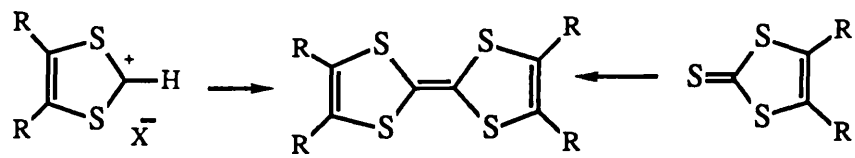
1,3-Dithioles

7.1 Introduction

The charge-transfer complex of tetrathiafulvalene (TTF) (**456**, R=H) with tetracyano-*p*-quinodimethane (TCNQ) was found to have an unusually high solid-state electrical conductivity. This triggered off extensive investigations of 1,3-dithiolium salts which form an important class of intermediates for the synthesis of tetrathiafulvalene derivatives.[129]

An essential feature for efficient charge-transfer organic donors and acceptors is that the donors form a new aromatic sextet not present in the neutral donor when it loses an electron and the acceptors form an aromatic sextet not present in the neutral acceptor when it gains an electron.[130]

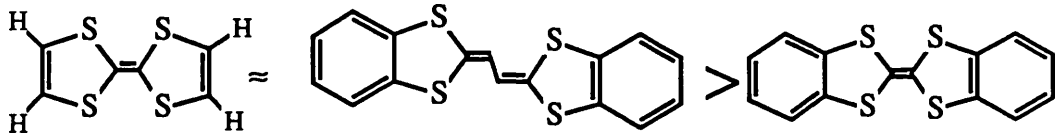
The major routes to TTF derivatives are by coupling 1,3-dithiolium salts (**457**) or 1,3-dithiole-2-thiones (**458**).



457 **456** **458**

Much work has been carried out on the chemistry of 1,3-dithiolium salts (**457**).[131,132]

The order of electron donating ability of some tetrathiafulvalenes is as follows:

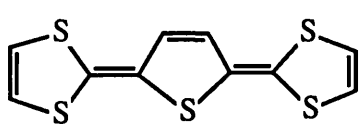


456
TTF

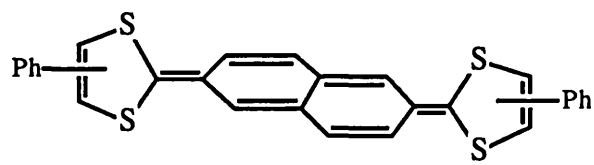
460

459

Compounds (**461**) and (**462**) analogous to (**460**) but with more extended delocalisation have recently been reported.[133] It was found that the more conjugated tetrathiafulvalenes are stronger donors.

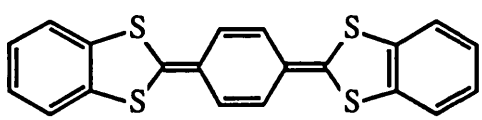


461

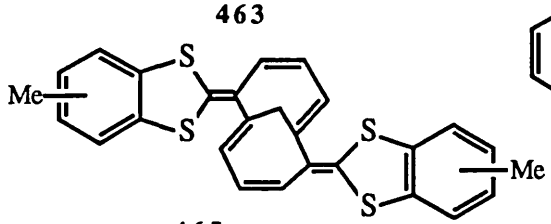


462

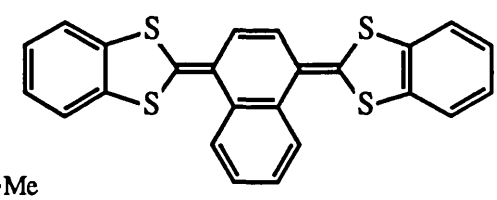
Various compounds (**463-466**) analogous to (**459**) have also been synthesised.[129]



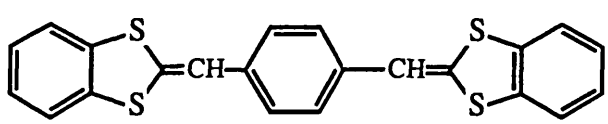
463



465



464



466

Compound (**466**) is of particular interest to us and it will be discussed

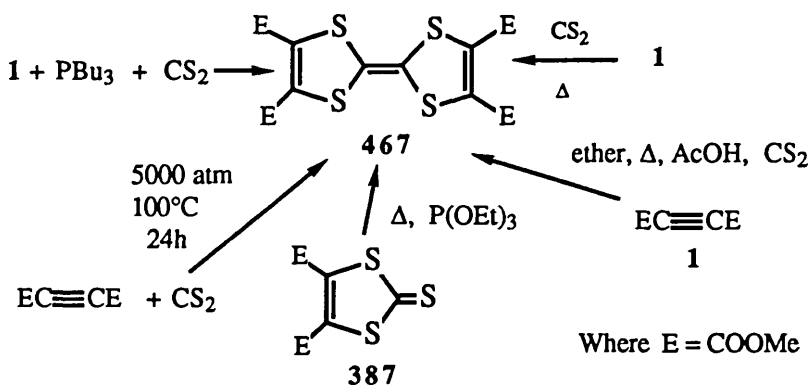
in more detail later.

7.2 Tetrathiafulvalenes

Though it has been known for 128 years that when an aliphatic phosphine was added to carbon disulphide a complex was formed, very little work has been carried out on this complex.[134]

Tetrathiafulvalenes with electron-withdrawing groups present on the ring have been synthesised by the addition of activated acetylenes to a mixture of tributyl phosphine and carbon disulphide.[135]

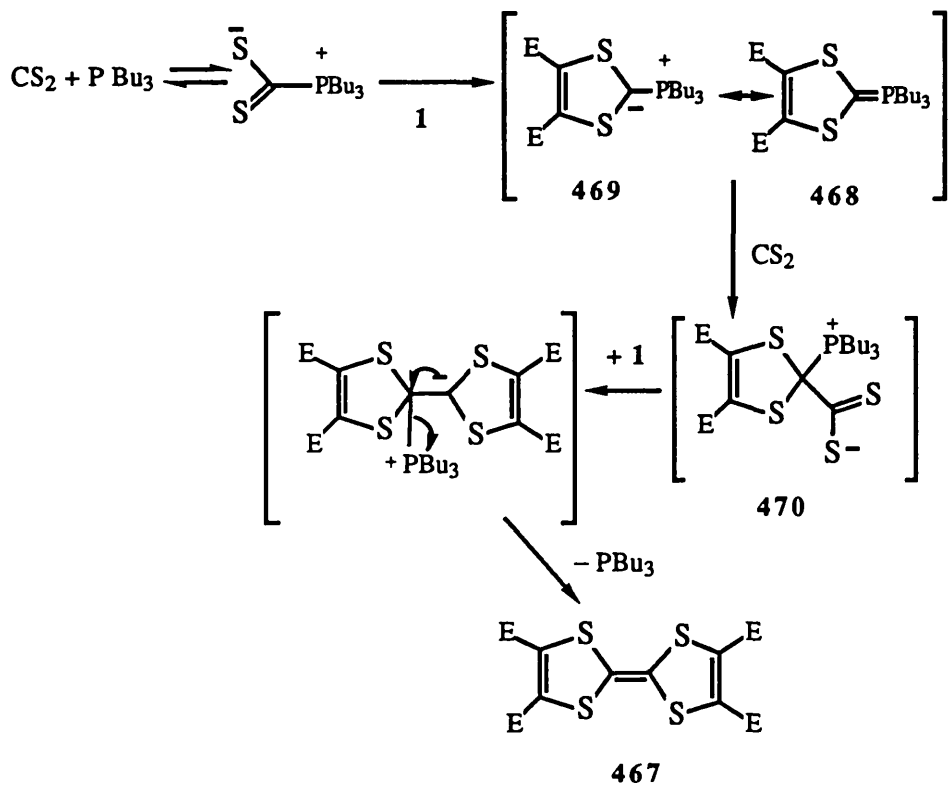
Tetramethyl tetrathiafulvalenetetracarboxylate (**467**) was obtained in poor yield when DMAD (**1**) was added to the tributyl phosphine-carbon disulphide complex.[135] Compound (**467**) was synthesised either by refluxing DMAD (**1**) in carbon disulphide (10% yield) or by subjecting dimethyl 2-thiono-1,3-dithiole-4,5-dicarboxylate (**387**) (see Chap.5) to desulphurisation with triethyl phosphite (52%).[136]



The tetrathiafulvalene (**467**) was also synthesised by refluxing DMAD with carbon disulphide in presence of acetic acid (10% yield).[137] Tetrathiafulvalene (**467**) was obtained in 87% yield when DMAD was treated with carbon disulphide under a pressure of 5000 atmospheres.[137]

We repeated the reaction of DMAD with the tributyl phosphine-carbon disulphide complex and obtained the tetrathiafulvalene (**467**) in 18% yield.

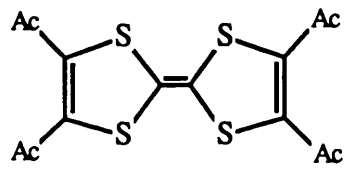
A probable mechanism for the formation of tetrathiafulvalene (**467**) from DMAD and tributyl phosphine-carbon disulphide complex has been proposed.[135]



Tributyl phosphine reacts with carbon disulphide to form the zwitterion which undergoes a 1,3-dipolar cycloaddition with DMAD (**1**) to form dithiol-2-ylidene-tributyl phosphorane (**468**) the dipolar form of which (**469**), being an 8π-system, rapidly undergoes reaction with carbon disulphide to form (**470**) which reacts further with DMAD, followed by elimination of tributyl phosphine to form tetramethyl tetrathiafulvalenetetracarboxylate (**467**).

By analogy with this DMAD reaction, we added hex-3-yne-2,5-dione (**295**) to the tributyl phosphine-carbon disulphide complex at –78°C in the hope of forming tetra-acetyltetrathiafulvalene (**389**). The reaction was monitored by t.l.c and found to be very complex, giving at least five products which could not be

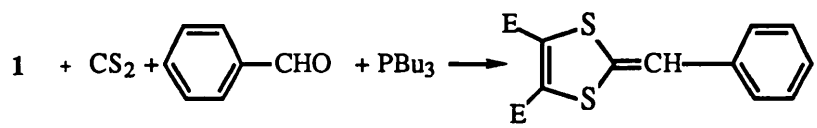
separated.



389

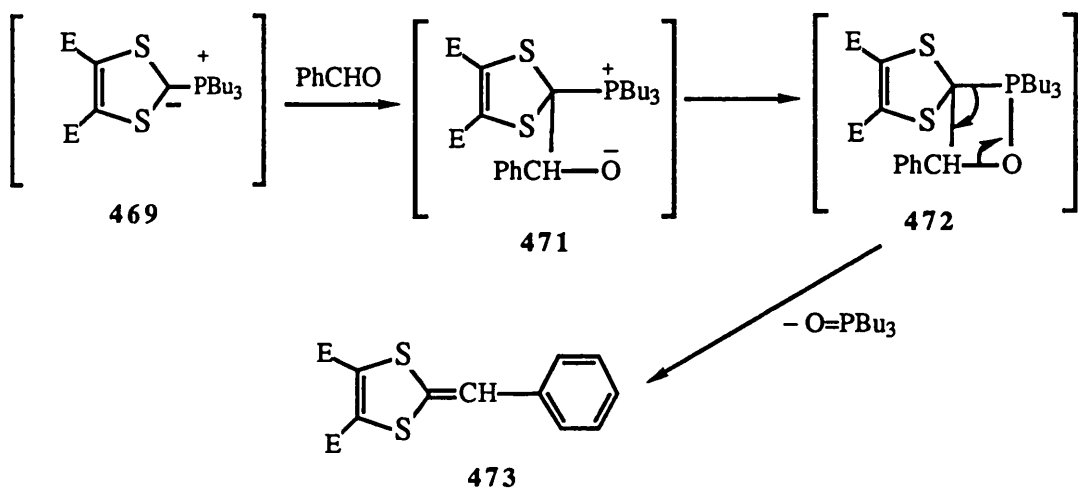
7.3 2-Arylidene-1,3-dithioles

The tributyl phosphine-carbon disulphide complex forms 2-benzylidene-1,3-dithiole (**473**) when treated with DMAD (**1**) and benzaldehyde at –23°C.[135,138]



473

The resonable mechanism is as shown:

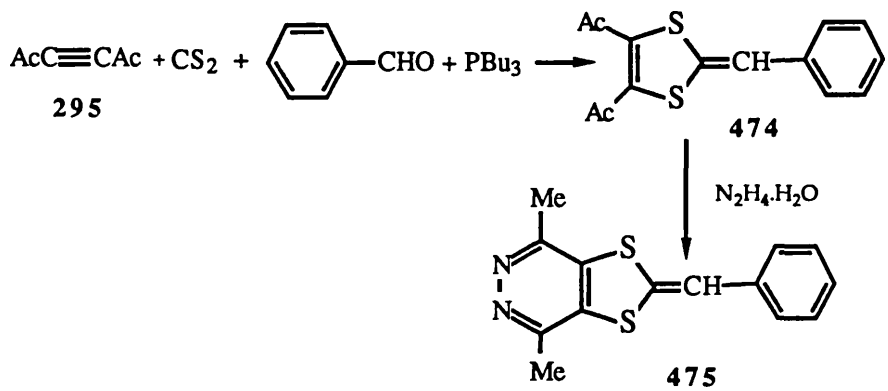


469 471 472 473

The intermediate (**469**) reacts with benzaldehyde to form the betaine (**471**)

which collapses to the oxaphosphetane (**472**) which eliminates tributyl phosphine oxide to form (**473**). The literature[138] reports a yield of 48% for compound (**473**), but we could only obtain a much lower yield (7%).

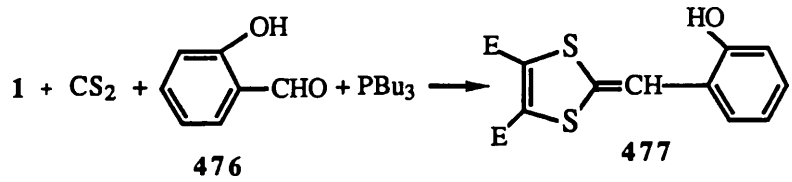
Under analogous conditions, except that the temperature was lower (–40°C), hex-3-yne-2,5-dione (DAA) (**295**) formed 4,5-diacetyl-2-benzylidene-1,3-dithiole (**474**), analytically pure, as a dark red viscous oil, though again in low yield (6%).



Compound (**474**), when treated with hydrazine hydrate in glacial acetic acid, afforded the corresponding pyridazine derivative (**475**) (81%) as a yellow solid, m.p. 141-145°C.

Since the reaction of DMAD (**1**), carbon disulphide and tributyl phosphine with aldehydes appears to have been done only with benzaldehyde and *p*-vinylbenzaldehyde we decided to extend the reaction to substituted aromatic aldehydes.

1,3-Dithiole (**477**) (16%) was obtained from salicylaldehyde (**476**) under the same conditions.

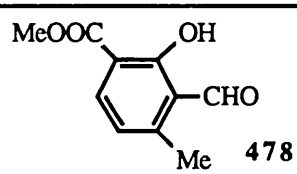
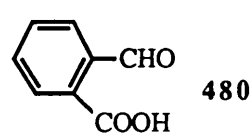
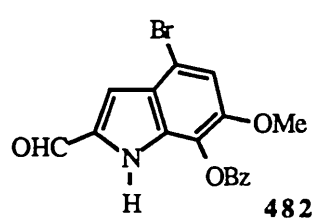


476 477

Similarly the substituted benzaldehyde (**478**)[139], *o*-phthalaldehydic acid (**480**), and the indole-aldehyde (**482**)[140] gave the 1,3-dithioles shown in rather low yields (see Table 4).

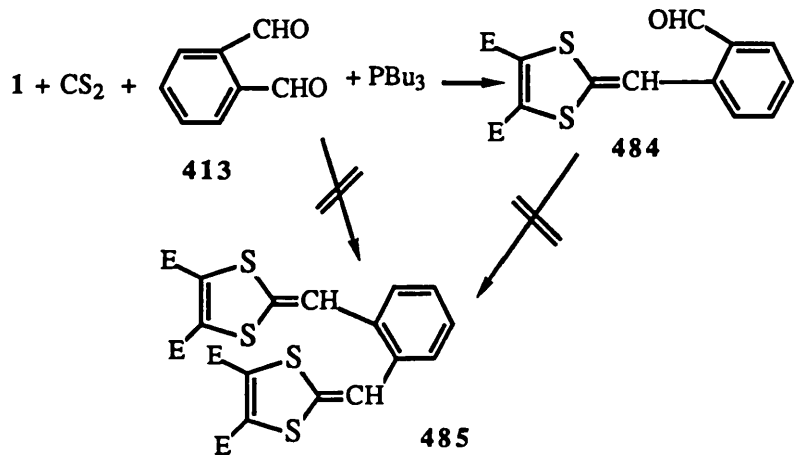
TABLE 4

Synthesis of 2-Arylidene-1,3-dithioles

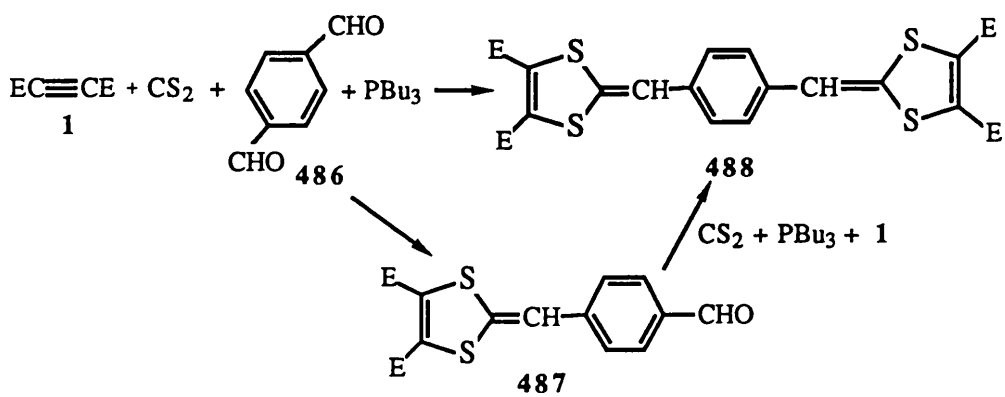
Aldehydes	Yield of 1,3-Dithioles
 **478**	**479** (49%)
 **480**	**481** (67%)
 **482**	**483** (22%)

o-Phthalaldehyde (**413**) reacted with phosphorane (**469**) to form the mono-1,3-dithiole (**484**) (19%).

