FACIAL SELECTIVITY IN THE DIELS-ALDER REACTIONS OF 1,3-CYCLOHEXADIENES BEARING ALLYLIC OXYGEN SUBSTITUTION

JAMES R. GILLARD

π-FACIAL SELECTIVITY IN THE DIELS-ALDER REACTIONS OF 1,3-CYCLOHEXADIENES BEARING ALLYLIC OXYGEN SUBSTITUTION

by

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Abstract

The Diels-Alder reaction of *cis*-3,5-cyclohexadiene-1,2-diol (**121**) and a number of its acyclic derivatives, *cis*-1,2-diacetoxy-3,5-cyclohexadiene (**109**), *cis*-1,2-bis-(trimethylsiloxy)-3,5-cyclohexadiene(**122**)and*cis*-1,2-dimethoxy-3,5-cyclohexadiene(**124**) were found to add *N*-phenylmaleimide in a kinetically controlled manner to yield adducts that arose mainly by attachment of the dienophile to the face of the diene *syn* to the oxygen atoms. Some cyclic derivatives of **121**, *cis*-3a,7a-dihydro-2,2-dimethyl-1,3-benzodioxole(**114**),*cis*-3a,7a-dihydro-2,2-dimethyl-1,3,2-benzodioxasilole(**123**)and*cis*-2-ethyl-3a,7a-dihydro-2,1,3-benzoboradioxole (**125**), afforded nearly equal quantities of both *syn* and *anti* adducts. Benzylidene-protected derivatives (2α,3aβ,7aβ)-3a,7a-dihydro-2-phenyl-1,3-benzodioxole (**132**) and (2α,3aα,7aα)-3a,7a-dihydro-2-phenyl-1,3-benzodioxole (**133**) also reacted with *N*-phenylmaleimide, but they gave predominantly *anti*-addition products.

1,3,5-Cyclohexatriene-1,2-oxide (**142**) and its more substituted derivatives, 1,2-dimethyl-1,3,5-cyclohexatriene-1,2-oxide (**148a**) and 10-oxatricyclo[4.3.1.0]deca-2,4-diene (**148b**) reacted also with *N*-phenylmaleimide to give only products that resulted from addition of the addends to the face of the diene *anti* to the epoxide oxygen.

The results obtained have been discussed in the context of the many theories that attempt to define the controlling factors involved in determining (*syn*/*anti*) π-facial selectivity of plane-nonsymmetric dienes bearing an allylic heteroatom. Steric effects and stereoelectronic effects are invoked in this study to rationalize the results we report here. In particular, our contrasting results with the diol-derived dienes and the benzene oxides are consistent with *syn*-addition being determined by the presence of a favorable

secondary orbital interaction between the LUMO of the dienophile and the components of the highest occupied molecular orbitals that reside on the allylic oxygens of the dienes.

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Glossary of Abbreviations

Ac	acetyl
APT	attached proton test
COSY	^{1}H-^{1}H correlation spectrum
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DMAD	dimethyl acetylenedicarboxylate
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
EDG	electron-donating group
EWG	electron-withdrawing group
GC-MS	gas chromatography-mass spectrometry
HOMO	highest occupied molecular orbital
ir	infrared [spectroscopy]
LUMO	lowest unoccupied molecular orbital
MA	maleic anhydride
MMPP	magnesium monoperoxyphthalic acid
mp	melting point
ms	mass spectrometry
*m*CPBA	*meta*-chloroperoxybenzoic acid
nmr	nuclear magnetic resonance [spectroscopy]
n.O.e.	nuclear Overhauser enhancement
n.O.e.d.	nuclear Overhauser enhancement difference [spectrum]
NPM	*N*-phenylmaleimide

PTAD	4-phenyl-1,2,4-triazoline-3,5-dione
*p*TsOH	*para*-toluenesulfonic acid
TCNE	tetracyanoethylene
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
uv	ultraviolet [spectroscopy]

To my wife, Ann, and my children, Joshua and Simon

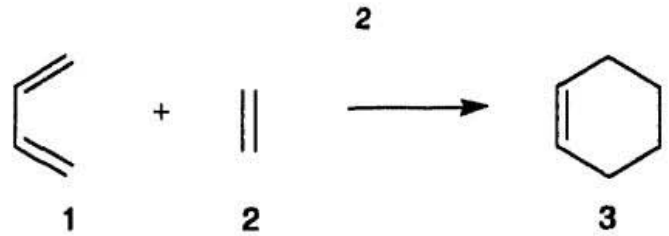
You make it all worth it.

INTRODUCTION TO THE DIELS-ALDER REACTION

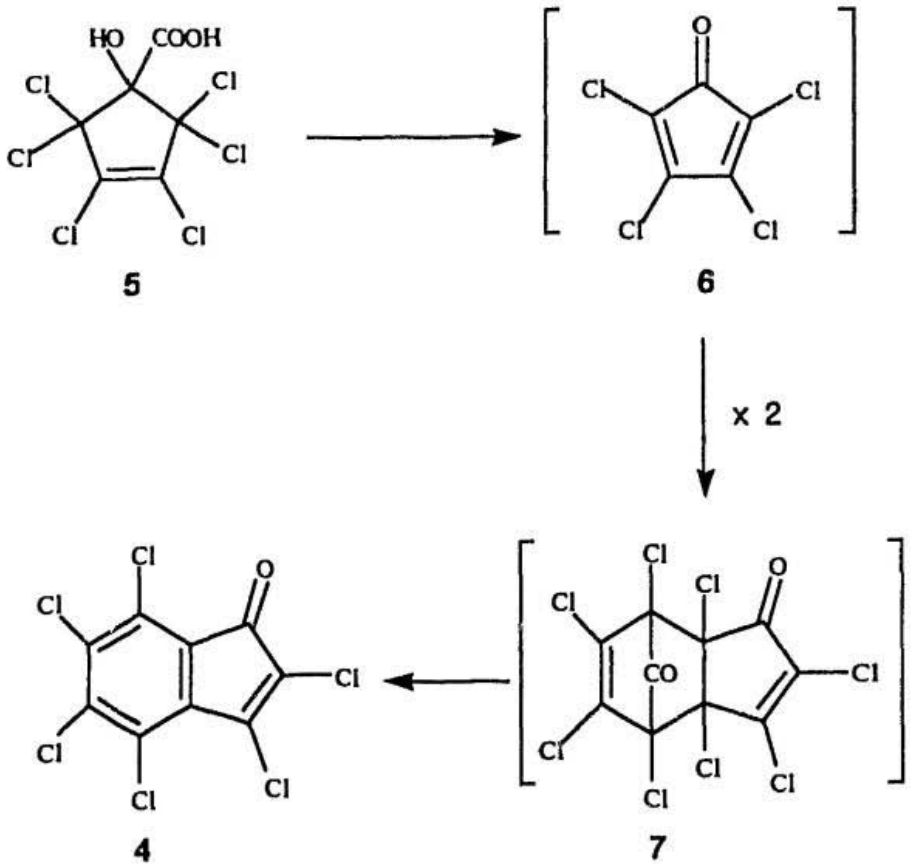
The first formal reports of what we now know as the Diels-Alder reaction (**1** + **2** → **3**, Scheme 1) appeared in the literature about 100 years ago. Sauer[1] described how Zincke,[2] in 1893, proposed that the formation of perchloroindenone **4** by the pyrolysis of 2,2,3,4,5,5-hexachloro-1-hydroxycyclopent-3-ene-1-carboxylic acid **5** occurred through the dimerization of perchlorocyclopentadienone **6**, with subsequent elimination of carbon monoxide and two atoms of chlorine from the dimeric adduct **7** (Scheme 2). Onishchenko[3] also pointed out that Ipatieff[4] had synthesized dipentene **9** by the dimerization of isoprene **8** in 1897 (Scheme 3).

Less than ten years later, in 1906, Albrecht[5] reported a mixed addition reaction of a 1,3-diene with a substituted alkene (cyclopentadiene and *para*-benzoquinone), but he proposed an incorrect structure **10** as the product. It was not until over 20 years later, in 1928,[6] that the pioneer work of Otto Diels and Kurt Alder resulted in the elucidation of the correct structure **11** for this product. In fact, they obtained evidence that the addition of 1,3-dienes with substituted alkenes was indeed a general phenomenon, and so was discovered the reaction that now bears their names.

Since that time the Diels-Alder reaction has become one of the most intensively researched transformations in organic chemistry. The total body of knowledge accumulated so far has resulted in the publication of numerous books[3,7] and review articles. To give the reader an appreciation of the amount of interest generated in the Diels-Alder reaction, especially in the last 10 years, consider the following: the 4th Collective Index (1937-46) of *Chemical Abstracts* has 24 listings under the subject

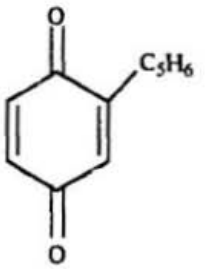


Scheme 1. The Diels-Alder reaction



Scheme 2. The synthesis of perchloroisoindanone

Scheme 3. The dimerization of isoprene



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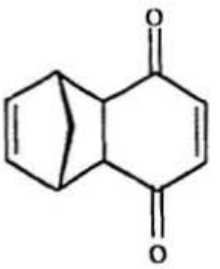

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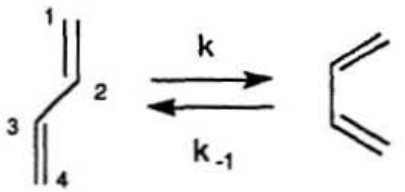
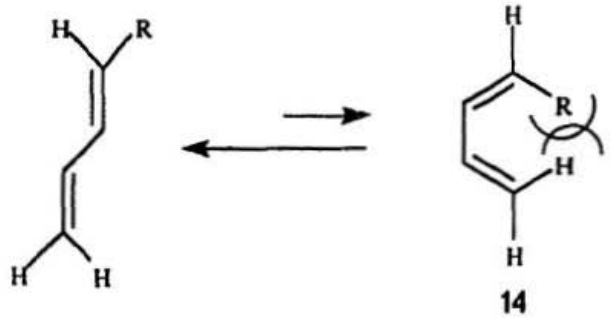


12 s-*trans* 13 s-*cis*

Scheme 4. The s- *cis* and s- *trans* conformers of 1,3-butadiene



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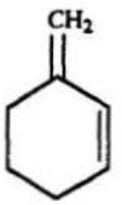

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16

heading "Diels-Alder reaction". Under the same heading of the General Subject Index of Volume 113 (July-Dec, 1990), *Chemical Abstracts* has almost 250 listings, encompassing only a six month span of the published literature. Thus, it is not surprising that the Diels-Alder reaction has evolved to be one of the most powerful tools employed by the synthetic chemist.[8] Its importance rests with its ability to generate two carbon-carbon σ bonds simultaneously, and up to four stereogenic centres in one synthetic operation. Thus it is a convenient method of generating a highly functionalized six-membered ring.

The Diels-Alder reaction is but one member of a broader class of transformations called cycloadditions.[9] These transformations are processes whereby two (or more) molecules condense to form a ring, with the formation of new σ bonds at the expense of the π bonds of the substrates. Two other examples are the [2+2] photoaddition of alkenes and [3+2] dipolar additions.

The application of orbital theory by Woodward and Hoffman[10] to pericyclic reactions (those reactions in which the bond-making and bond-breaking processes occur simultaneously, via a cyclic transition state[9]) provided great insight into the mechanism of cycloadditions. The use of frontier orbital theory,[11] in which one is restricted to consideration of the molecular orbitals of the reactants most important for reactivity, has led to the development of a simple, concise description of the reactivity, stereoselectivity and regioselectivity of Diels-Alder reactions.

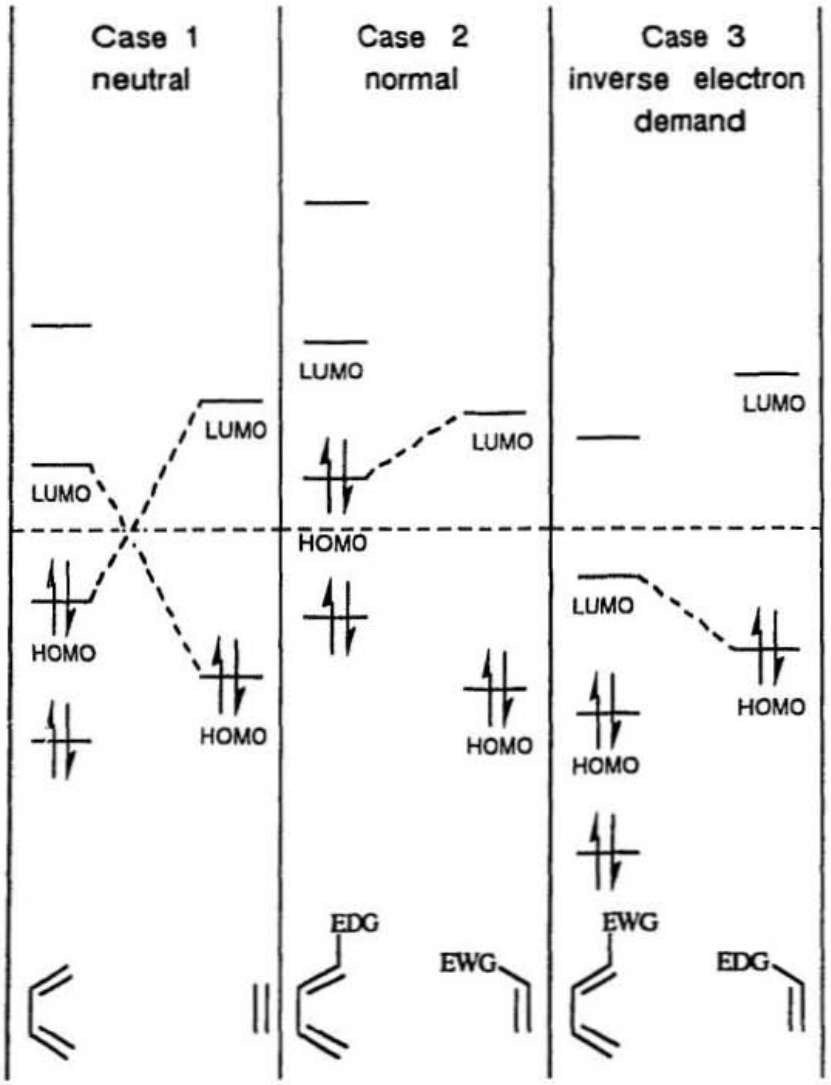
It has become widely accepted,[11] based on the conservation of orbital symmetry,[10] that the Diels-Alder reaction is a concerted, thermally allowed [$4\pi_s + 2\pi_s$] condensation of a diene **1** and a dienophile **2** (Scheme 1). Characteristics of the reaction that are excluded are zwitterionic and biradical intermediates.[11] Although other directions of approach of the addends can be analyzed by the rules of orbital symmetry, i.e. [$4\pi_s +$

$2\pi_s]$, $[4\pi_s + 2\pi_a]$ and $[4\pi_a + 2\pi_a]$, there is still no definite experimental evidence for these types of reactions of dienes and dienophiles.

With any two reacting partners there are several salient features of the Diels-Alder reaction that need to be considered, and which will ultimately determine its outcome. Not all of these factors operate in any one reaction. A short description will be given of each of these factors to encompass what is known experimentally regarding the course of Diels-Alder reactions in general.[7c] In all, there are seven factors.

i) *Diene conformation* For acyclic 1,3-dienes, there are many possible conformations that the carbon chain may adopt through rotation about the C_2-C_3 bond axis.[12] For 1,3-butadiene, two important forms are shown as *s-trans* **12** and *s-cis* **13** (Scheme 4), where k and k_{-1} are the rates of exchange. In order for a Diels-Alder reaction to occur, the diene must adopt the *s-cis* orientation. If rotation about the C_2-C_3 bond is hindered, as in **14**, or restricted, as in **15**, the Diels-Alder reaction may proceed slowly or not at all. Cyclic dienes **16** obviously do not have this problem as long as both double bonds are in the same ring. In general, reaction rates involving cyclic dienes proceed faster and with greater stereo- and regiocontrol than do acyclic dienes.

ii) *Substitution patterns on diene/dienophile* Diels-Alder reactions may be classified into three types,[11] depending on the substitution patterns on the diene and dienophile (Figure 1). This classification is based on which of the frontier molecular orbitals of the diene and dienophile are most important during reaction. Figure 1 illustrates the relative orbital energies of both addends for each type of Diels-Alder reaction.



EDG = OCH_3, OTMS, R, NR_2
EWG = COR, CO_2R, CHO, CNR, CN, CONR

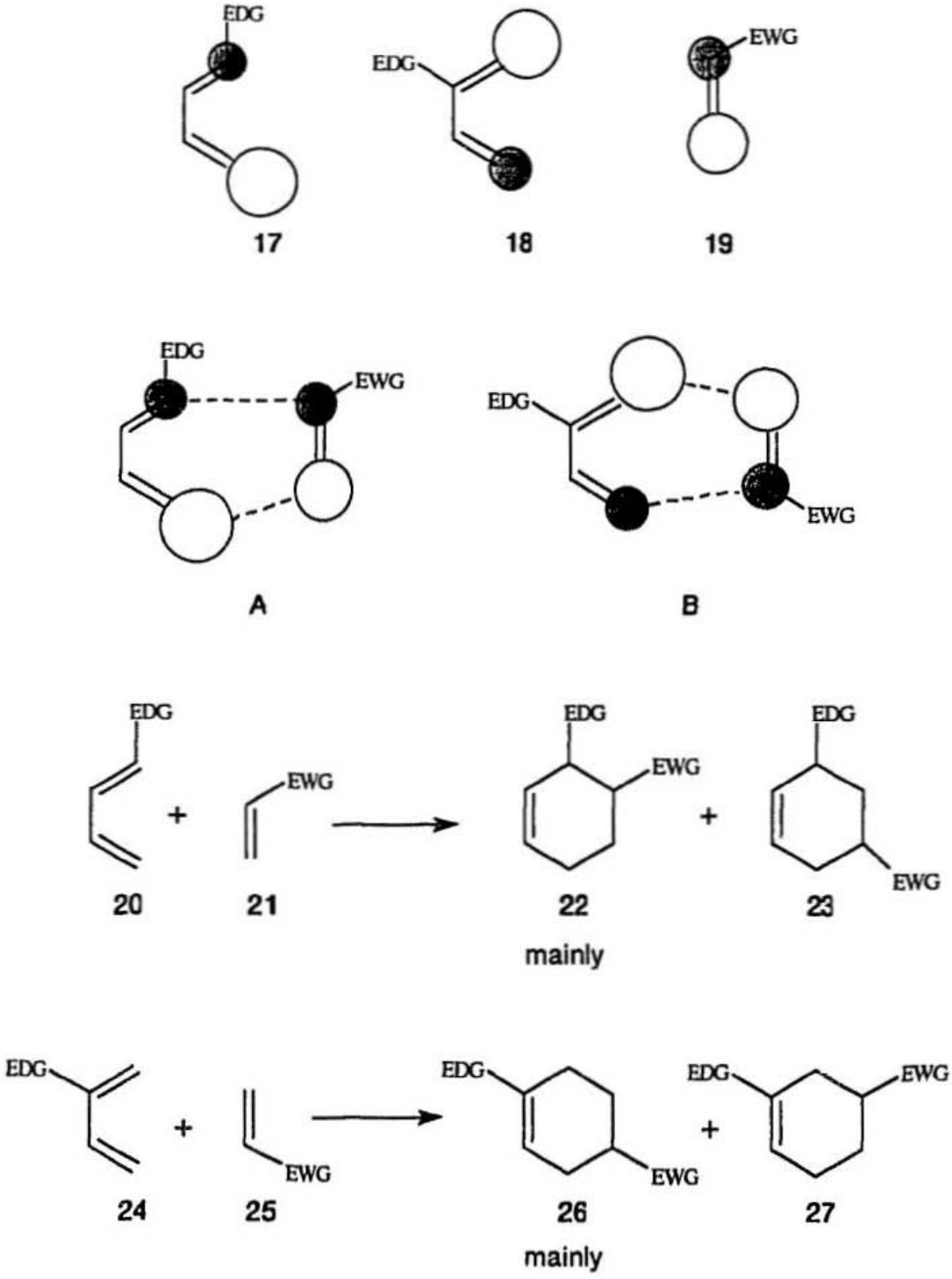
Figure 1. Orbital energy diagram for neutral, normal, and inverse electron demand Diels-Alder reactions

For the unsubstituted scenario (Case 1, 1,3-butadiene and ethylene) both the HOMO and the LUMO orbitals for each addend are of very similar energy. Therefore, cycloaddition may proceed via overlap of $HOMO_{diene}$ - $LUMO_{dienophile}$ as well as by $HOMO_{dienophile}$ - $LUMO_{diene}$. If groups placed on either addend (or both) do not significantly alter the orbital energies, then reactions of this type are termed "neutral" Diels-Alder reactions.

In Case 2, placement of an electron-donating group (EDG) on the diene serves to raise the orbital energy of the diene. Similarly, an electron-withdrawing group (EWG) on the dienophile will lower the orbital energy of the dienophile. As shown in Figure 1, the difference in energy between $HOMO_{diene}$ - $LUMO_{dienophile}$ is less than the energy difference between $HOMO_{dienophile}$ - $LUMO_{diene}$. Therefore, cycloaddition occurs involving the former interaction. Such a substitution pattern, common for most [4+2] cycloadditions, is called a "normal" Diels-Alder reaction.

Case 3 is a reversal of the substitution patterns found in Case 2. Thus, an EWG on the diene and an EDG on the dienophile serve to raise and lower their respective orbital energies. Now the $HOMO_{dienophile}$ - $LUMO_{diene}$ interaction becomes the more important one. Reactions of this type are referred to as "inverse-electron-demand" Diels-Alder reactions.

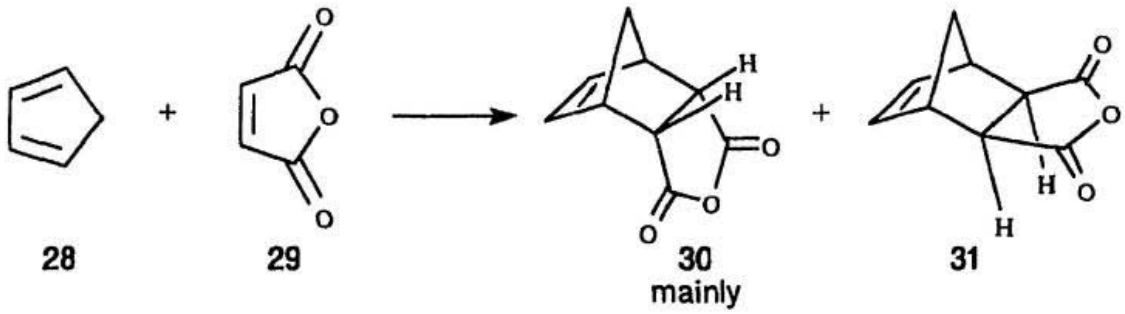
While the substitution patterns shown in Case 2 and Case 3 serve to enhance the reactivity of each reactant, it has been predicted that a normal Diels-Alder reaction involves a higher degree of synchronous character than does the inverse-electron-demand reaction.[11]



Scheme 5. Regiochemical control of the Diels-Alder reaction

iii) *Regioselectivity* The high degree of regioselectivity associated with a Diels-Alder reaction when both addends are unsymmetrically substituted can be readily envisioned when consideration is given to the effects of the substituents on the π systems.[9] Structures **17** and **18** (Scheme 5) show the relative contributions of the localized p-orbitals of the diene HOMO when substituted at the 1 or 2 positions. The view is perpendicular to the molecular plane. A shaded circle signifies a positive component of the wavefunction, and unshaded, a negative component. The size of the circle signifies relative size of the coefficient. Likewise, structure **19** gives the orbital picture of a dienophile bearing an EWG. It has been shown by Anh[13a] and others[13b-d] that condensation will occur so as to bring together the termini with the larger coefficients as shown for **A** and **B** in Scheme 5. Thus, the "ortho" product **22** is obtained predominantly from **20** and **21**, while the "para" product **26** predominates in the reaction of **24** and **25**. In generalized terms, this is referred to as the "ortho-para rule" (Scheme 5).

iv) *Stereoselectivity, the "cis principle", and the Alder "endo rule"* One of the more important features of the Diels-Alder reaction, and strong evidence for a concerted, one-step mechanism, is the high degree of stereoselectivity inherent to most [4+2] cycloadditions. It was recognized early on that *cis*- or *trans*-substituted dienophiles react with dienes to give adducts in which the *cis* or *trans* arrangement of the substituents in the dienophile is retained. This observation was formulated by Alder and Stein as the "*cis* principle".[14] An extension of this is the "*endo* rule". Consider the reacting partners **28** and **29**, which give the isomeric adducts **30** and **31**



Scheme 6. The Diels-Alder reaction of cyclopentadiene and maleic anhydride

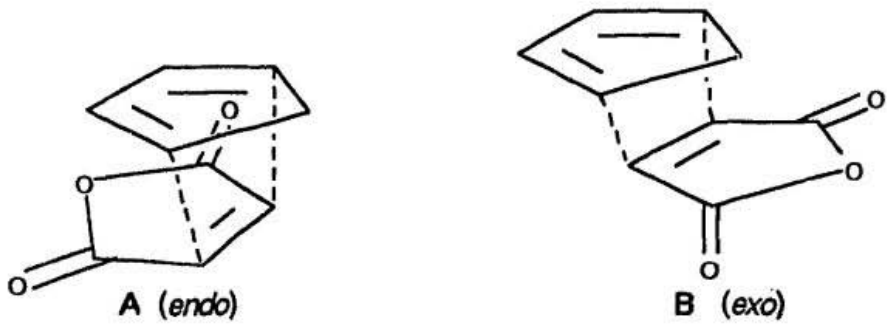


Figure 2a. The orientation of cyclopentadiene and maleic anhydride in the *endo* and *exo* transition states

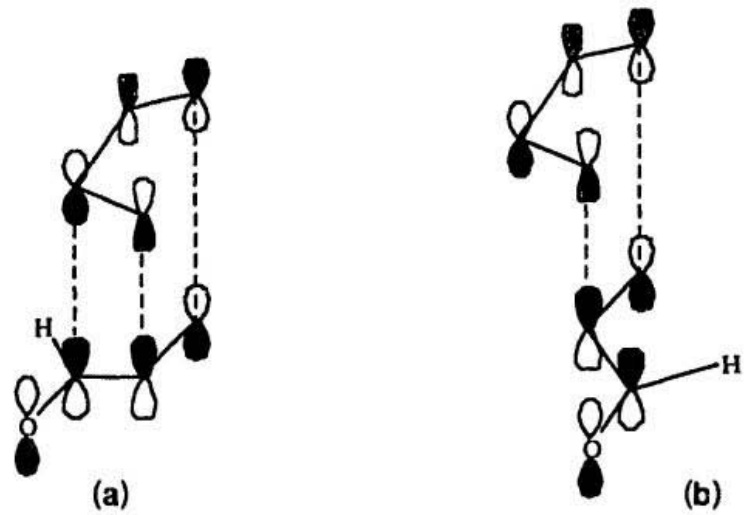


Figure 2b. Frontier orbital picture of the *endo* (a) and *exo* (b) transition states in the Diels-Alder reaction of 1,3-butadiene and acrolein

(Scheme 6). Compound **30** arises from an orientation of the substituent on the dienophile under the diene, as shown in **A** (*endo*), whereas **31** arises from the other orientation, **B** (*exo*) (Figure 2a). Based on a steric argument, inspection of **A** and **B** might lead one to predict that **31** should be the preferred product, because those parts of the molecules that are not bonding are pointing away from each other in **B**. However, with only a few exceptions, products arising from **A** predominate. The "*endo* rule" calls for "maximum concentration" of double bonds[14] in the transition state. This would not only include the π systems directly involved in the reaction, but also those of the activating group(s) on the dienophile.

A more rigorous explanation invokes frontier orbital interactions.[9,10] Figure 2b illustrates the HOMO-LUMO interaction in the transition state for *endo*-addition (**a**) and *exo*-addition (**b**) of 1,3-butadiene and butenone. In the *endo* orientation there is a favorable secondary orbital interaction, i.e. an in-phase orbital overlap, between portions of the HOMO and LUMO other than those at the centers of new bond formation. In the *exo* orientation, the acyl function is directed away from the diene's π system, so there is no secondary orbital overlap. The presence of this secondary effect serves to lower the activation energy leading to the transition state to give products of *endo*-addition. The difference in activation energy between *endo* and *exo* transition states is quite small,[15] but a 9:1 *endo/exo* product ratio needs only about 5 kJ/mol difference in energy.

v) *Lewis acid catalysis* Lewis acids, such as $AlCl_3$ and $SnCl_4$, accelerate the rate of addition of addends in [4+2] cycloadditions[16] in which the

dienophile possesses an allylic C=O or C=N activating function. In addition, both regioselectivity and stereoselectivity are enhanced for the catalysed *versus* the uncatalysed reaction. It has been postulated[17] that the Lewis acid complexes with the carbonyl oxygen, or imine nitrogen, and increases the electron-withdrawing capacity of the substituent group(s). As such, the energies of the frontier orbitals are lowered, and the coefficients in the LUMO at the primary reacting centres are altered, which enhances regioselectivity. Also, the degree of secondary orbital overlap may increase in the *endo* transition state (causing a decrease in the activation energy), which increases the difference in the activation energy leading to the *endo* and *exo* transition states, to result in enhanced stereoselectivity.

vi) *Medium effects* The thermal Diels-Alder reaction occurs under a variety of conditions. In addition to reactions in traditional organic solvents, [4+2] cycloadditions may take place in the gas phase,[11] in low melting fused salts,[18] and under ultra-high pressures[19] in conventional solvents. The most startling results, however, have come from Diels-Alder reactions performed in aqueous media[20] and in solutions of $LiClO_4$-diethyl ether.[21]

In general, the influence of the solvent on the reaction rate is relatively small (independent of the system investigated), even over a wide range of solvent polarity, for both the normal and the inverse-electron-demand Diels-Alder reactions.[11] However, *endo/exo* ratios are both solvent and temperature dependent,[11,22] and gas phase reactions seem to occur as fast as those in a nonpolar liquid phase.[11]

Breslow reported in 1980 a dramatic increase in both the rate and the *endo/exo* ratio of some simple Diels-Alder reactions conducted in water[23] (as opposed to those reactions performed in organic solvents). Grieco confirmed this unusual solvent effect with more complex substrates.[24] The increase in rate was thought to be due to the "hydrophobic effect", which is the tendency of nonpolar species to aggregate in water solutions so as to decrease the hydrocarbon-water interfacial area.[20] Two hydrocarbon surfaces come together in a Diels-Alder transition state. In water this aggregation must be favored, with a net decrease in hydrocarbon surface area on going from reactants to products. Additionally, hydrocarbon solubility is a function of the hydrophobic effect. Increased hydrophobicity decreases hydrocarbon solubility, and this should lead to an enhancement of reaction rate. This was indeed found to be the true when reactions were run in aqueous solutions of LiCl or guanidinium chloride (GnCl). Lithium chloride is known to increase the hydrophobic effect of water and GnCl decreases it. Rates did increase in solutions of LiCl, and they decreased in GnCl solutions.[20]

Grieco later postulated that the increase in the rate and the *endo/exo* ratio in his systems was the result of micellar catalysis, a mutual binding of reactants in an aggregate.[24] Breslow discounted this idea based on additonal experiments[25] restating that the rates are due to hydrophobic effects (*vide supra*). He went on to propose that the increased *endo/exo* ratios in water reactions are due to the high polarity of the medium increasing the charge-transfer interaction that results from secondary

orbital overlap in the *endo* transition state. Thus, the hydrophobic effect should also favour the more compact *endo* transition state.

In a more recent paper, Grieco[21] proposed that the high internal solvent pressure of water may also be responsible for the rate acceleration by compressing the reactants, in much the same manner as the application of external pressure in ultra-high pressure Diels-Alder reactions. He observed that the rates of a number of Diels-Alder reactions are greatly enhanced when conducted in solutions of 5M $LiClO_4$-diethyl ether, a solvent medium that possesses a high internal solvent pressure. Shortly afterwards, however, Dailey[26] provided evidence that suggests that the increases in rate in $LiClO_4$-diethyl ether solutions are due to Lewis acid catalysis of the reaction by the Li^+ ion, which may be the first example of catalysis of Diels-Alder reactions by a weak Lewis acid.

vii) *Syn-anti or π-facial selectivity* In addition to the regiochemical and topological (*endo/exo*) aspects of the Diels-Alder reaction, there is another form of stereoselectivity. This arises when the two sides, or faces, of the π-system of the diene or dienophile are differentiated.[7c] An example of this π-facial selectivity is illustrated in Figure 3. The side of the diene possessing the group Z is called the *syn* face, and the opposite side is referred to as the *anti* face. When addition of a dienophile occurs on to the *syn* face, the *syn* adduct **A**, is the result. Likewise, for *anti*-face addition, the *anti* adduct **B**, forms. The terms *syn* and *anti* are relative, and refer to the mode of addition. *Syn/anti* or π-facial selectivity will be discussed in detail in the following section.