We subjected the mono-1,3-dithiole (**484**) to a similar reaction in the hope of forming the bis-1,3-dithiole (**485**). The reaction was monitored by t.l.c and found to be complex, and the products could not be separated. When we



carried out a similar reaction with *o*-phthalaldehyde (**413**) and a large excess of carbon disulphide and tributyl phoshine, the reaction was complex and the products could not be separated. The mass spectra of the various fractions indicated the absence of the bis-1,3-dithiole (**485**).

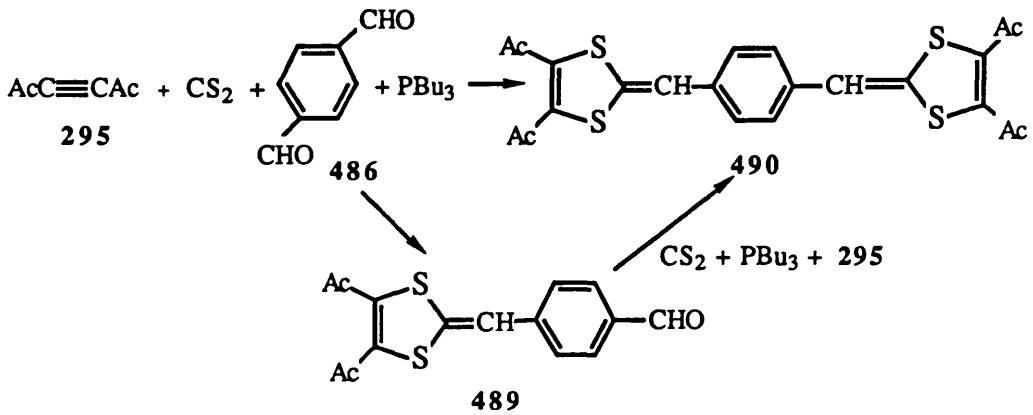


Terephthalaldehyde (**486**) forms the mono-1,3-dithiole (**487**) (58%) under analogous conditions, but with excess of carbon disulphide and tributyl phosphine it does form the bis-1,3-dithiole (**488**) (7%).

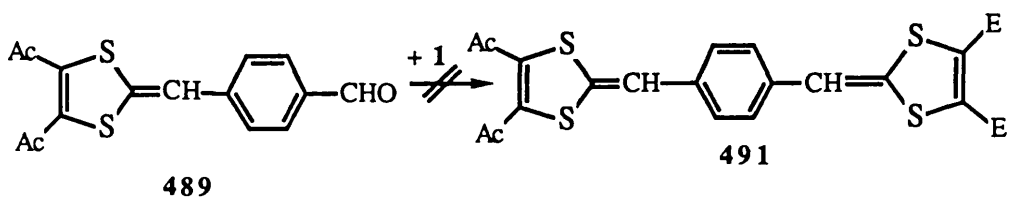
When subjected to a similar reaction 1,3-dithiole (**487**) formed the bis-1,3-dithiole (**488**) in 21% yield.

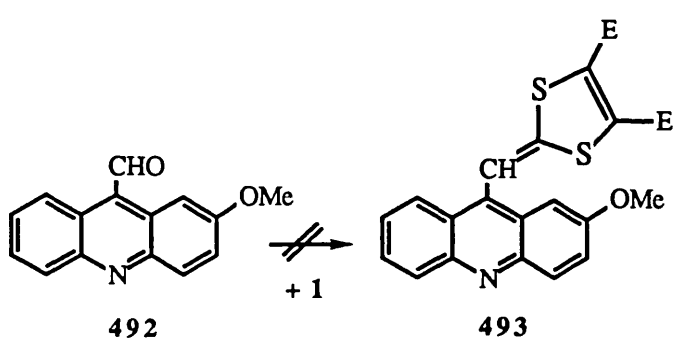
We also formed 1,3-dithiole (**489**) (47%) when hex-3-yne-2,5-dione (**295**) was added to terephthalaldehyde (**486**), carbon disulphide and tributyl phosphine. Compound (**489**) under analogous conditions affords the bis-1,3-dithiole (**490**)

(58%). The bis-1,3-dithiole (**490**) was obtained in 10% yield when terephthalaldehyde (**486**) was treated with excess of carbon disulphide and tributyl phosphine.



1,3-Dithiole (**489**) was subjected to a similar reaction with DMAD (**1**); none of the unsymmetrical bis-1,3-dithiole (**491**) was formed in contrast with the DMAD derived compound (**488**) and the hex-3-yne-2,5-dione derived compound (**490**).



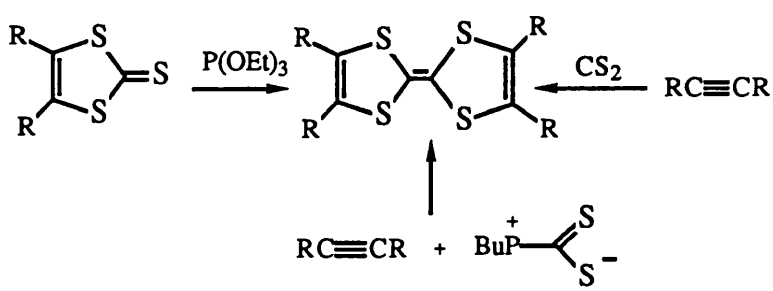


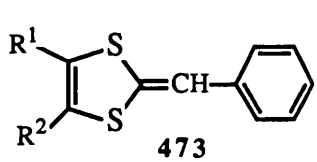
We also found that when we reacted the heteroaromatic aldehyde (**492**)[141] with DMAD (**1**), carbon disulphide and tributyl phosphine none of the product (**493**) was observed.

Compounds (**488**) and (**490**) are interesting molecules because structurally they are similar to compound (**466**). They could prove to be electron donating conjugated tetrathiafulvalenes.

7.4 Summary

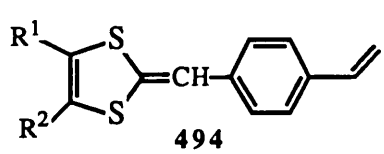
Tetrathiafulvalenes are electron donors which form charge-transfer complexes with electron acceptors. Many tetrathiafulvalenes have been synthesised as shown:





473

$R^1 = R^2 = COOMe$, Ph
$R^1 = H$, $R^2 = COOEt$, Ph

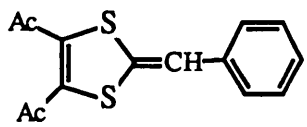


494

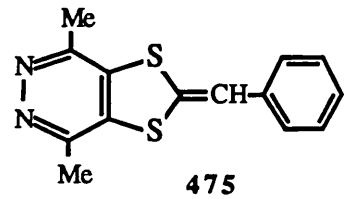
$R^1 = R^2 = COOMe$
$R^1 = H$, $R^2 = COOEt$, Ph

Compounds (**473**) and (**494**) are the only examples of 2-arylidene-1,3-dithioles prepared by the reaction of activated alkynes with carbon disulphide and tributyl phosphine in the presence of an aromatic aldehyde.

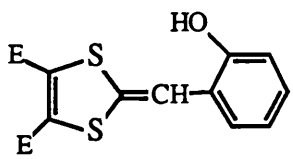
We have extended this reaction to the synthesis of the 2-arylidene-1,3-dithioles shown:



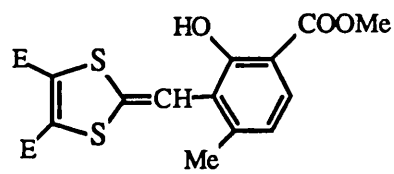
474



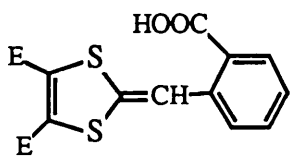
475



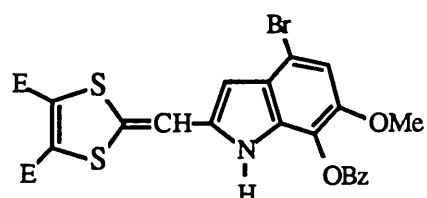
477



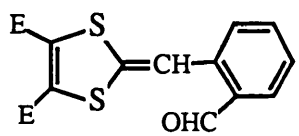
479



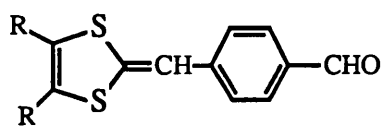
481



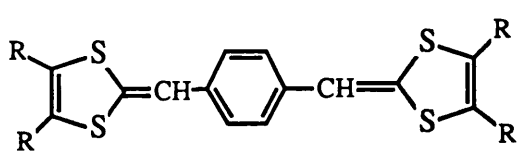
483



484



487, 489 R= E , Ac



488, 490 R= E , Ac

Where E = COOMe

The reaction appears to provide a general route to 2-arylidene-1,3-dithioles.

CHAPTER EIGHT

Experimental

8.1 Introduction

8.1.1 *Solvents and Reagents*

Commercially available solvents and reagents were used without purification except for those given below which were purified as stated.

Light petroleum, b.p. 40-60°C, was redistilled before use. Diethyl ether and THF were dried by distillation from potassium-benzophenone ketyl. Benzene, toluene, and xylene were dried by standing over sodium wire for several days. Dichloromethane was distilled from phosphorus pentoxide. Tetralin was washed with excess of concentrated sulphuric acid until the acid layer remained colourless, then washed with aqueous sodium carbonate followed by distilled water, dried ($CaSO_4$), filtered and fractionally distilled under reduced pressure from BaO.[142] Decalin was stirred with concentrated sulphuric acid for six hours, then the organic phase was separated, washed with water, saturated aqueous sodium carbonate and water, dried ($CaSO_4$), filtered and distilled under pressure.[143] *o*-Dichlorobenzene was shaken with concentrated sulphuric acid, washed with water, dried with ($CaSO_4$) and distilled from calcium hydride.[144] Dimethyl sulphoxide was dried with Linde type 4Å molecular sieves, by prolonged contact and passage through a column of the material, then distilled under reduced pressure and stored over 4Å molecular sieves.[145]

8.1.2 *Chromatography*

Dry flash chromatography carried out on silica (Merck Kieselgel 60H)[146] was used throughout unless otherwise stated. The mixture was used pre-adsorbed onto silica and applied to a pre-packed column (approximately 30g per gram of the mixture to be separated). The columns were eluted initially with the least polar solvent then with binary mixtures increasing in polarity.

Preparative plate chromatography was carried out using 20 x 20cm glass plates coated with silica (Merck Kieselgel 60 GF_{254}) (approximately 20-25g of silica coated on each glass plate), to which the mixture to be purified was applied as a solution in the minimum quantity of solvent. This was then run with an appropriate solvent and the separate compounds were eluted from the silica by washing with ethyl acetate or chloroform.

Thin layer chromatography (t.l.c) was used to analyse purity of compounds, monitor reactions and to analyse column fractions; aluminium backed silica plates (Merck Kieselgel 60 F_{254}) were used for this. The plates were viewed under u.v light at 254 and 300nm and developed in iodine vapour.

8.1.3 *Spectra*

Infra-red spectra were recorded either on a Perkin-Elmer 298 spectrometer and calibrated against polystyrene at 1602cm^{-1} or Perkin-Elmer 1710FT spectrometer with internal calibration.

Proton nuclear magnetic resonance spectra were recorded at 60MHz on a Varian EM360, at 90MHz on a Perkin-Elmer R32 or a Jeol FX90Q spectrometer, at 250MHz on a Brüker WM250, at 270MHz on a Jeol GSX270 and at 500MHz on a Brüker AM500 spectrometer. Chemical shifts are given in parts per million relative to tetramethylsilane as an internal reference. Carbon-13 n.m.r spectra were recorded at 62.9MHz on a Brüker WM250, at 69MHz on a

Jeol GXS270, and at 126MHz on a Brüker AM500 spectrometer.

Low resolution mass spectra and accurate mass spectrometer measurements were recorded on an AE1 MS12 mass spectrometer or a VG Micromass 7070B mass spectrometer using impact ionisation. Certain low resolution and CI mass spectra were recorded on a VG Analytical ZAB-E instrument at the S.E.R.C mass spectrometry centre, Swansea.

8.1.4 *Other Data*

Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. Elemental micro-analyses were carried out in the Imperial College Chemistry Department Micro-analytical Laboratory under the supervision of Mr K.I.Jones.

8.2 For Chapter Four

Chemistry of Hex-3-yne-2,5-dione

Hex-3-yne-2,5-dione (295)

A solution of sodium dichromate (126.5g, 1265mmol), water (800ml) and concentrated sulphuric acid (360ml) was added to hex-3-yne-2,5-diol (37.1g, 325mmol) in dichloromethane (600ml) at 38-40°C over 1.75h and stirred at room temperature for 0.5h. The dark green solution was extracted with dichloromethane (3x50ml) and the combined dichloromethane portions were washed with saturated aqueous sodium hydrogen carbonate, water and brine, dried ($MgSO_4$), and evaporated to give hex-3-yne-2,5-dione (DAA) (**295**) (21.4g, 59.8%), b.p. 50-56°C/0.3mmHg (lit.[97] 26-38°C/0.1mmHg); $\upsilon_{max.}(CCl_4)$ 1692 (CO), 1360, and 1226cm^{-1}; δ_H (60MHz; $CDCl_3$) 2.49 (s); δ_C(126MHz ; $CDCl_3$) 31.77, 83.63, and 182.33.

Conversion of Hex-3-yne-2,5-dione (295) into Oligomers

General Procedure

Hex-3-yne-2,5-dione (841mg, 7.6mmol), iodobenzene (1ml; initially added as "heavy-atom" solvent) and benzene (24ml) were heated at reflux temperature for 45h. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (30g). Diethyl ether (32 to 40%) in light petroleum eluted 4,5-*diacetyl*-2-*methyl*-3-(1,2-*dioxopropyl*)-*furan* (**367**) (41mg,

4.5%) as a yellow solid, m.p. 78-81°C (diethyl ether) (Found: C, 61.25; H, 5.1. $C_{12}H_{12}O_5$ requires C, 61.0; H, 5.1%); $\upsilon_{max.}(CCl_4)$ 1717s (COCOMe, 1,2-diketone), 1690vs (COMe), 1576, 1541s, 1408, 1360s, 1158s and 887cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.45 (3H, s, Me), 2.57 (3H, s, COMe), 2.6 (3H, s, COMe), 2.65 (3H, s, COCOMe); δ_C (62.9MHz; $CDCl_3$) 14.0, 24.6, 27.0, 31.0, 119.0, 131.6, 147.2, 162.0, 187.4, 187.9, 198.0, and 198.5; *m/z* (110°C) 236 (M^+, 0.7%), 218 (0.3), 193 (M^+-CH_2CO, 100), 151 (26), 123 (5) and 43 ($COMe^+$, 63).

Further elution with diethyl ether (44 to 48%) in light petroleum gave 1,4,5,6-*tetra-acetyl*-4,7-*dihydro*-3,7-*dimethyl*-4,7-*epoxy*-2-*benzofuran* (**366**) (35mg, 4%) as yellow needles, m.p. 156-158°C (diethyl ether) (Found: C, 65.5; H, 5.5. $C_{18}H_{18}O_6$ requires C, 65.45; H, 5.45%); $\upsilon_{max.}(CHCl_3)$ 3027, 1730vs (COMe), 1673vs (COMe), 1588s, 1364s, 1302 and 1285cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.09 (3H, s, Me), 2.23 (3H, s, Me), 2.301 (3H, s, COMe), 2.302 (3H, s, COMe), 2.44 (3H, s, COMe), 2.46 (3H, s, COMe); *m/z* (110°C) 330 (M^+, 3%), 315 (M^+-Me, 2), 288 (10), 287 (M^+-COMe,12), 273 (6.5), 260 (2), 245 (20), 227 (3), 220 (M^+-$C_6H_6O_2$, 13), 217 (5), 203 (10), 177 (23) and 43 ($COMe^+$, 100).