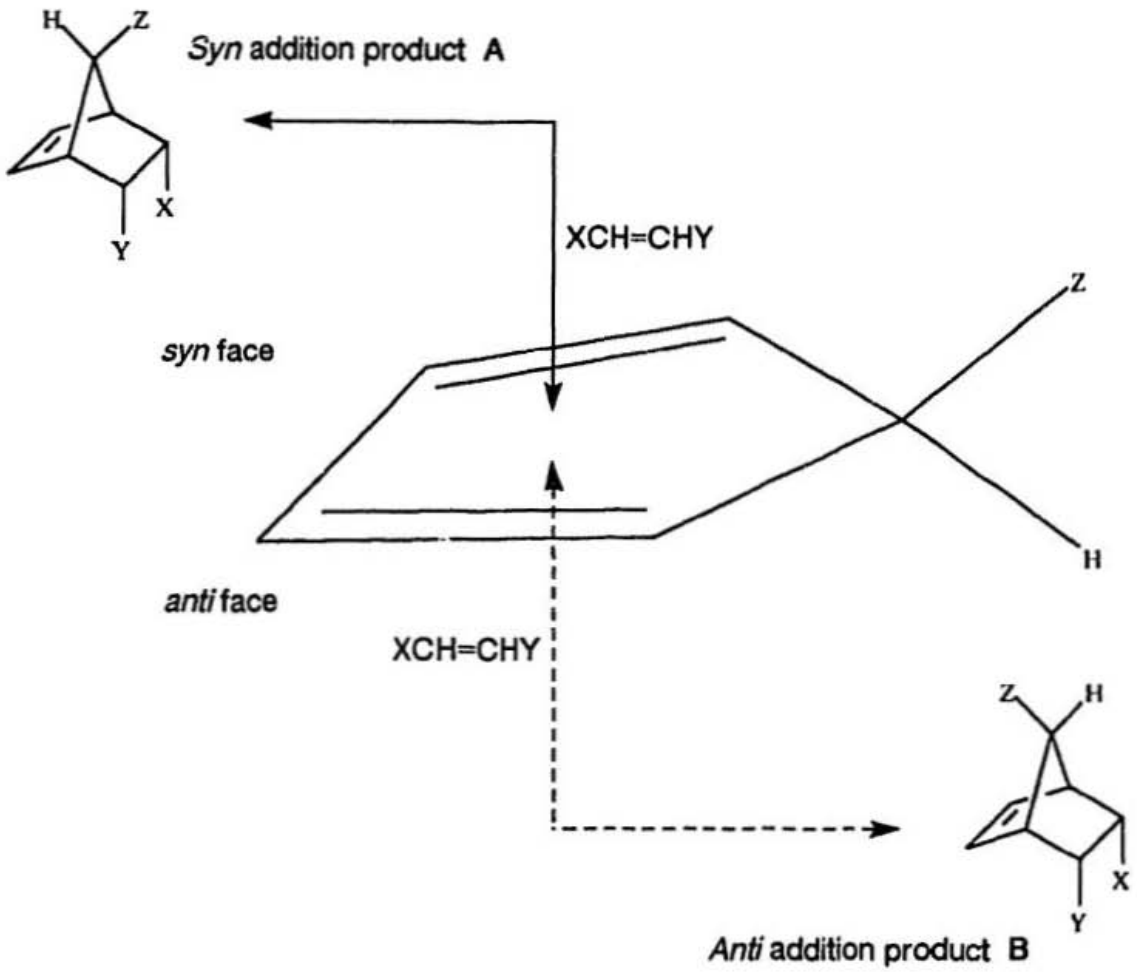


Figure 3. The addition of a dienophile *syn* and *anti* to a plane-nonsymmetric diene

SYN/ANTI OR π-FACIAL SELECTIVITY

π-Facial stereocontrol has long been recognized as an essential element in asymmetric synthesis.[2] In any reaction involving a planar substrate or intermediate, in which there are two reactive faces, two or more enantiomeric or diastereomeric products may be formed. It is often desired, however, that only one face react in a stereocontrolled manner. This *π*-facial selectivity may also be applied to the Diels-Alder reaction in which at least one chiral or pseudochiral centre on one of the addends causes one face of the diene or dienophile to react faster than the other, with the preferential formation of one product. *π*-Facial stereocontrol is usually observed in one of two circumstances: (i) by the influence of a chiral auxiliary or catalyst in which one face of an addend is blocked in the transition state; or (ii) by the influence of a plane-nonsymmetric substituent in the allylic position of either the diene or the dienophile.

The utility of the first approach as applied to asymmetric synthesis has already been well demonstrated,[2c] especially in instances involving chiral dienophiles. This treatise will focus on the *π*-facial selectivity arising from the latter case, or, more specifically, the consequence of heteroatom substitution at the allylic position of cyclic plane-non-symmetric dienes.

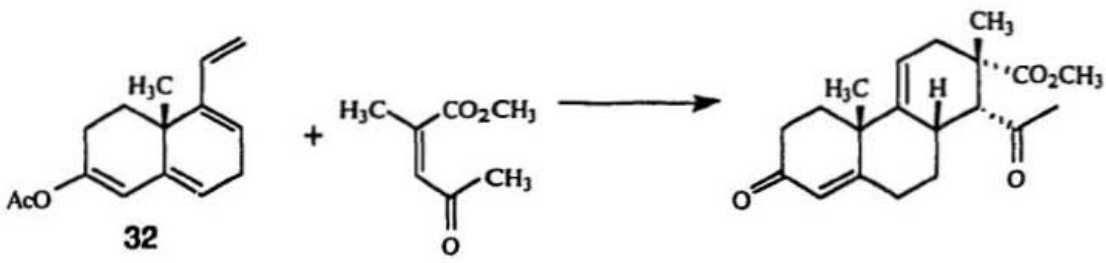
A number of systems have been studied to probe the causative factors involved in the *π*-facial selectivity exhibited by dienes possessing a stereogenic allylic centre. These can be classified into two general categories: (i) carbocyclic network, where there is alkyl, or carbon-based substitution at the allylic position, and (ii) heteroatom substitution (O, N, S, etc.) of the allylic position of cyclic, semicyclic and acyclic dienes.

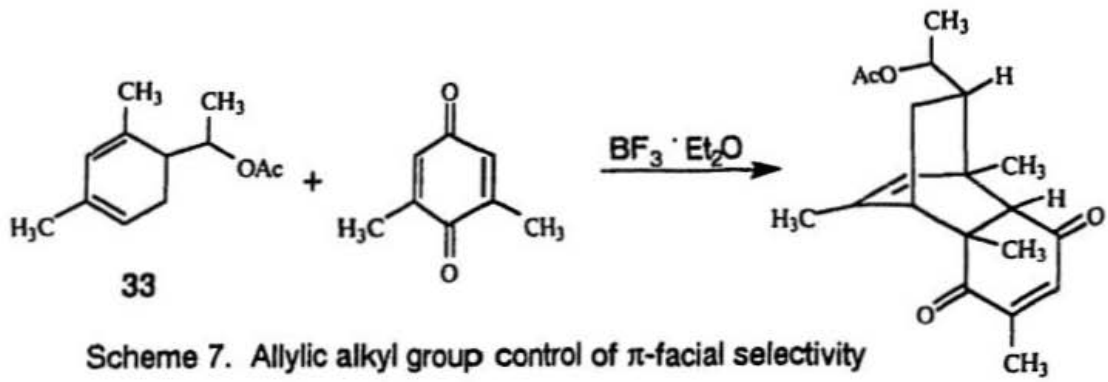
Allylic Alkyl Substitution

Experiments performed by Valenta and coworkers[27,28] demonstrated complete π-facial stereocontrol, as shown in Scheme 7, with dienes **32** and **33**. Similarly, the prostaglandin synthesis by Corey[29] utilized an alkyl substituent at the 5-position of a cyclopentadiene moiety **34** to c2ontrol the Diels-Alder addition as shown in Scheme 8. In both instances, the adduct obtained was that arising from addition of the dienophile *anti* to the sterically inhibiting allylic alkyl group. A more subtle demonstration of this steric effect is shown in Scheme 9, in which progressing from a dichloromethyl group in **35a**, to the larger dibromomethyl group in **35b**, gave enhanced addition *anti* to the dihalomethyl moiety.[30]

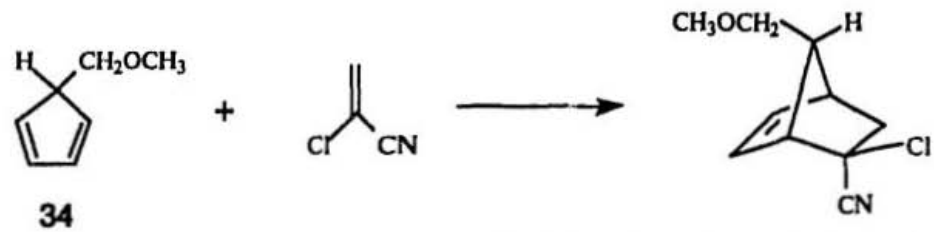
More rigorous studies of the steric requirements of the Diels-Alder reaction have been reported by Burnell and Valenta[31,33] and also by Paquette[34] using 5-alkyl substituted cyclopentadienes. The results are summarized in Scheme 10. There are two notable features presented in this work. Firstly, the adduct ratios arising from the Diels-Alder reactions of dienes **36-39** are strikingly similar, typically 80-85% in favor of the major product with a variety of dienophiles. Secondly, the results obtained for dienes **36** and **37** indicated that the methine hydrogen (C1-H) is more sterically demanding than the methylene hydrogens (C3-H) in the Diels-Alder addition. Molecular modelling calculations[35] supported this postulate. The possibility of some sort of σ/π interaction (*vide infra*) controlling the π-facial selectivity was not consistent with the similarity in the adduct ratios.

A somewhat anomalous result was that shown in Scheme 11 in which the "double adduct" **42**, formed from the reaction of tetraene **40** with DMAD, could only have arisen

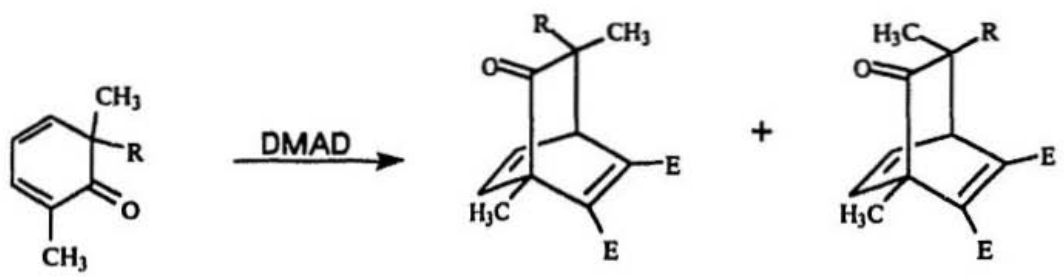




Scheme 7. Allylic alkyl group control of π-facial selectivity

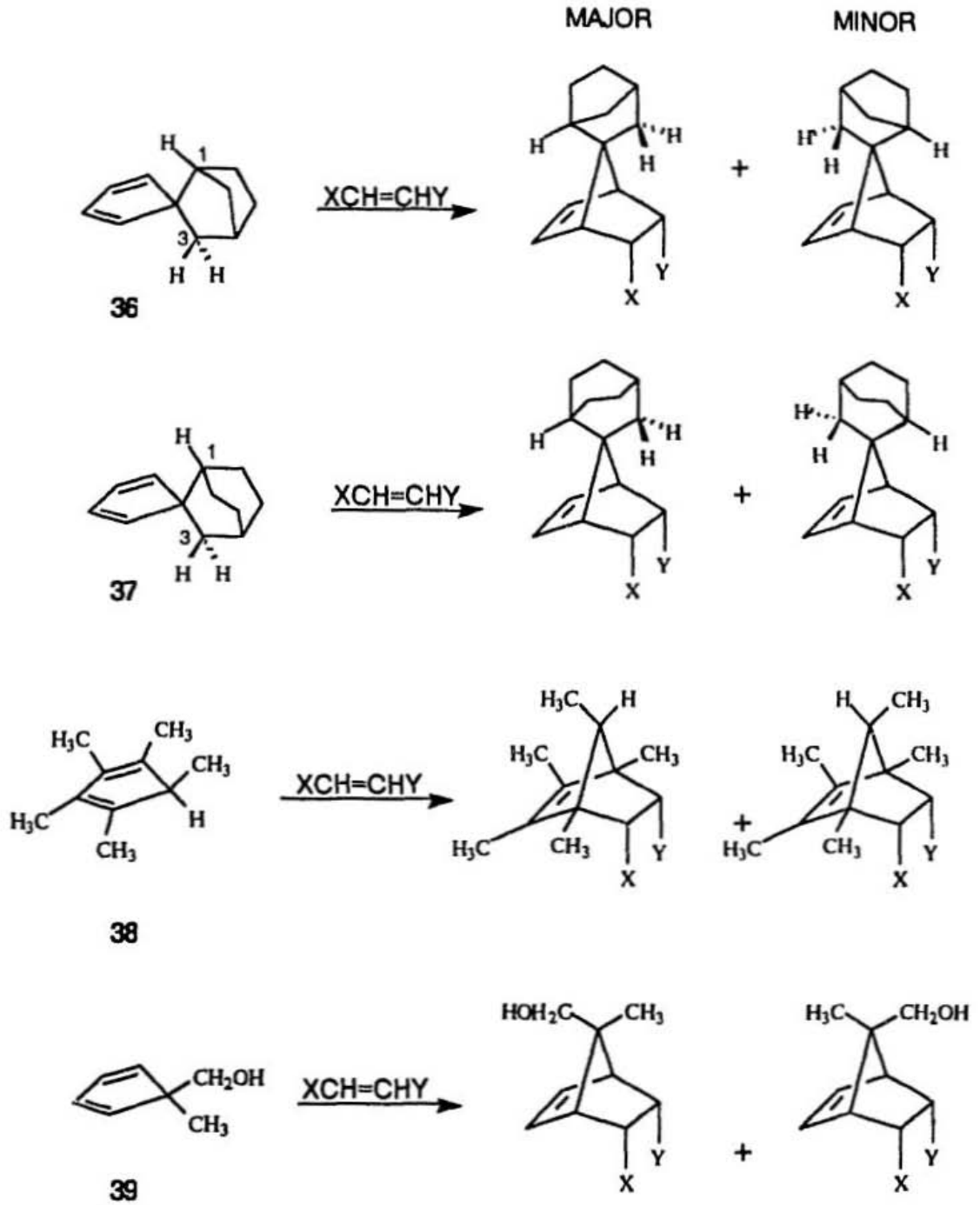


Scheme 8. Allylic alkyl group control of π-facial selectivity in the synthesis of prostaglandins



35a	R = $CHCl_2$	6	:	1	product ratio
35b	R = $CHBr_2$	8	:	1	

Scheme 9. π-Facially selective Diels-Alder reactions of dienones



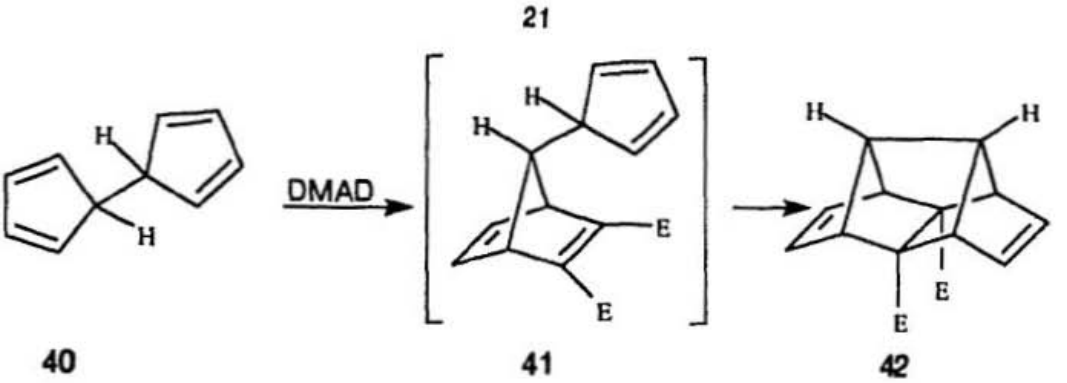
Scheme 10. π-Facial selectivity in the Diels-Alder reaction of 5-alkyl substituted cyclopentadienes

from addition of the dienophile *syn* to the cyclopentadiene substituent[36] to give intermediate **41**.

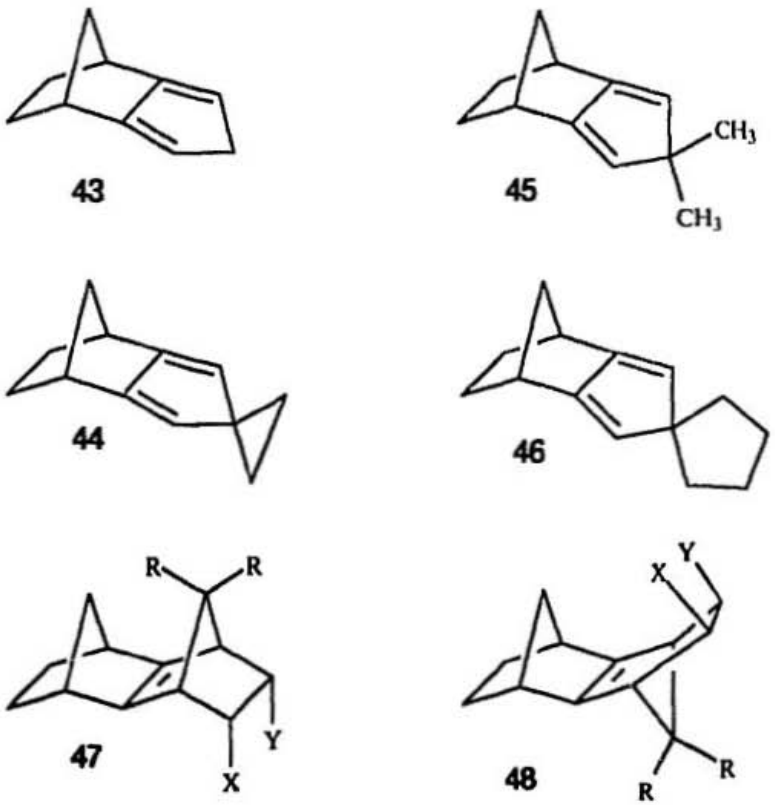
The pioneer work of Paquette *et al.*[37] on the isodicyclopentadiene systems **43-46** afforded some interesting observations. Many experiments revealed that **43** undergoes Diels-Alder reactions with various dienophiles to give only adducts of type **47**, i.e., arising from bonding to the "bottom", or *endo* face, of the diene (Scheme 12). It was claimed[37] that this result could not be due to a steric effect because the incoming dienophile must approach the diene face *syn* to the larger ethano bridge. The cyclopropane derivative **44** behaved in a similar manner. In contrast, the cyclopentane analogue **46** and the gem-dimethyl **45**, gave mainly adducts of type **48**.

It has been postulated[37] that these, and similar results, are due to mixing of the σ orbitals of the norbornyl framework with the π orbitals of the diene. This σ/π interaction perturbs the π_s of the diene unit, but not the π_a (or HOMO). For both **43** and **44**, this causes a disrotatory tilt of the terminal π lobes towards the methano bridge, as shown in **A** (Figure 4). Conversely, the central π lobes rotate in the opposite direction. The net effect is a minimization of closed-shell antibonding interaction between the π_s of the diene and the HOMO of the dienophile on the *endo* surface during dienophile approach, as shown in **C**. In contrast, dienes **45** and **46** experience a conrotatory tilt of the terminal π lobes (**B** of Figure 4), thereby minimizing any antibonding interactions on the "top" or *exo* surface during cycloaddition, as shown in **D**.

It should be noted, however, that molecular modelling calculations by Houk[38] suggested that the π-facial selectivity displayed by these and other isodicyclopentadiene systems was due to a combination of torsional and steric effects. In addition, studies on



Scheme 11. Diels-Alder reaction of 5-(cyclopentadienyl)cyclopentadiene with dimethyl acetylenedicarboxylate (E= CO_2CH_3)



R = H, $-CH_2CH_2-$ R = CH_3, $-(CH_2)_4-$

Scheme 12. π-Facial selectivity in the Diels-Alder reaction of isodicyclopentadienes

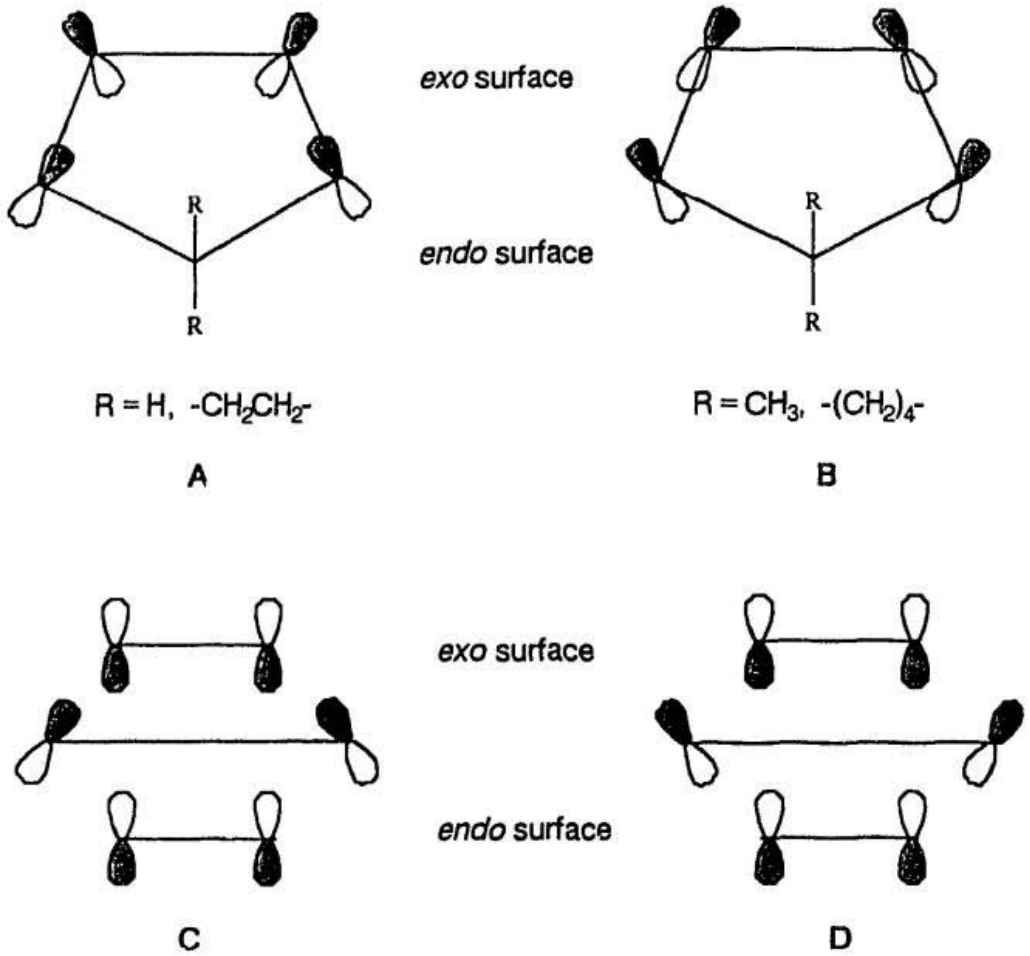


Figure 4. Orbital tilting postulate for the π-facial selectivity of isodicyclopentadienes

49 50

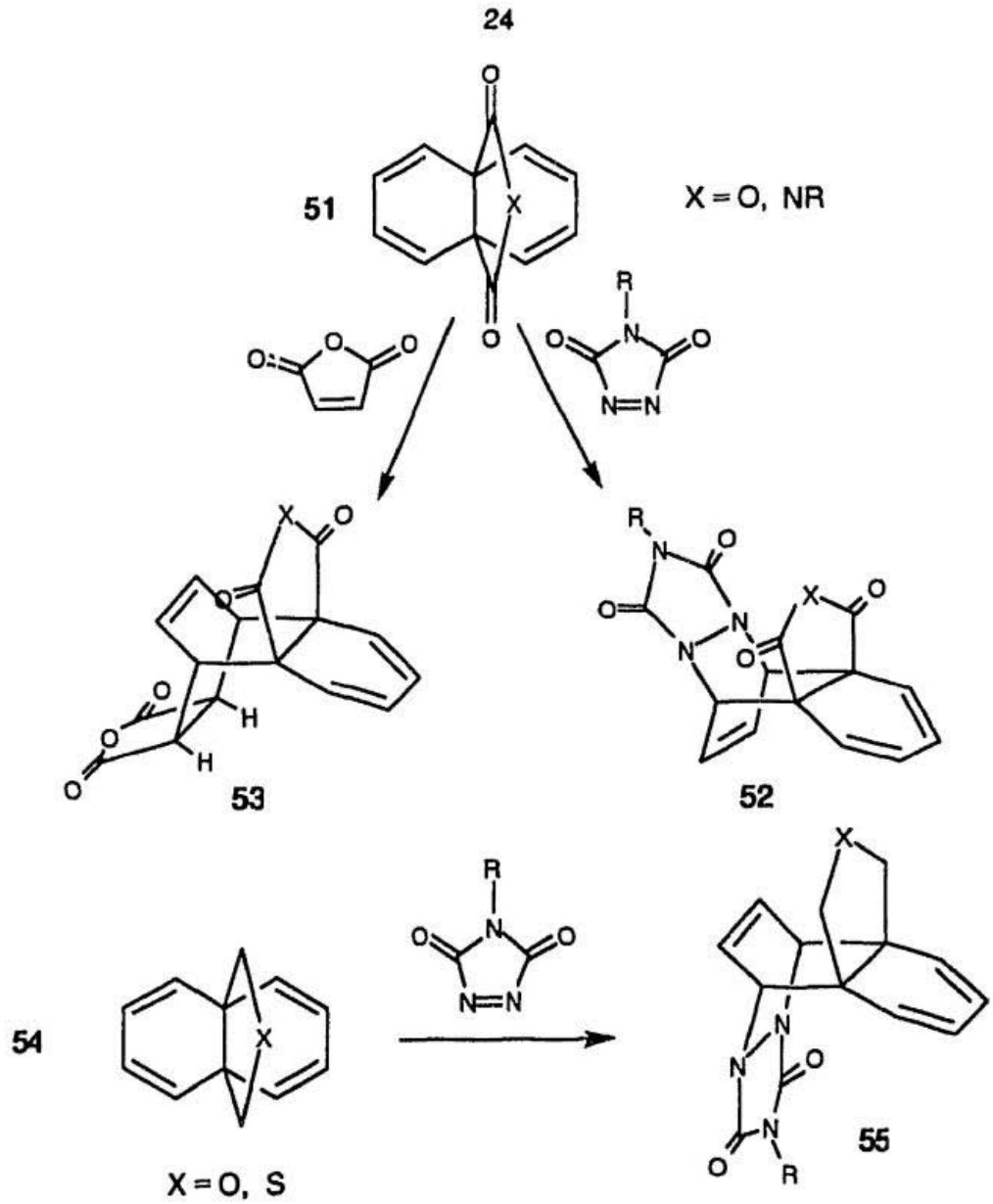
the cycloaddition of dienophiles **49** and **50** with various dienes indicated that the π-facial selectivity displayed by these substrates was essentially due to steric effects.[39]

Other examples of π-facial selectivity displayed by dienes with a carbon-based allylic substituent are the propellane systems investigated by Ginsburg *et al.*[40] It was discovered that addition of a nitrogen-based dienophile gave exclusively a *syn* adduct **52** with dienes **51** (Scheme 13), while a carbon-based dienophile gave exclusively an *anti* adduct **53**. In contrast, the nitrogen-based dienophiles reacted *anti* with propellanes **54**, to give adducts **55**.

The Diels-Alder reaction giving rise to adducts **52** was considered to be due to secondary orbital overlap between the π system of the anhydride moiety (with X = O) with the lone-pair orbitals on the nitrogens of the dienophile, as shown in Figure 5. The lone pair orbitals of the incoming diazo groups overlap favorably with the π^* orbitals of the carbonyls. This was predicted to occur at distances for which the $HOMO_{diene}$ - $LUMO_{dienophile}$ interaction leading to cycloaddition had not become significant.[40b] It should be pointed out that addition of the PTAD should experience no such overlap if approach is from the face of diene **51** *anti* to the carbonyls, and, of course, if the same dienophile reacts *syn* to dienes **54**. Considering also the *anti* adduct **53**, which arose from the addition of a carbon-based dienophile to **51**, it may be reasonably stated that the secondary orbital interaction shown in Figure 5 favors *syn* addition, when possible, and when not, steric effects favor *anti* addition.

Allylic Heteroatom Substitution

The last decade has witnessed an expansion of research efforts directed at unlocking the mechanism of heteroatom-directed π-facial diastereoselectivity in the Diels-



Scheme 13. π-Facial selectivity in the Diels-Alder reactions of propellanes

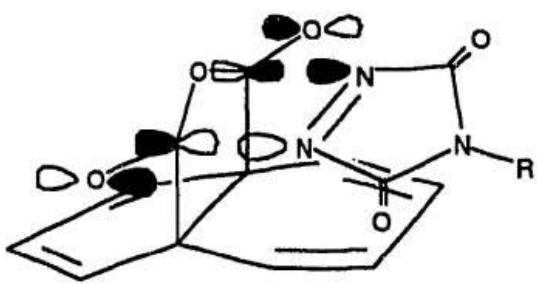


Figure 5. Secondary orbital overlap in the approach of an azo dienophile *syn* to an anhydride bridged propellane

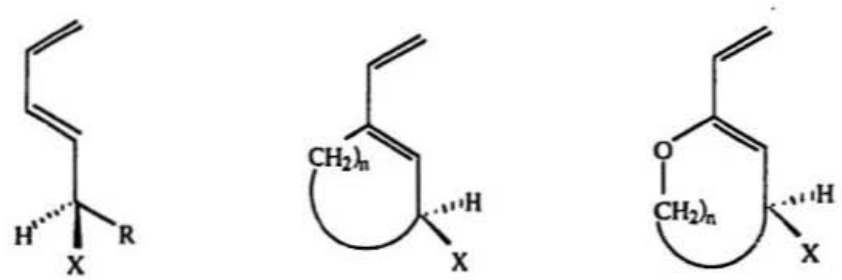
Alder reaction. It was discovered early on that an atom other than carbon placed at the allylic position of a diene can have a profound effect on the relative reactivities of the two-faces of the diene. In some systems, cycloaddition takes place preferentially by capture of the dienophile on the face of the diene *anti* to the heteroatom, while other systems exhibit the formation of adducts arising from an apparently contrasteric *syn* additions.

The systems that have been studied to date can be classified into four general categories (Scheme 14): the acyclic dienes I, which have free-rotation of the allylic centre, the semicyclic species II and III, which are more restricted in their degrees of conformational flexibility, and the cyclic derivatives IV, in which the diene moiety is constrained within a ring and the heteroatom is held rigidly in place. Examples and a discussion will be presented to overview the Diels-Alder behaviour of these four structural types. A review follows of the current theories dealing with π-facial diastereoselectivity in cases in which the cycloaddition affords seemingly contrasteric products.

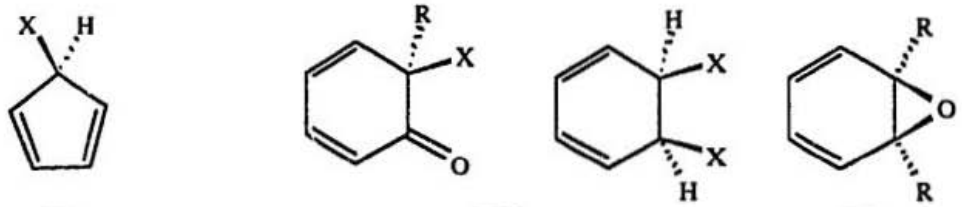
Type I dienes

A note on product description should be made at this point. In contrast to acyclic systems, the stereochemical descriptors *syn* and *anti*, which describe an adduct in terms of the facial approach of addends, are adequate for semicyclic and cyclic dienes because the heteroatom is reasonably well fixed in space with respect to the *Re* and *Si* faces of the diene.

For acyclic systems, due to free rotation about the C_1-C_2 bond axis (Figure 6), the heteroatom may adopt a number of conformations with respect to the two faces of the diene. This is a major problem in interpreting the π-facial selectivity of acyclic dienes. For acyclic systems the general practice is to describe the mode of addition of dienophiles



I II n = 1,2 III n = 1, furanose n = 2, pyranose



IV a cyclopentadienes

IV b 1,3-cyclohexadienes

IV c benzene oxides

X = Heteroatom

Scheme 14. Structural types of 1,3-dienes bearing allylic heteroatom substitution

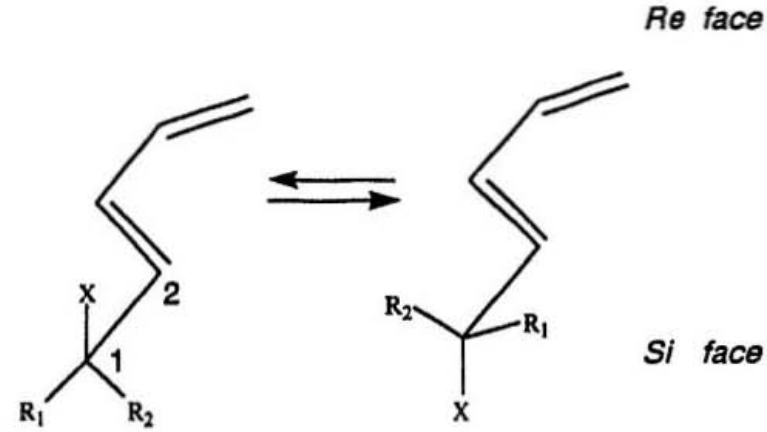


Figure 6. Free rotation of the allylic center of acyclic1,3-dienes

in terms of "like" and "unlike". (This is based on the Seebach-Prelog[41] convention for describing the relative topicities of approach to the faces of an enantiomer.) Reactant approach to the *Re* face of a double bond with an adjacent *R* allylic centre is termed "like" addition, and approach to the *Si* face is termed "unlike" addition. Similarly, for an *S* chiral centre, approach to the *Re* face is "unlike", and approach to the *Si* face is "like" (Figure 7). However, for consistency, many authors use a predetermined priority, which may differ from the "normal" convention, for assigning the *R* or *S* configuration of the chiral centre and the *Re* and *Si* assignments of the diene faces.[42] For the purposes of the present discussion, "like" addition is termed *syn*, and "unlike" is termed *anti*. This convention is used by other authors.[43,44] This does not imply, however, that the heteroatom is in any fixed position with respect to the diene.

The results of cycloadditions of a number of acyclic dienes containing a chiral allylic centre bearing a heteroatom are given in Table 1. When a stereogenic centre is incorporated into the diene the products of cycloaddition are diastereomeric, and remain so because the stereogenic centre still exists in the product. Taking entry 4 of Table 1 as an example (Scheme 15), addition of *N*-phenylmaleimide to compound **56** resulted in the formation of diastereomers **57** and **58** (both by *endo* addition) in a 83:17 ratio, respectively, in which the major adduct **57** arose from *syn* addition, and the minor adduct **58** from *anti* addition (Figure 8).

Table 1 does not include all of the many examples of the *π*-facial selectivity observed in acyclic dienes. It is only meant as an overview (see Ref. 44b for a more complete reference list). However, several observations can be made from the data contained therein.

1. Facial selectivity is sensitive to dienophile type (compare entries 5 and 9).

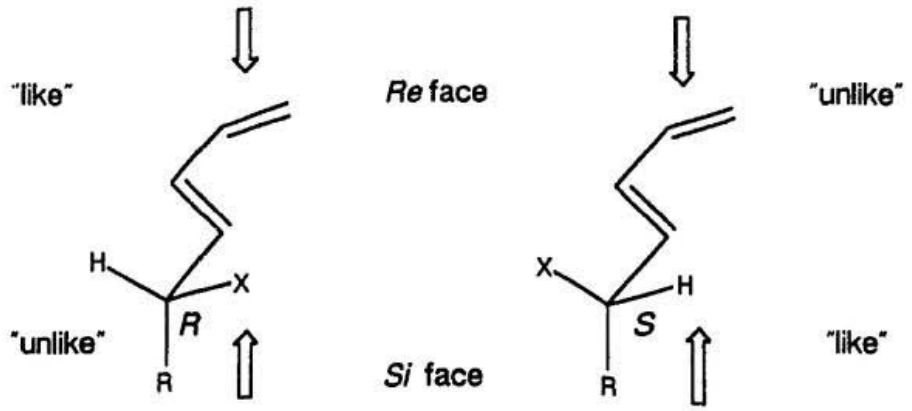
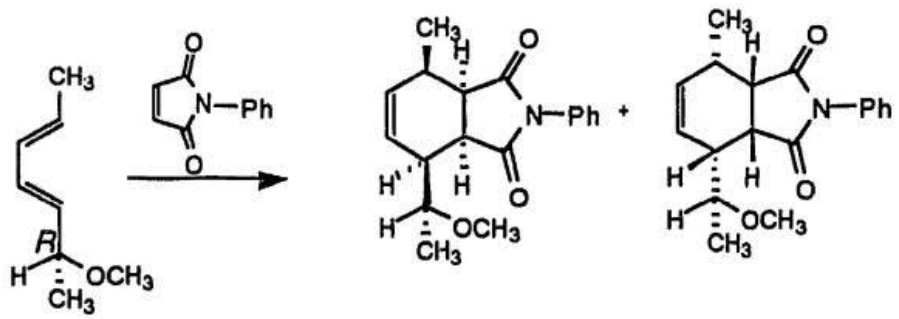


Figure 7. "Like" and "unlike" additions to acyclic 1,3-dienes



Scheme 15. Diels-Alder reaction of an acyclic 1,3-diene with an *R* allylic center

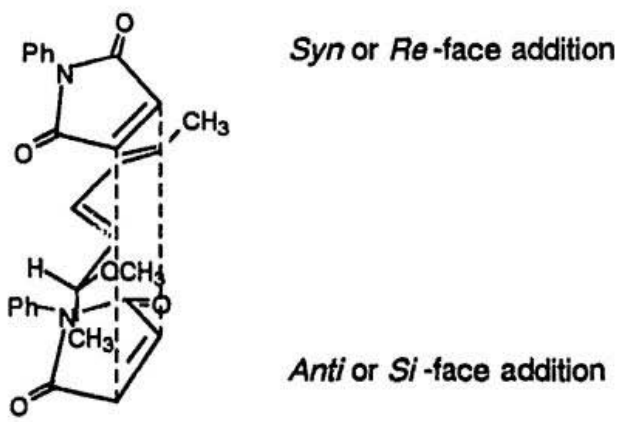


Figure 8. Approach of *N*-phenylmaleimide *syn* and *anti* to compound **56**

Table 1. π -Facially selective Diels-Alder reactions of acyclic dienes

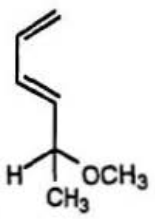
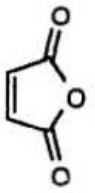
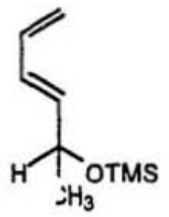
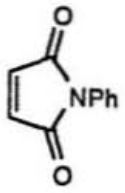
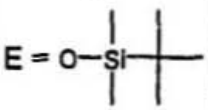
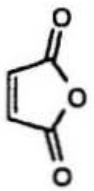
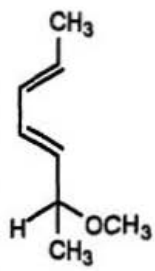
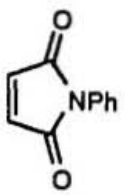
entry	diene	dienophile	% *syn* / % *anti*	Ref.
1			73 / 27	42b
2			80 / 20	42b
3	 		82 / 18	42b
4	 **56**		83 / 17	42a

Table 1. continued

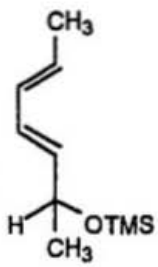
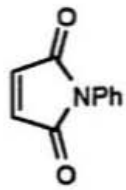
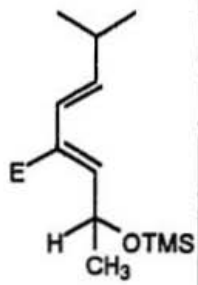
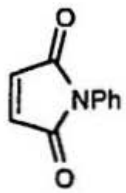
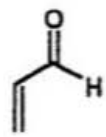
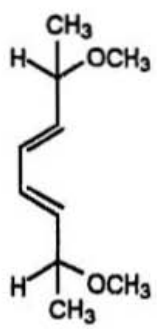
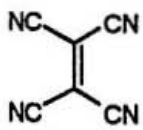
entry	diene	dienophile	% *syn* / % *anti*	Ref.
5			88 / 12	42
6	 E = OCH_2OCH_3		100 / 0	45
7	〃		100 / 0	45
8			15 / 85	46

Table 1. continued

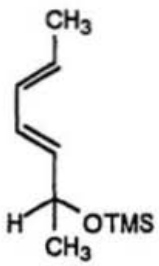
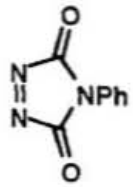
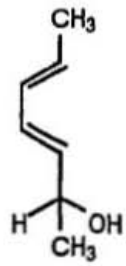
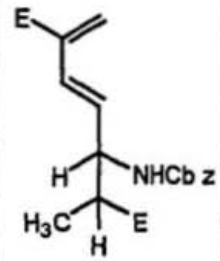
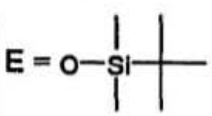
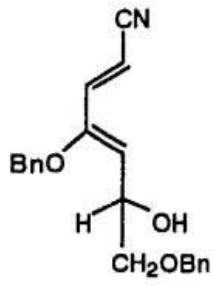
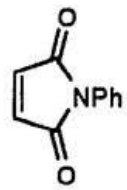
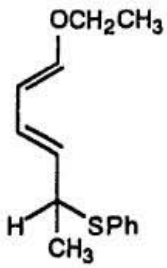
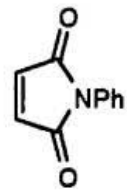
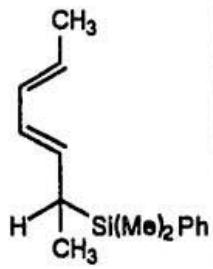
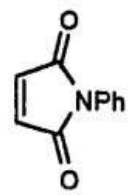
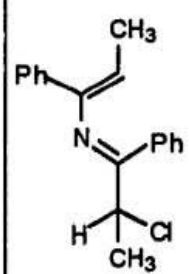
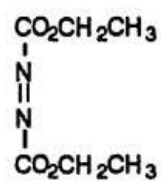
entry	diene	dienophile	% *syn* / % *anti*	Ref.
9			15 / 85	42b
10			27 / 73	42b
11	 		37 / 63	47

Table 1. continued

entry	diene	dienophile	% *syn* / % *anti*	Ref.
12			76 / 24	48
13			60 / 40	49
14			18 / 82	50
15			93 / 7	51

2. Even highly substituted acylics are able to display high levels of selectivity (entries 6, 7, 11-12, 15).
3. Allylic hetereoatoms other than oxygen are able to influence facial selectivity (entries 13-15).
4. Heterodienes also display selectivity (entry 15).
5. If strict attention is paid to dienophile type, the facial selectivity is generally predictable (entries 1-6, 12).

The previously mentioned difficulty associated with the interpretation of π-facial selectivity of acyclic dienes has its basis in the determination of the conformation of the allylic centre in the transition state. Figure 9 illustrates six possible conformations for an acyclic diene with an *R* allylic centre. Complications arise from the necessity of determining the relative contributions and reactivities of the various conformers. Is the heteroatom aligned "inside" (**E** and **F**) based on electronic factors, or "outside" (**B** and **C**) as favored on steric grounds?

Hehre[43] suggested that *syn* addition occurs from the *Re* face attack of conformer **C**, but no evidence was given to justify why this should be the preferred conformation in the transition state.

Houk and coworkers calculated the relative energies for some staggered transition states for the electrophilic dipolar addition of nitrile oxides to chiral alkyl ethers.[52] (They had shown earlier that the allylic substituents are staggered in cycloaddition transition states.[53]) They had determined that the allylic ethers prefer the "inside" position, and alkyl substituents prefer the sterically less crowded *anti* conformation (Scheme 16). This was termed the "inside alkoxy" effect. Houk argued that when bond formation occurs during electrophilic attack, the π-bond becomes electron deficient, and "Electron-donor

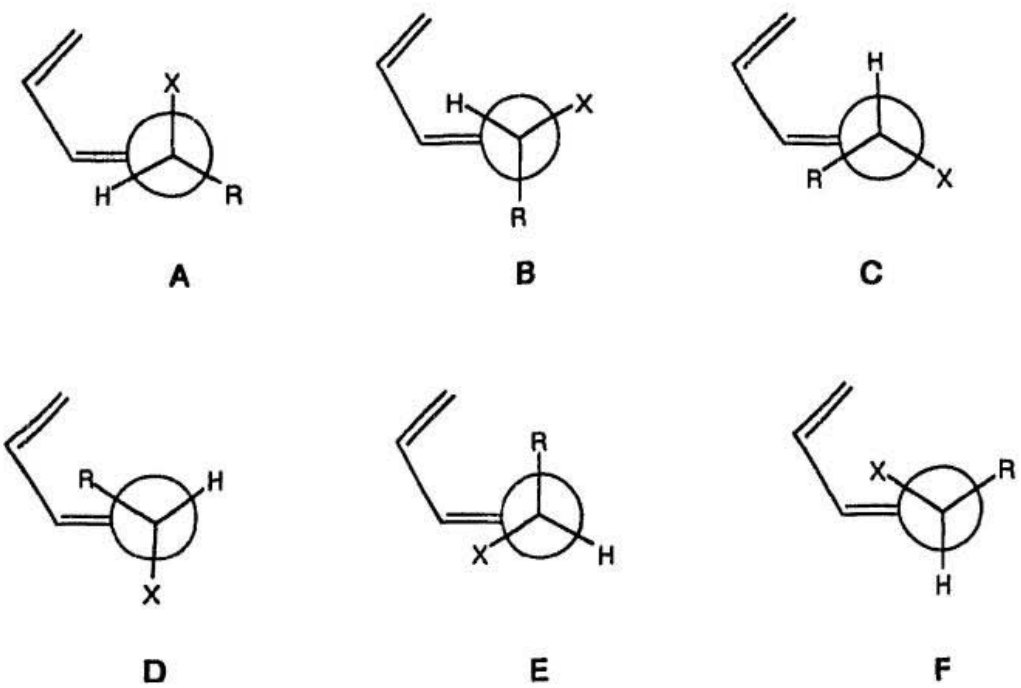
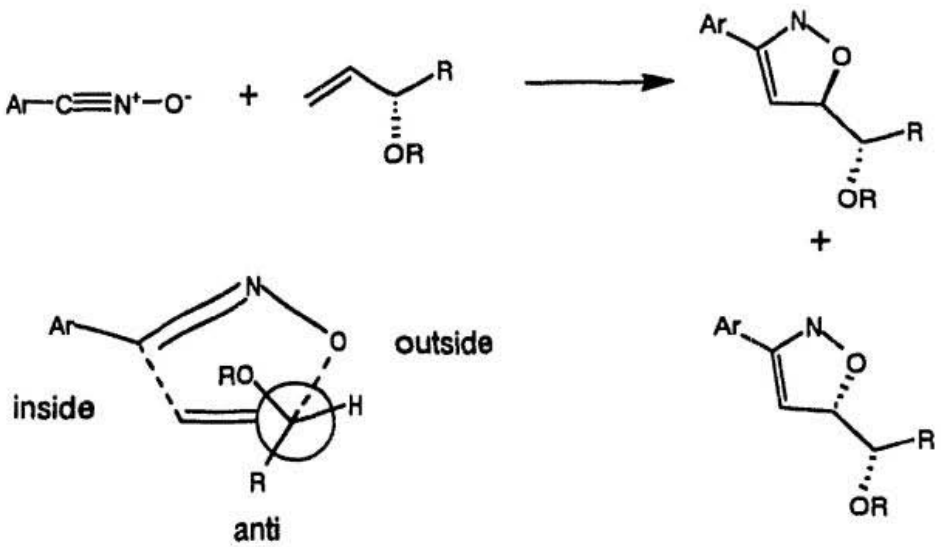


Figure 9. Important conformations of the allylic center of acyclic 1,3-diene



Scheme 16. Dipolar additions to alkenes containing ether substitution at the allylic positions

substituents on the alkene stabilize the transition state, while electron-withdrawing substituents destabilize the transition state. When the allyl ether is *anti*, the CHROR' group is electron-withdrawing, since the σCO orbital overlaps with, and withdraws electron density from, the alkene π orbital. When the CO is 'inside', it is near the plane, and overlap of σCO with π is minimized. Now, overlap of electron-donating σCH and σCR orbitals with the π orbital is maximized, and the transition state is stabilized".[52]

This generalization agreed well with the experimental results obtained by Houk for dipolar additions. However, Franck[42b] argued that this would predict the *Si* facial attack of dienophiles to conformer **E** (or *anti* addition), the opposite of that observed[42b] by Franck and others (see references in Table 1). Franck reasoned instead that *Re* face addition to conformer **B** should be preferred. MacDougal[45] also favored this conformation, based on arguments put forward by McGarvey[54] and Fleming[55] for the electrophilic alkylation of ester enolates.

Additional support that favored **B** as the more likely conformation in the transition state came from results with acetylenic dienophiles (entries 10 and 11, Table 1). Kozikowski[47c,58] proposed that for acetylenic dienophiles the electron withdrawing group of the dienophile would experience unfavorable steric interactions with the outside heteroatom of conformer **B** (see Figure 11a). This steric interaction would be smaller for ethylenic dienophiles. The preferred conformation in the transition state then would be **E** (Figure 11b), that in which the heteroatom is inside, and the dienophile would prefer to add *anti* to the larger R group to give the *Si* face addition product (or *anti* addition, *Si* face of *R* centre).

Meanwhile, Dannenberg and coworkers[57] modelled the conformations of some (*E*,*E*)-5-alkoxy-1,3-hexadienes (**59a-d**, Figure 10) in the transition states for both *Re* and

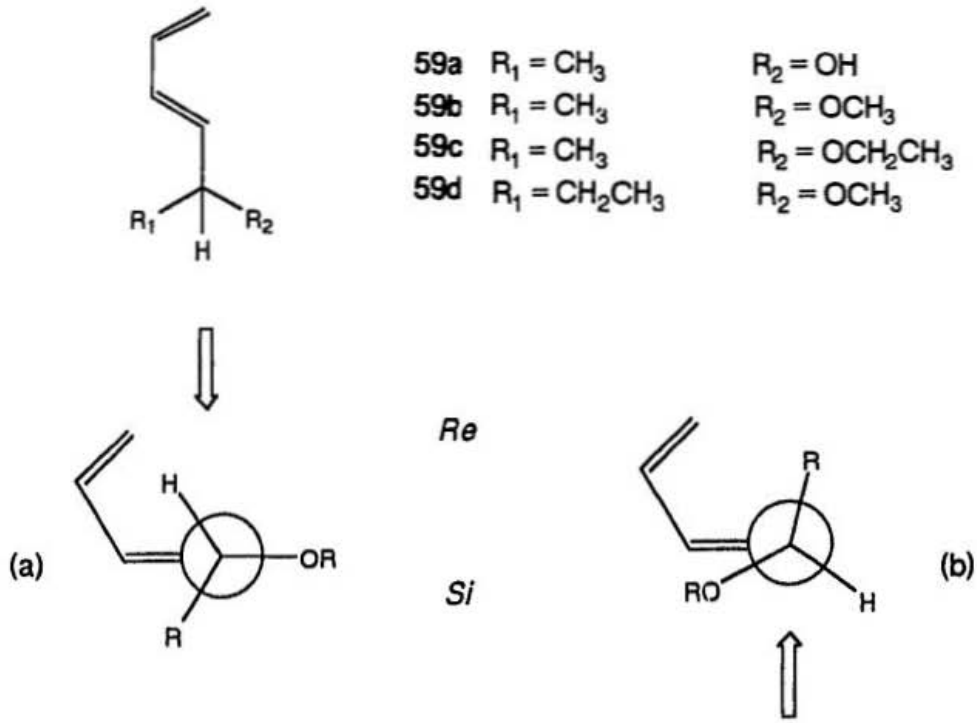


Figure 10. Preferred conformation of the allylic oxygen in the transition state of acyclic 1,3-dienes upon reaction with ethylenic dienophiles (a) and with acetylenic dienophiles (b)

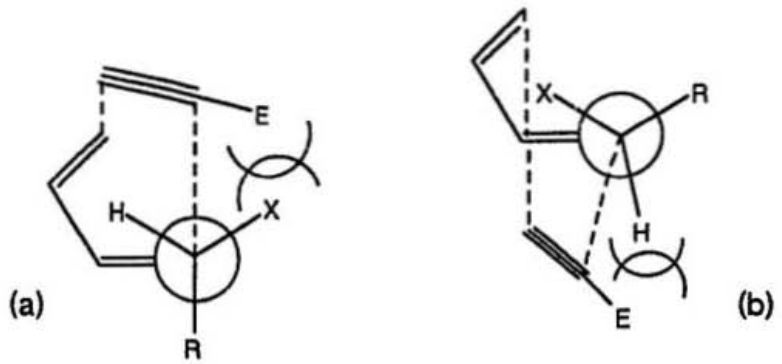
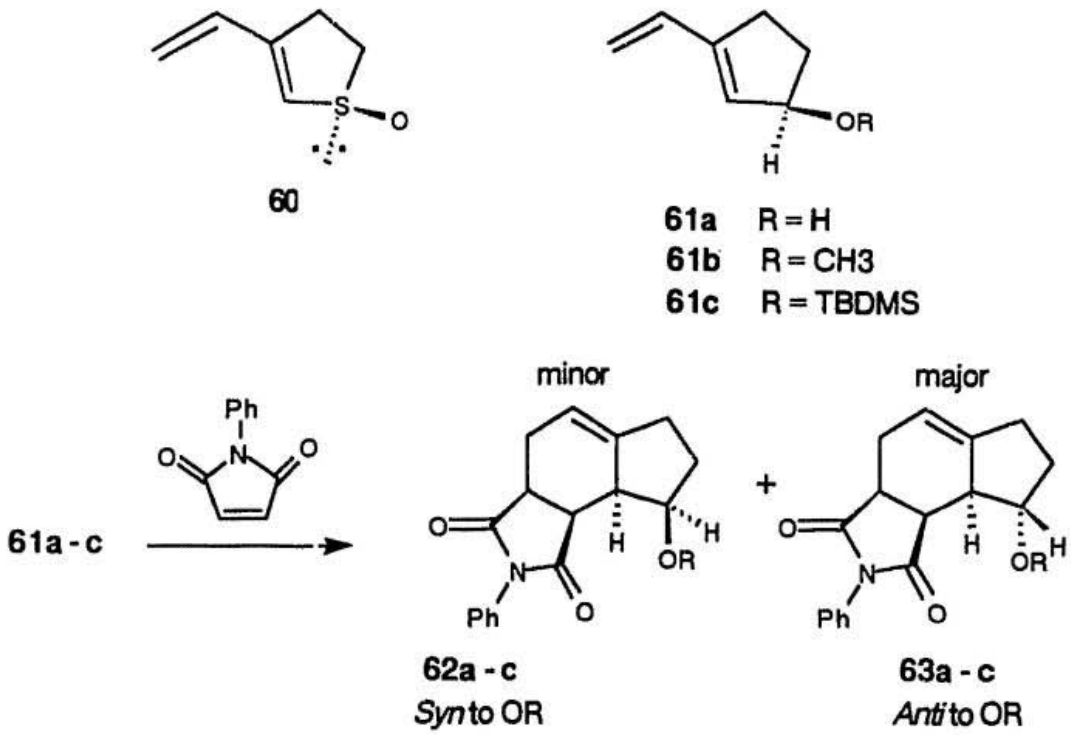


Figure11. Approach of an acetylenic dienophile to the *Re* (a) and *Si* (b) faces of an acyclic 1,3-diene

Si facial approach of ethylene. In all cases *Re* face approach to an *R* chiral centre (or *syn* addition) was the favored transition state. In addition, the OR group adopted an anti-coplanar orientation with respect to the diene (Figure 10a). In this conformation, the dienophile may approach *syn* to the hydrogen (*Re* face) or *anti* to the hydrogen (*Si* face). The alkoxy group prefers to be approximately in the plane of the diene in the transition states for both *syn* and *anti* additions. The dienophile approaches from what would be the less hindered side. Dannenberg's results suggested that the face selectivity is "due to a combination of steric and electronic effects", although it was unclear what the electronic effects are, and why the OR should prefer an anti-coplanar orientation. For the reaction with acetylenic dienophiles, it was determined that the OR instead would attain a syn-coplanar orientation (Figure 10b), to lessen the interaction between the dienophile and the OR in the transition state. This is in accord to the postulate proposed earlier.[56]

Type II dienes

Only two reports have been published to date with the semicyclic dienes of type II. Overman and coworkers[58] reported the synthesis and cycloadditions of two diene systems bearing a chiral allylic centre, the sulfoxide **60** and the alcohol **61a** with derivatives **61b** and **61c** (Scheme 17). Selected cycloaddition results with these dienes with *N*-phenylmaleimide (NPM) and tetracyanoethylene (TCNE) are given in Table 2. The sulfoxide **60** displayed exclusive *anti* addition in a number of solvents with NPM. In nearly every instance dienes **61a-c** also showed a relatively high degree of *π*-facial selectivity in favor of the *anti* adduct in three solvents (toluene, methanol, tetrahydrofuran). Only one experiment afforded a modest excess of the *syn* addition product (entry 2). The preference for *anti* addition was accounted for by the apparently unfavorable steric and/or



Scheme 17. π-Facial selectivity in the Diels-Alder reaction of vinyl cyclopentenes

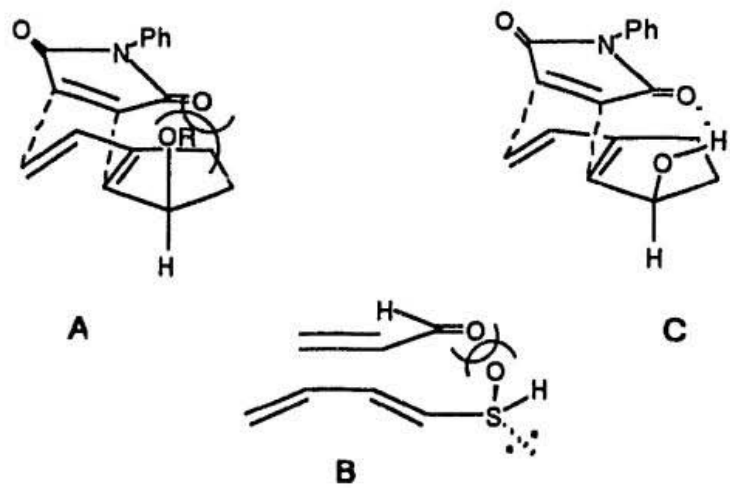


Figure 12. Interactions postulated in the control the π-facial selectivity of vinyl cyclopentenes

Table 2. π-Facial selectivity in the Diels-Alder reactions of vinylcyclopentenes (reactions performed in toluene, except where indicated)

Entry	Diene	Dienophile	%*syn* to OR	% *anti* to OR
1	**60**	NPM	0	100
2	**61a**	NPM	64	36
3*	**61a**	NPM	20	80
4	**61a**	TCNE	25	75
5	**61b**	NPM	3	97
6	**61b**	TCNE	3	97
7	**61c**	NPM	0	100
8	**61c**	TCNE	31	69

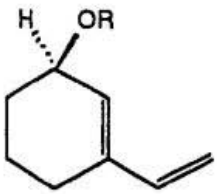
* methanol

electrostatic interactions that exist in the transition state leading to the *syn* addition product (**A** of Figure 12). Indeed, it has been calculated that the distance between the dienophile oxygen and the sulfoxide oxygen in transition state **B** (Figure 12) is only approximately 2.4Å.[58]

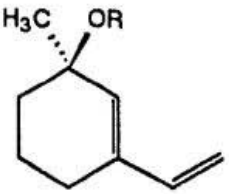
That diene **61a** showed a small preference for *syn* addition with NPM in an aprotic solvent (entry 2) may be due to intermolecular hydrogen bonding between the OH group of the diene and the carbonyl of the dienophile (**C** of Figure 12). When the same reaction was performed in a protic solvent (entry 3), the π-facial selectivity reversed. Also, protection of the alcohol as an ether, which eliminated H-bonding interactions, afforded mainly, and in some cases exclusively, *anti* adducts.

The one other study[59] of Type II semicyclic dienes bearing an allylic heteroatom involved the placement of one of the double bonds in a six-membered ring. This provided the molecules with more flexibility, and this in turn had an impact on the interpretation of the Diels-Alder behaviour of the dienes. In total, six substrates were synthesized, **64a-c** and **65a-c** (Scheme 18). Selected results from the published data are given in Table 3.

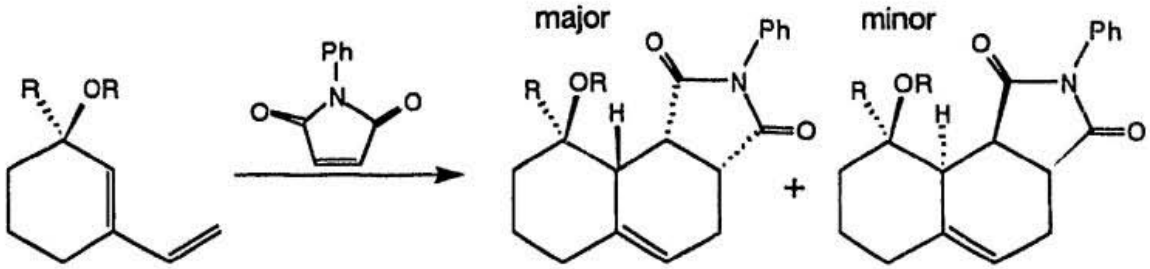
In nearly all instances involving the cycloaddition of dienes **64a-c** and **65a-c**, the major product obtained was **66a-c** (Scheme 18), that arising from the addition of the dienophile to the face of the diene *anti* to the allylic oxygen function. Even the replacement of the allylic hydrogen at C-3 of **64b-c**, with a methyl group still resulted in preferential *anti* addition (compare entries 3 and 4 with entries 7 and 8, Table 3), although the proportion of *anti* adducts was somewhat reduced. The only cases in which there was a preference for the formation of *syn* adducts **67a** and **69a** (Scheme 18) were those involving the dienes **64a** and **65a**, (entries 1 and 5, respectively). However, repeating the reactions of these dienes in a polar protic solvent resulted in a reversal in the *syn*/*anti* π-



64a R = H
64b R = CH_3
64c R = TMS



65a R = H
65b R = CH_3
65c R = TMS



64a - c
65a - c

66a - c
68a - c
Anti to OR

67a - c
69a - c
Syn to OR

Scheme 18. π-Facial selectivity in the Diels-Alder reaction of vinyl cyclohexenes

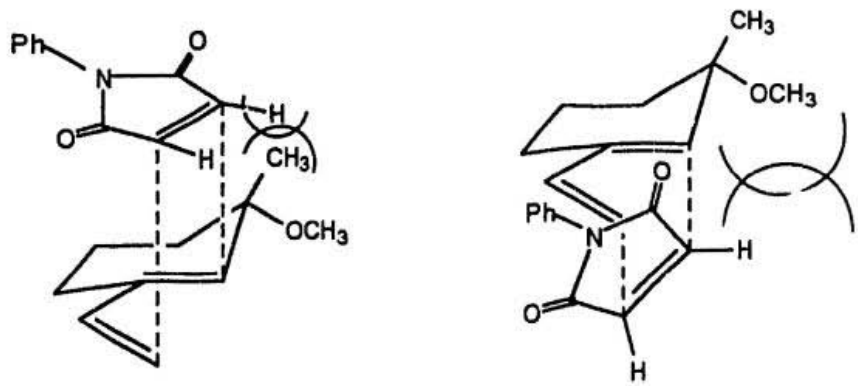


Figure 13. Steric effects postulated in the control of π-facial selectivity of vinyl cyclohexenes

Table 3. π-Facial selectivity in the Diels-Alder reactions of vinylcyclohexenes (reactions performed in benzene except where indicated)

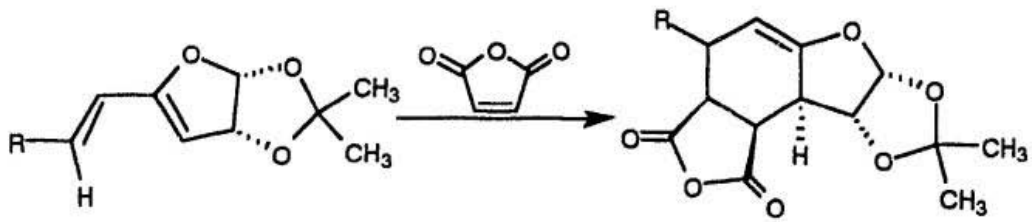
Entry	Diene	Dienophile	% *syn* to OR	% *anti* ot OR
1	**64a**	NPM	63	37
2[a]	**64a**	NPM	17	83
3	**64b**	NPM	11	89
4	**64c**	NPM	9	91
5	**65a**	NPM	92	8
6[a]	**65a**	NPM	45	55
7	**65b**	NPM	25	75
8	**65c**	NPM	23	77
9	**64a**	DMAD	20	80
10	**64c**	DMAD	8	92
11[b]	**64a**	PTAD	0	100

[a] DMF [b] CH_2Cl_2 / THF

facial selectivity (entries 2 and 6). This outcome was very similar to that found by Overman (*vide supra*). The results summarized in Table 3 have been rationalized in terms of steric effects alone. For dienes **64a** and **65a** (H *versus* OH and CH_3 *versus* OH) the Diels-Alder reactions with NPM in benzene showed preferred *syn* addition. However, in DMF it was postulated that hydrogen bonding between the substrate and the solvent increased the effective size of the hydroxyl group, thereby sterically hindering *syn* approach of the dienophile. For dienes **64b** and **64c** (H *versus* OCH_3 and H *versus* OTMS) the facial selectivity was dependent on the size of the substituent on the oxygen. When H was replaced by CH_3 in **65b** and **65c** (CH_3 *versus* OCH_3 and CH_3 *versus* OTMS), again the formation of *anti* adducts was due to steric effects. It was postulated that the OR substituent would assume a pseudo-equatorial position. Figure 13 illustrates the trajectory of approach of NPM to the faces *syn* and *anti* to the OR substituent. The outcome of the reaction could then be judged by the steric interactions between the vinyl hydrogen of the dienophile and the allylic substituents. It should be noted that, according to the Vogtle-Forster[60] model of determining group volume, OCH_3 is a larger group than CH_3.

Type III dienes

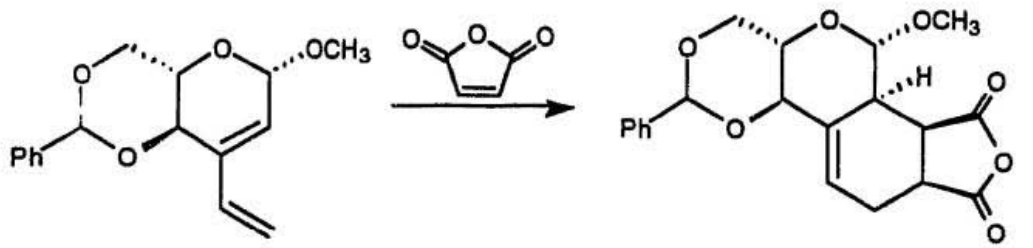
These carbohydrate-derived dienes have only recently received attention. Fraser-Reid and coworkers had reported that furanose derivatives **70a**[61a] and **70b**[61a,b] reacted with maleic anhydride to afford products **71a** and **71b**, respectively (Scheme 19), which arose from cycloaddition of the dienophile exclusively to the face of the diene *anti* to the allylic oxygen. The face *syn* to the oxygen was postulated to be sufficiently blocked by the acetonide group to exclude *syn* addition.