Further elution with diethyl ether (64 to 68%) in light petroleum gave 6,7,8-*triacetyl*-5,8-*dihydro*-1,4,5-*trimethyl*-5,8-*epoxy*-2-*benzopyran*-3-*one* (**364**) (461mg, 55%) as yellow cubic crystals, m.p. 137-142°C (diethyl ether) (Found: C, 65.4; H, 5.3. $C_{18}H_{18}O_6$ requires C, 65.45; H, 5.45%); $\upsilon_{max.}(CCl_4)$ 1730, 1702, 1675cm^{-1}; δ_H (500MHz; $CDCl_3$) 2.03 (3H, s), 2.07 (3H, s), 2.2 (3H, s), 2.21 (3H,s), 2.36 (3H, s), 2.38 (3H, s); δ_C (62.9MHz; $CDCl_3$) 11.2, 15.8, 16.5, 26.55, 30.16, 30.6, 91.15, 93.2, 116.97, 118.1, 146.6, 149.8, 153.9, 155.9, 163.25, 194.1, 198.4, and 201.8; *m/z* (110°C) 330 (M^+, 58%), 288 (M^+-CH_2CO, 22), 260 (36), 245 (73), 220 (M^+-$C_6H_6O_2$, 56), 218 (42), 117 (10), 173 (3), 145 (2), 107 (4), 65 (2) and 43 ($MeCO^+$, 100).

Further elution gave products which could not be purified. The oligomerisation reactions were carried out several times to maximise the yield of the individual oligomers and only the oligomer in question was purified (see Chap.5, Tables 2 & 3).

6,7,8-*Triacetyl*-5,8-*dihydro*-1,4,5-*trimethyl*-5,8-*epoxy*-2-*benzopyran*-3-*one* (**364**).–Hex-3-yne-2,5-dione (193mg, 1.8mmol) and xylene (16ml) were heated at reflux for 7h. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Ethyl acetate (26 to 31%) in light petroleum eluted 6,7,8-triacetyl-5,8-dihydro-1,4,5-trimethyl-5,8-epoxy-2-benzopyran-3-one (**364**) (121mg, 63%) as yellow cubic crystals, m.p. 137-142°C (diethyl ether), identical with that described above.

3-*Acetyl*-1,4,6,8-*tetramethyl*-7-*prop*-1-*ynyl*-4,8-*epoxy*-4H-*furo*[3,4-*c*]-*oxocin*-9(8H)-*one* (**365**).–Tetrasulphur tetranitride (460mg, 2.5mmol), hex-3-yne-2,5-dione (2.34g, 21mmol) and benzene (50ml) were heated at reflux temperature for 31h. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Dichloromethane (40 to 90%) in light petroleum eluted the 3-*acetyl*-1,4,6,8-*tetramethyl*-7-*prop*-1-*ynyl*-4,8-*epoxy*-4H-*furo*[3,4-*c*]*oxocin*-9(8H)-*one* (**365**) (170mg, 7.6%) as colourless rhombic crystals, m.p. 154°C (dichloromethane) (Found: C, 68.6; H, 5.8. $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.7%); $\upsilon_{max.}(CCl_4)$ 3000, 2940, 2920, 1710vs (CO), 1700vs (CO), 1635s, 1410, 1380, 1370, 1360, 1180, 1150s, 940s, 880cm^{-1}; δ_H (250MHz; $CDCl_3$) 1.58 (3H, s, Me), 1.96 (3H, s, Me), 1.97 (3H, s, Me), 2.07 (3H, s, Me), 2.53 (3H, s, Me), 2.68 (3H, s, MeCO); *m/z* (180°C) 314 (M^+, 9%), 299 (M^+-Me, 5), 272 (M^+-CH_2CO, 14), 271 (M^+-MeCO, 13), 257 (4), 243 (11), 229 (10.5), 201 (6.5), 193 (7), 187 (4), 159 (3), 151 (5), 121 (12), 109 (5), 77 (4), 51 (4) and 43

($MeCO^+$,100).

4,5-Diacetyl-2-methyl-3-(1,2-*dioxopropyl*)-*furan* (**367**).–Hex-3-yne-2,5-dione (252mg, 2.3mmol) and benzene (10ml) were heated at reflux temperature for 21h. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (30g). Diethyl ether (26 to 40%) in light petroleum eluted 4,5-diacetyl-2-methyl-3-(1,2-dioxopropyl)-furan (**367**) (36mg, 13%) as a yellow soild, m.p. 78-81°C (diethyl ether), identical with that described above.

Treatment of Hex-3-yne-2,5-dione with Acetic Acid

Hex-3-yne-2,5-dione (485mg, 4.4mmol) and glacial acetic acid (514mg, 8.6mmol) were heated at reflux for 17h. The reaction mixture was neutralised, extracted with diethyl ether, washed with water and brine, then dried ($MgSO_4$). The dried solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Ethyl acetate (9 to 10%) in light petroleum eluted 4,5-diacetyl-2-methyl-3-(1,2-dioxopropyl)-furan (**367**) (11mg, 2%) as a yellow solid, m.p. 78-81°C (diethyl ether), identical with that described above.

Further elution with ethyl acetate (14 to 18%) in light petroleum gave 3-(1-*acetoxy*-2-*oxopropyl*)-4,5-*diacetyl*-2-*methyl*-*furan* (**368**) (306mg, 49.6%) as yellow crystals, m.p. 108-110°C (diethyl ether) (Found: C, 59.85; H, 5.75. $C_{14}H_{16}O_6$ requires C, 60.0; H, 5.7%); (Found: M^+, 280.0945. $C_{14}H_{16}O_6$ requires 280.0942); $\upsilon_{max.}$($CHCl_3$) 3028, 1733vs (OCOMe), 1683vs (COMe), 1601, 1539s, 1362s, and 1235s cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.14 (3H, s, Me), 2.22 (3H, s, Me),

2.4 (3H, s, Me), 2.5 (3H, s, Me), 2.6 (3H, s, Me), 6.02 (1H, s, H); δ_C (62.9MHz; $CDCl_3$) 12.7, 20.3, 26.2, 26.56, 31.1, 71.7, 116.3, 131.0, 148.0, 155.6, 169.5, 187.0, 198.0, and 200.7; *m/z* (120°C) 280 (M^+,15%), 238 (M^+-CH_2CO, 20), 195 (100), 177 (25) and 43 ($MeCO^+$, 48).

8.3 For Chapter Five

Further Chemistry of Hex-3-yne-2,5-dione (DAA)

8.3.1 Nucleophilic Additions to Hex-3-yne-2,5-dione (DAA)

3-(*o-Toluidino*)*hex*-3-*ene*-2,5-*dione* (**383a**).– To a vigorously stirred solution of hex-3-yne-2,5-dione (337mg, 3mmol) in dry benzene (23ml) was added dropwise a solution of *o*-toluidine (1g, 9mmol) in dry benzene (13ml) at room temperature. The reaction mixture was stirred overnight. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (35g). Diethyl ether (13.3%) in light petroleum eluted 3-(*o-toluidino*)*hex*-3-*ene*-2,5-*dione* (**383a**) (384mg, 57.8%) as a yellow oil, (Found: C, 72.1; H, 7.2; N, 6.5. $C_{13}H_{15}NO_2$ requires C, 71.9; H, 6.9; N, 6.45%); $\upsilon_{max.}$($CHCl_3$) 3011m, 1709s (COMe), 1621vs, 1575vs, 1504, 1460, 1395s, 1268vs, 1198w, 1183w, 1106w, 1020w, 989w, and 668cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.02 (3H, s, Me), 2.24 (3H, s, COMe), 2.39 (3H, s, COMe), 5.48 (1H, s, CH), 6.74-7.25 (4H, m, ArH), and 11.3 (1H, br, NH); δ_C (500MHz; $CDCl_3$) 17.49, 27.95, 29.7, 97.75, 121.71, 125.25, 126.58, 129.86, 130.77, 137.68, 155.57, 198.73, and 199.34; *m/z* (130°C) 217 (M^+, 19.3), 174 (M^+-MeCO, 100), 132 (31.1), 117 (4.2), 91 (22), 77 (3), 65 (15.6), and 43 ($MeCO^+$, 35.5).

3-(*m-Toluidino*)*hex*-3-*ene*-2,5-*dione* (**383b**).– To a vigorously stirred solution of hex-3-yne-2,5-dione (486mg, 4.4mmol) in dry benzene (13ml) was added dropwise a solution of *m*-toluidine (1g, 9mmol) in dry benzene (10ml) at room temperature. The reaction mixture was stirred overnight. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade

silica (35g). Diethyl ether (10 to 15%) in light petroleum eluted 3-(*m-toluidino*)*hex*-3-*ene*-2,5-*dione* (**383b**) (154mg, 16.1%) as a yellow oil, (Found: C, 71.8; H, 7.1; N, 6.4. $C_{13}H_{15}NO_2$ requires C, 71.9; H, 6.9; N, 6.45%); $\upsilon_{max.}(CHCl_3)$ 3027w, 3011w, 1708s (COMe), 1625s, 1609s, 1593s, 1572vs, 1493, 1395s, 1272vs, 1198w, 1173w, 1020w, 948w, 698w, and 666cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.1 (3H, s, Me), 2.2 (3H, s, COMe), 2.3 (3H, s, COMe), 5.4 (1H, s, CH), 6.7-7.2 (4H, m, ArH), and 11.4 (1H, br, NH); δ_C (126MHz.; $CDCl_3$) 21.0, 28.4, 29.9, 97.9, 118.3, 121.9, 125.8, 129.2, 139.0, 139.45, 155.2, 199.2, and 199.4; *m/z* (160°C) 217 (M^+, 20.2), 174 (M^+-MeCO, 100), 132 (34), 117 (2.4), 77 (6.4), 65 (14.5), and 43 ($MeCO^+$, 80.3).

3-(*p-Toluidino*)*hex*-3-*ene*-2,5-*dione* (**383c**).– To a vigorously stirred solution of hex-3-yne-2,5-dione (419mg, 3.8mmol) in dry benzene (16ml) was added dropwise a solution of *p*-toluidine (0.88g, 8mmol) in dry benzene (10ml) at room temperature. The reaction mixture was stirred overnight. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (35g). Dichloromethane (50 to 70%) in light petroleum eluted 3-(*p-toluidino*)*hex*-3-*ene*-2,5-*dione* (**383c**) (473mg, 57.2%) as a yellow crystals which turn dark green on standing, m.p. 78-82°C (dichloromethane) (Found: C, 71.8; H, 7.0; N, 6.4. $C_{13}H_{15}NO_2$ requires C, 71.9; H, 6.9; N, 6.45%); $\upsilon_{max.}(CHCl_3)$ 3012w, 1708s (COMe), 1623s, 1589s, 1569vs, 1516s, 1359s, 1270s, 1193w, 1132w, 1018w, 991w, 820w, and 667cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.05 (3H, s, Me), 2.21 (3H, s, COMe), 2.32 (3H, s, COMe), 5.41 (1H, s, CH), 6.84 (2H, d, J 8.25Hz), 7.11 (2H, d, J 8.25Hz), and 11.4 (1H, br, NH); δ_C(62.9MHz; $CDCl_3$) 20.80, 28.68, 30.07, 97.64, 121.72, 130.16, 135.19, 136.83, 155.87, 199.45, and 199.57; *m/z* (120°C) 217 (M^+, 21.5), 174 (M^+-MeCO, 100), 132 (31.2), 117 (1.9), 105 (3.8), 91 (15), 77 (2.2), 65 (11.6), and 43 ($MeCO^+$, 28.5).

8.3.2 Cycloaddition Reactions of DAA

Dimethyl 2-thiono-1,3-dithiole-4,5-dicarboxylate (**387**).–To a vigorously stirred solution of ethylene trithiocarbonate (104mg, 0.8mmol) in dry xylene (20ml) at reflux temperature, DMAD (**1**) (971mg, 7mmol) in dry xylene (5ml) was added and refluxed for 6h. The reaction mixture was allowed to cool to room temperature. The solvent was removed by evaporation and the residue purified by dry flash chromatography on 60H grade silica (25g). Diethyl ether (55%) in light petroleum eluted the thione (108mg, 55.7%) as yellow crystals, m.p. 69-71°C (lit.[115] 56%, m.p. 70°C).

Dimethyl 2-methyl-2$\lambda^5\sigma^3$*-acenaphtho[5,6-de]triazine-6,7-dicarboxylate* (**392**).–To a vigorously stirred solution of 2-methyl-2$\lambda^5\sigma^3$-acenaphtho[1,8-*de*]triazine (**390**) (194mg, 1.1mmol) in *o*-dichlorobenzene (11ml) at reflux temperature, DMAD (**1**) (3.23g, 23mmol) in *o*-dichlorobenzene (39ml) was added dropwise and refluxed for 5h. The reaction mixture was allowed to cool to room temperature. The solvent was removed by evaporation and the residue purified by preparative plate chromatography on 60 GF_{254} (25g). Diethyl ether (50%) in light petroleum eluted dimethyl 2-methyl-2$\lambda^5\sigma^3$-acenaphtho[5,6-*de*]triazine-6,7-dicarboxylate (**392**) (128mg, 37.4%) as bright red crystals, m.p. 224-225°C (lit.[34] m.p. 225-226°C); δ_C (126MHz; $CDCl_3$) 52.12, 55.92, 103.63, 112.78, 118.55, 124.91, 125.43, 132.79, 143.66, and 166.35.

6,7-*Diacetyl-2-methyl-2*$\lambda^5\sigma^3$*-acenaphtho[5,6-de]triazine* (**393**).–Hex-3-yne-2,5-dione (1.072g, 10mmol) in DMSO (29ml) was added dropwise over 7h

to a refluxing solution of 2-methyl-2$\lambda^5\sigma^3$-naphtho[1,8-*de*]triazine (**390**) (105mg, 0.6mmol) in DMSO (11ml). The solution was allowed to cool and poured into water (10ml) and extracted with ethyl acetate (5x10ml). The organic layer was washed with water, brine, and dried ($MgSO_4$). The solvent was removed by evaporation and the residue was purified by dry flash chromatography on 60H grade silica (35g) several times before being purified by preparative plate chromatography on Merck Kieselgel $60GF_{254}$ (25g). Diethyl ether (33.3%) in dichloromethane eluted 6,7-*diacetyl*-2-*methyl*-2$\lambda^5\sigma^3$-*acenaphtho*[5,6-*de*]*triazine* (**393**) (53mg, 31.7%) as a red solid, m.p. 201-202°C (dichloromethane) (Found: M^+, 291.101; $C_{17}H_{13}N_3O_2$ requires 291.1005); $\upsilon_{max.}(CHCl_3)$ 2928s, 2856m, 1710w, 1655m, 1613w, 1384vs, 1191m, 1168m, and 1069cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.96 (6H, s, COMe), 5.01 (3H, s, MeN), 8.08 (2H, d, J 7.5Hz), and 9.06 (2H, d, J 7.5Hz); δ_C (126MHz; $CDCl_3$) 31.4, 56.1, 104.8, 113.3, 119.8, 124.4, 132.6, 135.1, 144.15, and 199.7; *m/z* (200°C) 291 (M^+, 39.5%), 276 (M^+-Me, 100), 248 (M^+-COMe, 5.4), 205 (M^+-2COMe, 6.3), 177 (5.5), 163 (3.9), 150 (3.6), 75 (2.3), and 43 ($MeCO^+$, 17).

Besides this, two very minor unidentified red products (5mg total) were also eluted but could not be purified.

2,3-*Dimethyl bicyclo*[2.2.1]*hept*-2,5-*diene*-2,3-*dicarboxylate* (**396**)[117].–To freshly cracked cyclopentadiene (10ml) at –60°C, DMAD (**1**) (235mg, 1.7mmol) was added dropwise over a period of 30mins and stirred at –60°C for 4h. The temperature was allowed to warm to room temperature overnight. The reaction mixture was dissolved in diethyl ether (10ml) and purified on 60H grade silica (25g). Light petroleum (100%) eluted 2,3-dimethyl bicyclo[2.2.1]hept-2,5-diene-2,3-dicarboxylate (**396**) (147mg, 42.7%) as yellow oil, $\upsilon_{max.}(CHCl_3)$ 2952m, 2844m, 1718vs (COOMe), 1627m, 1560w, 1436s, 1324s, 1294vs, 1151s, 1101s,

1020m, 953w, 919w, and 870cm^{-1}; *m/z* (100°C) 208 (M^+, 69.6%), 193 (19.6), 176 (60.9), 161 (13.6), 149 (M^+-COOMe, 63.2), 118 (24.8), 105 (12.7), 90 (25), 77 (13.6), 66 ($C_5H_6^+$, 100), and 59 ($COOMe^+$, 27.3).