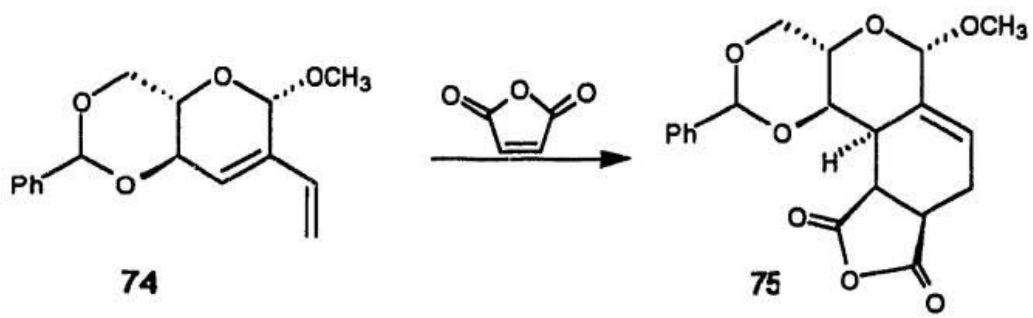
70a R = H
70b R = $CH_2OTBDMS$

71a R = H
71b R = $CH_2OTBDMS$

Scheme 19. Addition of maleic anhydride to furanose dienes



72 **73**



74 **75**

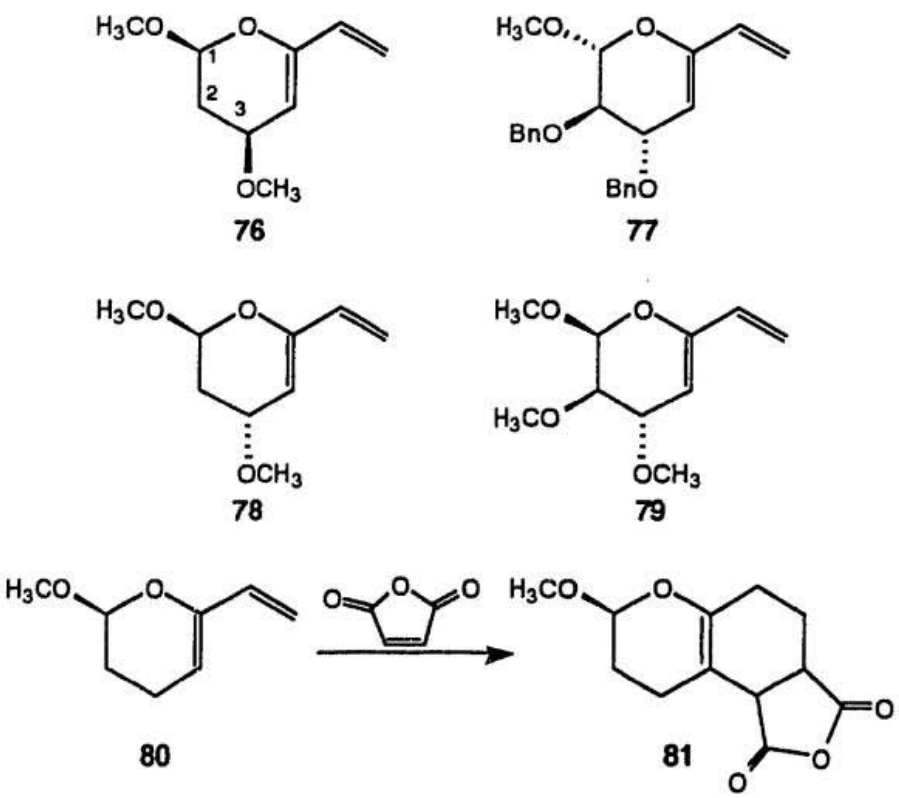
Scheme 20. Addition of maleic anhydride to pyranose dienes

In two more recent and concurrent publications,[62,63] pyranose derivative **72** was found to add maleic anhydride,[62,63] DMAD,[62,63] dimethyl fumarate,[63] benzoquinone[63] and naphthoquinone[63] exclusively from the face of the diene *anti* to the anomeric methoxyl group (i.e., **73**, Scheme 20). The isomeric diene **74**[62] behaved similarly with DMAD and with maleic anhydride (to afford, for instance, **75** in Scheme 20).

These Diels-Alder results were also attributed to steric effects in which dienophiles preferred approach *anti* to the axially oriented allylic methoxyl group.[62] This seemed to override any *syn*-directing effect of the allylic oxygen at C-5 in both **72** and **74**.

In an effort to determine the extent of anomeric *versus* allylic directing ability for π-facial selectivity, a number of pyranose dienes **76-79** (Scheme 21) were synthesized and their Diels-Alder reactions with maleimide were examined.[64] A summary of these results is given in Table 4. Addition of maleimide to **76** yielded only adduct **82**, that arising from approach of the dienophile *anti* to both the C-1 anomeric and the C-3 allylic oxygens. Reversing the configurations at C-1 and at C-3 for **77** also afforded the *anti* addition product **83**. Reaction of **78**, in which methoxy groups at C-1 and C-3 are on opposite sides of the molecule, gave two adducts, **84** (*syn* to allylic OMe) and **85** (*anti* to allylic OMe), in ratio of 81:19, respectively. The inclusion of an additional methoxyl group at C-2 had little effect on the *syn*/*anti* ratio obtained with **79**.

The adducts from the Diels-Alder reactions of dienes **76-79** indicated a strong tendency for dienophiles to react *anti* to the anomeric substituent. In light of the previously discussed results obtained by Franck[59] with dienes **64a-c** and **65a-c**, the formation of only *anti* adducts from **76** and **77** was entirely predictable. The relative position of the allylic oxygen in **64a-c** and **65a-c** is similar to that in **76** and **77**. For dienes **78** and **79**, steric interactions between the allylic substituents and the incoming



Scheme 21. Anomeric *versus* allylic heteroatom control of π-facial selectivity of pyranose dienes

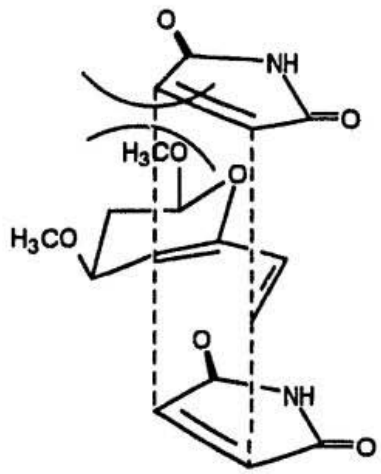
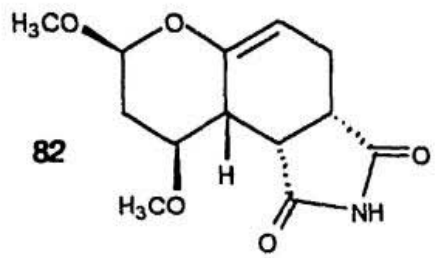
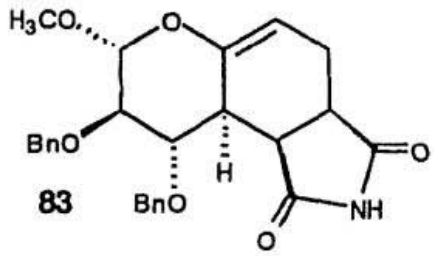
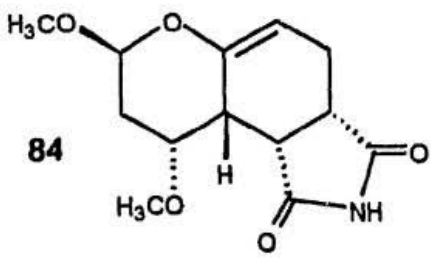
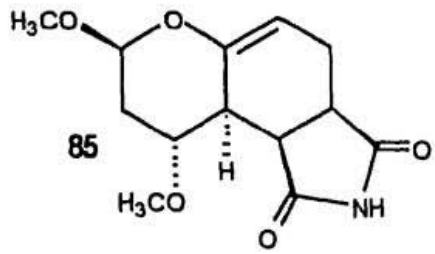
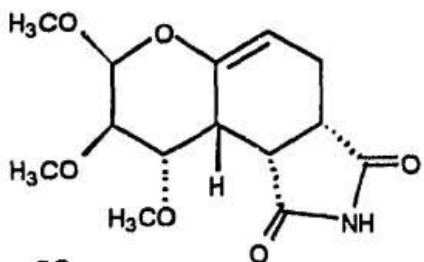
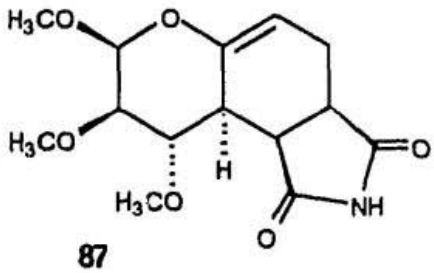


Figure 14. Postulated steric control in the π-facial selectivity of pyranose dienes

Table 4. Anomeric *versus* allylic heteroatom control of π-facial selectivity of pyranose dienes

Diene	*Syn* to allylic O	*Anti* to allylic O	% *Syn* / % *Anti*
76		 **82**	0 / 100
77		 **83**	0 / 100
78	 **84**	 **85**	81 / 19
79	 **86**	 **87**	75 / 25

dienophile would also be predicted to lead to the formation of *anti* adducts. While the anomeric and allylic groups of **78** and **79** are on opposite faces with respect to the diene moiety, the anomeric centre is somewhat remote from the reacting centres. That the products obtained were the result of mainly *syn* addition to the allylic function (and hence *anti* to the anomeric group) suggested that, for pyranose dienes, the anomeric group directs the π-facial selectivity in the Diels-Alder reaction. The cycloaddition of **80** might have given a better indication of this anomeric-directing effect. However, reaction of **80** with maleimide resulted in the isolation only of **81** (Scheme 21).

It has been postulated that for diene **76** the molecule prefers to adopt a half-chair conformation (Figure 14) with the anomeric substituent oriented in the pseudo-axial position as predicted by the anomeric effect (^{1}H nmr coupling constants and molecular mechanics calculations support this assumption[64]). It is suggested then that diene **76**, in its ground state conformation, would seriously encumber the approach of a dienophile *syn* to the allylic and anomeric substituents. For dienes **78** and **79** the anomeric group acts as a better blocking agent then the allylic group. The possibility that the conformations of the dienes may be different in the transition state should not be ruled out, however.

Type IV dienes

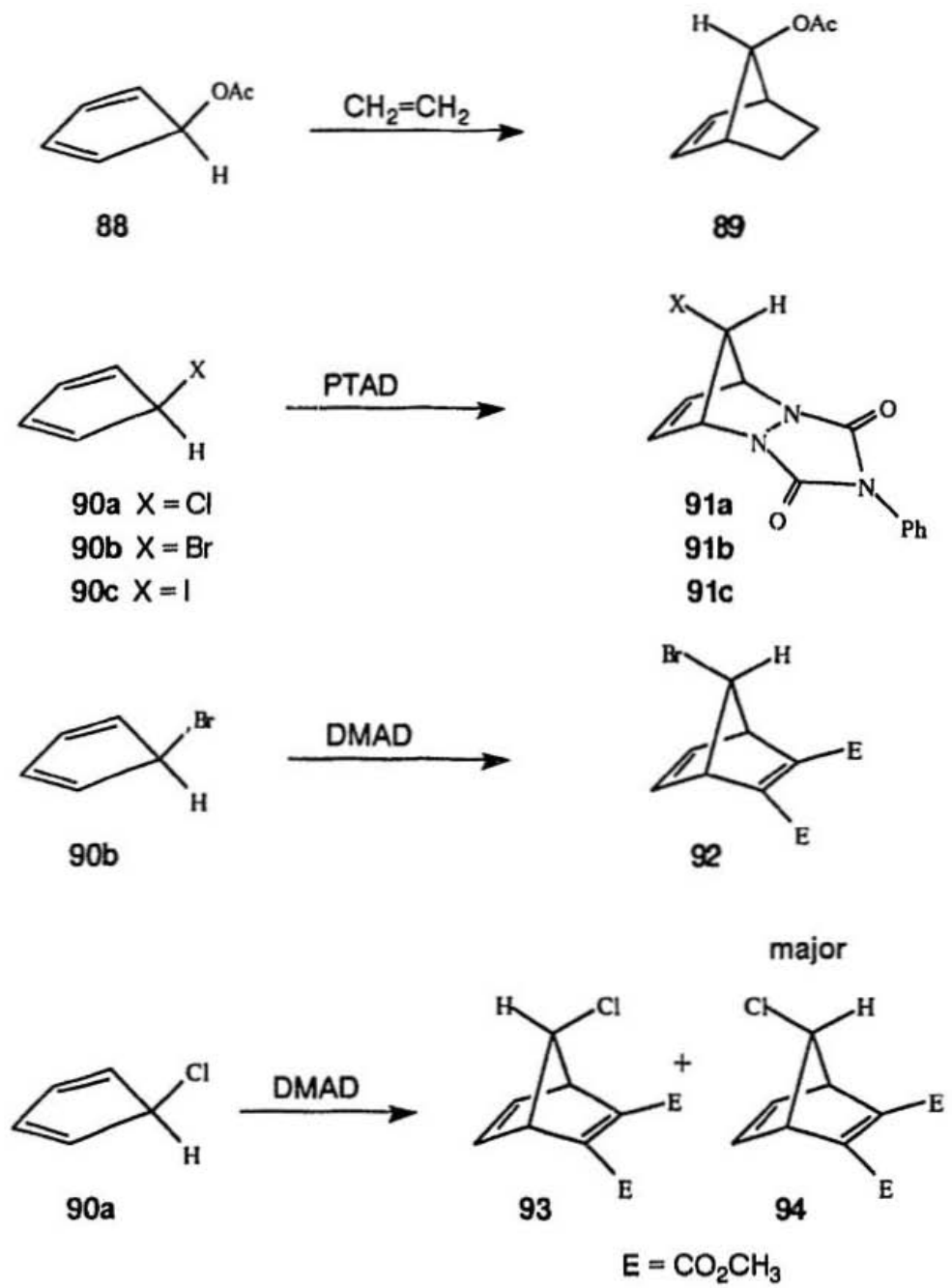
Type IV dienes (Scheme 14) have a very important structural feature that makes them especially well suited as probes to study heteroatom controlled π-facial selectivity. Not only is the diene constrained in a rigid cyclic species, but the topological placement of the heteroatom is particularly strategic with respect to the diene moiety in the molecule. Previous systems had the heteroatom attached to a position that interfered

directly with the activating group(s) on the dienophile as it approached *endo* and to the face of the diene *syn* to the heteroatom[58,59] (see Figure 12a). In type IV dienes, in contrast, the heteroatom is more remote from the activating group(s) on the dienophile as it approaches the *syn* face. That the allylic substituent on Type IV dienes has an effect on the π-facial selectivity of these dienes is quite apparent from the results obtained by Burnell and Valenta[33] on the Diels-Alder reaction of 1,2,3,4,5-pentamethylcyclopentadiene (Scheme 10). Another advantage of type IV dienes is that they are plane-nonsymmetric, so they do not suffer from the same conformational ambiguity as the other diene types do. Also, because most of the Type IV dienes studied thus far, including those in this report, contain a vertical mirror plane, reactions of these dienes with a symmetrically activated dienophile yield symmetrical adducts. This makes the process of elucidating the structures of the adducts easier.

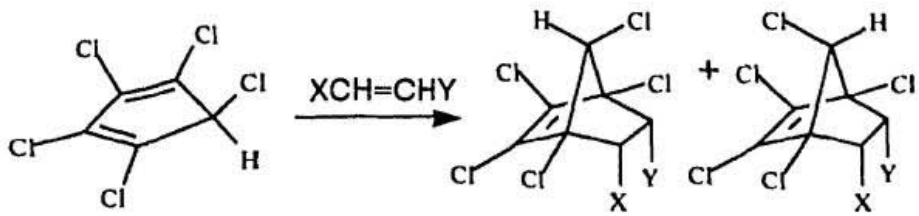
Most work that has been done on type IV dienes has involved cyclopentadienes. Examples from the literature will be reviewed, along with the theories that have been put forward to account for π-facial selectivity. This will be followed by a general synopsis of the cycloadditions involving 1,3-cyclohexadienes IVb and IVc.

5-Heterosubstituted cyclopentadienes IVa

Unlike most of the previous examples in which the allylic heteroatom was oxygen, a wide array of heteroatoms have been employed in the study of π-facial selectivity with cyclopentadienes. A number of metals in the 5-position have been employed: mercury,[65a] tin,[65a,66] platinum,[65b] and magnesium.[66] Magnesium and tin dienes add dienophiles *anti* to the metal;[66] however, the modes of cycloaddition to mercury and platinum dienes have not been elucidated.[65] 5-(Trimethylsilyl)cyclopentadiene reacted *anti*.[67] 5-Bromopenta-



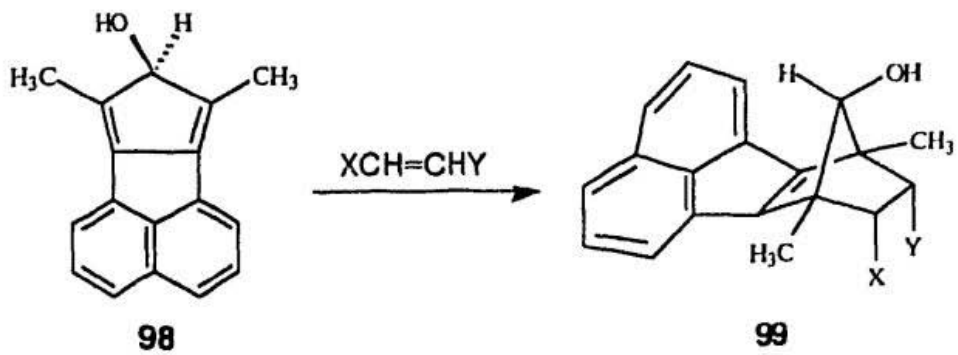
Scheme 22. π-Facial selectivity in the Diels-Alder reaction of some 5-heteroatom substituted cyclopentadienes



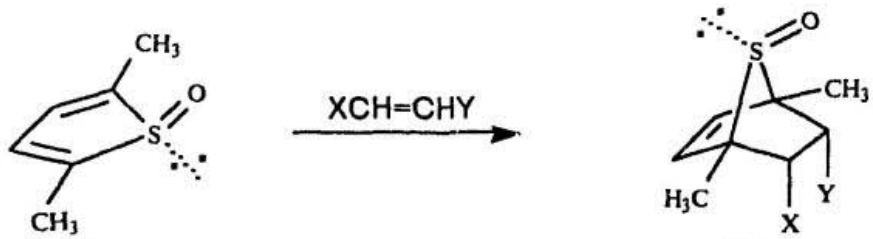
Scheme 23. The *endo-syn* (**96**) and *endo-anti* (**97**) adducts from the Diels-Alder reaction of 1,2,3,4,5-pentachlorocyclopentadiene with various dienophiles

Table 5. Summary of the addition of various dienophiles to pentachloro **95**

XCH=CHY	**96** % *endo-Syn*	**97** % *endo-Anti*
maleic anhydride	91	9
benzoquinone	60	40
acrylonitrile	83	17
meytyl acrylate	59	41
vinyl acetate	51	49
vinyl bromide	58	42
vinyl chloride	53	47
styrene	38	62
propene	31	69

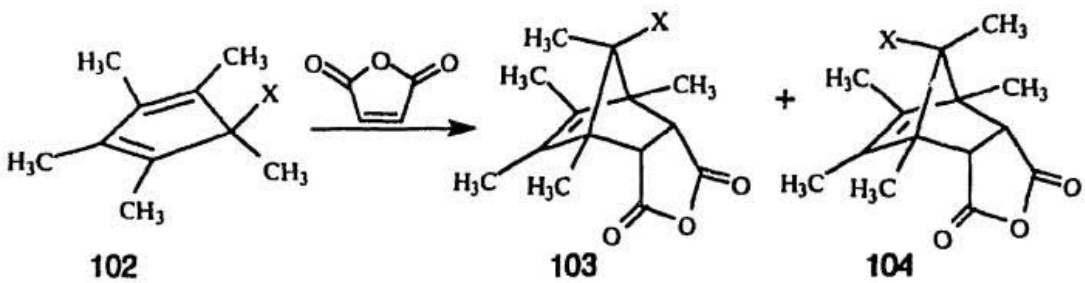


Scheme 24. The Diels-Alder reactions of a 5-hydroxycyclopentadiene derivative



100 101

Scheme 25. The Diels-Alder reaction of a thiophene oxide derivative with various dienophiles



102 103 104

Scheme 26. The Diels-Alder reactions of various 5-heteroatom substituted 1,2,3,4,5-pentamethylcyclopentadienes (102)

Table 6. Summary of the addition of maleic anhydride to dienes 102

X =	% 103	% 104
Cl	100	0
OH	100	0
OCH_3	100	0
NH_2	100	0
NHAc	100	0
SH	55	45
SMe	10	90
SCH_2Ph	3	97
SOMe	0	100
SO_2Me	0	100

chlorocyclopentadiene[68] reacted with a number of dienophiles, but the configuration at the 7-position of the adducts was not determined. 5-Acetoxycyclopentadiene **88** with ethylene gave only **89**, the adduct arising from addition to the face *syn* to the oxygen[69] (Scheme 22). Also, the 5-halo derivatives **90a-c**, reacted with PTAD[70] to provide *anti* addition products **91a-c**, while **90a** gave both *syn* and *anti* adducts **93** and **94**,[71] respectively. DMAD gave more of the *anti* isomer, but **90b** provided only **92**[71] with DMAD (Scheme 22).

Williamson *et al.*[72] established that 1,2,3,4,5-pentachlorocyclopentadiene **95** reacted with some dienophiles to give addition mainly *syn* to the 5-chloro substituent (adducts **96**), while other dienophiles yielded mainly the *anti* addition products **97** (Scheme 23 and Table 5). Jones[73] found that diene **98** also gave only the *syn* addition adduct **99** with several dienophiles (Scheme 24).

Much more recently, Naperstkow *et al.*[74] determined that 2,5-dimethylthiophene oxide **100** reacted with a number of dienophiles to give only adducts **101** by addition of the dienophiles only to the face of the diene *syn* to the sulfoxide oxygen (Scheme 25). A systematic study of heteroatom-directed π-facial selectivity was recently published for cyclopentadienes by Macaulay and Fallis.[44] Selected results are summarized in Table 6, and Scheme 26. Substitution of the 5-position of **102** with chlorine, oxygen or nitrogen directed addition of maleic anhydride to the face of the diene *syn* to the heteroatom, to give only **103** while sulfur substitution clearly favored addition to the *anti* face to give mainly **104**.

What factors determine whether a dienophile will add *syn* or *anti* to 5-heteroatom substituted cyclopentadienes? With 1,2,3,4,5-pentachlorocyclopentadiene, Williamson[72b] claimed a combination of steric effects and dipolar attraction controlled the selectivity.

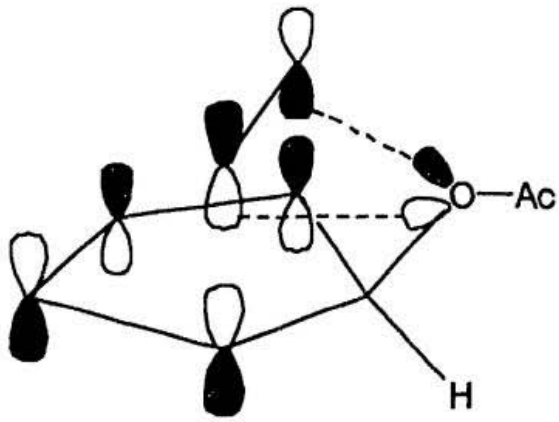


Figure 15. Anh's postulate

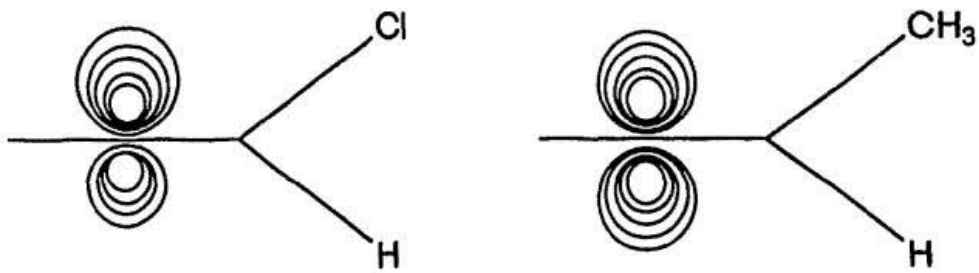


Figure 16. Fukui's postulate

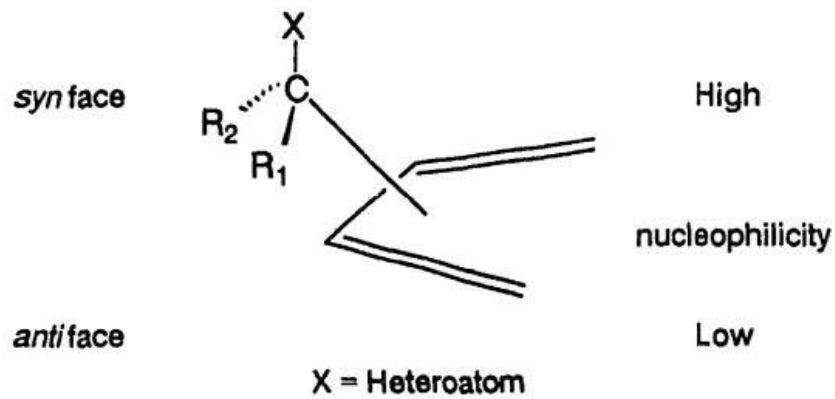


Figure 17. Hehre's postulate

Anh[75] envisioned a direct orbital interaction between the localized lone pair orbitals of the heteroatom with the LUMO of the incoming dienophile. This secondary orbital interaction was postulated to guide the dienophile to the *syn* face of the diene (Figure 15). An alternative view from Fukui's group,[76a] more recently expanded upon,[76b] invoked the mixing of low lying σ orbitals into the π-HOMO, thereby causing a perturbation of the electron density distribution on the two faces of the diene. Figure 16 shows the π-electron density distribution on the *syn* and *anti* faces of 5-chloro- and 5-methyl-cyclopentadiene.[76a] In the 5-methyl case, the electron density on both faces of the diene was determined to be about equal, therefore the addition of dienophiles were expected to be only under steric control. The chloro analogue, however, was believed to have its π- electron density biased in favor of the face *syn* to the chlorine. A highly electron poor dienophile would then prefer addition *syn* to the chlorine, whereas more electron rich dienophiles would be directed *anti*.

Kahn and Hehre[43] proposed an electrostatic model as the basis for selectivity. For dienes with the general structure shown in Figure 17 (the diene could be acyclic, semi-cyclic or cyclic) the face of the diene bearing a lone pair-containing substituent, i.e., the *syn* face, should have a higher nucleophilicity than the *anti* face. Thus, "Additions, involving ... electron-poor dienophile should occur onto the diene face which is the more nucleophilic".[43] It was predicted that electrophiles should prefer addition *syn* to a lone pair-containing allylic substituent, and *anti* to an electropositive allylic substituent. These generalizations did not take into account any overriding steric effects that might control the π-facial selectivity,[58,59] nor could it account for the *anti* facial selectivity displayed by sulfur substitution on cyclopentadienes (*vide supra*).

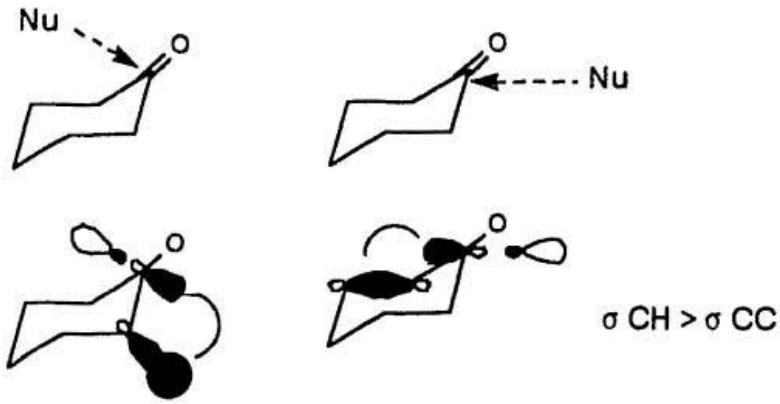
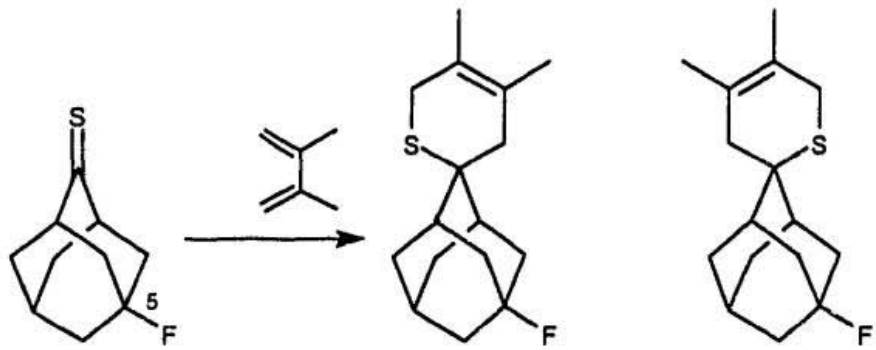
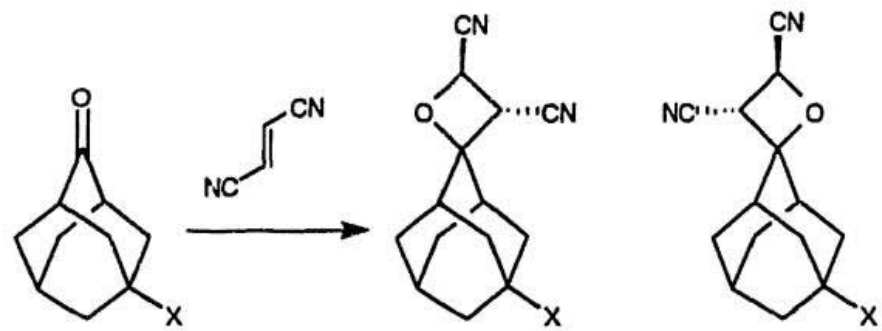


Figure 18. Cieplak's postulate for the preferred axial attack of nucleophiles to cyclohexanone

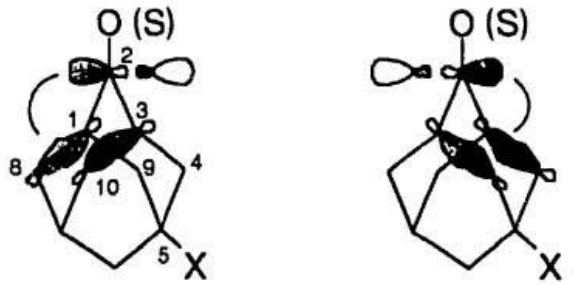


105 Ratio 65 : 35



106 X = OH, Br, Cl, F Ratio ca. 57:43

Scheme 27. π-Facial selectivity in the cycloaddition reactions of adamantyl derivatives



X = OH, Br, Cl, F σC_1C_8, σC_3C_{10} > σC_3C_4, σC_1C_9

Figure 19. σ Bond donation model applied to the π-facial selectivity observed in the cycloaddition of adamantyl derivatives

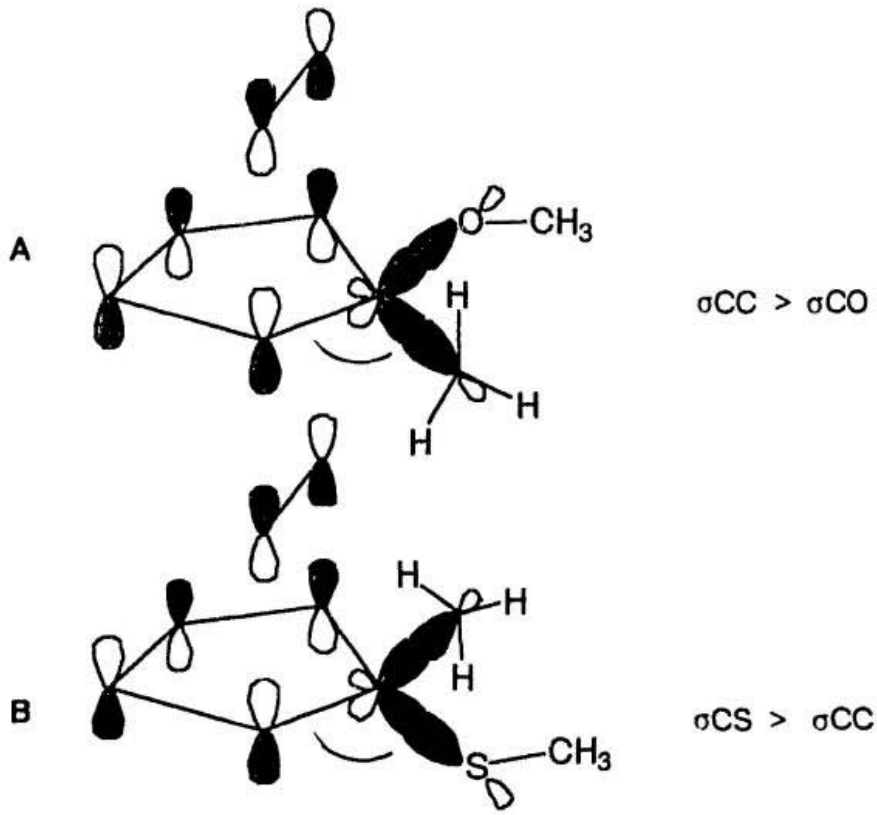


Figure 20. σ Bond donation model applied to the π-facial selectivity observed in the Diels-Alder reactions of 5-hetero substituted cyclopentadienes

Based on a model proposed by Cieplak *et al.*[77] for the π-facial selectivity of the nucleophilic attack on 3-substituted cyclohexanones and the electrophilic attack on 3-substituted-1-methylene cyclohexanes, Macaulay and Fallis[44] invoked hyperconjugation and σ bond-donor ability to explain π-facial selectivity. The Cieplak model suggests that transition state stabilization occurs through σ-electron donation into the vacant σ* orbital associated with the developing bond. This will arise from hyperconjugation of the antiperiplanar σ bond with the σ* orbital. For example, cyclohexanone prefers the axial approach of nucleophiles because the σC-H bond is a better electron donor than the σC-C bond (see Figure 18).

This proposal correctly accounted for the π-facial selectivity observed in the Diels-Alder reaction of **105** and the photocycloaddition of **106**, in which addition took place preferentially to the face bearing the C-5 substituents (Scheme 27). The electronegative group, X, at C-5 (Figure 19) caused the C1-C8 and C3-C10 σ bonds to become better donors than the C3-C4 and C1-C9 σ bonds. Accordingly, the more reactive face should be the one *anti* to the better σ donor. Putting this into the context of the cycloaddition results obtained by Macaulay and Fallis, this was summarized: "on the basis of hyperconjugation and the beneficial interaction with the incipient bond one should expect the cycloaddition of the cyclopentadienes to display a preference for *anti* addition to the antiperiplanar σ bond that is the better donor".[44] The common atom combinations, listed in order of their σ donor ability are as follows σCO < σCN < σCCl < σCC < σCH < σCS.[79] Thus, in transition state **A** (Figure 20), in which a σCO bond is pitted against a σCC bond, addition would be expected to occur on the face of the diene *anti* to the better donor, i.e., the σCC, to give the *syn* adduct **103** (Scheme 26). For a σCC bond *versus* a σCS bond, transition state **B** is stabilized, and so the *anti* addition product **104**

should form. This hypothesis, however, would not predict the result observed on the addition of DMAD to **90a** (Scheme 22), in which the major product was that which arose from cycloaddition *anti* to the chlorine. The above ranking of σ donor ability has σCH > σCCl, therefore addition *syn* to the chlorine would be predicted.

1,3-Cyclohexadienes IVb *and* IVc

In contrast to the preceding section, very little information has been acquired regarding the π-facial selectivities of plane-nonsymmetric 1,3-cyclohexadienes possessing heteroatom substituents. Early reports of the Diels-Alder reaction of dienes **107a**[80] and **107b**[81] with maleic anhydride had assumed that the dienophile had added to the face *anti* to the oxygens to give adducts **108a** and **108b**, respectively (Scheme 28). It was later reported that the reaction of **109** with 4-(*p*-bromophenyl)-1,2,4-triazoline-3,5-dione afforded **110**;[82] the structure of **110** was established unequivocally by x-ray analysis (Scheme 28). However, it is expected that *endo* approach of the triazoline dienophile to the *syn* face of **109** would result in unfavorable electrostatic interactions between the lone pairs on the oxygens of the diene with those on the nitrogens of the dienophile. This is complimentary, but opposite in effect, to the observations made by Ginsburg.[42,83]

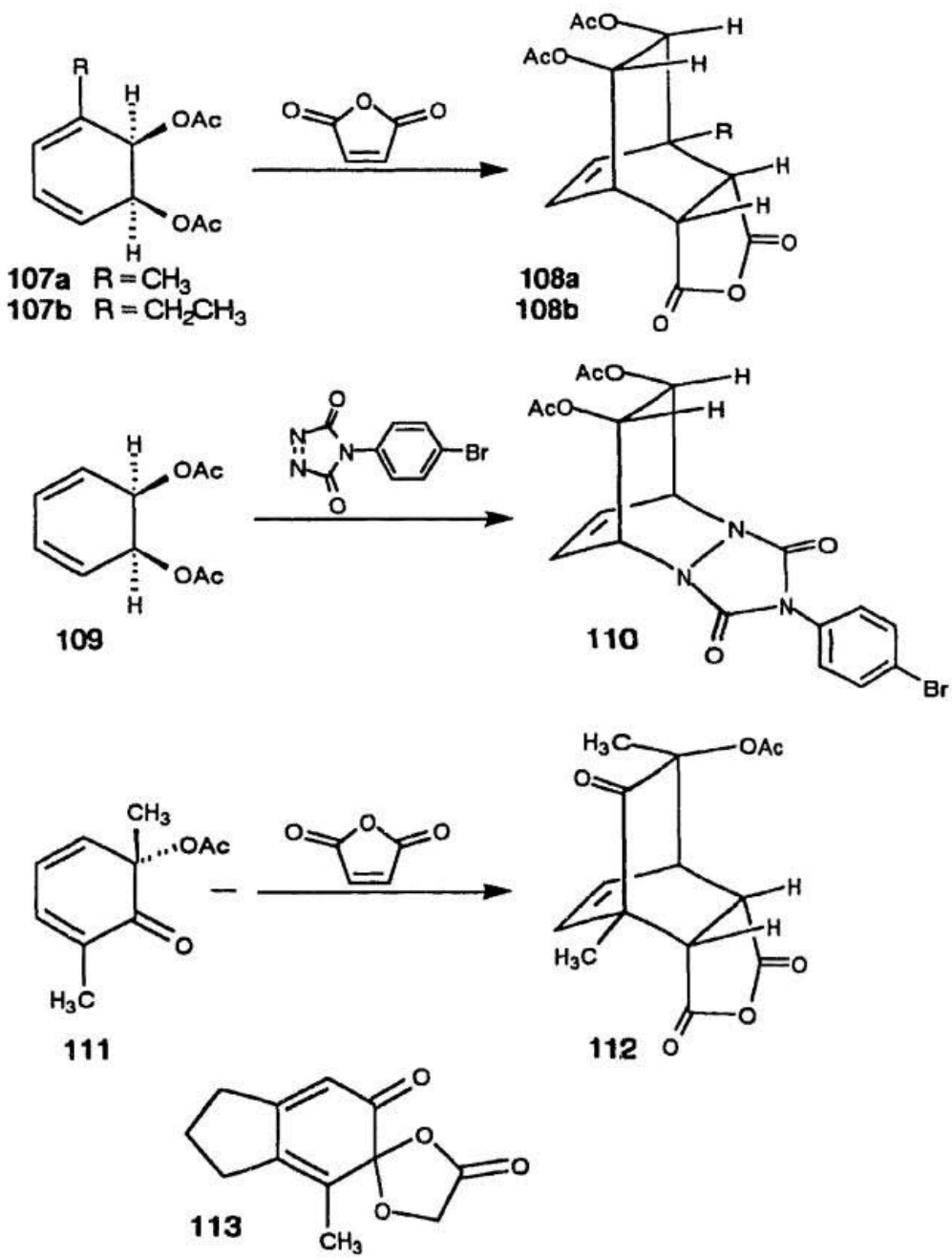
Yates and Auksi[84] had determined that maleic anhydride adds *endo* and *syn* to the oxygen-bearing face of **111** to give **112** as the only product (Scheme 28). This result could be attributed to steric effects (approach *syn* to OAc, as opposed to approach *syn* to methyl). The diene **113** was reported to have no facial selectivity at all.[85]

In a more recent report, details were published that indicated that diene **114** reacted with a number of dienophiles to give adducts of structure **115**.[86] However, it has also been determined that reaction of **116** with *N*-ethylmaleimide yielded both the *syn*

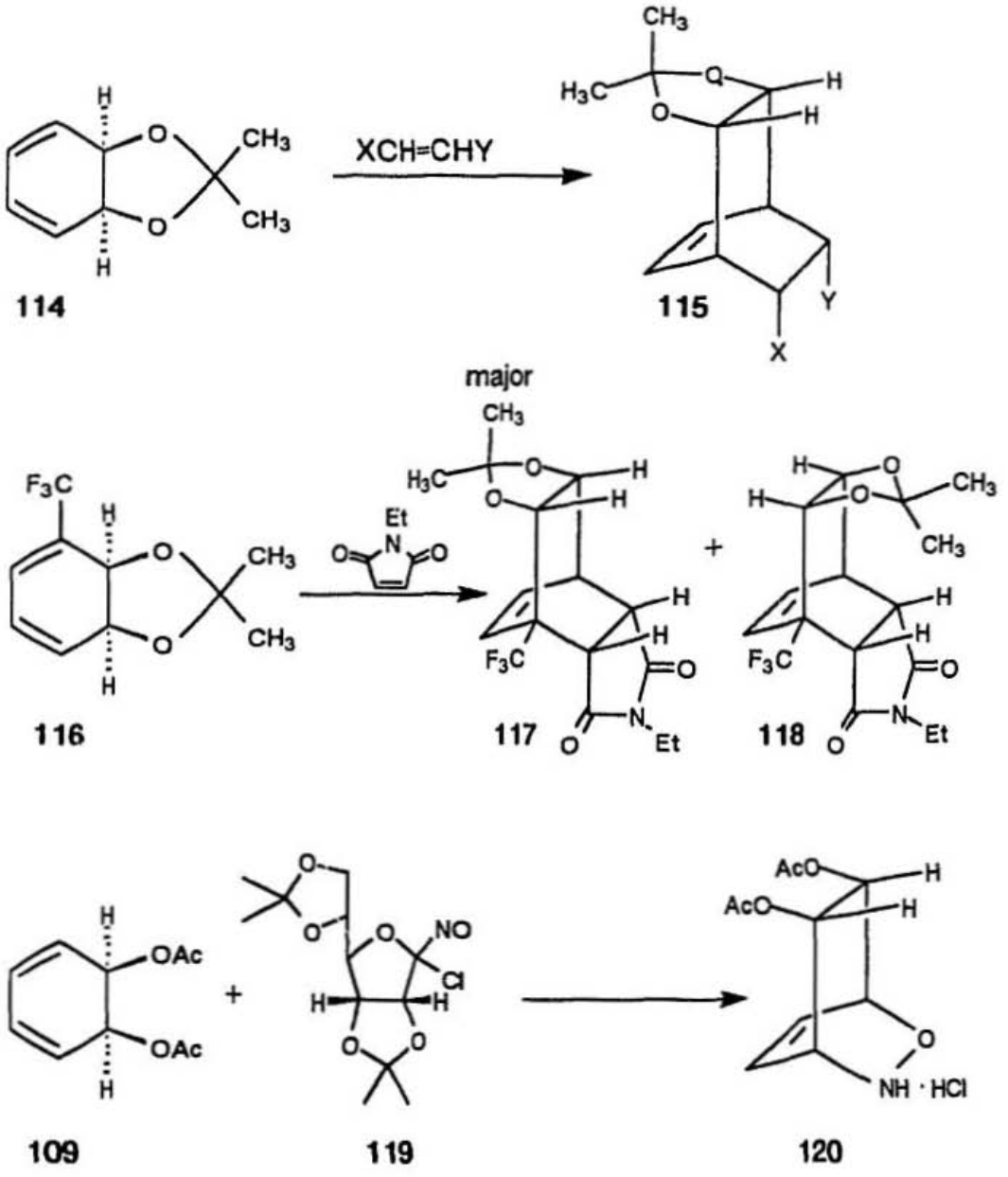
addition product **117** and the *anti* addition product **118**, with the *anti* isomer being the major adduct[87] (Scheme 29). In another example, **109** was reported to undergo *anti* addition with **119** to yield **120** after workup.[88] Diels-Alder-like photochemical additions of singlet oxygen afforded in only one case *anti* addition[89] with derivatives of *cis*-3,5-cyclohexadiene-1,2-diol (**121**), and in other cases both *syn* and *anti* adducts were formed.[90]

A close relative of both diene types IVa and IVb are the benzene oxides IVc (Scheme 14). These compounds are an elegant marriage of *cis*-1,2-disubstituted-3,5-cyclohexadiene and 5-substituted cyclopentadienes. The diene unit is still constrained in a six-membered ring, but the relative position of the allylic heteroatom is one that bisects the molecule, as it does in the cyclopentadienes. The structures of the Diels-Alder adducts obtained from benzene oxides with carbon-based dienophiles were not rigorously proven.[91] In one case, reaction of a benzene oxide derivative with 4-phenyl-1,2,4-triazoline-3,5-dione was shown by x-ray crystallography to provide an adduct that resulted from addition *anti* to the oxygen.[92] However, it has also been determined that on acetone-sensitized excitation, diazomethane added to benzene oxide to the face *syn* to the oxygen.[93]

Since the outcome of the Diels-Alder reactions of allylically substituted cyclohexadienes was ambiguous, it was deemed important to determine if they would display π-facial selectivity in line with that of the cyclopentadienes. It was also hoped that the results would aid in determining the factors that control the contrasteric additions of dienophiles to some allylic-heteroatom-substituted dienes.



Scheme 28. Diels-Alder reactions of 1,3-cyclohexadienes bearing an allylic oxygen substituent



Scheme 29. Diels-Alder reactions of 1,3-cyclohexadienes bearing an allylic oxygen substituent

DIENE SYNTHESIS

The microbial oxidation of benzene by *Pseudomanas putida* (Scheme 30) provides an efficient source of the plane-nonsymmetric diene, *cis*-3,5-cyclohexadiene-1,2-diol (**121**).[80,81]

This diol was conveniently derivatized to dienes **109**, **114**, and **122-125**, each requiring only one synthetic step as shown in Scheme 31. Thus, treatment of **121** with either chlorotrimethylsilane in pyridine, or acetic anhydride in pyridine, provided dienes **122** and **109**, respectively, in good yields. Transketalization of **121** with 2,2-dimethoxypropane as the reagent and solvent, with acid catalysis, gave the acetonide derivative **114**, also in good yield. The "siliconide" **123** was synthesized by addition of diacetoxydimethylsilane* to a solution of **121** in $CDCl_3$ in the presence of a catalytic amount of pyridine.[94] Following the reaction by ^1H nmr spectroscopy showed that a quantitative conversion of **121** to **123** was realized after only ten minutes. Because of its sensitivity to moisture, **123** could not be isolated using standard methods. However, a small amount of impure material (*ca.* 10% yield) was obtained by evaporation of all volatiles. The Diels-Alder reaction with **123** was conveniently achieved by addition of the dienophile to the nmr solvent immediately after **123** was formed.

The dimethoxy diene **124** was prepared in a phase-transfer reaction utilizing a procedure by Merz[95] with dimethyl sulfate as the methylating agent. The moisture-sensitive ethyl boronate ester **125** was prepared, using a recent literature procedure.[96] Addition of lithium triethylborohydride to **121** in dry tetrahydrofuran (THF) gave **125** in a

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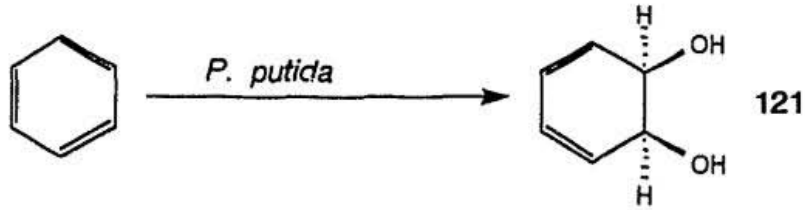
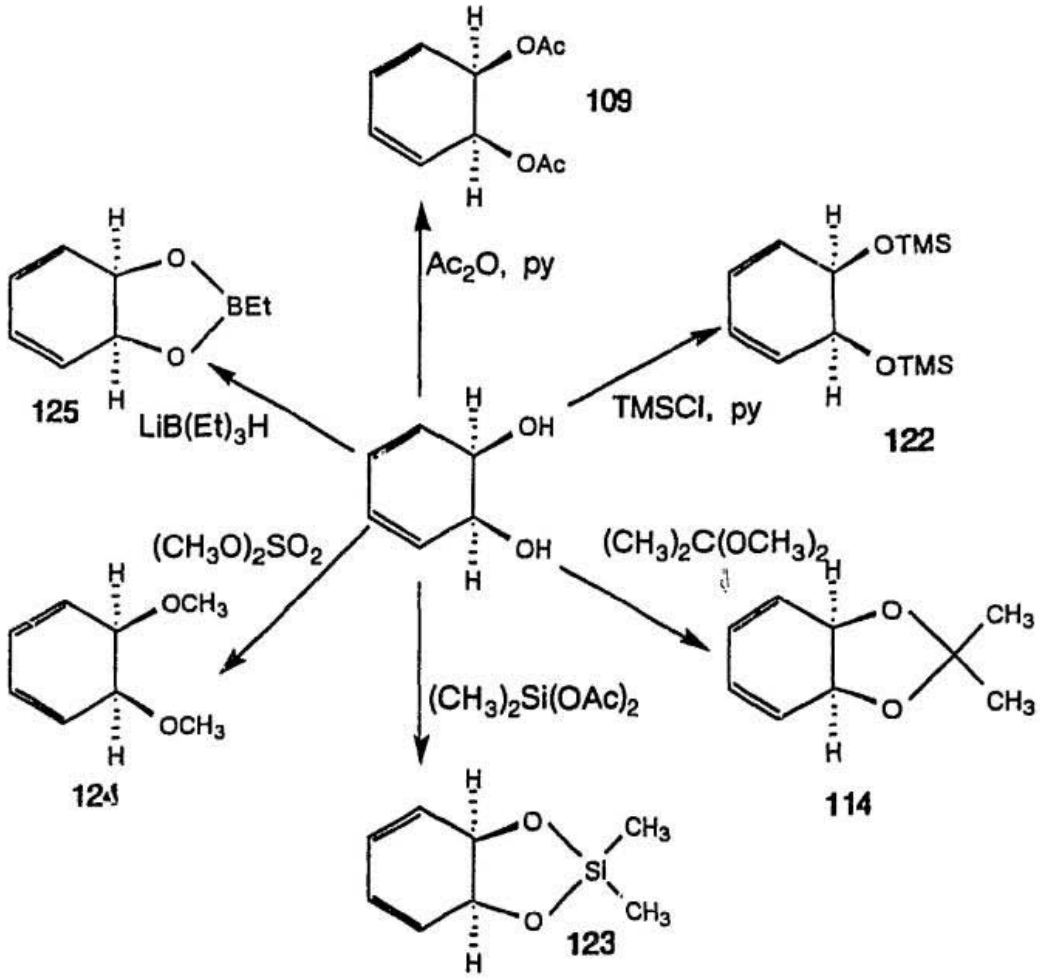
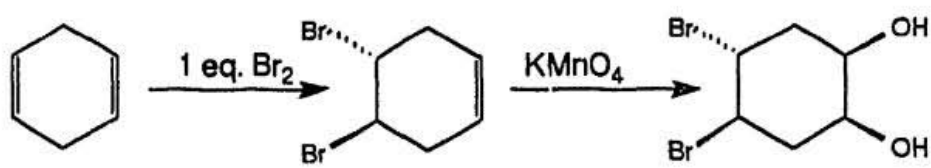
* This reagent was kindly provided by Dr. James C. Orr.



Scheme 30. Microbial oxidation of benzene



Scheme 31. Derivatization of diol diene **121**



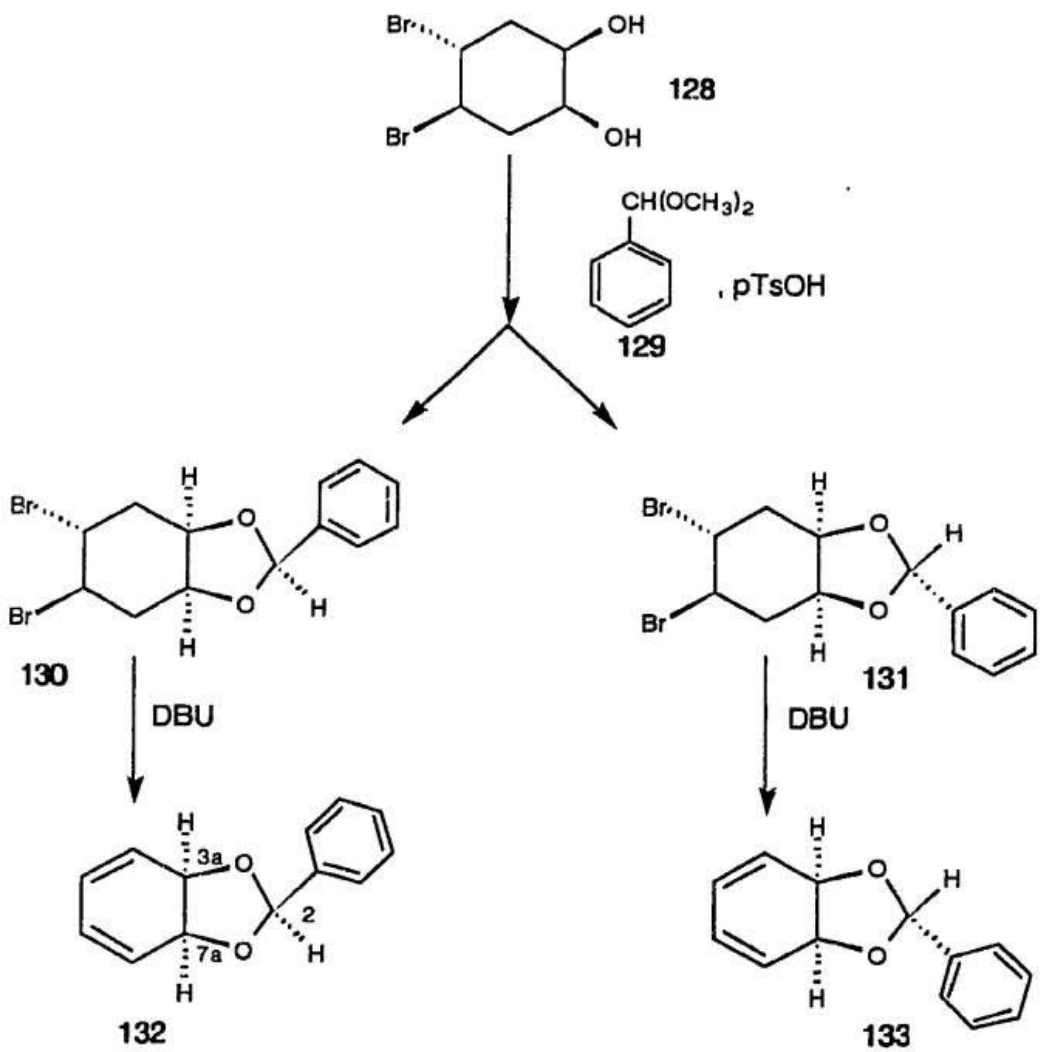
Scheme 32. Synthesis of dibromo diol precursor **128**

meager 30% yield after work-up. This was used immediately for the Diels-Alder reaction. Interestingly, the literature procedure did not report that any of the boronate esters were moisture sensitive.

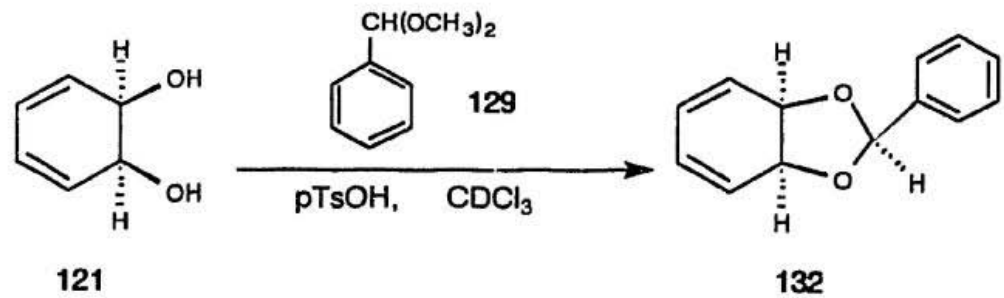
Schemes 32 and 33 provide an outline of the synthetic sequence leading to benzylidene-protected dienes **132** and **133** starting from 1,4-cyclohexadiene **126**. Addition of one molar equivalent of Br_2 in the cold to **126**,[97] followed by *cis*-hydroxylation[98] of purified **127**, gave the dibromodiol **128** in 40-45% yield from **127**. Acid catalysed transacetalization of **128** with a large excess of benzaldehyde dimethyl acetal **129** gave approximately equal quantities of **130** and **131** after fractional recrystallization and chromatography in a combined yield of 68%. Double dehydrobromination of **130** then of **131** with DBU in boiling benzene gave the *cis*-phenyl diene **132** and the *trans*-phenyl diene **133**, respectively. Diene **133** could not be purified by chromatography or by distillation (due to decomposition and dimerization, respectively), but **132** could be purified by chromatography.[98]

The synthesis of **132** could also be accomplished directly from the diol diene **121** (Scheme 34) under equilibrating conditions using one molar equivalent of **129** with *para*-toluenesulfonic acid (*p*TsOH) as a catalyst in $CDCl_3$. The ^1H nmr spectrum of the product confirmed that only isomer **132** was produced, indicating that this is the more stable isomer. This synthesis was not very efficient, giving only a 15% isolated yield after rotary thin-layer chromatography. In addition, the amount of *p*TsOH was crucial; too much, or insufficient mixing on addition of the catalyst, gave rapid elimination of water from diol **121** to give phenol.

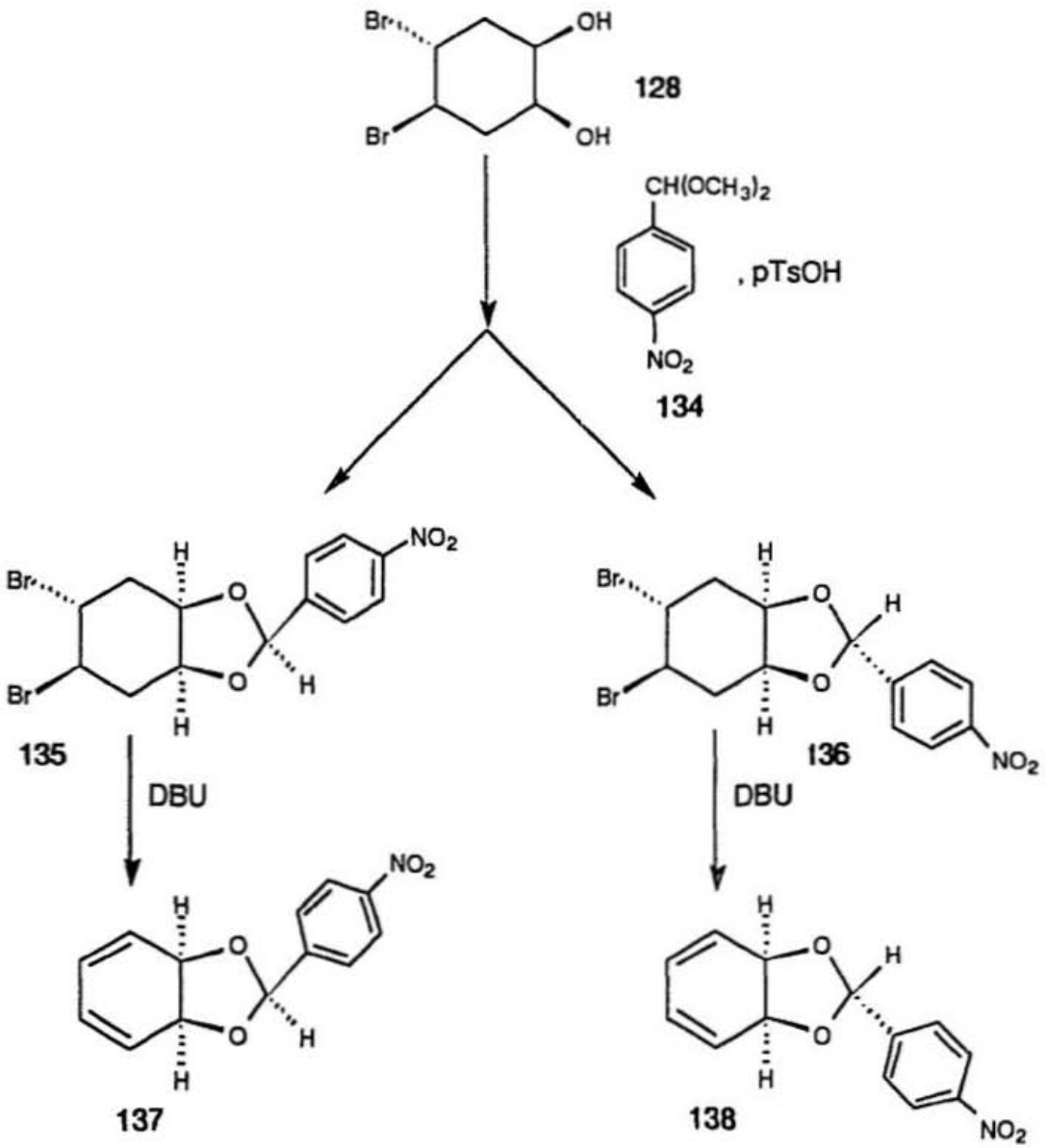
The syntheses of dienes **137** and **138** were analogous to those of **132** and **133**. Treatment of **128** with approximately one molar equivalent of *para*-nitrobenzaldehyde



Scheme 33. Synthesis of *cis* (**132**) and *trans* (**133**) benzylidene dienes



Scheme 34. Synthesis of *cis* benzylidene diene directly from **121**

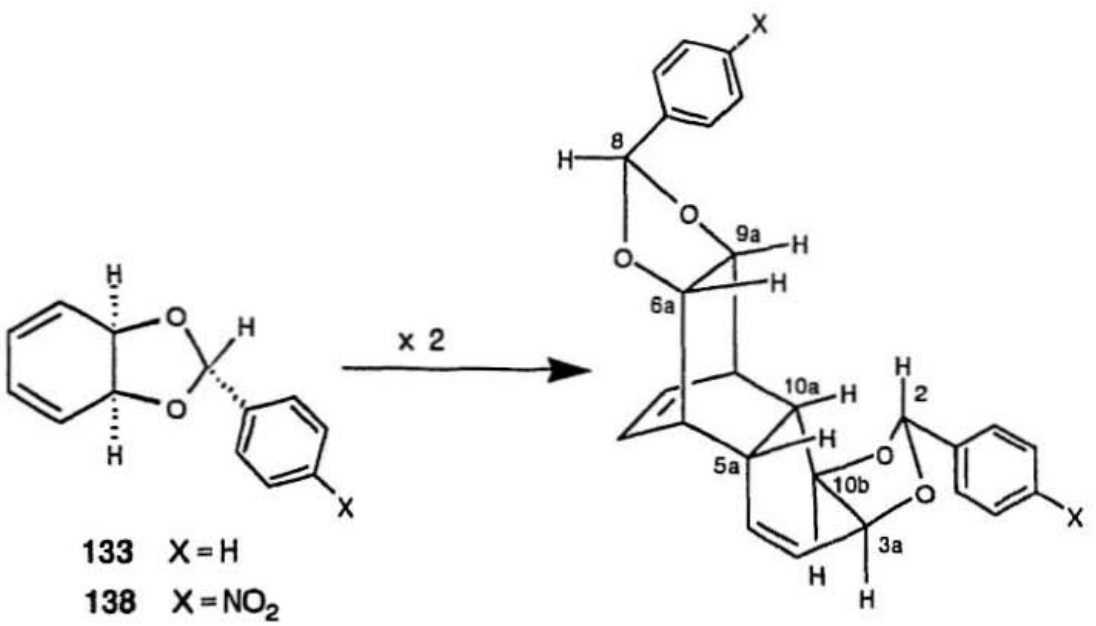


Scheme 35. Synthesis of *cis* (137) and *trans* (138) *p*-nitro benzylidene dienes

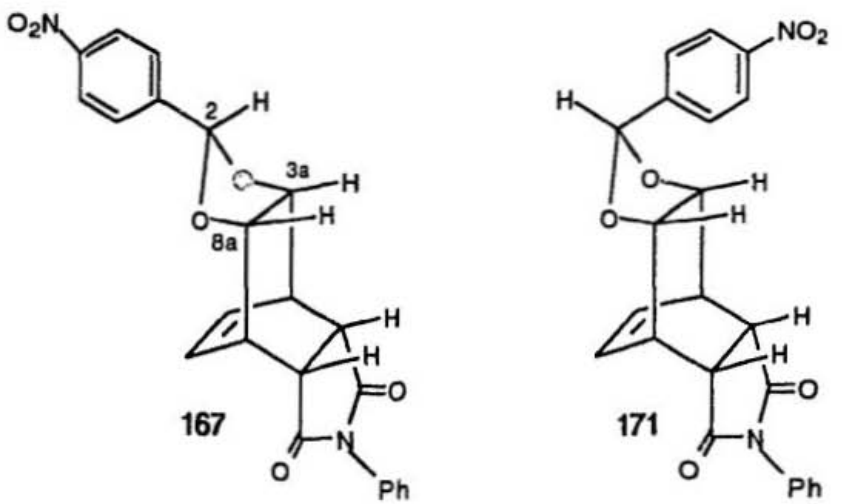
dimethyl acetal **134**, gave roughly equal amounts of **135** and **136** after work-up and chromatography in 60% overall yield. Double dehydrobromination gave the *cis*-phenyl diene **137** and the *trans*-phenyl diene **138** from **135** and **136**, respectively (Scheme 35).

The configuration of the phenyl ring for *cis*-phenyl dienes **132** and **137** was confirmed by nuclear Overhauser enhancement difference (n.O.e.d.) experiments. For example, saturation of the signal due to the hydrogens on C-3a and C-7a of **132** gave a significant enhancement (8.5%) of the signal for the hydrogen on C-2. Likewise, saturation of the C-2H signal gave a 4% enhancement of the C-3aH and C-7aH signal.

Previous reports of *trans*-phenyl diene **133** had mentioned that dimerization occurred on attempted distillation,[98] (Scheme 36) but no other details were given. In an endeavour to confirm this, and in order to determine the product of the cycloaddition, a freshly prepared sample of **133** was allowed to stand at room temperature overnight as a neat liquid. Analysis of the ^{1}H nmr spectrum of the resulting solid showed signals for residual unreacted **133** and one dimeric compound. Nuclear Overhauser enhancement experiments on the purified dimer indicated that it had the structure **139**, which could have arisen only from cycloaddition *endo* and *anti* with respect to the diene, and *anti* with respect to the dienophile. Due to the concave shape of the adduct, saturation of only one signal was sufficient to establish all of the relative stereochemistry of **139**. Thus, saturation of the signal due to the hydrogens on C-5a and C-10a gave a significant enhancement (13%) of the C-6a and C-9a hydrogens' signal, and enhancement of the signal of the hydrogen on C-2 (3%). The absence of any enhancement of the C-2 hydrogen signal on saturation of the signal due to the hydrogens on C-3a and C-10b aided in the structure elucidation and confirmed that epimerization of the C-2 centre had not occurred. That epimerization of the C-8 centre had also not occurred either was suggested by the rather



Scheme 36. Dimerization of *trans* benzylidene dienes **133** and **138**



small enhancement of the C-8 hydrogen signal (2%) upon saturation of the signal due to the hydrogens on C-6a and C-9a. If the C-8H were *cis* to C-6aH and C-9aH, then a very large enhancement would have been expected. This observation was found to be consistent with a number of Diels-Alder adducts from dienes **132**, **133**, **137**, and **138**. For example, saturation of the C-3a and C-8a hydrogen signal of **167** gave a very large enhancement of the signal due to the hydrogen on C-2. However, the analogous nmr experiment on **171** gave only a 4% enhancement of the C-2 hydrogen signal.

Diene **138** was also found to dimerize quite readily. In fact, **138** melted (*ca.* 130°C) and quickly resolidified to remelt at a much higher temperature (*ca.* 250°C). Heating a larger sample of **138** to 250°C for ten minutes gave a compound which proved to be insoluble in most conventional solvents. Analysis of the ^{1}H nmr spectrum of the crude material showed only one set of signals, corresponding to dimer **140**. Nuclear Overhauser enhancement experiments revealed structural information that led to the assignment of the relative stereochemistry in much the same way as that for **139**.