2,3-*Diacetylbicyclo*[2.2.1]*hept*-2,5-*diene* (**397**).–To hex-3-yne-2,5-dione (462mg, 4mmol) at –78°C was added freshly cracked cyclopentadiene (10ml). The temperature was allowed to warm to –12°C slowly and left at this temperature overnight. The reaction mixture was dissolved in diethyl ether (10ml) and purified on 60H grade silica (35g). Diethyl ether (26.7 to 40%) in light petroleum eluted 2,3-*diacetylbicyclo*[2.2.1]*hept*-2,5-*diene* (**397**) (411mg, 55.6%) as a colourless solid, m.p. 36-40°C (diethyl ether) (Found: C, 74.8; H, 6.8. $C_{11}H_{12}O_2$ requires C, 75.0; H, 6.8%); $\upsilon_{max.}$($CHCl_3$) 2997m, 2873w, 1663vs (CO), 1599s, 1422m, 1360s, 1312m, 1292vs, 1237s, 1195w, 1149m, 1090w, 917w, and 891cm^{-1}; δ_H (250MHz; $CDCl_3$) 1.87-2.04 (2H, ddt, J 1.5Hz, CH), 2.13 (6H, s, COMe), 3.7-3.86 (2H, dd, J 1.9Hz, CH), 6.75-6.77 (2H, t, J 1.9Hz); *m/z* (120°C) 176 (M^+, 48.9%), 161 (M^+-Me, 9.2), 133 (M^+-COMe, 34.1), 119 (8.3), 105 (8.5), 91 (14.5), 77 (4.9), 66 ($C_5H_6^+$, 80), and 43 ($MeCO^+$, 100).

2,3-*Dimethyl* 1,4-*diphenyl*-1,4-*epoxy*-1,4-*dihydronaphthalene*-2,3-*dicarboxylate* (**400**).–To a vigorously stirred solution of 1,3-diphenylisobenzofuran (195mg, 0.7mmol) in dry benzene (40ml) was added at room temperature DMAD (430mg, 3mmol). The reaction mixture was stirred for 22h. Evaporation of the solvent gave white crystals (268mg, 90%), m.p. 159-160°C (diethyl ether) (lit.[118] m.p. 158-160°C, 98%).

2,3-*Diacetyl*-1,4-*diphenyl*-1,4-*epoxy*-1,4-*dihydronaphthalene* (**401**).–To a vigorously stirred solution of 1,3-diphenylisobenzofuran (363mg, 1mmol) in dry diethyl ether (80ml) was added at room temperature hex-3-yne-2,5-dione (592mg, 5mmol) in dry diethyl ether (125ml). The reaction mixture was stirred for 22h. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (35g). Diethyl ether (33.3 to 40%) in light petroleum eluted 2,3-*diacetyl*-1,4-*diphenyl*-1,4-*epoxy*-1,4-*dihydronaphthalene* (**401**) (450mg, 88%) as colourless crystals, m.p. 120-125°C (diethyl ether) (Found: C, 81.9; H, 5.3. $C_{26}H_{20}O_3$ requires C, 82.1; H, 5.3%); $\upsilon_{max.}$($CHCl_3$) 1678vs, 1600w, 1455m, 1359m, 1308s, 1275m, 1008w, 703s, 647w, and 614cm^{-1}; δ_H (270MHz; $CDCl_3$) 2.11 (6H, s, Me), 7.18-7.22 (2H, q, ArH), 7.43-7.53 (5H, m, ArH), 7.55-7.59 (2H, q, ArH), 7.68-7.72 (5H, m, ArH); δ_C (69MHz; $CDCl_3$) 30.9, 94.5, 122.3, 126.1, 128.4, 129.0, 129.5, 133.3, 149.2, 159.7, and 198.9; *m/z* (100°C) 380 (M^+, 1.6%), 364 (M^+-O, 0.7), 337 (M^+-COMe, 57.9), 295 (4.4), 270 (M^+-DAA, 100), 209 (70), 193 (4.9), 77 (47.5), and 43 ($MeCO^+$, 18).

1,4-*Dimethyl*-5,10-*epoxy*-5,10-*dihydronaphtho*[2,3-*d*]*pyridazine* (**402**).–To a vigorously stirred solution of 2,3-diacetyl-1,4-diphenyl-1,4-epoxy-1,4-dihydronaphthalene (**401**) (103mg, 0.3mmol) in acetic acid (20ml) at room temperature was added hydrazine hydrate (0.2ml). The colour of the reaction mixture turns from yellow to pale green then back to yellow again. The reaction mixture was stirred for 2h 35min at room temperature and then poured into water (20ml) and extracted with ethyl acetate (5x10ml). The organic phase was washed with water, brine, and dried ($MgSO_4$). The solvent was removed by evaporation and the residue purified by dry flash chromatography (25g). Diethyl ether (100%) eluted 1,4-*dimethyl*-5,10-*epoxy*-5,10-*dihydronaphtho*[2,3-*d*]*pyridazine* (**402**) (74mg, 72.6%) as pale yellow crystals, m.p. 198-199°C

(dichloromethane) (Found: C, 82.9; H, 5.4; N, 7.2. $C_{26}H_{20}N_2O$ requires C, 83.0; H, 5.3; N, 7.45%); $\upsilon_{max.}(CHCl_3)$ 3009s, 2918s, 1733w, 1456s, 1389vs, 1353s, 1307m, 1110m, 1024s, and 870cm^{-1}; δ_H (270MHz; $CDCl_3$) 2.39 (6H, s, Me), 7.18-7.21 (2H, q, ArH), 7.5-7.58 (5H, m, ArH), 7.64-7.67 (2H, q, ArH), 7.85-7.88 (5H, m, ArH); δ_C (126MHz; $CDCl_3$) 20.0, 91.4, 123.1, 126.6, 128.9, 129.4, 129.8, 132.7, 148.65, 150.1, and 152.1; *m/z* (120°C) 376 (M^+, 100%), 347 (10.6), 333 (3.1), 320 (1.6), 305 (3.5), 270 (M^+-$C_6H_6N_2$, 17.7), 252 (1.7), 193 (M^+-$C_{12}H_{11}N_2$, 1.9), 175 (2), 99 (5.9), 77 (19.8), and 41 (MeCN, 14.2).

1,4-*Diphenylphthalazine* (**403**).–To a vigorously stirred solution of 1,3-diphenylisobenzofuran (14.8mg, 0.05mmol) and methanol (10ml), hydrazine hydrate (0.1ml) was added. Formation of precipitate was observed 10 min later. The solvent was removed and the residue was purified by preparative plate chromatography (25g). Dichloromethane (50%) in light petroleum eluted 1,4-diphenylphthalazine (**403**) (4.5mg, 29%) m.p. 196-197°C (lit.[119] 197.5-198.5°C).

o-Dibenzoylbenzene bis(phenyl hydrazone) (**406**).–To a vigorously stirred solution of 2,3-diacetyl-1,4-diphenyl-1,4-epoxy-1,4-dihydronapthalene (**401**) (114mg, 0.3mmol) and methanol (30ml) was added phenylhydrazine (0.2ml). The yellow reaction mixture turned colourless, greenish yellow, then yellow. It was poured into water and extracted with diethyl ether (5x10ml). The organic phase was washed with water, brine and dried over $MgSO_4$. Evaporation of the solvent gave yellow crystals (40mg, 28.6%); $\upsilon_{max.}(CHCl_3)$ 1603vs, 1557w, 1503s, 1494s, 1311w, 1252m, 1130m, 1068w, and 693cm^{-1}; *m/z* (130°C) 466 (M^+,4.7%), 435 (0.4), 372 (1.1), 359 (100), 268 (57.4), 190 (9), 165 (13.3), 93 (5.7), 77 (15.9), 65 (6.5), and 51 (3.7).

Phthalic acid.–To a vigorously stirred solution of 1-acetoxy-1,3-butadiene (64mg, 0.6mmol) in dry xylene (10ml) at reflux temperature, DMAD (222mg, 1.6mmol) was added and the reaction was then refluxed for 7h. The reaction mixture was allowed to cool to room temperature. The solvent was removed by evaporation and the residue purified by dry flash chromatography on 60H grade silica (25g). Diethyl ether (40 to 47%) in light petroleum eluted dimethyl phthalate (46mg, 41.5%) as a yellow oil, (lit.[57] 43%).

To dimethyl phthalate (46mg, 0.2mmol) in aq.EtOH (80%), sodium hydroxide (5g, 125mmol) was added and the reaction was then refluxed for 4h. The cooled reaction mixture was acidified with 30% sulphuric acid and extracted with diethyl ether (8x20ml), dried over $MgSO_4$, and filtered through charcoal. The filtrate on concentration gave phthalic acid in quantitative yield as white crystals, m.p. 208-209°C (lit. [57] m.p. 210-211°C).

1,2-*Diacetylbenzene* (**417**).–To a vigorously stirred solution of 1-acetoxy-1,3-butadiene (1.52g, 14mmol) in dry xylene (18ml) at reflux temperature, hex-3-yne-2,5-dione (575mg, 5mmol) in dry xylene (25ml) was added over a period of 25 min. The reaction was then refluxed for 6h. The reaction mixture was allowed to cool to room temperature. The solvent was removed by evaporation and the residue purified by dry flash chromatography on 60H grade silica (45g). Diethyl ether (32 to 36%) in light petroleum eluted 1,2-diacetylbenzene (**417**) as a yellow oil, which on trituration gave colourless crystals, (481mg, 56.8%), m.p. 38-40°C (lit.[97,120]m.p. 39-41°C) (diethyl ether) (Found: C, 73.8; H, 6.4 $C_{10}H_{10}O_2$ requires C, 74.1; H, 6.2%); (Found: M^+, 162.0681.Calc. for $C_{10}H_{10}O_2$ 162.0678); $\upsilon_{max.}$($CHCl_3$) 3013w, 2978w, 1694vs, 1268s, 1112w, and 961cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.46 (6H, s, COMe) and 7.5 (4H, s, ArH); *m/z* (120°C) 162 (M^+, 2.2%), 147 (M^+-Me, 100), 105 (4.2), 91 (23.2), 77 (6.1), and 43 ($COMe^+$,

14.8).

Further elution with diethyl ether (50 to 60%) in light petroleum eluted an unidentified red oil (1mg) as a minor product.(Found: M^+, 364.131. $C_{22}H_{20}O_5$ requires 364.1305); $\upsilon_{max.}(CHCl_3)$ 3693w, 3025w, 1745w, 1708vs, 1603w, 1357m, and 896cm^{-1}; *m/z* (190°C) 364 (M^+, 20.1%), 321 (M^+-COMe, 33.5), 220 (65.7), 192 (45.5), 177 (5.5), 147 (17.7), 105 (3.9), 91 (6.6),77 (4.4), and 43 ($COMe^+$, 100).

8.4 For Chapter Six

Substituted Norbornadien-7-ones

Dimethyl 3,4,5,6-*tetraphenylbenzene*-1,2-*dicarboxylate* (**421**).–To a vigorously stirred solution of tetracyclone (141mg, 0.4mmol) in *o*-dichlorobenzene (15ml) at reflux temperature, DMAD (**1**) (956mg, 7mmol) in *o*-dichlorobenzene (15ml) was added dropwise. The reaction mixture was refluxed for 20min and then allowed to cool to room temperature. The precipitate formed was filtered off and washed several times with light petroleum to afford dimethyl 3,4,5,6-tetraphenylbenzene-1,2-dicarboxylate (**421**) (106mg, 57.9%) as white crystals, m.p. 259-260°C (lit.[121], 89%, m.p. 257-258°C).

1,2-*Diacetyl*-3,4,5,6-*tetraphenylbenzene* (**423**).–To a vigorously stirred solution of tetracyclone (268mg, 0.7mmol) in dry xylene (10ml) at reflux temperature was added hex-3-yne-2,5-dione (1.7g, 15.5mmol) in dry xylene (40ml) over 30min and the solution was refluxed for a further 2h 30min. The reaction was cooled, the solvent removed by evaporation and the residue purified by dry flash chromatography on 60H grade silica (45g). Diethyl ether (5 to 10%) in light petroleum eluted 1,2-*diacetyl*-3,4,5,6-*tetraphenylbenzene* (**423**) (60mg, 18.4%) as white solid, m.p. 265-268°C (diethyl ether) (Found: C, 87.5; H, 5.7. $C_{34}H_{26}O_2$ requires C, 87.55; H, 5.6%); $\upsilon_{max.}$($CHCl_3$) 2928m, 1794w, 1727vs (CO), 1682w, 1605vs, 1496w, 1447w, 1371w, and 1026cm^{-1}; δ_H (270MHz; $CDCl_3$) 1.88 (6H, s,COMe), 6.7-6.74 (5H, q, Ph), 6.80-6.90 (5H, t, Ph), 6.99-7.02 (5H, q, Ph), and 7.13-7.12 (5H, t, Ph); δ_C (126MHz; $CDCl_3$) 31.8 (Me), 125.9, 126.8, 127.3, 127.9, 130.6, 131.1, 137.3, 138.3, 138.6, 140.8, 141.9, and 207.15 (CO); *m/z* (180°C) 466 (M^+, 40%), 451 (M^+-Me, 100), 389 (M^+-Ph, 2.8), 302 (6.8),

224 (4.4), 200 (2.4), 77 (Ph^+, 13.8), and 43 ($MeCO^+$, 16.4).

Dimethyl 3,6-*dimethyl*-4,5-*diphenylbenzene*-1,2-*dicarboxylate* (**426**).–To a vigorously stirred solution of 2,5-dimethyl-3,4-diphenylcyclopentadienone (375mg, 1.4mmol) in dry xylene (20ml) at reflux temperature, DMAD (1.69g, 12mmol) in dry xylene (10ml) was added dropwise and refluxed for 5h. The reaction mixture was then allowed to cool to room temperature. The solvent was removed by evaporation and the residue was washed several times with dichloromethane after filtration to afford dimethyl 3,6-dimethyl-4,5-diphenyl-benzene-1,2-dicarboxylate (**426**) (361mg, 66.9%) as white crystals, m.p. 214-216°C (lit.[121a] 90%, m.p.212°C).

Dimethyl 3,6-*diethyl*-4,5-*diphenylbenzene*-1,2-*dicarboxylate* (**429**).–To a vigorously stirred solution of 2,5-diethyl-3,4-diphenylcyclopentadienone (135mg, 0.5mmol) in dry benzene (10ml) at reflux temperature, DMAD (236mg, 1.7mmol) in dry benzene (10ml) was added dropwise. The reaction mixture was refluxed for 1h 30min and then allowed to cool to room temperature. The precipitate formed was filtered off and washed several times with light petroleum to afford dimethyl 3,6-diethyl-4,5-diphenylbenzene-1,2-dicarboxylate (**429**) (91mg, 48.3%) as white crystals, m.p. 217-219°C

1,2,3,4-*Tetraphenylnaphthalene* (**432a**).–To a vigorously stirred solution of tetracyclone (70mg, 0.2mmol) in dry dichloromethane (10ml) at –78°C, 1-aminobenzotriazole (41mg, 0.3mmol) in dry dichloromethane (10ml) and lead tetra-acetate (112mg, 0.25mmol) in dry dichloromethane (10ml) were added dropwise simultaneously. After 20min the reaction mixture turned colourless. The reaction

mixture was allowed to warm up to room temperature over 3h. The solvent was removed by evaporation and the residue was purified by dry flash chromatography on 60H grade silica (25g). Diethyl ether (7%) in light petroleum eluted 1,2,3,4-tetraphenylnaphthalene (**432a**) (73mg, 92.7%) as pale yellow crystals, m.p. 197-199°C (lit.[121&122] 93%, m.p. 203-204°C).

1-*Methyl*-2,3,4-*triphenylnaphthalene* (**432b**).–To a vigorously stirred solution of 2-methyl-3,4,5-triphenylcyclopentadienone (39mg, 0.1mmol) in dry dichloromethane (10ml) at –78°C, 1-aminobenzotriazole (40mg, 0.3mmol) in dry dichloromethane (10ml) and lead tetra-acetate (252mg, 0.6mmol) in dry dichloromethane (10ml) were added dropwise simultaneously. After 3min the reaction mixture turned colourless. The reaction mixture was allowed to warm up to room temperature over 3h. The solvent was removed by evaporation and the residue was purified by dry flash chromatography on 60H grade silica (25g). Diethyl ether (7%) in light petroleum eluted 1-methyl-2,3,4-triphenylnaphthalene (**432b**) (40mg, 88%) as pale yellow crystals, m.p. 164-165°C (lit.[122] 64%, m.p. 165-166°C).

1,4-*Diethyl*-2,3-*diphenylnaphthalene* (**432c**).–To a vigorously stirred solution of 2,5-diethyl-4,5-diphenylcyclopentadienone (61mg, 0.2mmol) in dry dichloromethane (10ml) at –78°C, 1-aminobenzotriazole (49mg, 0.4mmol) in dry dichloromethane (10ml) and lead tetra-acetate (286mg, 0.6mmol) in dry dichloromethane (10ml) were added dropwise simultaneously. A few min after complete addition, the reaction mixture turned colourless. The reaction mixture was allowed to warm up to room temperature over 3h. The solvent was removed by evaporation and the residue was purified by dry flash chromatography on 60H grade silica (25g). Diethyl ether (7%) in light petroleum

eluted 1,4-diethyl-2,3-diphenylnaphthalene (**432c**) (44mg, 61.8%) as pale yellow crystals, m.p. 140-141°C (lit.[122] 60%, m.p. 141-142°C).