The benzene oxides* **142**, **148a**, and **148b**, were synthesized using established literature methods. Reaction of **127** with *meta*-chloroperoxybenzoic acid yielded **141** as a yellow oil. Very careful crystallization from cold hexane was necessary to obtain pure material. Double dehydrobromination with DBU in ether at room temperature provided benzene oxide **142** (Scheme 37), which displayed a single set of signals in its ^{1}H nmr spectrum. Vogel and Gunther[99] demonstrated that this is really an average of the signals of benzene oxide (**142**) and its valence tautomer, oxepin (**143**). They also determined that the relative amounts of each tautomeric form present in solution is dependent on solvent

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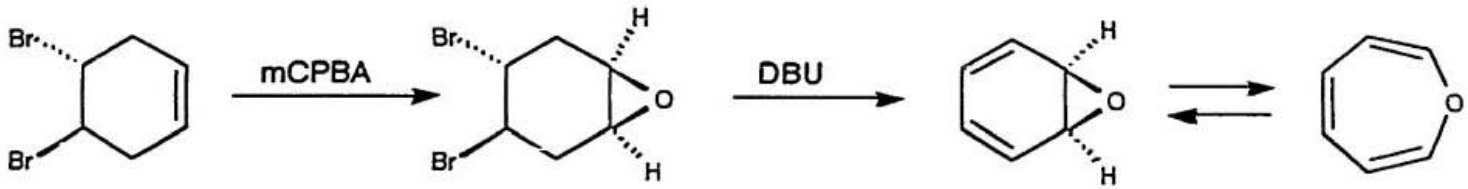
* Even though the benzene oxides **142**, and **148a** have been shown to exist mainly in the form of the oxepin tautomers **143** and **149a**, respectively, the benzene oxide tautomers will be referred to only for convenience and consistency.

polarity, with more polar media favouring the benzene oxide form. This indicates that the dipole moment for **142** is larger than that for **143**, and more polar media are able to stabilize the former more so than do nonpolar media.

The more substituted, and seemingly more sterically hindered benzene oxides **148a** and **148b** (Scheme 38), were synthesized in the following manner. Birch reduction of *o*-xylene **144a** and indan **144b** gave the substituted 1,4-cyclohexadienes **145a** and **145b**, respectively. Oxidation with the magnesium salt of monoperoxyphthalic acid (MMPP)[100] provided the mono-epoxides, **146a** and **146b**. Purification of **146a** then **146b** by chromatography, followed by addition of slightly less than one molar equivalent of Br_2 in the cold, gave the dibromides **147a** and **147b**, respectively. Following the procedure by Paquette and Barrett,[101] **147a** and **147b** were doubly dehydrobrominated in ether with potassium *tert*-butoxide, which provided **148a** and **148b**, respectively.

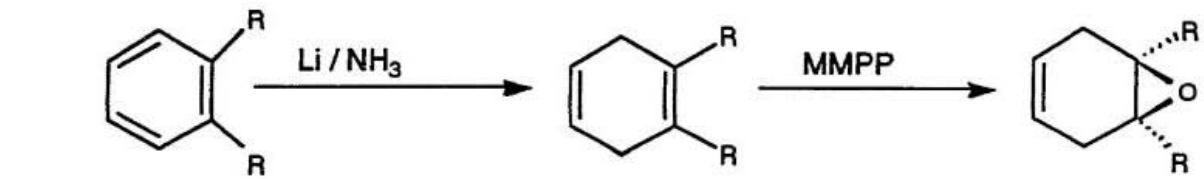
Vogel[99] had shown that for **148a** the **148a** ⇌ **149a** equilibrium favours the oxepin tautomer **149a**, presumably due to the eclipsing of the two methyl groups in the benzene oxide form **148a**. In contrast, the **148b** ⇌ **149b** equilibrium of the benzene oxide derived from indan lies in favour of **148b**. This is not surprising, since a considerable amount of angle strain would be expected in the oxepin **149b**.

The following section will report the results of the cycloadditions of dienes **109**, **114**, **121** - **125**, **132**, **133**, **137**, **138** and the benzene oxides **142**, **148a**, and **148b**.

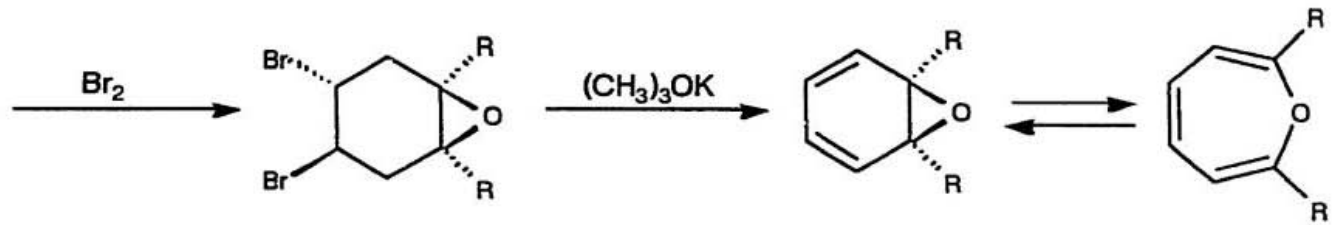


127 141 142 143

Scheme 37. The synthesis of benzene oxide 142



144a , b 145a , b 146a , b



147a , b 148a , b 149a , b

a R = CH_3, CH_3

b R = $CH_2CH_2CH_2$

Scheme 38. The synthesis of *o*- xylene-1,2-oxide (**148a**) and indan oxide (**148b**)

DIELS-ALDER REACTIONS

The addition of *N*-phenylmaleimide to a chloroform solution of *cis*-3,5-cyclohexadiene-1,2-diol (**121**) produced, after heating at reflux overnight and evaporation of the solvent, a colourless solid in nearly quantitative yield. Analysis of the ^{1}H nmr spectrum of this sample indicated clean conversion of addends to Diels-Alder adducts. Two sets of signals, corresponding to a major and a minor isomer, were evident in a ratio of 95:5. Repeated recrystallization of the crude product mixture afforded crystals of the major isomer. The structure of the major isomer **150** (Scheme 39), arising from the *endo*-addition of the dienophile to the diene, *syn* to the diol unit, was established by x-ray crystallography (Figure 21). The structure of the minor isomer **151**, resulting from addition of the dienophile *endo* and *anti* to the diol diene, was also established by x-ray crystallography (Figure 22). Compound **151** was not isolated from the above Diels-Alder reaction. However, ample quantities of **151** were obtained from the acid-catalysed hydrolysis of Diels-Alder adduct **153** (Scheme 41). The signals in the ^{1}H nmr spectrum of the hydrolysis product of **153** coincided with the signals due to the minor isomer in the ^{1}H nmr spectrum of the crude product mixture from the addition of **121** and NPM.

To confirm that the product distribution of the Diels-Alder addition of **121** and NPM was roughly independent of the solvent, this reaction was performed in a number of solvents. The results are summarized in Table 7.* The **150/151** ratio was found to vary only slightly from solvent to solvent. Using dielectric constant (ε) as an estimate of

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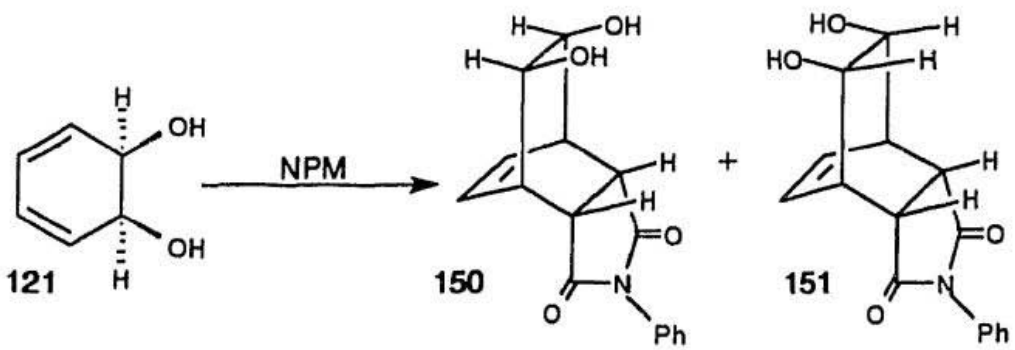
* All adduct ratios reported in Tables 7, 8 and 9 were determined by integration of the ^{1}H nmr spectra of the crude adduct mixtures.



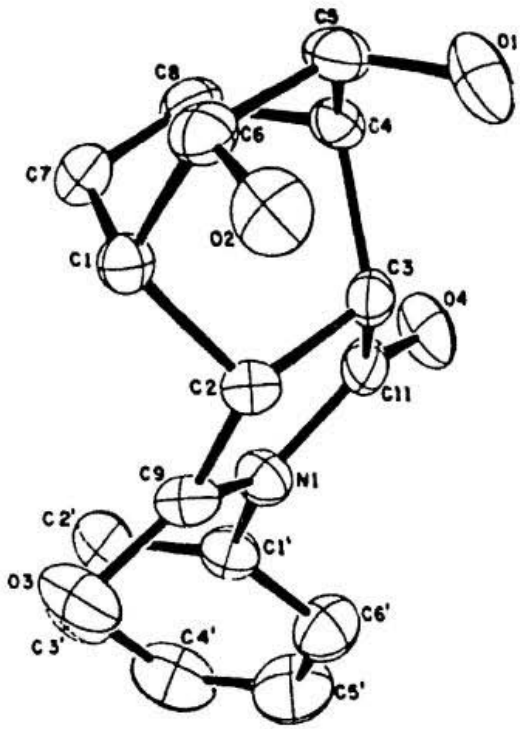
Scheme 39. Diels-Alder reaction of *cis*-3,5-cyclohexadiene-1,2-diol **121** with *N*-phenylmaleimide

Table 7. Reaction of diol diene **121** with *N*-phenylmaleimide in various solvents (reactions heated at reflux, except where indicated)

Solvent	ε	% *syn* **150**	% *anti* **151**	% yield [a]
pyridine [b]	12	95	5	90
acetone	21	95	5	93
chloroform	5	95	5	93
methanol	33	93	7	80
benzene	2	92	8	91
DMSO [b]	47	92	8	87
acetonitrile	38	88	12	94

[a] Based on mass recovery of adducts, and sample purity as determined by ^{1}H nmr

[b] Heated at 80 °C in an oil bath



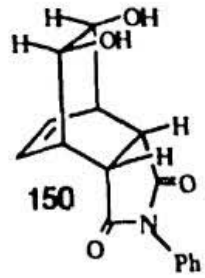
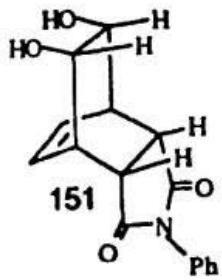


Figure 21. Perspective view of **150**



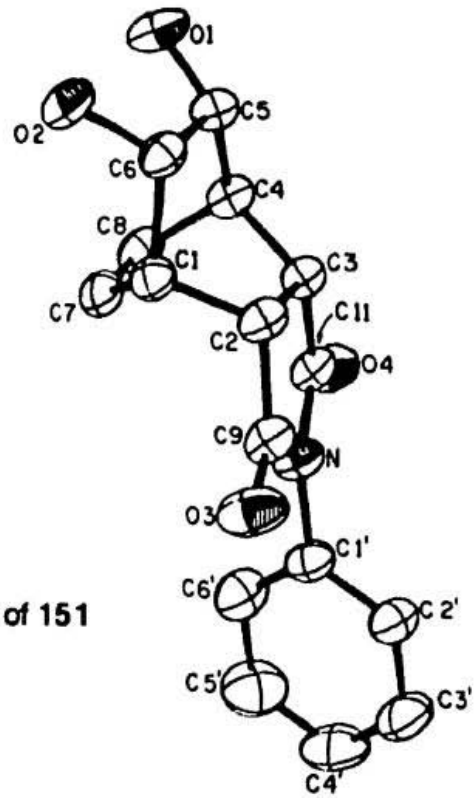
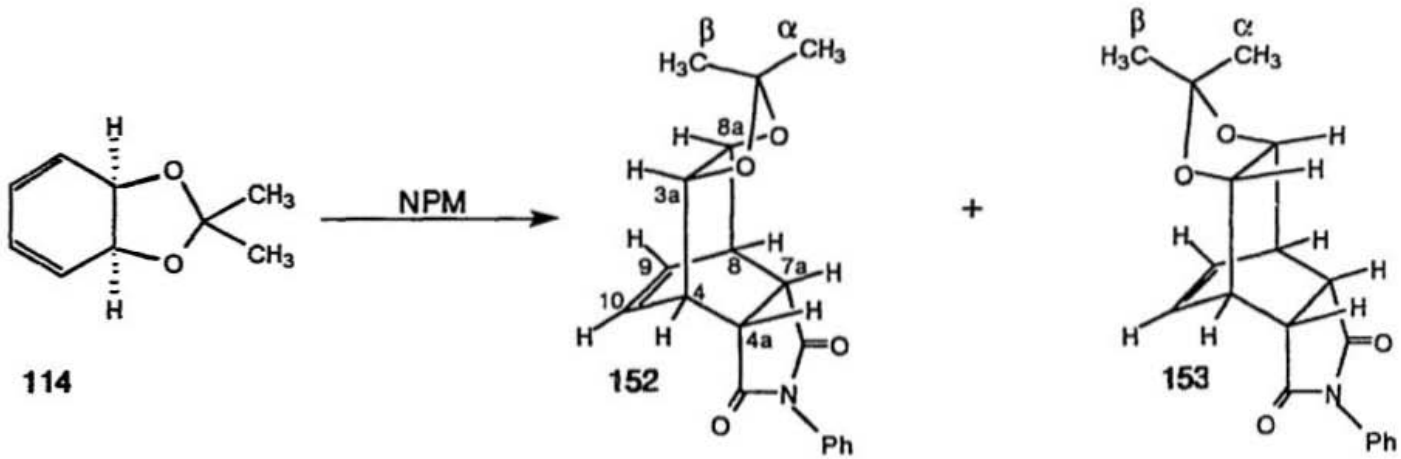


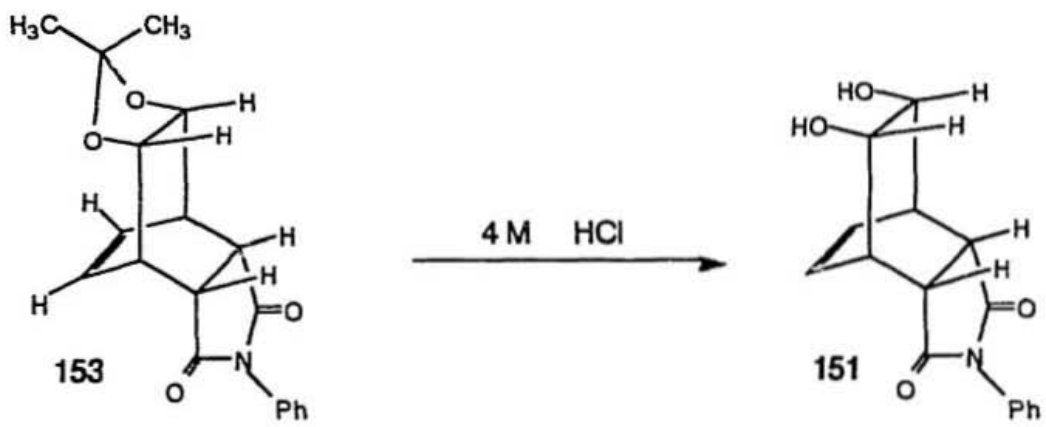
Figure 22. Perspective view of **151**

solvent polarity, it was originally expected that highly polar solvents, which are capable of strong hydrogen-bonding interactions with the hydroxyl substituents of **121**, would increase the effective size of the diol units. This in turn would cause increased steric interactions between diene and a dienophile approaching the *syn* face of the diene. However, as Table 7 shows there was no correlation between the **150/151** ratio and the dipole moment of the solvent. Obviously, if polar solvents did coordinate around the hydroxyl substituents, this had little effect on the relative reactivity of the *syn* face of **121**.

The acetonide diene **114** reacted with NPM to yield adducts **152** and **153** in a 60:40 ratio (Scheme 40). The complete assignment of the ^{1}H nmr spectra of both of these adducts was done on the basis of chemical shift and ^{1}H nmr nuclear Overhauser enhancement difference spectral data. For example, compound **153** displayed low field signals at δ 7.35 - 7.18 and δ 6.17. These were assigned to the phenyl ring of the maleimide moiety and the vinyl portion of the bicyclo[2.2.2]octene unit, respectively. The signal at δ 4.32 was assigned to the hydrogens on C-3a and C-8a, which is the chemical shift that would be expected for a hydrogen attached to an ether carbon. The signal at δ 3.53, which appeared as a broad multiplet, was due to the bridgehead hydrogens at C-4 and C-8. Saturation of this signal enhanced the intensities of those signals at δ 6.17, δ 4.32 and δ 2.88. Only the bridgehead hydrogens are positioned such that this result could be obtained. It should be noted that saturation of the bridgehead hydrogens of a number of adducts gave similar results. The signal at δ 2.88 was therefore due to those hydrogens at C-4a and C-7a, α to the carbonyls of the maleimide function. The high field signals at δ 1.35 and δ 1.30 (each with an integration of 3 hydrogens) were assigned to be those due to the methyl groups of the acetonide unit.



Scheme 40. Diels-Alder reaction of acetonide diene **114**



Scheme 41. Hydrolysis of the *anti* acetonide adduct **153** to *anti* diol adduct **151**

With the hydrogen signals assigned, the assignment of the signals in the ^{13}C nmr spectrum of **153** was aided considerably by the use of ^{1}H - ^{13}C heteronuclear correlation experiments (HET-CORR). The carbon signals appearing at δ129.6, 77.1, 40.3 and 36.9 were found to be one-bond coupled to the hydrogen signals at δ6.17, δ4.32, δ3.53 and δ2.88, respectively. Nearly all adducts synthesized gave ^{1}H nmr and ^{13}C nmr spectra that were very similar in appearance to that of compound **153**, and the signal assignments for these were made in an analogous fashion.

The stereochemistries of both **152** and **153** were established unequivocally by nuclear Overhauser effect difference experiments. For compound **152**, saturation of the signal due to the α-CH_3 group gave enhancement (4%) of the signal due to the hydrogens on C-4a and C-7a. Saturation of the hydrogen signal due to the β-CH_3 group gave an n.O.e. (7%) to the C-3a and C-8a hydrogens' signal. Furthermore, a smaller n.O.e. (1.5%) was observed for the signal due to the hydrogens on C-9 and C-10 on saturation of the C-3a and C-8a hydrogens' signal. This showed conclusively that **152** must have arisen from *endo* addition of the dienophile to the *syn* face of diene **114**. Compound **153** displayed an enhancement (13%) of the C-4a and C-7a hydrogens' signal on saturation of the C-3a and C-8a hydrogens' signal. Also, saturation of the β-CH_3 hydrogens gave an n.O.e. (2.5%) for the C-9 and C-10 hydrogens' peak. This indicated that **153** arose from addition of the dienophile *endo* and to the *anti* face of diene **114**.

Table 8 gives a compilation of the *syn*/*anti* adduct ratios arising from the Diels-Alder additions of NPM to several dienes. The structures of the *syn* and *anti* adducts resulting from dienes **109**, **122** and **124**, were determined by derivatization of the diol adducts **150** and **151**, respectively. The Diels-Alder reaction of diacetate diene **109** with NPM yielded a colourless solid. The ^{1}H nmr spectrum of a sample of the crude product

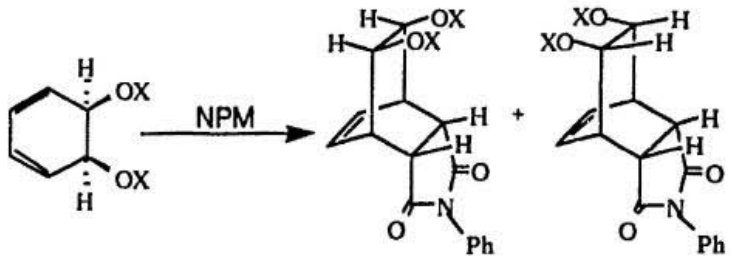
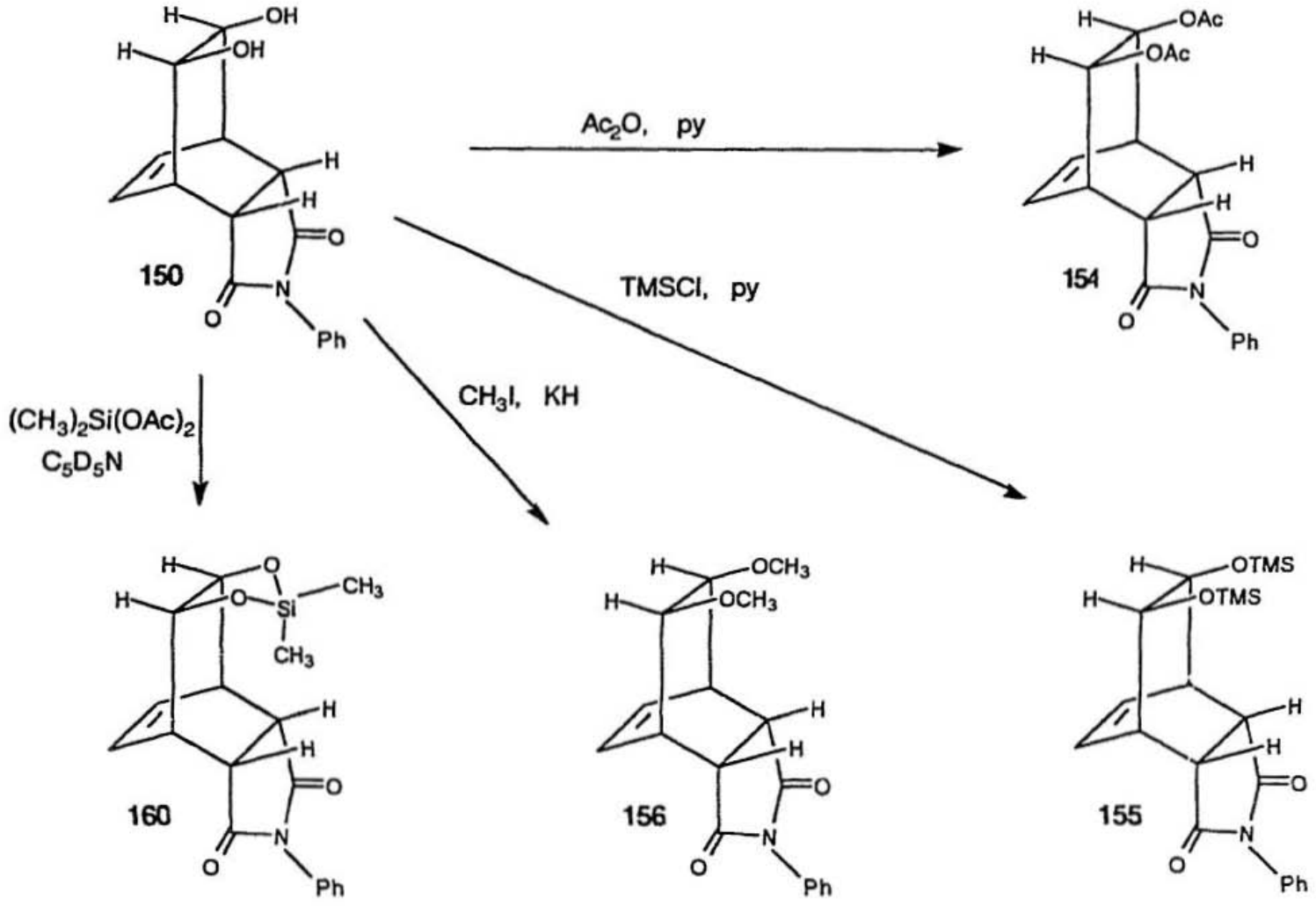


Table 8. Relative amounts of *syn* and *anti* adducts obtained, and the relative rates, for the Diels-Alder reaction of **121** and derivatives in $CHCl_3$ (reactions stirred at room temperature except where indicated)

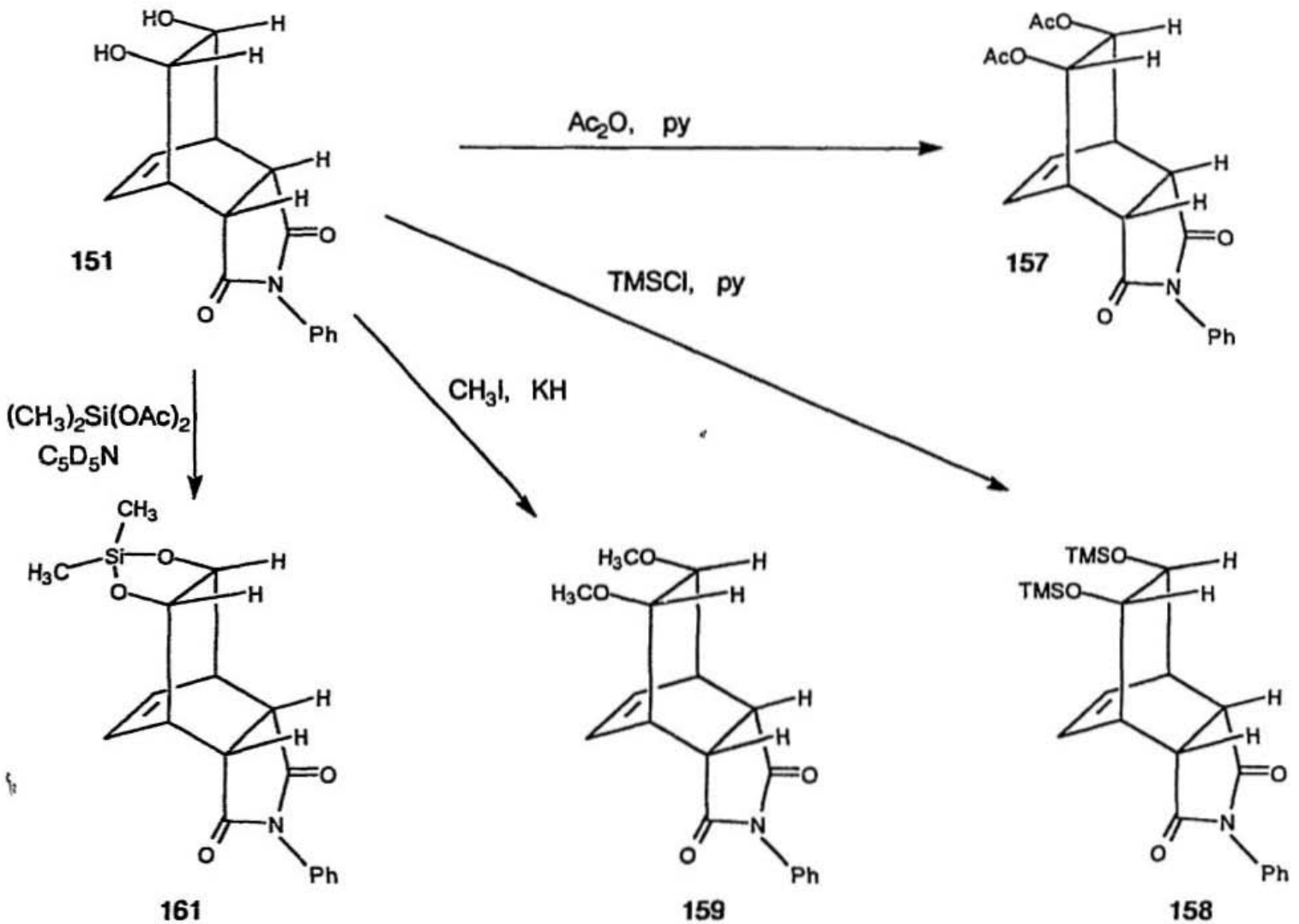
Diene	X =	% *syn*	% *anti*	Rate [a]
109 [b]	$COCH_3$	88	12	0.002
122	$Si(CH_3)_3$	100	0	0.03
121 [b]	H	95	5	0.1
124	CH_3	99	1	0.2
123	$-Si(CH_3)_2-$	60	40	2.7
114	$-C(CH_3)_2-$	60	40	> 100
125	$-B(CH_2CH_3)-$	45	55	——

[a] Rate relative to 1,3-cyclohexadiene (rate = 1)

[b] Heated under reflux



Scheme 42. Derivatization of *syn* diol adduct **150**



Scheme 43. Derivatization of *anti* diol adduct **151**

showed clearly two sets of signals, corresponding to a major and a minor adduct in a ratio of 88:12. Derivatization of **150** then **151** with acetic anhydride in pyridine provided the diacetate analogs **154** and **157**, respectively. Comparison of the ^{1}H nmr spectra of purified **154** and **157**, and the spectrum obtained from the crude product of the above addition showed that **154** corresponded to the major isomer and **157** to the minor isomer. Analyses of the products from the cycloadditions involving dimethoxy diene **124** and bis(trimethylsilyloxy) diene **122** were performed in the same manner. (See also Schemes 42 and 43.)

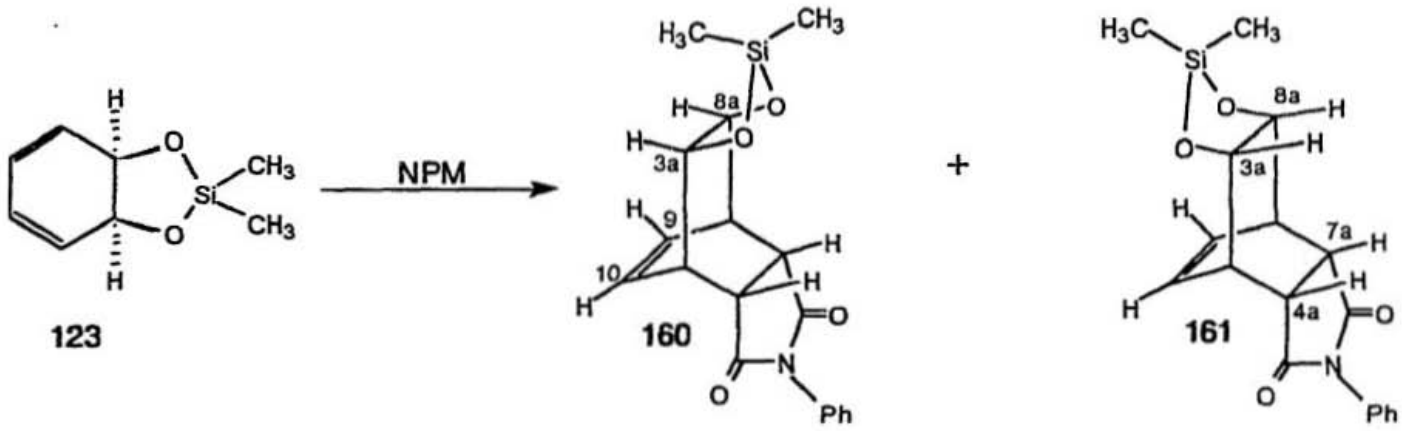
The Diels-Alder of diene **122** does deserve special mention. A stirred chloroform solution of **122**, with one molar equivalent of NPM, yielded, after evaporation of the solvent, a pale yellow solid, which was shown to consist of some unreacted **122**, unreacted dienophile and the *syn* Diels-Alder adduct **155**. No signals corresponding to the *anti* Diels-Alder adduct **158** could be detected in the ^{1}H nmr spectrum of the crude product.

The "siliconide" diene derivative **123** gave a quantitative conversion to a major and a minor adduct in a 60:40 ratio on reaction with NPM in $CDCl_3$ (Scheme 44). Attempted separation of these two adducts by flash chromatography resulted in the isolation of diol adducts **150** and **151** in a low combined yield. However, the ^{1}H nmr spectrum of the adduct mixture displayed good separation of some of the aliphatic hydrogen signals of the individual adducts. This allowed us to perform n.O.e.d. experiments directly on the adduct mixture, which gave the following pertinent results. Saturation of the signal due to the hydrogens on C-3a and C-8a of the minor adduct resulted in an enhancement (12%) of the signal due to the hydrogens on C-4a and C-8a, which indicated that the minor adduct was the *anti* isomer **161**. (This n.O.e. result was analogous to that found

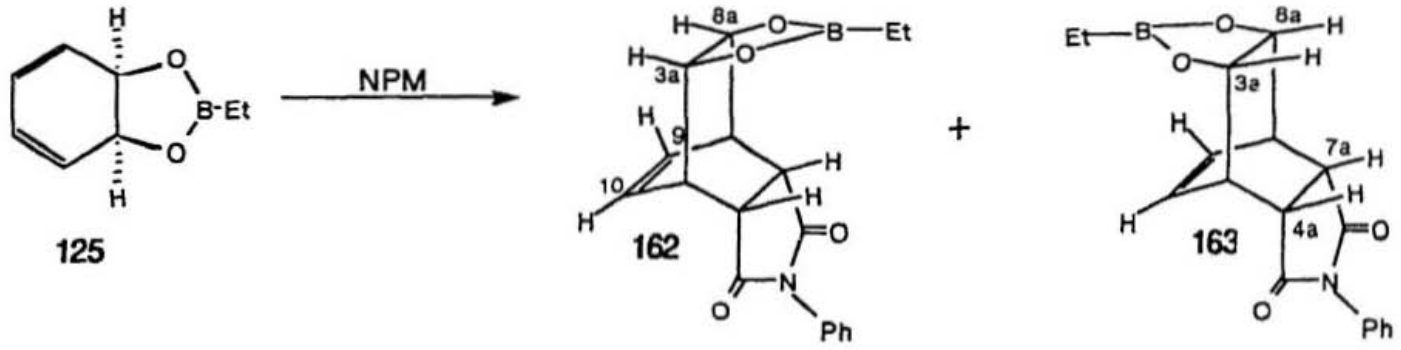
for the *anti*-acetonide adduct **153**.) Saturation of the signal due to the hydrogens on C-4a and C-7a of the major adduct gave a smaller signal enhancement (3%) of the signal due to the hydrogens on C-9 and C-10, which indicated that the major adduct corresponded to compound **160**, the *syn* addition product. (This n.O.e. result was reminiscent to that of the *syn* acetonide adduct **152**.) To confirm the structural assignments for the major and minor adducts, both of the pure diol adducts **150** and **151** were derivatized to the corresponding "siliconides" according to Schemes 42 and 43, respectively.

The Diels-Alder reaction of cyclic boronate ester **125** was done in a similar fashion as that for the siliconide diene **123**. Addition of approximately one molar equivalent of NPM to **125** in $CDCl_3$ resulted in clean conversion of the addends to two adducts in a 55:45 ratio (Scheme 45). A series of multiplets at δ 0.7 - 1.1 appearing in the ^1H nmr spectrum, and carbon signals at *ca.* δ 2.5 in the ^{13}C nmr spectrum, of the adduct mixture were entirely consistent with the spectral data reported for other ethyl boronate esters.[102a] Without separation of the adducts, n.O.e.d. experiments were performed on the product mixture. Saturation of the signal due to the hydrogens on C-3a and C-8a of the major isomer gave a large enhancement (12%) to the signal due to the hydrogens on C-4a and C-7a. Therefore, the major isomer was assigned structure **163**, that arising from *endo* addition of the dienophile to the face of diene **125** *anti* to the oxygens. Likewise, saturation of the signal due to the hydrogens on C-3a and C-8a of the major adduct gave the expected smaller enhancement (3%) of the signal due to the hydrogens on C-9 and C-10. The minor isomer was then assigned structure **162**, resulting from addition of the dienophile *endo* and *syn* to the oxygens of the diene.