1-*Isopropylidenaminobenzotriazole* (**434**).–1-Aminobenzotriazole (52mg, 0.4mmol) in acetone (10ml) was stirred at room temperature with molecular sieves 4Å for 16h. The solvent was evaporated and the residue was purified by dry flash chromatography on 60H grade silica (25g). Diethyl ether (47 to 73%) in light petroleum eluted 1-*isopropylidenaminobenzotriazole* (**434**) (55mg, 82%) as an oil, (Found: C, 62.4; H, 6.05; N, 32.3. $C_9H_{10}N_4$ requires C, 62.1; H, 5.75; N, 32.2%); $\upsilon_{max.}$($CHCl_3$) 3007s, 1636w, 1615w, 1594w, 1493w, 1449s, 1433w, 1383s, 1370s, 1289w, 1269s, 1241s, 1082s, 1049s, 996w, and 920cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.18 (3H, s, Me), 2.27 (3H, s, Me), and 7.25-7.93 (4H, m, ArH); δ_C (126MHz; $CDCl_3$) 20.76, 25.49, 109.61, 118.68, 123.56, 126.82, 130.16, 143.6, and 173.11; *m/z* (130°C) 174 (M^+, 100%), 131 (32), 117 (53.3), 103 (52.5), 90 (57.9), 78 (39.5), 63 (9.4), 56 (13), 50 (15.5), and 41 (15.3). This compound was prepared in a similar way in the literature but in the presence of potassium permanganate.[122b] Our work indicates that potassium permanganate is not required for the formation of 1-isopropylidenaminobenzotriazole (**434**).

9,14-*Diphenyl*-9,14-*dihydrodibenz*[*a,c*]*anthracene*-9,14-*methanone* (**267b**).–To a vigorously stirred solution of phencyclone (46mg, 0.12mmol) in dry dichloromethane (10ml) at –78°C, lead tetraacetate (LTA) (368mg, 0.8mmol) in dry dichloromethane (20ml) and 1-aminobenzotriazole (74mg, 0.55mmol) in dry dichloromethane (15ml) were simultaneously added dropwise over a period of 30min. The reaction mixture was allowed to warm to room temperature overnight. The solvent was removed by evaporation and the residue purified by dry flash chromatography on 60H grade silica (25g). Diethyl ether (0 to 7%) in

light petroleum eluted biphenylene (14mg, 33%) as pale yellow crystals, m.p. 110-114°C (lit.[122a] m.p. 113-114°C).

Further elution with diethyl ether (100%) gave 9,14-*diphenyl*-9,14-*dihydrodibenz*[*a*,*c*]*anthracene*-9,14-*methanone* (**267b**) (37mg, 67%) as colourless crystals, m.p. 163-167°C, with carbon monoxide evolution, (diethyl ether) (Found: C, 91.7; H, 4.9. $C_{35}H_{22}O$ requires C, 91.7; H, 4.8%); $\upsilon_{max.}(CHCl_3)$ 3066w, 3036w, 3011m, 1805vs (CO), 1500m, 1457m, 1110w, 1033w, 984w, 927w, 915w, and 810cm^{-1}; δ_H (500MHz; $CDCl_3$) 7.21-7.23 (2H, m), 7.32-7.35 (2H, m), 7.55-7.59 (2H, m), 7.77-7.79 (2H, m), 7.47-7.51 (10H, m), 8.04-8.07 (2H, m), and 8.69-8.72 (2H, m); δ_C (126MHz; $CDCl_3$) 123.51, 123.56, 125.85, 125.98, 126.11, 126.56, 126.97, 127.84, 128.53, 130.50, 132.60, 142.14, 144.72, and 194.90 (CO); *m/z* (180°C) 458 (M^+, 0.2%), 442 (0.8), 430 (M^+-CO, 100), 352 (21.1), 276 (2.9), 199 (7.6), 176 ($C_{14}H_8^+$, 15.4), and 77 (Ph^+, 30.2).

1,3-*Dihydro*-1,3-*diphenyl*-2-*keto*-2*H*-*cyclopenta*[*l*]*phenanthrene* (**446**).– Phencyclone (57mg, 0.2mmol) in tetralin (31ml) was heated at 110°C for 45min. The disappearance of the dark green colour of the reaction mixture indicated the completion of the reaction. The reaction mixture was allowed to cool to room temperature and the solvent was removed by evaporation under pressure. The residue, 1,3-dihydro-1,3-diphenyl-2-keto-2*H*-cyclopenta[*l*]phenanthrene (**446**) (10mg, 17%) was washed with light petroleum-dichloromethane (1:1) and dried; m.p. 314°C; $\upsilon_{max.}(CHCl_3)$ 1747cm^{-1} (lit.[125] m.p. 314°C, $\upsilon_{max.}(CHCl_3)$ 1747cm^{-1}); *m/z* (240°C) 384 (M^+, 100%), 356 (M^+-CO, 23.3), 279 (M^+-PhCO, 77.4), 265 (M^+-$PhCH_2CO$, 7.1), 252 (6.0), 178 (18.2), 163 (5.3), 150 (2.7), and 77 (Ph^+, 1.8). The i.r. absorption of phencyclone is 1705cm^{-1}. The i.r. absorption of 9,10,11,12-tetraphenyl-9,12-dihydrodibenz[*a*,*c*]naphthalene-9,12-methanone (**267a**) claimed to have been isolated was found to be 1750cm^{-1}.[86] The i.r. absorption

of bridged-carbonyl compounds are normally around 1780cm^{-1}; thus indicating that the product isolated by the Indian workers was not compound (**267a**) but was (**446**).

9,14-*Di-isopropyl*-9,14-*dihydrodibenz*[*a,c*]*anthracene*-9,14-*methanone* (**448**).–To a vigorously stirred solution of 1,3-di-isopropylcyclopenta[*l*]phenanthren-2-one (18mg, 0.06mmol) in dry dichloromethane (10ml) at –78°C, lead tetraacetate (LTA) (25mg, 0.06mmol) in dry dichloromethane (10ml) and 1-aminobenzotriazole (7mg, 0.05mmol) in dry dichloromethane (10ml) were simultaneously added dropwise over a period of 10min. The reaction mixture was allowed to warm to room temperature over 3h and then filtered. The fitrate was concentrated and the residue purified by preparative plate chromatography on Merck Kieselgel 60GF$_{254}$ (25g). Diethyl ether (50%) in light petroleum eluted a pale yellow solid, m.p. 125-130°C (diethyl ether) tentatively assigned as 9,14-*di-isopropyl*-9,14-*dihydrodibenz*[*a,c*]*anthracene*-9,14-*methanone* (**448**) (3mg, 13.4%); $\upsilon_{max.}$(CHCl$_3$) 1779vs (CO), 1603w, 1500w, 1459w, 1390w, and 950cm^{-1}; δ_H (500MHz; CDCl$_3$) 1.50 (6H, d, J 7Hz, Me), 1.56 (6H, d, J 7Hz, Me), 3.79 (2H, m, J 7Hz, CH), 7.06-7.09 (2H, m), 7.43-7.46 (2H, m), 7.57-7.63 (4H, m), 8.41-8.43 (2H, m), and 8.69-8.72 (2H,m); δ_C (126MHz; CDCl$_3$) 15.27, 18.68, 19.20, 121.84, 123.43, 124.49, 125.35, 126.14, 126.46, 128.01, 130.02, 141.68, 145.66, and 194.07 (CO); *m/z* (220°C) 390 (M^+, 8.2%), 362 (M^+-CO, 100), 347 (M^+-C_3H_7, 8.8), 332 (2.7), 316 (M^+-C_6H_4, 0.1), 305 (76.7), 287 (4.2), 274 (3.1), 202 (1.7), 190 (1.9), 165 (7.2), and 43 ($C_3H_7^+$, 6.1).

Dimethyl 1,4-*diphenyldibenz*[*a,c*]*naphthalene*-2,3-*dicarboxylate* (**449**).–To phencyclone (64mg, 0.2mmol) was added DMAD (658mg, 5mmol) under nitrogen and kept in the dark at room temperature for 3 days. The precipitate

formed was filtered, washed several times with diethyl ether and dried to give dimethyl 1,4-diphenyldibenz[*a*,*c*]napthalene-2,3-dicarboxylate (**449**) (54mg, 65%) as greenish yellow crystals, m.p. 269-271°C (lit.[127] 81%, m.p. 272-273°C).

9,14-*Diphenyl*-9,9*a*,13*a*,14-*tetrahydro*-9,14-*methanodibenz*[*a*,*c*]*anthracene*-10,13,15-*trione* (**450**).–A vigorously stirred solution of phencyclone (813mg, 2.1mmol) and *p*-benzoquinone (269mg, 2.5mmol) in chlorobenzene (20ml) was refluxed for 30min. The reaction mixture was allowed to cool to room temperature and methanol (5ml) was added. The pale yellow crystals precipitated were filtered off and washed several times with light petroleum to afford 9,14-diphenyl-9,9a,13a,14-tetrahydro-9,14-methanodibenz[*a*,*c*]anthracene-10,13,15-trione (**450**) (99mg, 94.9%), m.p. 270-271°C (lit.[127] 93%, m.p. 272-273°C).

9,14-*Diphenyldibenz*[*a*,*c*]*anthracene* (**455**).–9,14-Diphenyl-9,14-dihydrodibenz[*a*,*c*]anthracene-9,14-methanone (**267b**) (40mg, 0.1mmol) in dry benzene (30ml) was refluxed for 7h. The reaction mixture was allowed to cool to room temperature slowly. The solvent was removed by evaporation and the residue on purification by recrystallisation afforded 9,14-diphenyldibenz[*a*,*c*]anthracene (**455**) (20mg, 53.3%), m.p. 278-280°C (lit.[86] m.p. 276°C); $\upsilon_{max.}$($CHCl_3$) 3017m, 3012m, 1445m, 1427s, 1260m, 1151m, 1129m, 1110w, 961s, 919w, and 613cm^{-1}; absence of a strong carbonyl stretch at 1805cm^{-1} indicates that compound (**267b**) had undergone decarbonylation; *m/z* (150°C) 430 (M^+,100%), 352 (22.1), 199 (9.3), 187 (4.2), and 176 (12.9).

8.5 For Chapter Seven

1,3-Dithioles

Tetramethyl tetrathiafulvalenetetracarboxylate (**467**).–To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol) and carbon disulphide (0.8ml, 1.01g, 13.3mmol) was added DMAD (**1**) (765mg, 5.4mmol) at –23°C. The reaction mixture was allowed to warm to room temperature slowly. The black precipitate of compound (**467**) was filtered off and dried (209mg, 17.8%) m.p. 166-168°C (lit.[135] m.p. 169-170°C, 10%); $\upsilon_{max.}$(nujol) 1741vs, 1715vs, 1676m, 1572s, 1286s, 1253vs, 1099m, 1025s, 976m, 859w, 770m, and 712cm^{-1}; *m/z* (120°C) 436 (M^+, 100%), 378 (M^+-COOMe, 15.3), 320 (1.4), 262 (M^+-$C_6H_6O_4S$, 20.7), 204 (3.2), 178 (4.6), 134 (4.9), 122 (9.1), 92 (9.9), 76 (20.1), and 59 (COOMe$^+$, 19.9).

Dimethyl 2-benzylidene-1,3-dithiole-4,5-dicarboxylate (**473**).–To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and benzaldehyde (0.5ml, 522mg, 5mmol) at –23°C, DMAD (754mg, 5mmol) in dry diethyl ether (4ml) was added dropwise. The colour of the reaction mixture turns from deep reddish-purple to reddish orange. It was allowed to warm to room temperature slowly. The orange precipitate (99mg, 6.5%) was filtered off and dried, m.p. 96-97°C, $\upsilon_{max.}$(nujol) 1742vs, 1719vs, 1589s, 1555m, 1489w, 1343w, 1240vs, 1162w, 1095m, 1016m, 997m, 924w, 810m, 749m, and 686cm^{-1}; *m/z* (100°C) 308 (M^+,100%), 277 (M^+-OMe, 3.6), 250 (M^+-$COOCH_2$, 1.2), 189 (6.2), 165 (2), 134 (34.1), 102 (2.1), 90 (5.9), 77 (Ph$^+$, 2.3), and 59 (COOMe$^+$, 5.2), (lit.[135 & 138] m.p. 97-98°C, 48%); $\upsilon_{max.}$(nujol) 1740, 1720, 1590, 1550, and 1500cm^{-1}).

4,5-*Diacetyl*-2-*benzylidene*-1,3-*dithiole* (**474**).–To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and benzaldehyde (0.5ml, 522mg, 5mmol), hex-3-yne-2,5-dione (**295**) (551mg, 5mmol) in dry diethyl ether (2ml) was added at –40°C. The reddish-purple coloured reaction turned brown. The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Dichloromethane (100%) eluted 4,5-*diacetyl*-2-*benzylidene*-1,3-*dithiole* (**474**) (82mg, 6%) as a dark red viscous oil (Found: C, 61.1; H, 4.4. $C_{14}H_{12}O_2S_2$ requires C,60.9; H, 4.4%); $\upsilon_{max.}(CHCl_3)$ 1704vs, 1681s, 1584s, 1566vs, 1532s, 1360s, 1235vs, and 1202cm^{-1}; *m/z* (120°C) 276 (M^+, 100%), 234 (M^+-COMe, 61), 192 (42), 178 (3.8), 134 (M^+-$C_6H_6O_2S$, 47.8), 102 (M^+-$C_6H_6O_2S_2$, 4.4), 90 (M^+-$C_7H_6O_2S_2$, 10.2), 77 (Ph^+, 5.7), and 43 ($MeCO^+$, 55.8).

2-*Benzylidene*-4,7-*dimethyl*-1,3-*dithiolo*[4,5-*d*]*pyridazine* (**475**).–To a stirred solution of 4,5-diacetyl-2-benzylidene-1,3-dithiole (**474**) (68mg, 0.25mmol) and glacial acetic acid (5ml), hydrazine hydrate (0.5ml) was added slowly at room temperature. The reaction mixture was stirred for an hour at this temperature, then poured into water (20ml) and extracted with ethyl acetate; the organic layer was dried ($MgSO_4$) and evaporated to give 2-*benzylidene*-4,7-*dimethyl*-1,3-*dithiolo*[4,5-*d*]*pyridazine* (**475**) (54mg, 80.6%) as a yellow soild, m.p. 141-145°C (dichloromethane) (Found: C, 61.5; H, 4.4; N, 10.1. $C_{14}H_{12}N_2S_2$ requires C, 61.8; H, 4.4; N, 10.3%); $\upsilon_{max.}(CHCl_3)$ 3007m, 1588vs, 1569s, 1539w, 1495m, 1445m, 1430m, 1400s, 1243w, 1008w, and 932cm^{-1}; δ_H (500MHz; $CDCl_3$) 2.57 (3H, s, Me), 2.59 (3H, s, Me), 6.70 (1H, s, CH), and 7.25-7.43 (5H, m, ArH); *m/z* (170°C) 272 (M^+, 100%), 243 (0.5), 214 (0.1), 166 (M^+-$C_6H_6N_2$, 2.9), 134 (M^+-$C_6H_6N_2S$, 9.9), 102 (M^+-$C_6H_6N_2S_2$, 2.1), 90 (M^+-$C_7H_6N_2S_2$, 4.5), and 77 (M^+-$C_8H_7N_2S_2$, 2.8).

Dimethyl 2-(2-*hydroxybenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**477**).– To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and salicylaldehyde (1ml, 1.146g, 9mmol) in dry dichloromethane (10ml) at –45°C, DMAD (**1**) (699mg, 5mmol) in dry dichloromethane (5ml) was added. The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue was purified by preparative plate chromatography on Merck Kieselgel $60GF_{254}$ grade silica (25g). Light petroleum (100%) eluted *dimethyl* 2-(2-*hydroxybenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**477**) (259mg, 16.2%) as a red solid, m.p. 122-124°C (dichloromethane) (Found: C, 51.9; H, 3.8. $C_{14}H_{12}O_5S_2$ requires C, 51.9; H, 3.7%); $\upsilon_{max.}(CHCl_3)$ 1733s, 1582m, 1455m, 1336m, 1263vs, 1098m, and 1030cm^{-1}; δ_H (250MHz; $CDCl_3$) 3.83 (3H, s, MeOCO), 3.87 (3H, s, MeOCO), 5.14 (1H, br, OH), 6.53 (1H, s, CH), and 6.79-7.29 (4H, m, ArH); *m/z* (210°C) 324 (M^+, 100%), 293 (M^+-MeO, 4.7), 285 (4.4), 279 (2), 264 (2.6), 233 (1.8), 200 (17.1), 193 (1.1), 183 (1.4), 161 (9), 149 (46.3), 118 (M^+-$C_6H_6O_4S_2$, 23.9), 105 (1.7), 90 (8.8), 78 (6.2), and 59 ($MeOCO^+$, 8.3).

Dimethyl 2-(2-*hydroxy*-3-*methoxycarbonyl*-4-*methylbenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**479**).–To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and methyl 3-formyl-2-hydroxy-4-methylbenzoate (335mg, 1.7mmol) in dry dichloromethane (16ml) at –70°C, DMAD (535mg, 3.8mmol) in dry dichloromethane (10ml) was added. The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Diethyl ether (33%) in light petroleum eluted *dimethyl* 2-(2-*hydroxy*-3-*methoxycarbonyl*-4-*methylbenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**479**) (338mg, 49.4%) as a yellow solid, m.p. 89-93°C (dichloromethane) (Found: C, 51.15; H, 3.9. $C_{16}H_{16}O_7S_2$ requires C, 51.1; H,

4.2%); $\upsilon_{max.}(CHCl_3)$ 3031m, 3010m, 1733s, 1674s, 1615m, 1590s, 1490w, 1439s, 1332s, 1258vs, 1202s, 1155s, 1096m, 1030m, and 541cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.30 (3H, s, Me), 3.76 (3H, s, MeOCO), 3.82 (3H, s, MeOCO), 3.92 (3H, s, MeOCO), 6.27 (1H, s, CH), 6.73 (1H, d, J 7.5Hz), 6.68 (1H, d, J 7.5Hz), and 11.28 (1H, s, OH); *m/z* (160°C) 396 (M^+, 42.4%), 364 (100), 348 (0.4), 336 (7), 316 (0.5), 305 (5.8), 277 (2.4), 261 (3.9), 245 (1.2), 233 (0.8), 221 (2.8), 190 (M^+-$C_6H_6O_4S_2$, 11.6), 182 (6), 166 (15.1), 161 (5.9), 134 (6.5), 129 (1.4), 118 (2.6), 102 (2.3), 95 (1.4), 90 (4.1), 77 (1.3), and 59 ($MeOCO^+$, 3.8).

Dimethyl 2-(2-*carboxybenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**481**).– To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and 2-carboxybenzaldehyde (335mg, 2.2mmol) in dry dichloromethane (10ml) at –45°C, was added DMAD (**1**) (419mg, 3mmol). The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Diethyl ether (40 to 47%) in light petroleum eluted *dimethyl* 2-(2-*carboxybenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**481**) (530mg, 67.4%) as an orange solid, m.p. 136-138°C (dichloromethane) (Found: C, 51.0; H, 3.55. $C_{15}H_{12}O_6S_2$ requires C, 51.1; H, 3.4%); $\upsilon_{max.}(CHCl_3)$ 1768vs, 1586w, 1468w, 1437m, 1352w, 1286s, 1202m, 1130w, 1088m, 1067m,940m, 713w, and 692cm^{-1}; δ_H (250MHz; $CDCl_3$) 3.83 (3H, s, MeOCO), 3.86 (3H, s, MeOCO), 6.62 (1H, s, CH), 6.62-7.27 (4H, m, ArH); *m/z* (110°C) 352 (M^+, 9.8%), 339 (1.8), 315 (2.1), 279 (2.1), 255 (2.1), 248 (1.2), 219 (3.4), 205 (1.1), 197 (2.6), 189 (1.1), 179 (3.3), 163 (5.1), 133 (66.3), 122 (48.3), 105 (100), 77 (38.8), 59 ($MeOCO^+$,8.7), and 57 (9.7).

Dimethyl 2-(7-*benzyloxy*-4-*bromo*-6-*methoxyindole*-2-*methylidene*-1,3-*dithiole*-4,5-*dicarboxylate* (**483**).–To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and 7-benzyloxy-4-bromo-6-methoxyindole-2-carboxaldehyde (347mg, 0.96mmol) in dry diethyl ether (20ml) at –78°C, DMAD (**1**) (808mg, 5.7mmol) in dry diethyl ether (30ml) was added. The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue was purified by preparative plate chromatography on Merck Kielselgel $60GF_{254}$ grade silica (20g). Dichloromethane (50%) in light petroleum eluted *dimethyl* 2-(7-*benzyloxy*-4-*bromo*-6-*methoxyindole*-2-*methylidene*-1,3-*dithiole*-4,5-*dicarboxylate* (**483**) (121mg, 22.4%) as a dark purple solid, m.p.162-165°C (chloroform) (Found: M^+, 560.9915. $C_{24}H_{20}BrNO_6S_2$ requires M^+, 560.9911); $\upsilon_{max.}(CHCl_3)$ 1733vs, 1584w, 1525w, 1503w, 1456w, 1437m, 1265vs, 1203w, 1103w, 1027w, and 700cm^{-1}; δ_H (250MHz; $CDCl_3$) 3.85 (3H, s, OMe), 3.87 (3H, s, COOMe), 3.89 (3H, s, COOMe), 5.13 (2H, t, CH_2Ph), 6.24 (1H, s), 7.01 (1H, s, CH), 7.12-7.5 (6H, m, ArH), 7.77 (1H, br s, NH); *m/z* (180°C) 563 (M^+, 18.5%), 472 (M^+-$PhCH_2$, 18.9), 391 (9.1), 363 (15.8), 174 (3.4), 119 (2.5), 91 (64.1), and 65 (10.1).

Dimethyl 2-(2-*formylbenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**484**).–To a stirred solution of tributyl phosphine (2ml, 1.624g, 8mmol), carbon disulphide (5ml, 6.33g, 83mmol) and *o*-phthalaldehyde (140mg, 1mmol) at –20°C was added DMAD (**1**) (593mg, 4.2mmol). The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue was purified by preparative plate chromatography on Merck Kielselgel $60GF_{254}$ grade silica (20g). Dichloromethane (25%) in light petroleum eluted *dimethyl* 2-(2-*formylbenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**484**) (66mg, 18.8%) as an orange-red solid, m.p. 118-120°C (dichloromethane) (Found: C, 53.4; H, 3.5.

$C_{15}H_{12}O_5S_2$ requires C, 53.6; H, 3.6%); $\upsilon_{max.}$(nujol) 1711vs, 1690s, 1583s, 1431s, 1298vs, 1211m, 1192w, 1094w, 1039w, 922w, 813w, 759w, 709w, and 638cm^{-1}; δ_H (250MHz; $CDCl_3$) 3.82 (3H, s,MeOCO), 3.87 (3H, s, MeOCO), 7.37-7.84 (4H, m, ArH), 7.39 (1H, s, CH), 10.25 (1H, s, CHO); *m/z* (80°C) 336 (M^+, 20.5%), 305 (M^+-MeO, 2.7), 277 (M^+-MeOCO, 0.8), 166 (10.4), 161 (2.7), 134 (11.9), 121 (5.2), 102 (2.1), 90 (8.1), and 59 ($MeOCO^+$, 3.6).

Dimethyl 2-(4-*formylbenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**487**).– To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and terephthalaldehyde (317mg, 2.4mmol) in dry dichloromethane (5ml) at –32°C was added DMAD (785mg, 5.5mmol) in dry dichloromethane (2ml) over a period of 4min and after a further 20min at this temperature, the reaction mixture was allowed to warm to room temperature slowly. The orange precipitate was filtered, dried and recrystallised from dichloromethane to afford *dimethyl* 2-(4-*formylbenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**487**) (459mg, 57.7%) as an orange solid, m.p. 78-81°C (dichloromethane) (Found: C, 53.6; H, 3.5. $C_{15}H_{12}O_5S_2$ requires C, 53.6; H, 3.6%); $\upsilon_{max.}$(nujol) 1756s, 1741m, 1724m, 1713s, 1693vs, 1586s, 1547s, 1434m, 1291m, 1245vs, 1177s, 1094m, 853m, 795m, 773m, and 513cm^{-1}; δ_H (270MHz; $CDCl_3$) 3.87 (3H, s, MeOCO), 3.88 (3H, s, MeOCO), 6.50 (1H, s, CH), 7.35 (2H, d, J 7.5Hz), 7.87 (2H, d, J 7.5Hz), and 9.95 (1H, s, CHO); *m/z* (170°C) 336 (M^+, 100%), 305 (M^+-MeO, 3.5), 278 (1.4), 272 (0.6), 241 (0.7), 217 (1.8), 206 (M^+-$C_5H_6O_4$, 0.8), 161 (14.4), 134 (13.5), 133 (13), 121 (2.1), 105 (M^+-$C_8H_7O_4S_2$, 4.9), 89 (M^+-$C_8H_7O_5S_2$, 8.6), 77 (M^+-$C_9H_7O_5S_2$, 3.9) and 59 ($MeOCO^+$, 5.6).

4,5-*Diacetyl*-2-(4-*formylbenzylidene*)-1,3-*dithiole* (**489**).–To a stirred solution of tributyl phosphine (0.4ml, 325mg, 1.6mmol), carbon disulphide (0.7ml, 886mg, 11.7mmol), terephthalaldehyde (322mg, 2.4mmol) in dry dichloromethane (4ml) at –78°C was added hex-3-yne-2,5-dione (**295**) (275mg, 2.5mmol) in dry dichloromethane (5ml). The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (25g). Dichloromethane (50%) in light petroleum eluted 4,5-*diacetyl*-2-(4-*formylbenzylidene*)-1,3-*dithiole* (**489**) (345mg, 47.2%) as a bright red solid, m.p. 149-153°C (chloroform) (Found: C, 59.1; H, 3.9. $C_{15}H_{12}O_3S_2$ requires C, 59.2; H, 3.9%); $\upsilon_{max.}$(nujol) 1685vs, 1603m, 1568vs, 1553s, 1421w, 1356w, 1314w, 1231s, 1209s, 1167s, 982w, 850m, 793m, and 603cm^{-1}; δ_H (250MHz; $CDCl_3$) 2.41 (3H, s, Ac), 2.43 (3H, s, Ac), 6.54 (1H, s, CH), 7.36 (2H, d, J 7.5Hz), 7.86 (2H, d, J 7.5Hz), 10.94 (1H, s, CHO); *m/z* (180°C) 304 (M^+, 100%), 262 (M^+-$COCH_2$, 60), 220 (36.4), 191 (3.8), 167 (5.1), 161 (19.8), 149 (21.9), 133 (9), 121 (2.7), 112 (2.3), 100 (3.6), 89 ($C_7H_5^+$,15.7), 77 (2.4), and 43 ($MeCO^+$, 53.7).

Tetramethyl 1,4-*phthalalylidene*-2,2'-*bis*(1,3-*dithiole*)-4,4',5,5'-*tetracarboxylate* (**488**).

Method A – *from terephthalaldehyde*

To a stirred solution of tributyl phosphine (1.5ml, 1.218g, 6mmol), carbon disulphide (2ml, 2.52g, 33mmol) and terephthalaldehyde (702mg, 5.2mmol) in dry dichloromethane (10ml) at –40°C was added DMAD (**1**) (3.273g, 23mmol). The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Chloroform (100%) eluted *tetramethyl* 1,4-*phthalalylidene*-2,2'-

bis(1,3-*dithiole*)-4,4',5,5'-*tetracarboxylate* (**488**) (210mg, 7.5%) as a red solid, m.p. 226-228°C (chloroform) (Found: C, 48.8; H, 3.4. $C_{22}H_{18}O_8S_4$ requires C, 49.1; H, 3.35%); $\upsilon_{max.}$(nujol) 1734s (CO), 1587s, 1436m, 1265vs, 1096w, 1028w, 850w, and 512cm^{-1}; δ_H (250MHz; $CDCl_3$) 3.85 (6H, s, MeOCO), 3.86 (6H, s, MeOCO), 6.43 (2H, s, CH), and 7.21 (4H, s , ArH); *m/z* (180°C) 538 (M^+, 100%), 507 (M^+-MeO, 1.5), 480 (4.3), 364 (M^+-$C_6H_6O_4S$, 17), 352 (M^+-$C_7H_6O_4S$, 0.9), 320 (M^+-$C_6H_6O_4S_2$, 0.8), 306 (0.9), 269 (1.5), 261 (0.9), 245 (0.8), 221 (0.6), 210 (0.8), 202 (0.5), 190 (11.5), 182 (3.1), 178 (1.4), 158 (2.5), 145 (2.1), 134 (1.3), 102 (1.8), 95 (1.1), and 59 (MeOCO$^+$,2.4).

Method B – *from dimethyl* 2-(4-*formylbenzylidene*)-1,3-*dithiole*-4,5-*dicarboxylate* (**487**)

To a stirred solution of tributyl phosphine (0.5ml, 406mg, 2mmol), carbon disulphide (0.8ml, 1.01g, 13.3mmol) and dimethyl 2-(4-formylbenzylidene)-1,3-dithiole-4,5-dicarboxylate (**487**) (124mg, 0.4mmol) in dry dichloromethane (9ml) at –42°C was added DMAD (**1**) (195mg, 1.4mmol) in dry dichloromethane (10ml). The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by dry flash chromatography on 60H grade silica (20g). Chloroform (100%) eluted tetramethyl 1,4-phthalalylidene-2,2'-bis(1,3-dithiole)-4,4',5,5'-tetracarboxylate (**488**) (42mg, 21%) as a red solid, m.p. 226-228°C (chloroform), identical with that described above.

Tetra-acetyl-1,4-*phthalalylidene*-2,2'-*bis*(1,3-*dithiole*) (**490**)

Method A – *from terephthalaldehyde*

To a stirred solution of tributyl phosphine (1.8ml, 1.462g, 7.2mmol), carbon disulphide (15ml, 18.99g, 0.25mol) and terephthalaldehyde (142mg,

1.1mmol) at −78°C was added hex-3-yne-2,5-dione (**295**) (242mg, 2.2mmol) in dry dichloromethane (15ml). The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by preparative plate chromatography on Merck Kieselgel $60GF_{254}$ silica (20g). Dichloromethane (100%) eluted *tetra-acetyl*-1,4-*phthalalylidene*-2,2'-*bis*(1,3-*dithiole*) (**490**) (49mg, 9.8%) as a red solid, m.p. 232-234°C (dichloromethane) (Found: M^+, 474.0088 $C_{22}H_{18}O_4S_4$ requires M^+, 474.0084); $\upsilon_{max.}(CHCl_3)$ 1680vs (CO), 1651m, 1573vs, 1531m, 1359m, 1235m, 1195s, 839m, 607m, and 582cm^{-1}; δ_H (270MHz; $CDCl_3$) 2.40 (6H, s, Ac), 2.43 (6H, s, Ac), 6.48 (2H, s, CH), 7.28 (4H, s, ArH); *m/z* (250°C) 474 (M^+, 20.8%), 440 (9.3), 369 (3.4), 332 (M^+-$C_6H_6O_2S$, 5.1), 304 (9.8), 257 (M^+-$C_8H_9O_3S_2$, 3.4), 221 (10.8), 207 (6.2), 189 (26.6), 161 (12.9), 105 (8.3), 92 (100), 78 (56.2), and 43 ($MeCO^+$, 13.8).

Method B – *from* 4,5-*diacetyl*-2-(4-*formylbenzylidene*)-1,3-*dithiole* (**489**)

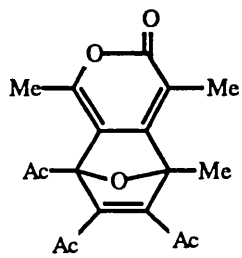
To a stirred solution of tributyl phosphine (1.5ml, 1.22g, 6mmol), carbon disulphide (10ml, 12.66g, 0.17mol) and 4,5-diacetyl-2-(4-formylbenzylidene)-1,3-dithiole (**489**) (73mg, 2.4mmol) at −78°C was added hex-3-yne-2,5-dione (**295**) (1.763g, 1.6mmol) in dry dichloromethane (15ml). The reaction mixture was allowed to warm to room temperature slowly. The solvent was evaporated and the residue purified by preparative plate chromatography on Merck Kieselgel $60GF_{254}$ silica (20g). Dichlorormethane (100%) eluted tetra-acetyl-1,4-phthalalylidene-2,2'-bis(1,3-dithiole) (**490**) (66mg, 58%) as a dark red solid, m.p. 232-234°C (dichloromethane), identical with that described above.

List of Compounds Prepared

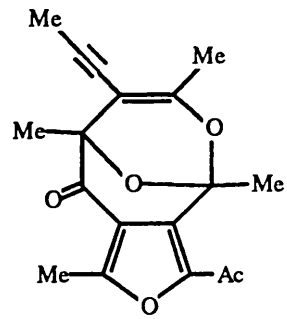
Compound numbers (**bold**) and page numbers in the experimental section are given.