The increase in the proportion of *anti* addition product with the cyclic dienes **114** and **123** can be attributed to increased steric hindrance experienced by the dienophile



Scheme 44. Diels-Alder reaction of "siliconide" diene 123



Scheme 45. Diels-Alder reaction of boronate diene 125

as it approaches the *syn* face of these dienes (see Discussion). In an effort to increase these steric demands and promote the formation of a higher proportion of *anti* adducts, *cis*-benzylidine dienes **132** and **137** were studied. In contrast, the epimeric *trans*-benzylidine dienes **133** and **138** should then decrease the steric demands and so might allow *syn* addition to occur with these cyclic derivatives. The results of the Diels-Alder reaction between dienes **132, 133, 137,** and **138** with NPM are summarized in Table 9.

The Diels-Alder reaction of both **132** and **137** with NPM (Schemes 46) proceeded smoothly to give very similar adduct ratios. As expected, both of these dienes afforded a marked increase in the proportion of *anti* adduct formed. In contrast, however, the *trans*-phenyl dienes **133** and **138** reacted with NPM to give the highest proportion of *anti* adducts of all of the cyclic diene derivatives of **121** studied (Schemes 47). The similarity in the adduct ratios obtained for dienes **132** and **137**, and, **133** and **138** indicated that the nitro group on dienes **137** and **138** had no significant long-range electronic effect on the *π*-facial selectivity of the Diels-Alder additions. The relative stereochemistries of all the adducts shown in Schemes 46 and 47 were determined by n.O.e.d. experiments.

The major adduct **165** from diene **132** gave a large signal enhancement of the signal due to the hydrogens on C-4a and C-7a (16%) and the signal due to the hydrogen on C-2 (18%) on saturation of the signal due to the hydrogens on C-3a and C-8a. This result indicated that C-3aH and C-8aH were *cis* to C-2H and also *cis* to C-4aH and C-7aH. This observation was in accord with *endo*-addition of NPM to the diene **132**, *anti* to the oxygens. Saturation of the signal due to the hydrogens on C-3a and C-8a of **164** gave increased signal intensity of the signals due to the hydrogens on C-2 (12%) and those on C-9 and C-10 (2%). In addition, saturation of the signal due to the hydrogens on C-4a and C-7a gave enhancement (3%) of the *ortho* protons at δ 7.52 on the phenyl

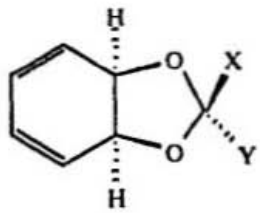
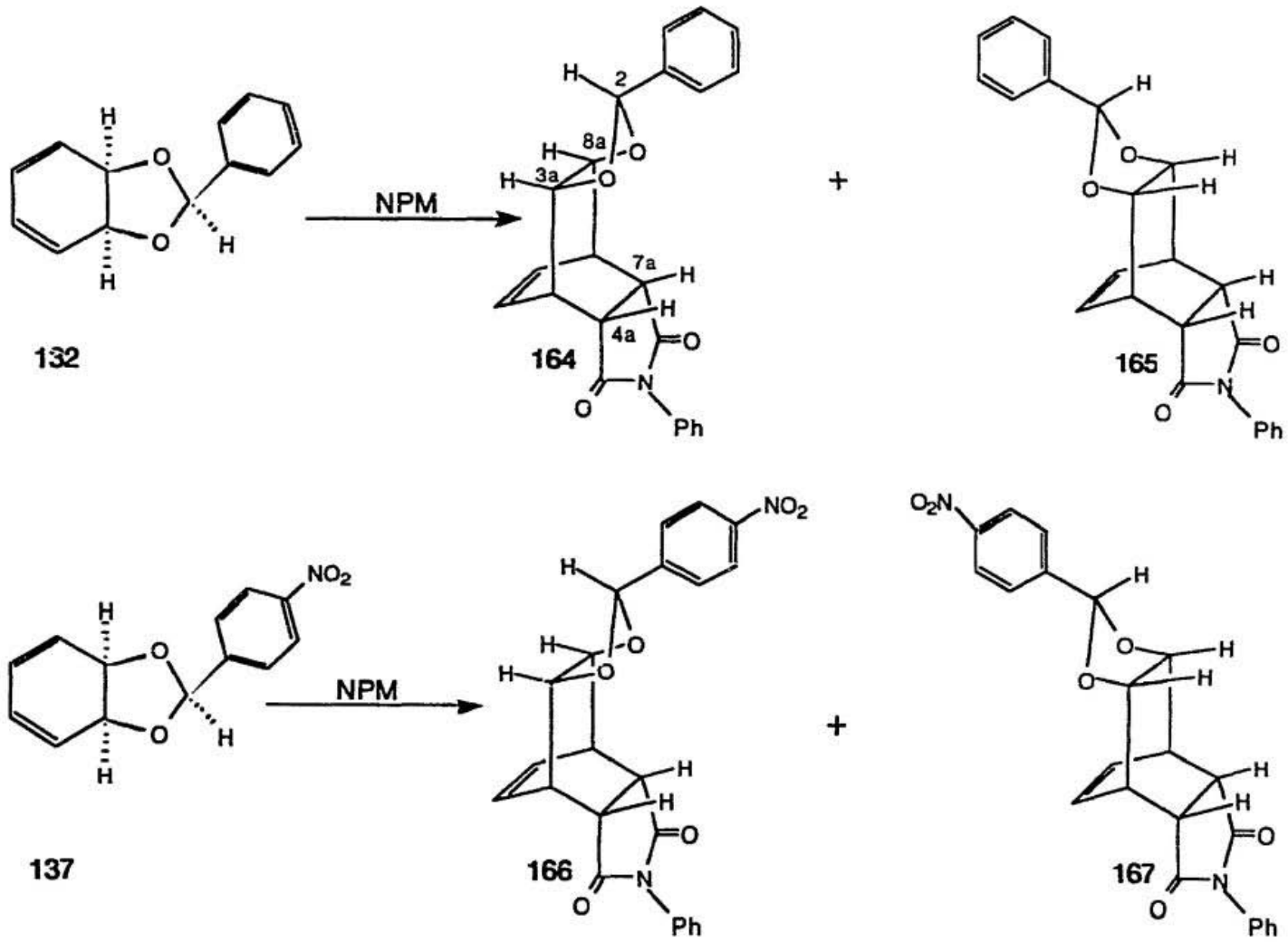
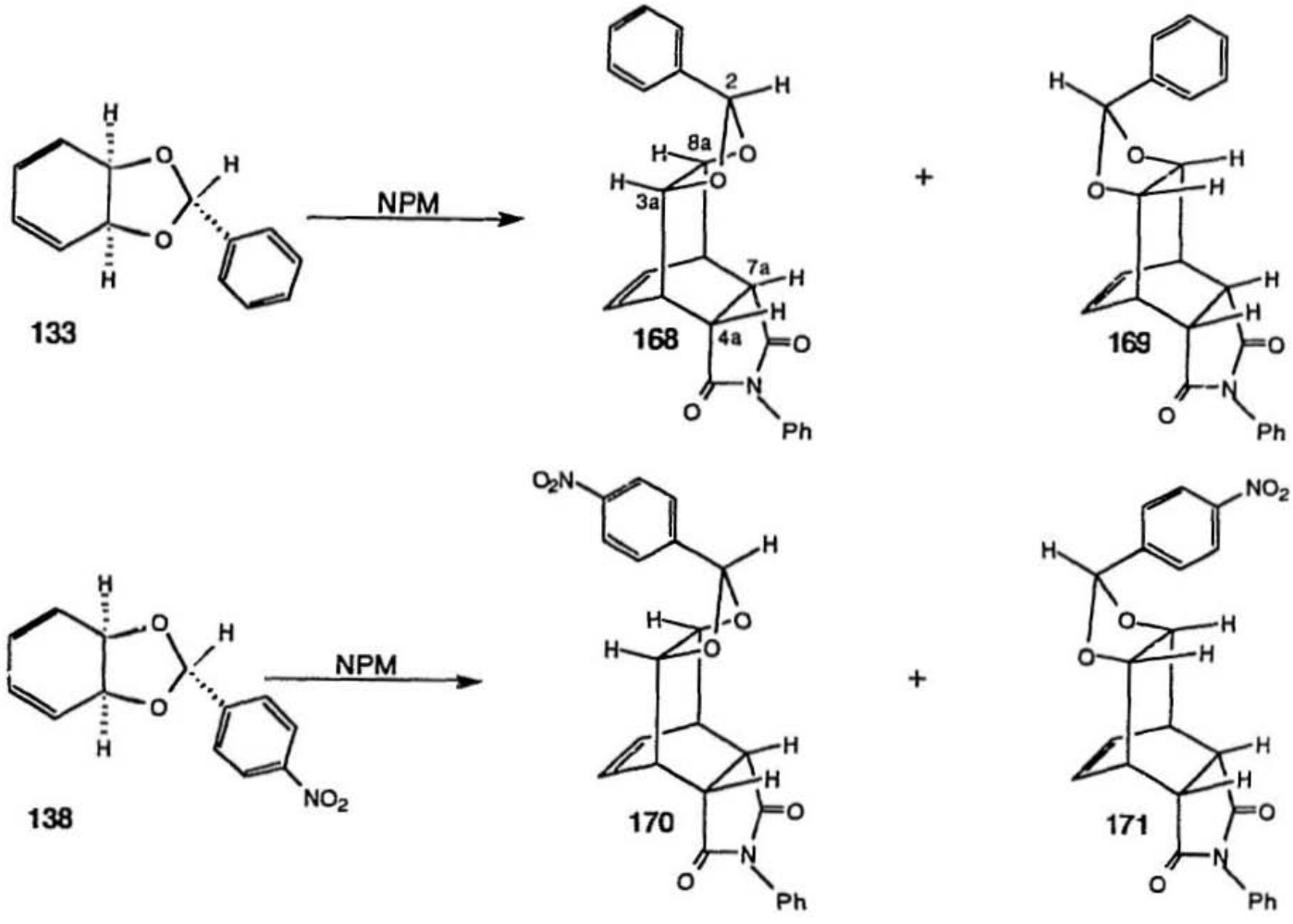


Table 9. Relative amounts of *syn* and *anti* adducts obtained from the Diels-Alder reaction of various benzylidene protected derivatives of **121** with *N*-phenylmaleimide (reactions performed in $CHCl_3$ at room temperature)

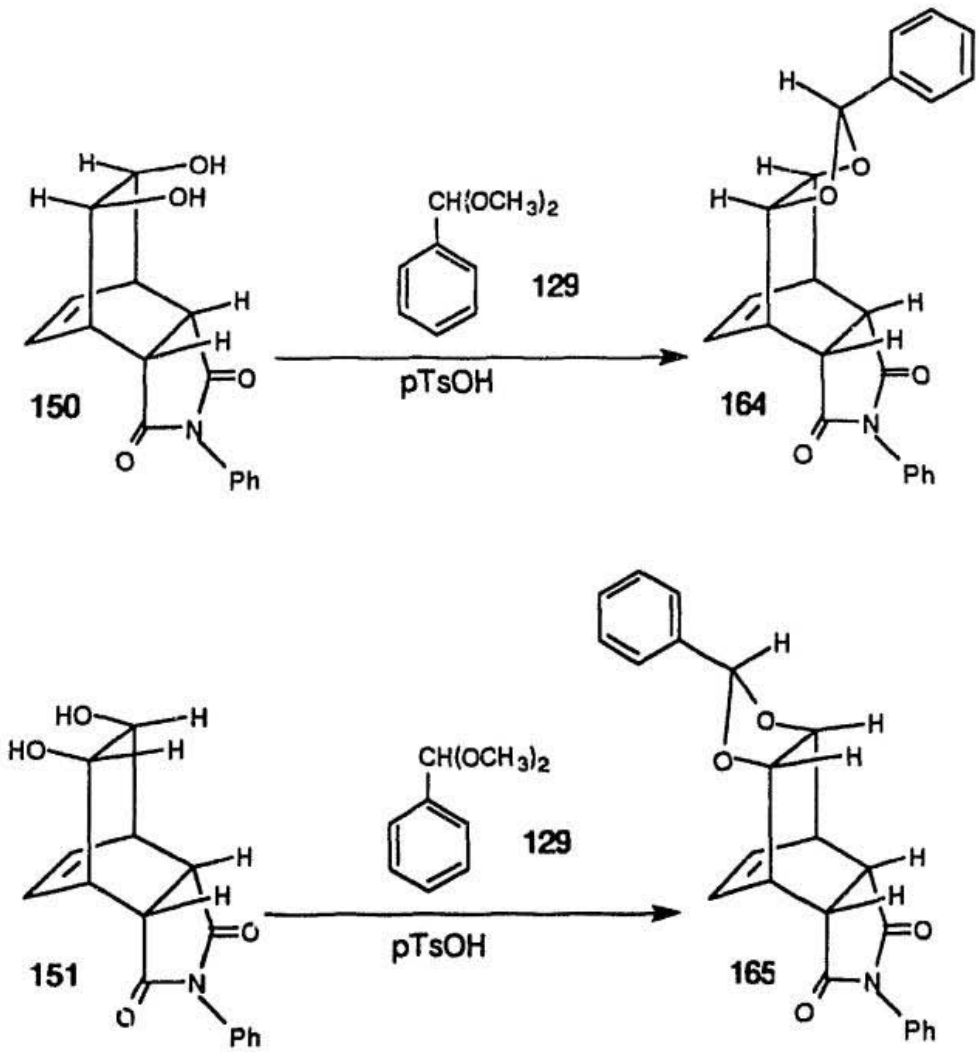
Diene	X =	Y =	% *syn*	% *anti*
132	Ph	H	28	72
137	Ph-pNO_2	H	27	73
133	H	Ph	4	96
138	H	Ph-pNO_2	5	95



Scheme 46. Diels-Alder reactions of *cis* benzylidene-protected dienes 132 and 137



Scheme 47. Diels-Alder reactions of *trans* benzylidene-protected dienes **133** and **138**



Scheme 48. Derivatization of diol adducts **150** and **151** to the *cis* benzylidene-protected adducts **164** and **165**

ring. The spectral information therefore indicated that C-3aH and C-8aH were *cis* to C-2H and also *cis* to C-9H and C-10H, and that C-4aH and C-7aH were *cis* to the phenyl ring. This could only have arisen by *endo*-addition of the dienophile to the *syn* face of diene **132**. Adducts **166** and **167** exhibited similar spectral behaviour to **164** and **165**, respectively. It is of interest to note that reaction of **150**, then of **151**, with **129** (Scheme 48) under equilibrating conditions gave only **164** and **165**, respectively, which suggested that the relative stereochemistry of the substituent at the C-2 position was the thermodynamically preferred one.

The minor adduct **168** arising from diene **133** displayed signal enhancement (9%) of the signal due to the hydrogen on C-2 upon saturation of the signal due to the hydrogens on C-4a and C-7a. Also, saturation of the signal due to the hydrogens on C-3a and C-8a gave a smaller enhancement (2.5%) to the signal due to the hydrogens on C-9 and C-10. The stereochemical relationship that must have existed was C-2H being *cis* to C-4aH and C-7aH (and consequently C-2H was *trans* to C-3aH and C-8aH), and C-3aH and C-8aH were *cis* to C-9H and C-10H. This was consistent with the dienophile adding *endo* and *syn* to the oxygen function of diene **133**.

For compound **169**, the major isomer isolated from diene **133**, saturation of the signal due to its hydrogens at C-4a and C-7a resulted in a large signal enhancement (14%) of the signal due to the hydrogens on C-3a and C-8a. In addition, an enhancement (4%) of the signal due to the hydrogen on C-2 was observed when the signal due to the hydrogens on C-9 and C-10 was saturated. These results corresponded to the structure shown in which a *cis* relationship exists between C-3aH and C-8aH, and C-4aH and C-7aH, and C-2H was *cis* to C-9H and C-10H. Compounds **170** and **171** displayed similar n.O.e.d. spectra to those of **168** and **169**, respectively.

Information regarding the relative reactivities of various dienes was obtained in addition to the *syn*:*anti* product ratios. The relative reaction rates for a number of dienes are shown in Table 8, in which the rates of reaction in Diels-Alder additions were measured relative to 1,3-cyclohexadiene. These experiments were done competitively by combining one molar equivalent of each of a pair of dienes in $CDCl_3$ (e.g. **121** and 1,3-cyclohexadiene, **121** and **109**, etc.) with one molar equivalent or less of NPM. After stirring overnight, the ^1H nmr spectrum of the mixture was studied. Based on the integration of the signals of the adducts formed and those of any unreacted dienes, a relative rate was determined using the following formula:[102b]

$$\frac{kA}{kB} = \frac{\log [A] - \log ([A] - [Ax])}{\log [B] - \log ([B] - [Bx])}$$

in which (kA/kB) is the rate of reaction of diene A relative to diene B, [A] and [B] are the initial concentrations of dienes A and B, and [Ax] and [Bx] are the final concentrations of the adducts derived from A and B, respectively.

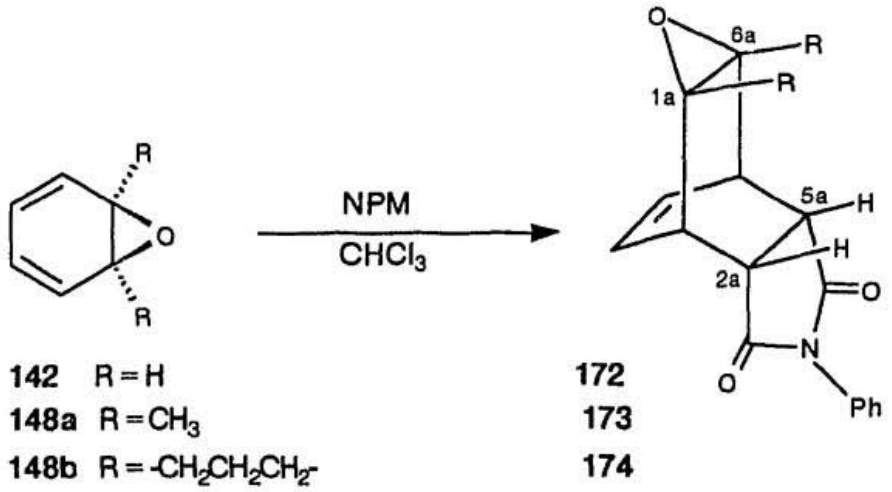
Finally, to ensure that the kinetically preferred adducts had formed in our Diels-Alder additions, a number of major adducts (**150, 152, 154, 155, 165, 167, 169,** and **171**) and minor adducts (**151, 153, 157, 159, 164, 166,** and **168**) were heated under reflux for an extended period (*ca.* 36 hours). In no instance did we find evidence for the formation of an isomeric adduct.

The Diels-Alder reactions of benzene oxides **142, 148a,** and **148b** with NPM were readily achieved, and the results are summarized in Scheme 49. The cycloadditions were performed in $CHCl_3$ at room temperature, except for **148a**, which required reflux conditions. All three benzene oxides displayed π-facial diastereospecificity. In contrast to the general outcome from the cycloaddition of **121** and its acyclic derivatives, the

structurally related benzene oxides added the dienophile *anti* to the oxygen substituent. Reaction of **148b** with *N*-methylmaleimide and the sterically less demanding dimethyl acetylenedicarboxylate still proceeded to give exclusively *anti* addition products (Scheme 49).

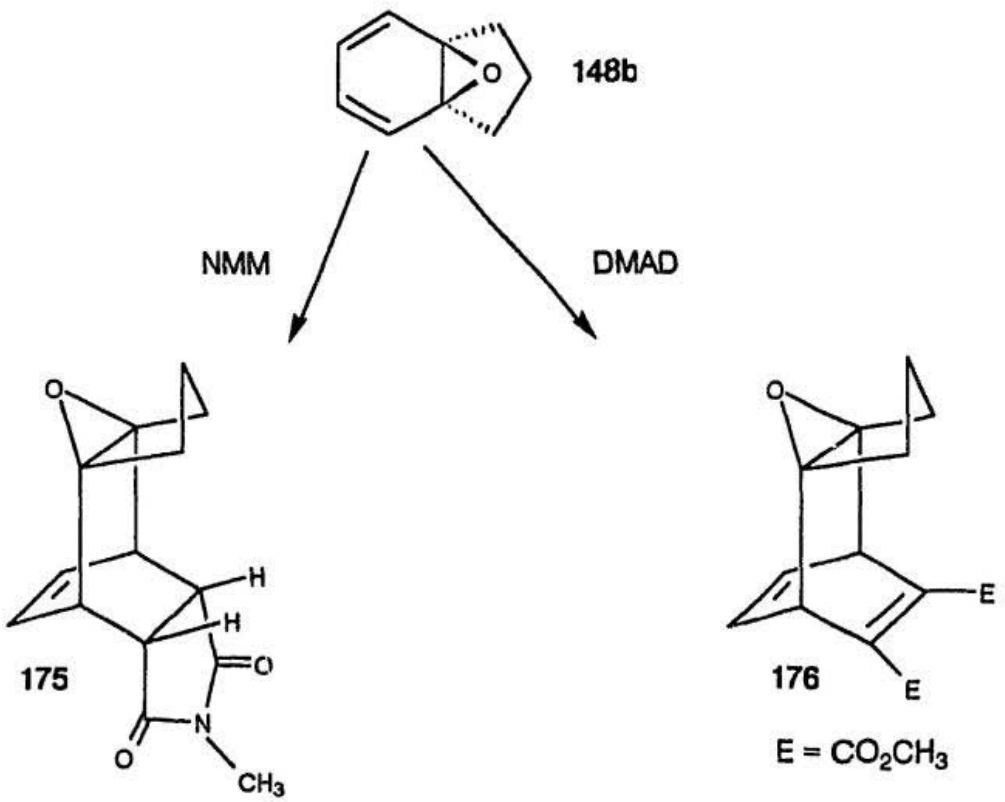
The structure of compound **172** was elucidated using n.O.e.d. spectroscopy. Saturation of the signal due to the hydrogens at C-2a and C-5a gave enhancement (6%) of the signal due to the hydrogens at C-1a and C-6a, indicating that the dienophile added *endo* and *anti* to the epoxide oxygen of **142**. In light of this outcome, and given the precedent we had established with the diol derivatives, it was considered prudent to confirm this structural assignment by x-ray crystallography (Figure 23). The n.O.e.d. experiments, however, served as a precedent for the structure determination of compounds **173-175**. Unfortunately, the structure of compound **176** could not be determined using n.O.e. difference methods. However, its structure was determined by x-ray crystallography, also (see Figure 24).

To confirm that the formation of only anti adducts that arose from the additions to **148b** was due to kinetic control, rather than thermodynamic control, the following test was carried out. A chloroform solution of **174** and *N*-methylmaleimide was heated under reflux for about 2 days. Likewise, a solution of **175** and *N*-phenylmaleimide were also heated. In neither case could any exchange product be detected. These results ensured that the Diels-Alder additions to **148b** and, presumably, those of **142** and **148a**, proceeded to give the kinetically preferred adducts.



142 R = H
148a R = CH_3
148b R = -$CH_2CH_2CH_2$-

172
173
174



Scheme 49. Diels-Alder reactions of the benzene oxides **142**, **148a** and **148b**

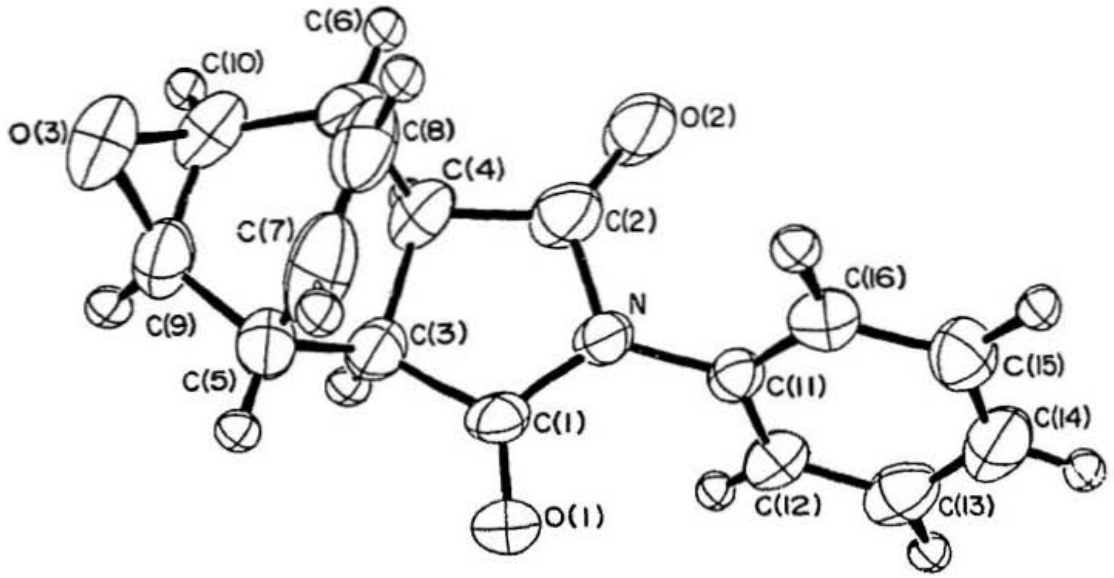


Figure 23. Perspective view of 172. Hydrogen atoms have been included to show relative stereochemistry.

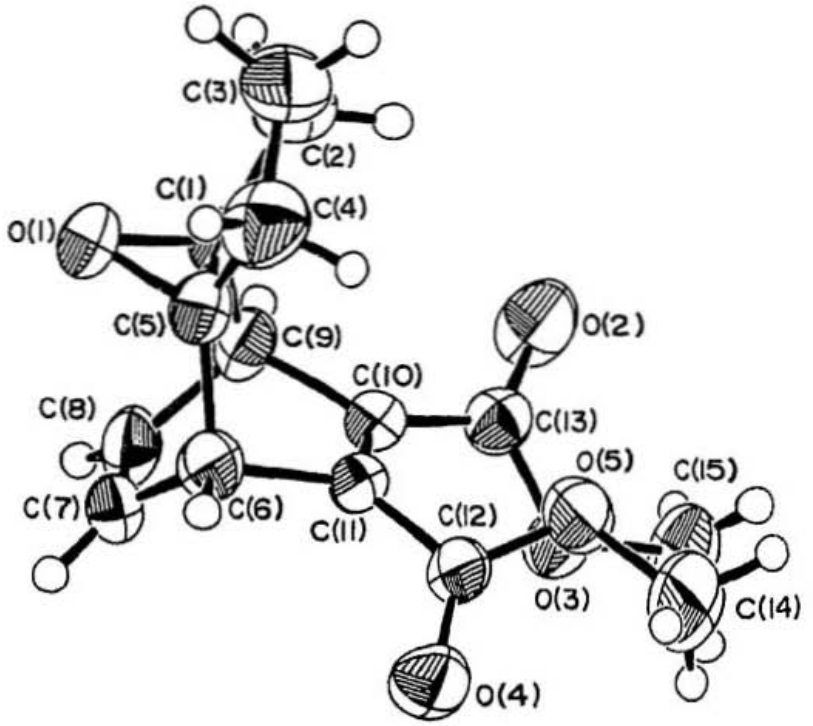


Figure 24. Perspective view of 176. Hydrogen atoms have been included to show relative stereochemistry.

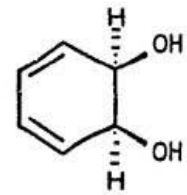
DISCUSSION

The Diels-Alder addition of *N*-phenylmaleimide to diol **121** clearly proceeded in a contrasteric manner, to give very predominantly the *syn* addition product. This high proportion of *syn* adduct was formed in both non-polar, polar aprotic, and polar solvents. This fact excluded direct hydrogen-bonding interactions between the reactants as a controlling factor that would facilitate *syn* addition.[58] Furthermore, this also suggested that if the effective size of the OH groups were to increase due to coordination with the solvent, this would not affect the *π*-facial selectivity.[59] The cycloadditions of **109**, **122**, and **124** to give mainly *syn* adducts did not agree with Franck's postulate for semicyclic dienes; that is, that the facial selectivity should be dependent on the size of the substituent on the oxygens. Indeed, diene **122**, which bears the group with the greatest potential for steric inhibition of the *syn* approach of a dienophile, gave exclusively the *syn* addition product.

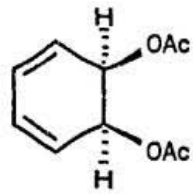
A parallel cannot be postulated between the Diels-Alder behaviour in this study and the results obtained for the cycloaddition of acyclic dienes, or with those obtained for the pyranose systems. Questions regarding the position of the heteroatom with respect to the diene have not yet been resolved with the acyclic dienes. In the latter case, the presence of a distal anomeric substituent seems to inhibit sterically *syn*-approach of dienophiles. As expected, the *syn*-addition to dienes **109**, **121**, **122**, and **124** is most similar to the observations by Woodward, Jones and Fallis for cyclopentadiene systems. Therefore, the information acquired in this study will be discussed in the context of the existing theories developed for cyclopentadienes.

The slower rate of cycloaddition for dienes **109**, **121**, **122**, and **124** relative to 1,3-cyclohexadiene was at variance with what would be expected if the electron density of the π-system were to be biased in favor of the face *syn* to the oxygens, as suggested by Fukui[76a] and Inagaki.[76b] This would also exclude any direct donation of electron density by the oxygens to the π-system. The slower rates may actually be due to the electronegativity of the oxygens, which might withdraw electron density by induction from the carbon framework. This would account for the higher rate of **124** (CH_3 is an electron-donating group) relative to **109** (acyl is an electron withdrawing group). However, some other "electronic" factor must be active to facilitate *syn*-addition.

The postulate that the *anti* substituent is the controlling factor for π-facial selectivity espoused by Macaulay and Fallis[44] and by leNoble[78] also does not agree with the rate behaviour. Although the electronic nature of the oxygens would be expected to change (thereby altering the σCO bond-donor ability) the *anti*-substituents of our dienes were always hydrogens. The σCO bond of diene **124** would be a better donor than the σCO bond of diene **109**. If the ability of the σCH bond to hyperconjugate and donate electron density remains constant for both dienes, then the Cieplak model[77] would predict a higher *syn*/*anti* ratio, and a higher rate of cycloaddition for diene **109**. That the opposite was true on both counts makes it difficult to extrapolate the results obtained with this model. The *syn*/*anti* ratio obtained for the boronate diene **125** further suggested that σ bond donation may not be the controlling force. The planar nature of boron should not greatly increase the amount of steric hindrance on the *syn* face of the diene, relative to **114**. If the boronate **A** is considered to be an electron withdrawing group *via* the resonance form **B** (Figure 25), then the σCO donor ability of this substrate would be much reduced compared to the σCO donor ability of **124**. This would predict the formation of a high



121



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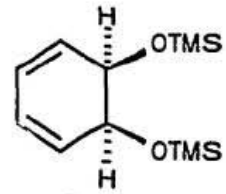

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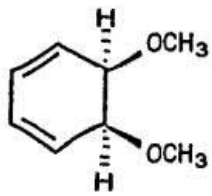

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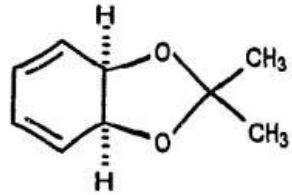

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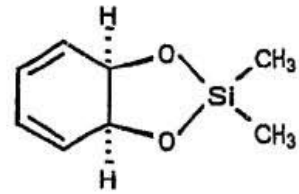

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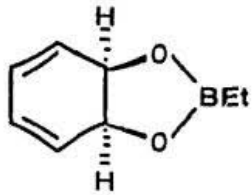

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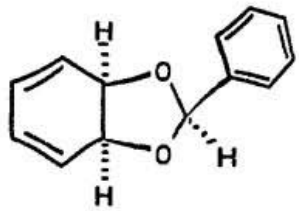

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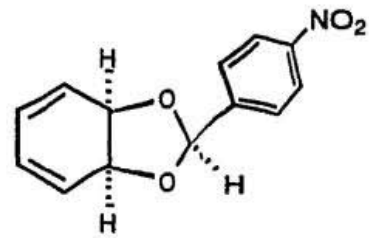

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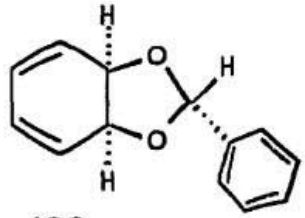

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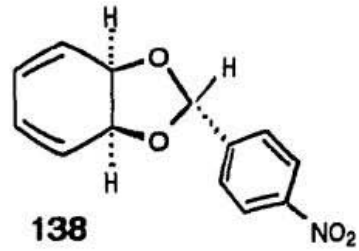


138

Figure 25. Possible resonance forms of a boronate ester

proportion of *syn* adduct. That the reactivity of both the *syn* and *anti* faces was approximately the same indicated that σ bond donation was again not operative. However, the higher percentage of *anti* adduct did indicate that the electronic nature of the oxygens was significantly altered.

The higher reaction rate of the cyclic derivatives **114** and **123** relative to 1,3-cyclohexadiene could be attributed to the fact that the *cis*-3a,7a-dihydro-1,3-benzodioxole ring system would have the cyclohexadiene moiety constrained in a more planar conformation, thus increasing the reactivity of the diene. That the amount of *syn* adduct formed is quite considerably lower for derivatives **114** and **123** compared to their acyclic counterparts **124** and **122** may be due to the increase in steric hindrance on the *syn* face of the diene. Compound **114**, for example, may adopt conformations **A** and **B** (Figure 26). While conformer **A** leaves the *syn*-face relatively unencumbered, conformer **B** would seriously inhibit the approach of a dienophile from that direction. If the energy barrier is low for the **A**⇌**B** interconversion, then a dienophile may have an approximately equal chance of encountering either conformer as it approaches the *syn* face.

An indication of the importance of steric effects in the control of π-facial selectivity was readily demonstrated with the *cis*-phenyl dienes **132** and **137**. Compound **132** would be expected to adopt conformers **C** and **D**. Conformer **D**, with the phenyl group oriented pseudo-axially over the *syn* face of the diene, would hinder *syn*-addition of dienophiles. However, a significant proportion of molecules must also exist in conformer **C** allowing some *syn*-addition, to give the result obtained.