CHAPTER FOUR

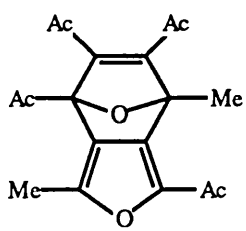
295
135



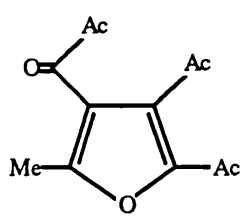
364
136 & 137



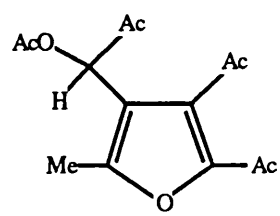
365
137



366
136

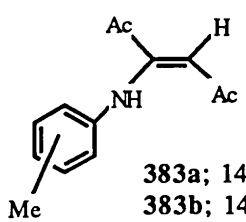


367
135 & 138

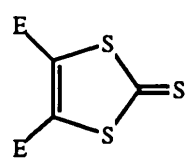


368
138

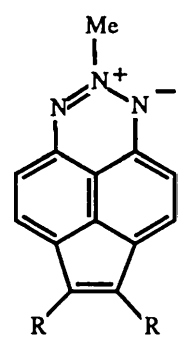
CHAPTER FIVE



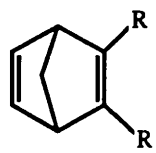
383a; 140
383b; 140
383c; 141



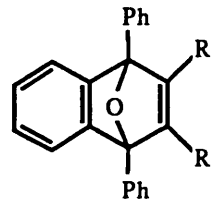
387
142



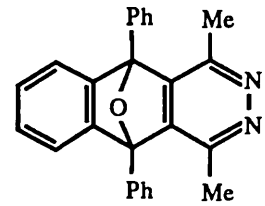
392 R=COOMe
393 R=Ac
142



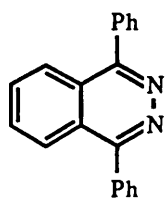
396 R=COOMe ; 143
397 R=Ac; 144



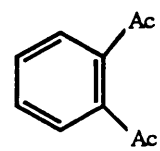
400 R=COOMe; 144
401 R=Ac; 145



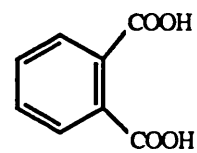
402
145



403
146

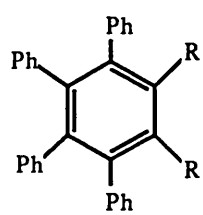


417
147

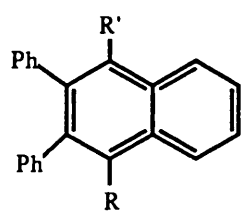


147

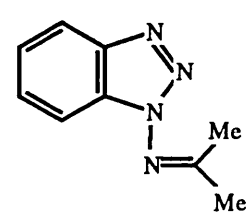
CHAPTER SIX



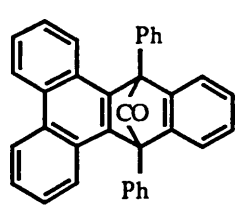
421 R=COOMe; 149
423 R=Ac; 149



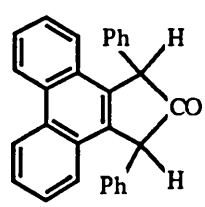
432a R'=R=Ph; 150
432b R'=Me, R=Ph; 151
432c R'=R=Et; 151



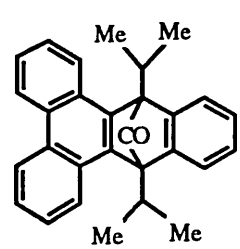
434
152



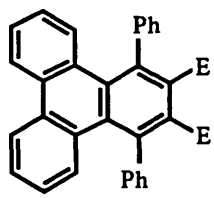
267b
152



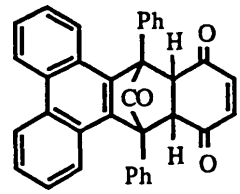
446
153



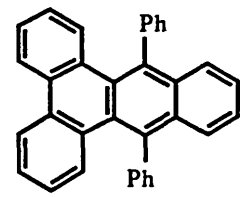
448
154



449
154

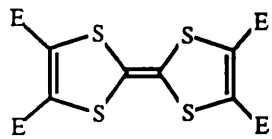


450
155

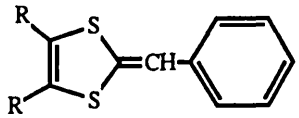


455
155

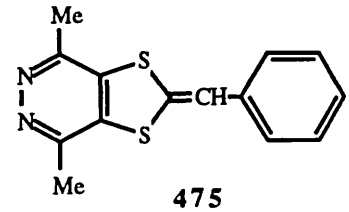
CHAPTER SEVEN



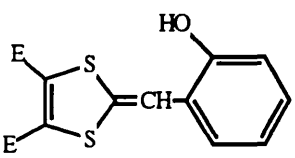
467
156



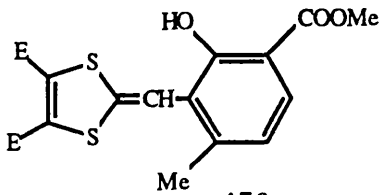
473 R=COOMe; 156
474 R=Ac; 157



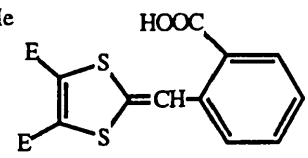
475
157



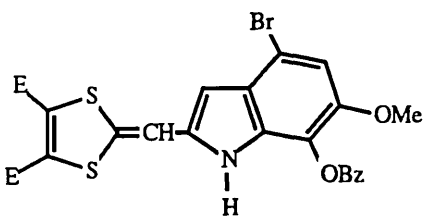
477
158



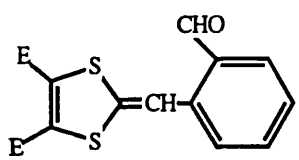
479
158



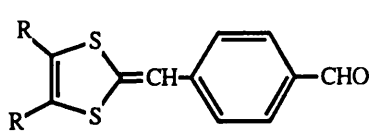
481
159



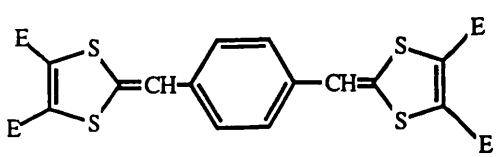
483
160



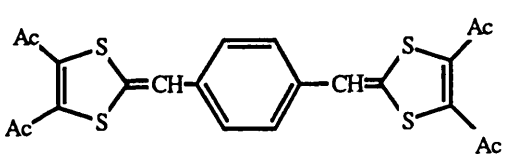
484
160



487 R=COOMe; 161
489 R=Ac; 162



488
162



490
163

*X-Ray Data**

Chapter Four

6,7,8-Triacetyl-5,8-dihydro-1,4,5-trimethyl-5,8-epoxy-2-benzopyran-3-one (364)

Crystal data: $C_{18}H_{18}O_6$, M = 330.3, monoclinic, a = 9.132 (2), b = 13.235 (2), c = 13.592 (2) Å, β = 90.87 (1)°, V = 1643Å^3, space group $P2_1/c$, Z = 4, D_c = 1.34gm^{-3}, Cu radiation, λ = 1.54178Å, μ(Cu-K_α) = 8cm^{-1}, F(000) = 696. Data were measured on a Nicolet R3m diffractometer with Cu-K_α radiation (graphite monochromator) using ω-scans. 1974 Independent reflections ($20 \leq 110°$) were measured, of which 1846, had $|F_o| > 3\sigma(|F_o|)$, and were considered to be observed. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied. The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. A ΔF map revealed two halfweight orientations for the hydrogen atoms on C(11) and C(16). The leading protons on the methyl groups on the sp^2 centres were located from a ΔF map. The positions of the remaining hydrogen atoms were idealised, C-H = 0.96Å, assigned isotropic thermal parameters, U(H) = 1.2 U_{eq}(C), and allowed to ride on their parent carbon atoms. The methyl groups were refined as rigid bodies. Refinement was by block-cascade full-matrix least-squares to R = 0.040, R_w = 0.049 [$w^{-1} = \sigma^2(F) + 0.00028F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.14 and -0.14eÅ^{-3} respectively. The mean and maximum shift/error in the final refinement were 0.003 and 0.013 respectively. Computations were carried out on an Eclipse S140 computer using the SHELXTL program system.

* Kindly supplied by Dr D.J.Williams of this department.

3-Acetyl-1,4,6,8-tetramethyl-7-prop-1-ynyl-4,8-epoxy-4*H*-furo [3,4-*c*]oxocin-9(8*H*)-one (365)

Crystal data: $C_{18}H_{18}O_5$, M = 314.3, triclinic, a = 7.914 (1), b = 8.455 (1), c = 12.629 (2) Å, α = 76.49 (1), β = 77.13 (1), γ = 86.97(1)°, V = 801Å^3, space group $P\bar{1}$, Z = 2, D_c = 1.30gm^{-3}, Cu radiation, λ = 1.54178Å, μ(Cu-K_α) = 8cm^{-1}, F(000) = 332. Data were measured on a Nicolet R3m diffractometer with Cu-K_α radiation (graphite monochromator) using ω-scans. 2007 independent reflections ($2\theta \leq 110°$) were measured, of which 1801, had $|F_o| > 3\sigma(|F_o|)$, and were considered to be observed. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied. The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. The leading protons on the methyl groups on the planar centres were located from a ΔF map. The positions of the hydrogen atoms were idealised, C-H = 0.96Å, assigned isotropic thermal parameters, U(H) = 1.2 U_{eq}(C), and allowed to ride on their parent carbon atoms. The methyl groups were refined as rigid bodies. Refinement was by block-cascade full-matrix least-squares to R = 0.045, R_w = 0.052 [$w^{-1} = \sigma^2(F) + 0.00048F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.31 and -0.21eÅ^{-3} respectively. The mean and maximum shift/error in the final refinement were 0.012 and 0.044 respectively. Computations were carried out on an Eclipse S140 computer using the SHELXTL program system.

1,4,5,6-Tetra-acetyl-4,7-dihydro-3,7-dimethyl-4,7-epoxy-2-benzofuran (366)

Crystal data: $C_{18}H_{18}O_6$, M = 330.3, monoclinic, a = 14.313 (2), b = 8.177 (1), c = 14.685 (3) Å, β = 9107.57 (1)°, V = 1639Å^3, space group $P2_1/c$, Z = 4, D_c = 1.34gm^{-3}, Cu radiation, λ = 1.54178Å, μ(Cu-K_α) = 8cm^{-1}, F(000) = 696. Data

were measured on a Nicolet R3m diffractometer with Cu-K_α radiation (graphite monochromator) using ω-scans. 2203 Independent reflections ($20 \leq 116°$) were measured, of which 1954, had $|F_o| > 3\sigma(|F_o|)$, and were considered to be observed. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied. The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. The leading protons on the methyl groups on the sp^2 centres was located from a ΔF map. The positions of the remaining hydrogen atoms were idealised, C-H = 0.96Å, assigned isotropic thermal parameters, U(H) = 1.2 U_{eq}(C), and allowed to ride on their parent carbon atoms. The methyl groups were refined as rigid bodies. Refinement was by block-cascade full-matrix least-squares to R = 0.042, R_w = 0.049 [$w^{-1} = \sigma^2(F) + 0.00041F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.18 and -0.18eÅ^{-3} respectively. The mean and maximum shift/error in the final refinement were 0.102 and 0.563 respectively. Computations were carried out on an Eclipse S140 computer using the SHELXTL program system.

Chapter Six

9,14-Diphenyl-9,14-dihydrodibenz[*a*,*c*]anthracene-9,14-methanone (267b)

Crystal data: $C_{35}H_{22}O$, M = 458.6, triclinic, a = 9.625 (4), b = 14.800 (7), c = 17.818 (10) Å, α = 96.25 (4), β = 105.18 (4), γ = 100.22(4)°, U = 2378Å^3, space group $P\bar{1}$, Z = 4 (2 crystallographically independent molecules), D_c = 1.28gm^{-3}, Cu radiation, λ = 1.54178Å, μ(Cu-K_α) = 5cm^{-1}, F(000) = 960. Data were measured on a Nicolet R3m diffractometer with Cu-K_α radiation (graphite monochromator)

using ω-scans. 6380 Independent reflections ($20 \leq 116°$) were measured, of which 5355, had $|F_o| > 3\sigma(|F_o|)$, and were considered to be observed. The data were corrected for Lorentz and polarisation factors; no absorption correction was applied. The structure was solved by direct methods. The non-hydrogen atoms were refined anisotropically. The positions of the hydrogen atoms were idealised, C-H = 0.96Å, assigned isotropic thermal parameters, $U(H) = 1.2\ U_{eq}(C)$, and allowed to ride on their parent carbon atoms. The methyl groups were refined as rigid bodies. Refinement was by block-cascade full-matrix least-squares to R = 0.053, $R_w = 0.060$ [$w^{-1} = \sigma^2(F) + 0.00146F^2$]. The maximum and minimum residual electron densities in the final ΔF map were 0.24 and -0.23eÅ^{-3} respectively. The mean and maximum shift/error in the final refinement were 0.040 and 0.181 respectively. Computations were carried out on an Eclipse S140 computer using the SHELXTL program system.

References

1a A.Padwa, "1,3-Dipolar Cycloaddition Chemistry", Wiley-Interscience Publications, 1984, **1** & **2**.

1b S.Patai, "The Chemistry of the Carbon-Carbon Triple Bond", Wiley-Interscience Publications, 1978, **1**, Chap. 11, p. 447.

1c T.L.Gilchrist, R.C.Storr, "Organic Reactions and Orbital Symmetry", Cambridge University Press, 2nd Edition, 1978, Chap.4, p. 20, Chap.5, p. 136.

2 E.Buchner, *Chem. Ber.*, 1889, **22**, 842 & 2165.

3 R.Huisgen, G.Binsch, H.König, *Chem. Ber.*, 1964, **97**, 2884.

4 A.S.Katner, *J. Org. Chem.*, 1973, **38**, 825.

5 M.Franck-Neumann, C.Buchecker, *Angew. Chem. Int. Ed. Engl.*, 1973, **12**, 240.

6 M.Martin, M.Regitz, *Liebigs Ann. Chem.*, 1974, 1702.

7 W.Bethäuser, M.Regitz, W.Theis, *Tetrahedron Lett.*, 1981, **22**, 2535.

8 H.Neunhoeffer, G.Cuny, W.K.Franke, *Liebigs Ann. Chem.*, 1968, **713**, 96.

9 A.Michael, *J. Prakt. Chem.*, 1893, **48**[2], 94.

10 T.L.Gilchrist, G.E.Gymer, *Advances in Heterocyclic Chemistry*, 1974, **16**, 33.

11 S.K.Khetan, M.V.George, *Can. J. Chem.*, 1967, **45**, 1993; R.Huisgen, H.Knupfer, R.Sudtmann, G.Wallbillich, V.Weberndörfer, *Chem. Ber.*, 1967, **100**, 1580.

12 V.S.Abramov, L.A.Shapshinskaya, *Zh. Obshch. Khim.*, 1952, **22**, 1450; M.A.Ogliaruso, M.G.Romanelli, E.I.Becker, *Chem. Rev.*, 1965, **65**, 261.

13 Y.Nagawa, K.Honda, H.Nakanishi, *Bull. Chem. Soc. Jpn.*, 1987,

60, 2931.

14 T.Sasaki, K.Kanematsu, M.Murata, *Tetrahedron*, 1971, **27**, 5121.

15 T.Sasaki, K.Kanematsu, M.Murata, *J. Org. Chem.*, 1971, **36**, 446.

16 N.K.Kochetkov,S.D.Sokolov, *Advances in Heterocyclic Chemistry*, 1963, **2**, 365.

17 L.Erichomovitch, F.L.Chubb, *Can. J. Chem.*, 1966, **44**, 2095.

18 R.Huisgen, M.Christl, *Chem. Ber.*, 1973, **106**, 3291; K.Bast, M.Christl, R.Huisgen, W.Mack, *Chem. Ber.*, 1973, **106**, 3312.

19 Ch.Grundmann, *Forschritte der Chemischen Forchung*, 1966, **7**, 62.

20 H.Seidl, R.Huisgen, R.Knorr, *Chem. Ber.*, 1969, **102**, 904.

21 J.P.Fleury, J.P.Schoeni, D.Clerin, H.Fritz, *Helv. Chim. Acta*, 1975, **58**, 2018.

22 A.Padwa, L.Hamilton, *Tetrahedron Lett.*, 1965, 4363.

23 R.Huisgen, H.Gotthardt, H.O.Bayer, F.C.Schaefer, *Angew. Chem. Int. Ed. Engl.*, 1964, **3**, 136; R.Huisgen, H.Gotthardt, H.O.Bayer, F.C.Schaefer, *Chem. Ber.*, 1970, **103**, 2611.

24 W.E.McEwen, I.C.Mineo, Y.H.Shen, *J. Am. Chem. Soc.*, 1971, **93**, 4479.

25 R.Huisgen, H.Gotthardt, R.Grashey, *Chem. Ber.*, 1968, **101**, 536.

26 Y.Tamura, H.Hayashi, Y.Nishimura, M.Ikeda, *J. Heterocycl. Chem.*,1975, **12**, 225.

27 O.Tsuge,H.Samura, *Tetrahedron Lett.*, 1973, 597.

28 H.Marley, S.H.B.Wright, P.N.Preston, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1727.

29 K.T.Potts, J.L.Marshall, *J. Org. Chem.*, 1976, **41**, 129.

30 H.Koga, M.Hirobe, T.Okamoto, *Chem. Pharm. Bull.*, 1974, **22**, 482.

31 Ref. 1a, p. 789.

32 K.T.Potts, D.R.Choudhury, *J. Org. Chem.*, 1977, **42**, 1648.

33 S.R.Challand, S.F.Gait, M.J.Rance, C.W.Rees, R.C.Storr, *J. Chem. Soc., Perkin Trans. 1*, 1975, 26.

34 S.F.Gait, M.J.Rance, R.W.Stephenson, C.W.Rees, R.C.Storr, *J. Chem. Soc., Perkin Trans. 1*, 1975, 556.

35 C.W.Rees, R.W.Stephenson, R.C.Storr, *J. Chem. Soc., Chem. Commun.*, 1974, 941.

36 S.R.Challand, C.W.Rees, R.C.Storr, *J. Chem. Soc., Chem. Commun.*, 1973, 837.

37 E.F.Ullman, J.E.Milks, *J. Am. Chem. Soc.*, 1962, **84**, 1315; E.F.Ullman, J.E.Milks, *J. Am. Chem. Soc.*, 1964, **86**, 3814.

38 H.Gotthardt, M.C.Weisshuhn, K.Dörhöfer, *Angew. Chem. Int. Ed. Engl.*, 1975, **14**, 422.

39 H.Hamaguchi, T.Ibata, *Chem. Lett.*, 1975, 499.

40 H.Gotthardt, *Chem. Ber.*, 1972, **105**, 196.

41 J.E.Franz, L.L.Black, *Tetrahedron Lett.*, 1970, 1381.

42 R.K.Howe, J.E.Franz, *J. Chem. Soc., Chem. Commun.*, 1973, 524; R.M.Paton, *Chem. Soc. Rev.*, 1989, **18**, 33.

43 J.R.Grunwell, S.L.Dye, *Tetrahedron Lett.*, 1975, 1739.

44 K.T.Potts, E.Houghton, U.P.Singh, *J. Org. Chem.*, 1974, **39**, 3627.

45 A.Roberts, M.Ferrey, A.Foucaud, *Tetrahedron Lett.*, 1975, 1377.

46 D.B.J.Easton, D.Leaver, T.J.Rawlings, *J. Chem. Soc., Perkin Trans. 1*, 1972, 41; H.Behringer, J.Falkenberg, *Tetrahedron Lett.*, 1967, 1895.

47 D.H.Clemens, A.J.Bell, J.L.O'Brien, *Tetrahedron Lett.*, 1965, 3257.

48 H.E.Winberg, D.D.Coffman, *J. Am. Chem. Soc.*, 1965, **87**, 2776.

49 D.B.J.Easton, D.Leaver, T.J.Rawlings, *J. Chem. Soc., Chem. Commun.*, 1965, **22**, 585; G.Lang, J.Vialle, *Bull. Chem. Soc. Fr.*, 1967, 2865.

50 R.Huisgen, K.Herbig, *Liebigs. Ann. Chem.*, 1965, **688**, 98.

51 A.Crabtree, A.W.Johnson, J.C.Tebby, *J. Chem. Soc.*, 1961, 3497; R.M.Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds", Wiley-Interscience Publications, 3rd Edition, 1976, Chap.6, p. 330.

52 R.Huisgen, M.Morikawa, K.Herbig, E.Brunn, *Chem. Ber.*, 1967, **100**, 1094.

53 L.M.Gomès, *Bull. Soc. Chim. Fr.*, 1967, 1764.

54 R.Grigg, J.L.Jackson, *J. Chem. Soc., Chem. Commun.*, 1970, 552.

55 J.A.Reed, C.L.Schilling Jr., R.F.Tarvin, T.A.Rettig, J.K.Stille, *J. Org. Chem.*, 1969, **34**, 2188.

56 D.M.Lemal, E.P.Gosselink, S.D.McGregor, *J. Am. Chem. Soc.*, 1966, **88**, 582.

57 R.K.Hill, R.M.Carlson, *J. Org. Chem.*, 1965, **30**, 2414.

58 A.Demoulin, H.Gorissen, A.M.Hesbain-Frisque, L.Ghosez, *J. Am. Chem. Soc.*, 1975, **97**, 4409.

59 J.Barluenga, S.Fustero, V.Gotor, *Synthesis*, 1975, **3**, 191.

60 J.B.Hester Jr., *J. Org. Chem.*, 1974, **39**, 2137.

61 C.J.Moody, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2505; C.J.Moody, P.Shah, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1407.

62 H.Erfanian-Abdoust, U.Pindur, *Heterocycles*, 1989, **29**, 1709.

63 L.A.Paquette, M.J.Wyvratt, *J. Am. Chem. Soc.*, 1974, **96**, 4671; D.McNeil, B.R.Vogt, J.J.Sudol, S.Theodoropulos, E.Hedaya, *J. Am. Chem. Soc.*, 1974, **96**, 4673.

64 D.J.Cram, C.S.Montgomery, G.R.Knox, *J. Am. Chem. Soc.*, 1966, **88**, 515.

65 H.Wynberg, R.Helder, *Tetrahedron Lett.*, 1971, 4317.

66 Ref. 1a, **2**, Chap.15, 543.

67 T.Hiyama, H.Taguchi, H.Nozaki, *Bull. Chem. Soc. Jpn.*, 1974, **47**(11), 2909.

68 D.J.Cram, R.D.Partos, *J. Am. Chem. Soc.*, 1963, **85**, 1273.

69 N.Abe, Y.Tanaka, T.Nishiwaki, *J. Chem. Soc., Perkin Trans. 1*, 1978, 429.

70 Ref. 1a, **1**, Chap.1, p. 153.

71a J.R.Bailey, N.H.Moore, *J. Am. Chem. Soc.*, 1917, **39**, 279; J.R.Bailey, A.T.McPherson, *J. Am. Chem. Soc.*, 1917, **39**, 1322.

71b R.Huisgen, *Angew. Chem. Int. Ed. Engl.*, 1963, **2**, 565.

72 S.Evans, R.C.Gearhart, L.J.Guggenberger, E.E.Schweizer, *J. Org. Chem.*, 1977, **42**, 452.

73 S.Somner, *Angew. Chem. Int. Ed. Engl.*, 1979, **18**, 695; A.Eckell, R.Huisgen, *Chem. Ber.*, 1977, **110**, 559.

74 K.Burger, F.Hein, *Liebigs Ann. Chem.*, 1979, 133; K.Burger, F.Hein, C.Zettl, H.Schickaneder, *Chem. Ber.*, 1979, **112**, 2609; K.Burger, F.Hein, *Chem.-Ztg*, 1978, **102**, 152.

75 S.Yankelevich, B.Fuchs, *Tetrahedron Lett.*, 1967, 4945.

76 D.Wege, S.P.Wilkinson, *Aust. J. Chem.*, 1973, **26**, 1751.

77 D.M.Birney, J.A.Berson, *J. Am. Chem. Soc.*, 1985, **107**, 4553.

78 B.F.LeBlanc, R.S.Sheridan, *J. Am. Chem. Soc.*, 1985, **107**, 4554.

79 J.M.Landesberg, J.Sieczkowski, *J. Am. Chem. Soc.*, 1971, **93**, 972.

80 S.C.Clarke, B.L.Johnson, *Tetrahedron Lett.*, 1967, 617.

81 J.Meinwald, E.G.Miller, *Tetrahedron Lett.*, 1961, 253.

82 H.Tanida, T.Irie, *J. Org. Chem.*, 1979, **44**, 1002.

83 R.N.Warrener, R.A.Russell, I.G.Pitt, *J. Chem. Soc., Chem. Commun.*, 1984, 1675.

84 S.Mondal, A.J.Bhattacharya, *Current Science*, 1972, **41**, 217.

85 S.Mondal, T.K.Bandyopadhyay, A.J.Bhattacharya, *Indian J. Chem.*, 1983, **22B**, 225.

86 S.Mondal, T.K.Bandyopadhyay, A.J.Bhattacharya, *Indian J. Chem.*, 1983, **22B**, 448.

87 M.J.Plater, Ph.D Thesis, University of London, 1989.

88 P.D.Bartlett, W.P.Giddings, *J. Am. Chem. Soc.*, 1960, **82**, 1240.

89 S.C.Clarke, B.L.Johnson, *Tetrahedron*, 1971, **27**, 3555.

90 B.Halton, M.A.Battiside, R.Rehberg, C.L.Deyrup, M.E.Brennan, *J. Am. Chem. Soc.*, 1967, **89**, 5964.

91 D.Wege, S.P.Wilkinson, *J. Chem. Soc., Chem. Commun.*, 1973, 795.

92 R.W.Hoffmann, *Acc. Chem. Res.*, 1985, **18**, 248.

93 A.Rieman, R.W.Hoffmann, *Chem. Ber.*, 1985, **118**, 2544.

94 R.S.Atkinson, A.J.Clark, R.E.Overhill, *J. Chem. Soc., Chem. Commun.*, 1971, 535.

95 A.Chollet, J.-P.Hagenbuch, P.Vogel, *Helv. Chim. Acta*, 1979, **62**, 511; W.R.Roth, B.P.Scholz, *Chem. Ber.*, 1981, **114**, 3741.

96 B.P.Stark, A.J.Duke, "Extrusion Reactions", Pergamon Press, 1967, Chap.2, p. 16.

97 S.Goldschmidt, A.Zoeblein, *Chem. Ber.*, 1961, **94**, 169.

98 I.J.Turchi, M.J.S.Dewar, *Chem. Rev.*, 1975, **75**, 418.

99 G.Y.Kondrate, L.B.Medvedsk, Z.N.Ivanova, L.A.Shimelev, *Izv. Akad. Nauk S.S.S.R–Seriya Khimicheskaya*, 1971, **4-6**, 1363.

100 H.Dürr, W.Schmidt, *Liebigs Ann. Chem.*, 1974, 1140.

101 M.Franck-Neumann, D.Martina, *Tetrahedron Lett.*, 1975, 1767.

102 M.Franck-Neumann, C.Dietrich-Buchecker, *Tetrahedron Lett.*, 1976, 2069.

103 R.M.Acheson, M.G.Bite, M.W.Cooper, *J. Chem. Soc., Perkin Trans. 1*, 1976, 1908.

104 T.Uchida, K.Aoyama, M.Nishikawa, T.Kuroda, *J. Heterocycl.*

Chem., 1988, **25**, 1793.

105 A.M.Nour-el-Din, A.F.E.Mourad, *J. Prak. Chem.*, 1983, **325**(6), 908.

106 W.Flitsch, Batroff, *Liebigs Ann. Chem.*,1987, 621.

107 P.J.Dunn, C.W.Rees, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1585.

108 P.J.Dunn, C.W.Rees, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1579.

109 C.F.Huebner, E.Donoghue, L.Dorfman, F.A.Stuber, N.Danieli, E.Wenkert, *Tetrahedron Lett.*, 1966, 1185.

110 E.Winterfeldt, G.Giesler, *Angew. Chem. Int. Ed. Engl.*, 1966, **5**, 579.

111 E.LeGoff, R.B.LaCount, *Tetrahedron Lett.*, 1967, 2333.

112 J.C.Kauer, H.E.Simmons, *J. Org. Chem.*, 1968, **33**, 2720.

113 E.Winterfeldt, G.Giesler, *Chem. Ber.*, 1968, **101**, 4022.

114 I.M.Gverdtsiteli, L.P.Asatiani, A.A.Tskhvaradze, *Soobshch. Akad. Nauk Graz. S.S.R*, 1976, **81**(2), 353 & 361; (CA, 1976, **84**, 151162q).

115 D.B.J.Easton, D.Leaver,*J. Chem. Soc., Chem. Commun.*, 1965, 585.

116 E.Winterfeldt, *Chem. Ber.*, 1965, **98**, 1581.

117 O.Diels, K.Alder, *Liebigs Ann. Chem.*, 1931, **490**, 236; A.W.McCulloch, A.G.McInnes, D.G.Smith, J.A.Walter, *Can. J. Chem.*, 1976, **54**, 2013.

118 R.A.F.Matheson, A.W.McCulloch, A.G.McInnes, D.G.Smith, *Can. J. Chem.*, 1977, **55**,1422.

119 J.Sauer, G.Heinrichs, *Tetrahedron Lett.*, 1966, **41**, 4979.

120 F.Weygand, H.Weber, E.Maekawa, G.Eberhardt, *Chem. Ber.*, 1956, **89**, 1994.

121 L.F.Fieser, K.L.Williamson, "Organic Experiments"; D.C.Heath & Co.,4th Edition, 1979, Chap.43, p. 274; L.Fieser, M.J.Haddadin, *Can. J. Chem.*, 1965, **43**, 1599.

121a C.F.H.Allen, J.A.VanAllan, *J. Am. Chem. Soc.* , 1942, **64**, 1260.

122 B.Baigrie, J.I.G.Cadogan, J.R.Mitchell, A.K.Robertson, J.T.Sharp, *J. Chem. Soc., Perkin Trans. 2*, 1972, 2563; J.I.G.Cadogan, C.D.Murray, J.T.Sharp,*J. Chem. Soc., Perkin Trans. 2*, 1976, 583.

122a C.W.Rees, C.D.Campbell, *Proc. Chem. Soc.*, 1964, 296; C.W.Rees, C.D.Campbell, *J. Chem. Soc.(C)*, 1969, 742.

122b C.D.Campbell, C.W.Rees, *J. Chem. Soc. (C)*, 1969, **84**, 752.

123 J.I.G.Cadogan, J.B.Thomson, *J. Chem. Soc., Chem. Commun.*, 1969, 770.

124 S.Patai, "The Chemistry of Double-Bonded Functional Groups", Wiley & Sons, 1977, Pt.2, Chap.11, p. 1080.

125 B.A.Arbuzov, V.S.Abramov, L.A.Shapshinskaya, *Compt. rend. acad. sci. URSS*, 1945, **46**, 147; (CA, 1945, **39**, 4849[8]); B.A.Arbuzov, L.A.Shapshinskaya, G.A.Prytkova, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1962, 2084; N.O.V.Sonntag, S.Linder, E.I.Becker, P.E.Spoerri, *J. Am. Chem. Soc.*, 1953, **75**, 2283.

126 D.W.Jones, *J. Chem. Soc., Perkin Trans. 1*, 1977, 980.

127 T.Sasaki, K.Kanematsu, K.Iizuka, *J. Org. Chem.*, 1976, **41**, 1105; M.Yasuda, K.Harano, K.Kanematsu, *J. Org. Chem.*, 1980, **45**, 659.

127a S.Mondal, A.J.Bhattacharya, *Current Science*, 1984, **53**, 1229.

128 S.Hünig, *Angew. Chem.*, 1984, **96**, 447; A.Aumüller, S.Hünig, *Liebigs Ann. Chem.*, 1986, 142.

129 M.R.Bryce, *Aldrichimica Acta*, 1985, **18**, 73.

130 J.H.Perlstein, *Angew. Chem. Int. Ed. Engl.*, 1977, **16**, 519.

131 N.Lozac'h, M.Staraux, *Advances in Heterocyclic Chemistry*, 1980, **27**, 151.

132 G.Schukat, A.M.Richter, E.Fanghänel, *Sulphur Reports*, 1987, **7**(3), 155.

133 K.Takahashi, T.Nihira, *Tetrahedron Lett.*, 1989, **30**, 5903.

134 A.W.Hoffmann, *Liebigs Ann. Chem. Suppl.*, 1861, **1**, 26 & 59.

135 H.D.Hartzler, *J. Am. Chem. Soc.*, 1971, **93**, 4961; H.D.Hartzler, *J. Am. Chem. Soc.*, 1973, **95**, 4379.

136 M.Narita, C.U.Pittman Jr., *Synthesis*, 1976, 489.

137 A.Krief, *Tetrahedron*, 1986, **42**, 1209.

138 J.E.Mulvaney, D.M.Chang, *Macromolecules*, 1980, **13**, 240.

139 R.E.Bolton, C.J.Moody, C.W.Rees, G.Tojo, *J. Chem. Soc., Perkin Trans. 1*, 1987, 931.

140 G.B.Jones, C.J.Moody, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2449.

141 E.J.Griffen, unpublished results.

142 D.D.Perrin, W.L.F.Armarego, "Purification of Laboratory Chemicals", Pergamon, 3rd Edition, 1988, p. 284.

143 Ref. 142, p. 136.

144 Ref. 142, p. 143.

145 Ref. 142, p. 161.

146 L.M.Harwood, *Aldrichimica Acta*, 1985, **18**(1), 25.

Abbreviations

Å	Ångsröm unit
ABT	1-Aminobenzotriazole
Ac	Acetyl
AcO	Acetoxy
aq.	Aqueous
BaO	Barium oxide
$(Bu)_3P$	Tributyl phoshine
°C	° in Celsius
CS_2	Carbon disulphide
$CaSO_4$	Calcium sulphate
CCl_4	Carbon tetrachloride
DAA	Hex-3-yne-2,5-dione (Diacetylacetylene)
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
o-DCB	*o*-Dichlorobenzene
DCM	Dichloromethane
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMAD	Dimethylacetylene dicarboxylate
DMF	Dimethyl formamide
DMSO	Dimethyl sulphoxide
E	COOMe
h	Hours
Hg	Mercury
i.r.	Infra-red spectra
LTA	Lead tetra-acetate

mg	Milligram
min	Minutes
mmol	Millimol
n.m.r.	Nuclear magnetic resonance spectra
PDC	Pyridinium dichromate
Ph	Phenyl
RT	Room temperature
S	Sulphur
S_4N_4	Tetrasulphur tetranitride
THF	Tetrahydrofuran
t.l.c	Thin layer chromatography

OMM GUHAYANAMAHA