It was somewhat surprising that the *trans*-phenyl derivatives **133** and **138** reacted to give almost exclusively *anti* addition products. This outcome may be rationalized in terms of the placement of the substituents on the acetal centre in different conformations.

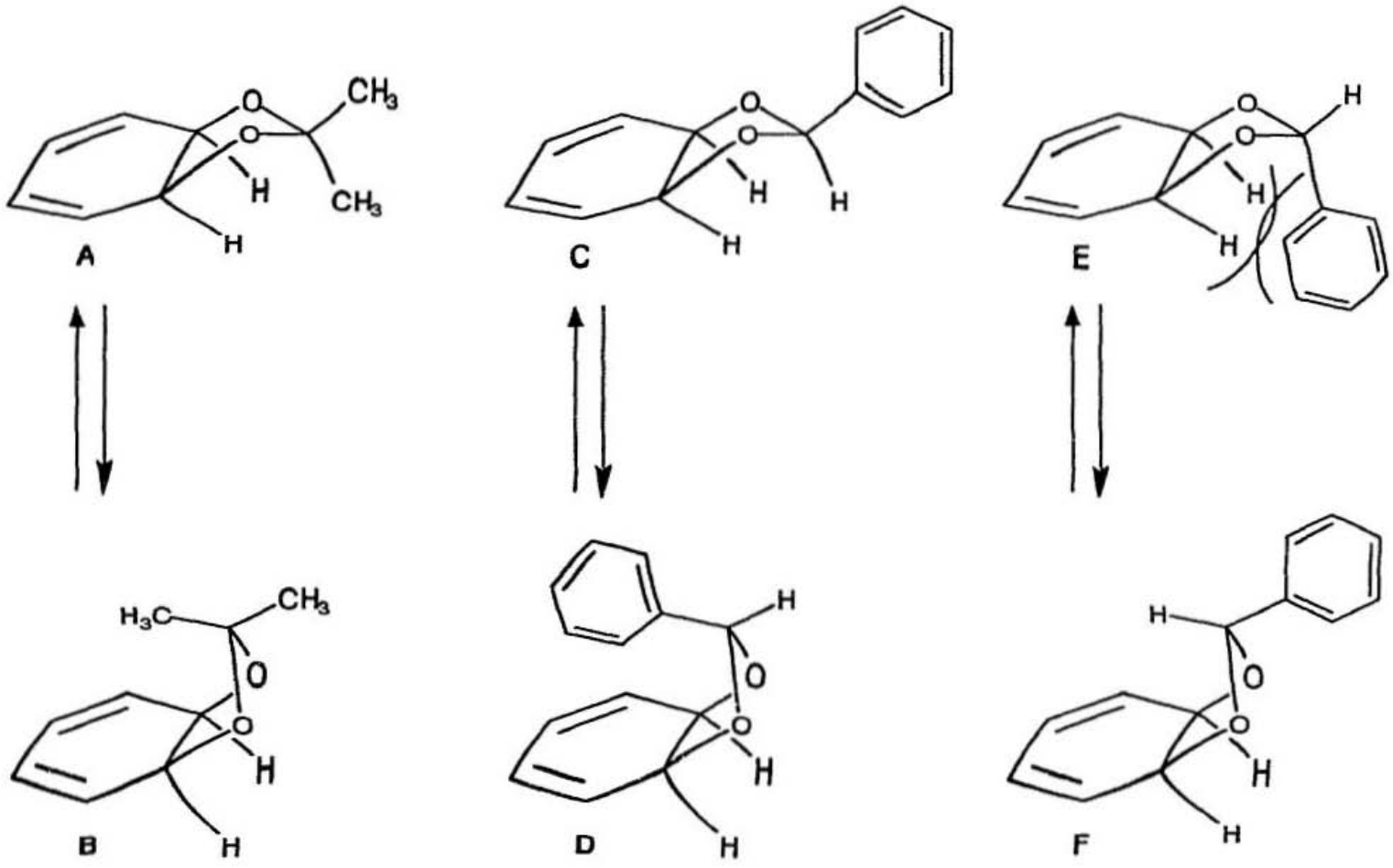
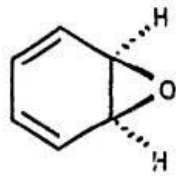


Figure 26. Important conformations of the acetonide and the benzylidene protected dienes

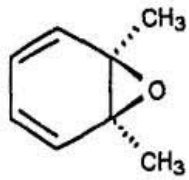
The phenyl ring would be expected to prefer to assume a pseudo-equatorial position on the 5-membered dioxolane ring, as in **F**, to avoid the steric crowding that must be present in conformer **E** between the phenyl ring and the allylic hydrogens. Conformer **F** has its acetal hydrogen directly over the cyclohexadiene ring, which must effectively block the *syn*-face of the diene. This is an example of the control that one well situated hydrogen atom can have on π-facial selectivity.

Given the tendency for *syn*-addition to **121** and its acyclic derivatives, it was somewhat surprising to encounter the exclusive addition of dienophiles *anti* to the oxygen substituent of the benzene oxides **142**, **148a**, and **148b**. These observations were contrary to postulate of Kahn and Hehre[43] stating that dienophiles add preferentially to the face *syn* to a lone-pair-bearing substituent. *Ab initio* calculations on **142** have shown that the π-electron density is only slightly biased in favor of the face *syn* to the oxygen.[103] Therefore, it is unlikely that the exclusive *anti* facial attachment of dienophiles arose by "orbital mixing" as described by Fukui and Inagaki.[78]

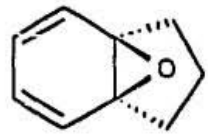
The *anti*-additions of dienophiles to the benzene oxides were, however, not really inconsistent with the model proposed by Macaulay and Fallis.[44] This model would predict *syn*-addition since the σCH bonds and the σCC bonds are better donors than the σCO bond. But this model also requires that the σ bonds be approximately perpendicular to the plane of the diene. An examination of the geometry of the benzene oxides shows that the oxygen is almost perpendicular to the plane of the diene, and the allylic R substituents are nearly coplanar (Figure 27). Even though the σCH and σCC bonds are better electron-donors, only the σCO bond possesses the proper orientation to enable it to hyperconjugate with the σ^* of the incipient bond. The σCH(R) bond is not far enough out-of-plane to interact properly in this manner to stablize effectively a *syn* transition state.



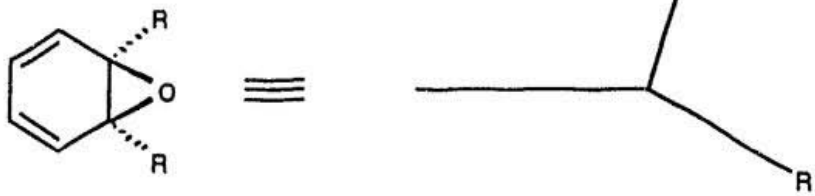
142

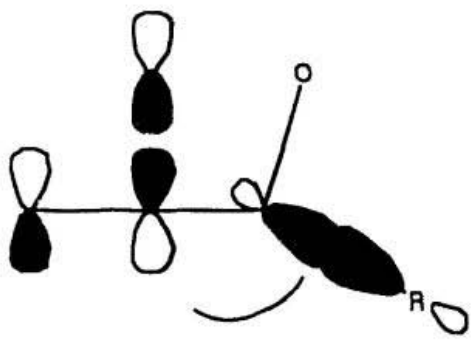


148a

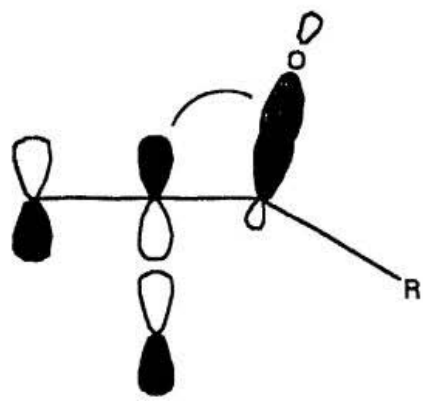


148b





Addition *syn* to O



Addition *anti* to O

Figure 27. σ-Bond donation as a possible controlling mechanism for the π-facial selectivity observed for the Diels-Alder reactions of the benzene oxides **142**, **148a** and **148b**

It should also be noted that as a consequence of the relative position of the oxygen in the benzene oxides, the approach of a dienophile to the *syn* face would be hindered, therefore it is plausible that the facial selectivity arose due to steric effects alone.

An alternative view of π-facial selectivity for cyclopentadienes, cyclohexadienes, and the benzene oxides involves the orbital components on the heteroatoms in the highest occupied molecular orbitals of the molecules as in Figures 28 and 29. (The highest occupied molecular orbital is labelled "1st HOMO". The next two molecular orbitals, the second highest and the third highest occupied molecular orbitals are labeled "2nd HOMO" and "3rd HOMO", respectively.) *Ab initio* calculations performed on various substrates generated the orbital pictures shown in Figures 28 and 29.[104] For 5-hydroxycyclopentadiene (Figure 28a) the "1st HOMO" has a small p-component situated on the oxygen that is out-of-phase with respect to the LUMO of the reacting dienophile. This antibonding relationship certainly would have a repulsive effect on the dienophile as it approaches to the *syn* face. However, in the "2nd HOMO" a substantially larger component is on the oxygen that is in-phase with the LUMO of the dienophile. If the difference in energy between the "1st HOMO" and the "2nd HOMO" is small, then the attractive effects of the favorable interaction might become more important than the repulsive effects of the unfavorable interactions. Recall from the work by Jones[73] that an OH group at the 5-position of a cyclopentadiene analogue gave exclusive *syn* addition. Likewise, for **121** (Figure 28b) in both the "1st HOMO" and the "2nd HOMO", there are components on the oxygens that are aligned in-phase with the LUMO of the dienophile. In contrast, for 5-chlorocyclopentadiene (Figure 29a), which adds preferentially *anti*,[71] a large component rests on the chlorine in the "1st HOMO" that is antibonding with the LUMO of the dienophile. Only in the "3rd HOMO" is there a component that is in-phase

with the LUMO. In this case, the repulsive interactions must overwhelm any attractive interactions between dienophile and the heteroatom.

Benzene oxide (**142**, Figure 29b) is most similar in structure to 5-hydroxycyclopentadiene in that its oxygen lies in the plane that bisects the diene. However, the "1st HOMO" has a large out-of-phase component on the oxygen, and neither the "2nd HOMO" nor the "3rd HOMO" has a component on the oxygen that is properly aligned in-phase with the LUMO of the dienophile. This implies that any electronic interaction between the dienophile and the oxygen would most certainly be repulsive if the dienophile were to approach the *syn*-face of the diene. Work is still in progress to generate orbital diagrams for other heteroatom-substituted plane-nonsymmetric cyclopentadienes and cyclohexadienes.

In retrospect, the postulate that is most similar with the above proposal was that extended by Anh.[75] However, Anh took the approach of "mixing orbitals" in his hypothesis. Figure 15 illustrates both a diene HOMO and localized lone pair orbitals on the oxygen in the same orbital diagram. Those illustrations shown in Figures 28 and 29 do not imply localized lone pair orbitals on the heteroatoms. Instead, those orbitals which are shown to be situated on the heteroatoms for a particular molecular orbital (1st HOMO, 2nd HOMO, and 3rd HOMO) are components of that molecular orbital.

In conclusion, the results obtained in this study have clearly shown that allylic heteroatom substitution on 1,3-cyclohexadiene will direct the addition of dienophiles to the face of the diene *syn* to the heteroatom. This facial selectivity can be nearly completely reversed by steric effects with appropriate derivatization. In addition, the hypothesis that π-facial selectivity may be controlled by favorable or unfavorable orbital interactions between the dienophile and that of the diene has also been extended.

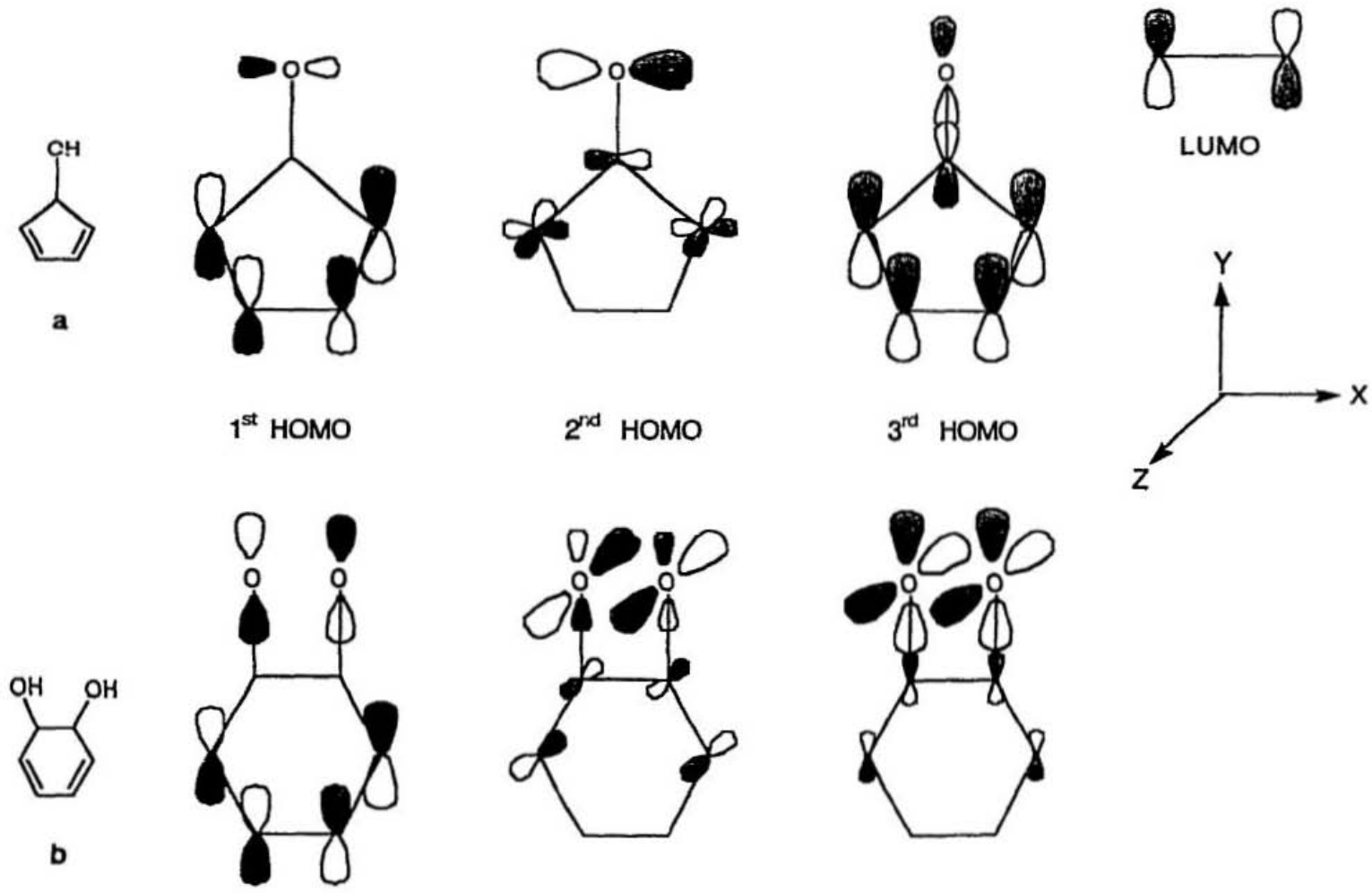


Figure 28. Possible secondary orbital interactions that may promote *syn* addition

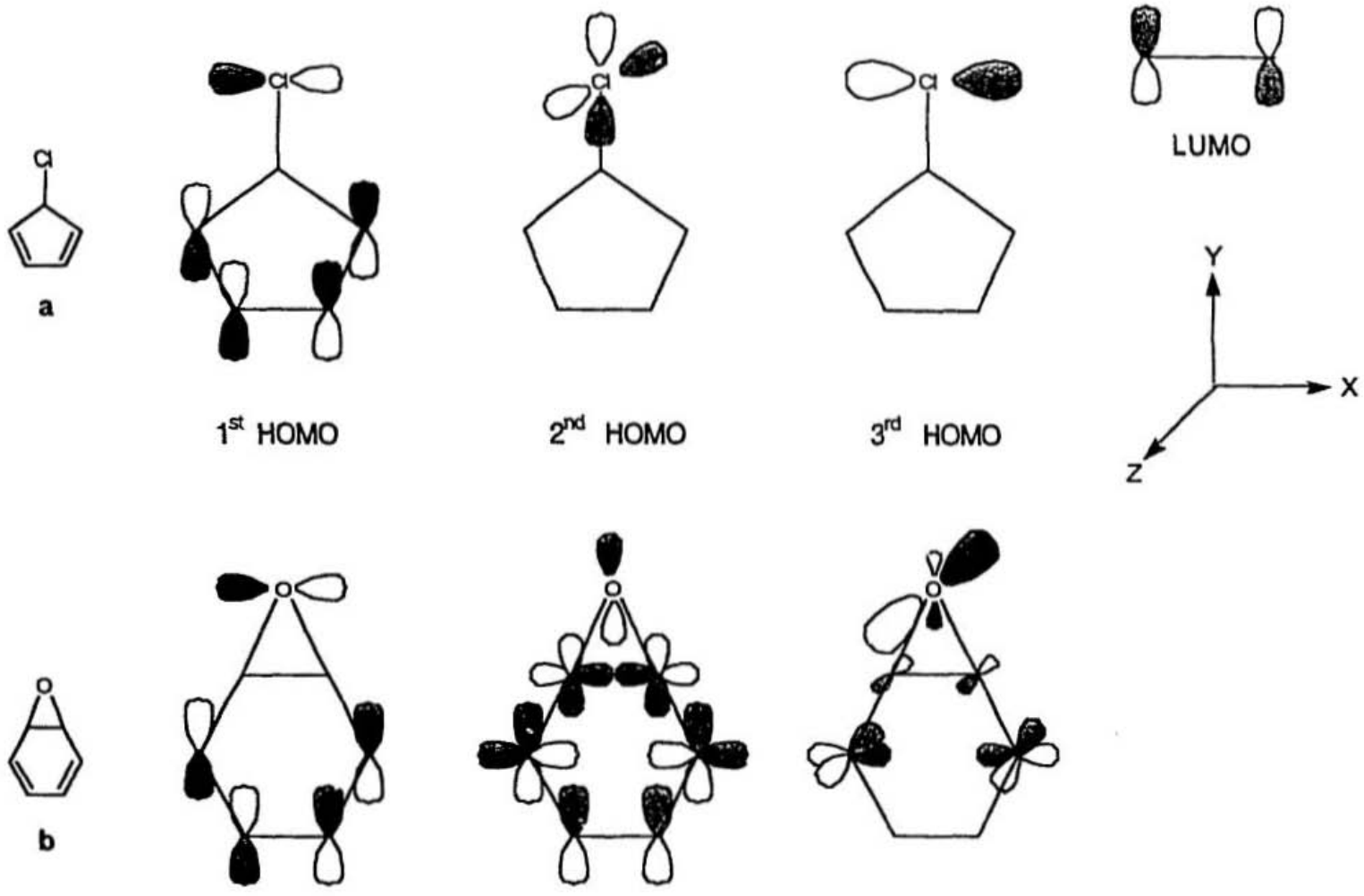


Figure 29. Possible secondary orbital interactions that may promote *anti* addition

EXPERIMENTAL

General

All solvents were purified by distillation. Benzene, dichloromethane, carbon tetrachloride and diethyl ether were distilled from calcium hydride (CaH_2). Pyridine was dried over anhydrous potassium hydroxide (KOH), distilled and stored over KOH. Tetrahydrofuran was distilled from sodium metal/benzophenone. Most reagents were not purified before use. Exceptions were: *N*-phenylmaleimide was crystallized from cyclohexene; *para*-toluenesulfonic acid was dried by refluxing in benzene with a Dean-Stark apparatus, followed by crystallization; chlorotrimethylsilane was distilled from CaH_2. Aqueous solutions are implied for saturated NaCl, etc. Reactions were run under an atmosphere of dry nitrogen, and monitored by thin-layer chromatography (TLC). Commercial TLC plates were Merck 60F-254. The plates were visualized by UV fluorescence, or by spraying with a solution of phosphomolybdic acid, ceric sulfate and sulfuric acid, followed by heating. Flash column chromatography was performed on Merck Type 60 silica gel, 230-400 mesh. Preparative TLC was carried out using Whatman 60A-PK6F commercial plates with a 1 mm plate thickness. Rotary TLC was performed using the Chromatotron (Harrison Research, Palo Alto, California) on plates coated (2 mm) with Merck type 60-PF254 TLC silica gel with calcium sulfate binder. Melting points (mp) were determined on a Fisher-Johns apparatus and are uncorrected. Ultraviolet (uv) spectra were run on a Perkin-Elmer 202 instrument. Infrared (ir) spectra were recorded on a Mattson FT instrument. Nuclear magnetic resonance (nmr) spectra were obtained on a General Electric GE 300-NB (300 MHz) instrument or a Varian 360 instrument. The

^1H nmr shifts of $CDCl_3$ solutions were measured relative to a tetramethylsilane internal standard, but in other solvents the shifts were calibrated to a solvent resonance. The ^{13}C shifts are relative to internal solvent resonance ($CDCl_3$ = δ 77.0, C_6D_6 = δ 128.0, C_5D_5N = δ 149.5 and $(CH_3)_2SO$ = δ 39.5). Multiplicities are described by the following abbreviations: s (singlet), d (doublet), dd (double doublet), ddd (doubled double doublet), m (multiplet), t (triplet), q (quartet). For some carbon resonances for which rigorous assignments are not provided the number of attached protons (by APT) may be indicated in parentheses after the chemical shift. The nmr assignments were aided by ^1H - ^1H correlation (COSY) and ^1H - ^{13}C correlation (HET-CORR) 2-D spectra, and nuclear Overhauser effect (n.O.e.) enhancement measurements, which also led to the assignment of stereochemistry. The n.O.e. measurements were made from sets of interleaved ^1H experiments (16K) of 8 transients cycled 12 to 16 times through the list of frequencies to be saturated. The decoupler was gated on in continuous wave mode for 6 seconds with sufficient attenuation to give a 70-90% reduction in intensity of the irradiated peak. Frequency changes were preceded by a 60 second delay. Four scans were used to equilibrate spins before data acquisition, but a relaxation delay was not applied between scans at the same frequency. The n.O.e. difference (n.O.e.d.) spectra[105] were obtained from zero-filled 32K data tables to which a 1 to 2 Hz exponential line-broadening function had been applied. The n.O.e. results are reported in the following format: δ saturated signal: enhanced signal (% enhancement). Mass spectral (ms) data were from a V.G. Micromass 7070 HS instrument. Gas chromatography-mass spectral (GC-MS) data were obtained on a Hewlett-Packard system comprised of a model 5890 gas chromatograph coupled to a model 5970 mass selective detector. Data for the x-ray structures were collected using either an Enraf-Nonius CAD-4 diffractometer or a Rigaku AFC6S

diffractometer, and the structures were determined by Dr. M.J. Newlands or Dr. J.N. Bridson of this Department.

cis-1,2-Diacetoxy-3,5-cyclohexadiene (**109**)

To a solution of *cis*-cyclohexa-3,5-diene-1,2-diol (**121**) (0.240 g, 2.14 mmol, Aldrich) in pyridine (1 mL) was added acetic anhydride (1 mL). This was stirred at room temperature for *ca.* 2 h, after which time TLC indicated no starting material was present. The solvent was evaporated on a vacuum pump for *ca.* 2 h, and chromatography (30% ethyl acetate/hexane) of the residue gave **109** (0.368 g, 88%) as a clear, colourless oil; uv (CH_3OH) λ_{max}: 256 nm (ε = 3900); ir (film) ν_{max}: 3054, 1740, 1371, 1241 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.07 (6H, s), 5.54 (2H, t, J = 1.2 Hz), 5.87 - 5.93 (2H, m), 6.14 (2H, m); ^{13}C nmr ($CDCl_3$) δ: 20.7 (3), 66.8 (1), 125.1 (1), 126.1 (1), 170.1 (0); ms *m/z* (%): 196 (M^+, 1), 154 (3), 136 (13), 112 (60), 95 (98), 94 (100), 78 (33), 77 (24), 66 (66), 43 (100). Exact mass calcd. for $C_{10}H_{12}O_4$: 196.0735; found: 196.0725.

cis-3a,7a-Dihydro-2,2-dimethyl-1,3-benzodioxole (**114**)

To a stirred solution of **121** (0.200 g, 1.78 mmol), in 2,2-dimethoxypropane (15 mL), was added *p*TsOH (10 mg). This solution was stirred at room temperature for 1 h after which dichloromethane (50 mL) was added. This was washed with 0.1 M NaOH (50 mL), saturated $NaHCO_3$ (50 mL) and saturated NaCl (100 mL), dried ($MgSO_4$) and the solvent evaporated. Chromatography of the residue (30% ethyl acetate/hexane) gave **114** as a colourless liquid (0.226 g, 83%); uv (CH_3OH) λ_{max}: 257 nm (ε = 3500); ir (film) ν_{max}: 2987, 1379, 1209, 1032 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.40 (3H, s), 1.43 (3H, s), 4.66 (2H, t, J = 1.7 Hz), 5.87 - 5.93 (2H, m), 6.00 (2H, m); ^{13}C nmr ($CDCl_3$) δ: 24.6 (3), 26.6 (3), 70.2

(1), 104.4 (0), 123.6 (1), 125.1 (1); ms *m/z* (%): 152 (M^+, 1), 137 (42), 109 (3), 95 (100), 94 (96), 77 (53), 66 (94), 65 (50), 43 (87). Exact mass calcd. for $C_8H_9O_2$ (M^+ -CH_3): 137.0602; found: 137.0599.

cis-1,2-Bis(trimethylsiloxy)-3,5-cyclohexadiene (**122**)

To a solution of **121** (0.232 g, 2.07 mmol) in pyridine (2 mL) was added chlorotrimethylsilane (600 μL, 4.73 mmol). This was stirred at room temperature for 1 h after which time CCl_4 (10 mL) was added, and the resultant solid was removed by filtration through a Kimwipe plug in a Pasteur pipette. The filtrate was concentrated under vacuum, and chromatography (10% ethyl acetate/hexane) of the residue gave **122** (0.456 g, 86%) as a clear, colourless oil; uv (CH_3OH) λ_{max}: 259 nm (ε = 4000); ir (film) ν_{max}: 2958, 1412, 1252, 1119, 840 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 0.15 (18H, s), 4.14 (2H, t, J = 1.1 Hz), 5.84 - 5.89 (2H, m), 5.94 - 5.99 (2H, m); ^{13}C nmr ($CDCl_3$) δ: 0.2 (3), 68.9 (1), 124.0 (1), 130.4 (1); ms *m/z* (%): 256 (M^+, 21), 191 (10), 167 (2), 147 (17), 73 (100), 45 (17). Exact mass calcd. for $C_{12}H_{24}O_2Si_2$: 256.1314; found: 256.1314.

cis-3a,7a-Dihydro-2,2-dimethyl-1,3,2-benzodioxasilole (**123**)

To a solution of **121** (0.141 g, 1.26 mmol) in $CDCl_3$ (*ca.* 0.5 mL) in an nmr tube was added pyridine (10 μL) and diacetoxydimethylsilane (222 μL, 1.26 mmol). The solution was stirred in the nmr probe (60 MHz, *ca.* 25°C). After 10 min there was a quantitative conversion of the **121** to **123**. The solvent could be removed under vacuum to provide a small amount (*ca.* 15%) of impure material; uv (CH_3OH) λ_{max}: 260 nm (ε = 3600); ir (film) ν_{max}: 3044, 2962, 2902, 1413, 1258 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 0.23 (3H, s), 0.27 (3H, s), 4.70 (2H, s), 5.82 - 5.90 (2H, m), 5.92 - 5.99 (2H, m); ^{13}C nmr ($CDCl_3$) δ: -1.9

(3), -1.3 (3), 69.1 (1), 123.2 (1), 126.3 (1); ms *m/z* (%): 168 (M^+, 90), 167 (100), 153 (99), 135 (21), 133 (17), 94 (45), 91 (40), 77 (36), 75 (64), 66 (24), 45 (34). Exact mass calcd. for $C_8H_{12}O_2Si$: 168.0606; found: 168.0587; calcd. for $C_8H_{11}O_2Si$ (M^+ - H): 167.0528; found: 167.0522.

cis-1,2-Dimethoxy-3,5-cyclohexadiene (**124**)

In a 250 mL 3-necked flask, fitted with a stirring motor and paddle, was added 50% NaOH/H_2O (50 mL) and CH_2Cl_2 (100 mL). To this was added **121** (0.311 g, 2.77 mmol), dimethylsulfate (2.10 g, 16.6 mmol), and tetra-*n*-butylammonium hydroxide 40% w/w in H_2O (1.0 g). This was stirred for three days at room temperature. Water (100 mL) was added, and the organic layer was removed and washed with water (100 mL), saturated $NaHCO_3$ (100 mL) and saturated NaCl (100 mL). The organic layer was dried over $MgSO_4$ and concentrated under vacuum. Chromatography of the residue (30% ethyl acetate/hexane) provided **124** (0.296 g, 76%) as a colourless liquid; ir (film) ν_{max}: 2929, 1464, 1122 cm^{-1}; uv (CH_3OH) λ_{max} (ε): 262 nm (ε = 2500); ^1H nmr ($CDCl_3$) δ: 3.44 (6H, s), 3.81 (2H, s), 5.99 - 6.08 (4H, m); ^{13}C nmr ($CDCl_3$) δ: 56.2 (3), 73.9 (1), 124.8 (1), 126.9 (1); ms (GC-MS) *m/z* (%): 140 (M^+, 18), 125 (7), 109 (14), 97 (23), 82 (21), 75 (100), 65 (50), 51 (30). Exact mass calcd. for $C_8H_{12}O_2$: 140.0837; found: 140.0834.

(1R*,2R*,4S*,5R*)-4,5-Dibromocyclohexane-1,2-diol (**128**)

A 5 litre, 3-necked flask fitted with a stirring motor, and containing 95% ethanol (2 L), water (1 L) and $MgSO_4$ (60 g), was cooled to -5 to -10°C with the aid of a Dry Ice/ isopropanol both. To this stirred mixture, **127**[100] (30.1 g, 0.125 mol) in acetone (10 mL) was added dropwise over 5 minutes. To this solution was added $KMnO_4$ (20.0 g, 0.125

mol) in water (1 L) over a period of 5 hours, making sure that the temperature did not go above -5°C. After the $KMnO_4$ addition was complete, the reaction was stirred overnight (*ca.* 16 h). The brown precipitate of MnO_2 was discharged by bubbling SO_2 through the stirred reaction mixture, after which the solution was filtered and reduced to a total volume of 1 L. This was then extracted with CH_2Cl_2 (10 x 100 mL), and the combined organic layers were washed with saturated NaCl (200 mL), dried over $MgSO_4$ and filtered. Evaporation of the solvent and crystallization of the residue from hot $CHCl_3$ afforded **128** (15.1 g, 44%) as an off-white powder: mp 103-105°C; ir (KBr) ν_{max}: 3380, 2910, 1445, 1295, 1060, 990 cm^{-1}; ^1H nmr (C_5D_5N) δ : 2.16 (1H, ddd, J = 2.2, 12.0, 13.8 Hz, C-6H_β), 2.70 (1H, ddd, J = 4.2, 4.5, 12.5 Hz, C-3H_β), 2.82 (1H, ddd, J = 2.9, 4.5, 13.8 Hz, C-6H_α), 2.92 (1H, ddd, J = 11.3, 12.0, 12.5 Hz, C-3H_α), 3.98 (1H, ddd, J = 2.8, 4.2, 11.3 Hz, C-2H), 4.25 (1H, m, $W_{1/2}$ = 8 Hz, C-1H), 4.39 (1H, ddd, J = 4.5, 10.7, 12.0 Hz, C-5H), 4.84 (1H, ddd, J = 4.5, 10.7, 12.0 Hz, C-4H), 6.60 (2H, broad s, OH's); ^{13}C nmr (C_5D_5N) δ: 41.2 (C-3), 42.9 (C-6), 54.8 (C-4), 55.6 (C-5), 70.2 (C-1), 70.7 (C-2); ms (GC-MS) m/z (%): 195 (M^+ - ^{79}Br, 14), 193 (M^+ - ^{81}Br, 14), 177 (20), 175 (21), 165 (4), 163 (5), 147 (23), 121 (6), 119 (5), 113 (13), 95 (67), 83 (14), 67 (100), 55 (79), 41 (82). Exact mass calcd. for $C_6H_8{}^{81}BrO$ (M^+ - Br - H_2O): 176.9734; found: 176.9728.

(2α,3aβ,5β,6α,7aβ)- (**130**) and (2α,3aβ,5β,6α,7aβ)-5,6-Dibromohexahydro-2-phenyl-1,3-benzodioxole (**131**)

To a solution of **128** (5.88 g, 21.5 mmol) in dry CH_2Cl_2 (150 mL) was added *p*TsOH (1.03 g) and benzaldehyde dimethylacetal (**129**) (16.3 g, 107 mmol) as a solution in dry CH_2Cl_2 (10 mL). This was stirred at room temperature for 2 days, after which the solution was washed with 20% $NaHSO_3$ (50 mL), 1M NaOH (100 mL), saturated $NaHCO_3$

(100 mL) and saturated NaCl (100 mL). After drying ($MgSO_4$) and evaporation of the solvent, hexane (50 mL) was added to the residue and the resulting solution was refrigerated at 0 - -5°C for a few days. The liquid was decanted from the colourless crystals that formed. These crystals were washed with hexane (4 x 5 mL) to provide **131** (1.77 g). The hexane washings were combined with the decanted solution, and this was concentrated to *ca.* 5 mL. Chromatography of the residue (10% ethyl acetate/hexane), gave an additional crop of **131** (0.88 g) after recrystallization from hexane (total yield: 2.66 g, 34%), and of **130** (2.61 g, 34%).

For **130**: mp 63 - 65°C; ir (KBr) ν_{max}: 1412, 1173, 1069, 1011 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.28 (1H, ddd, J = 5.2, 8.0, 15.0 Hz, C-4H_β), 2.49 (1H, ddd, J = 6.0, 6.7, 15.5 Hz, C-7H_α), 2.79 (1H, ddd, J = 3.8, 5.7, 15.0 Hz, C-4H_α), 2.84 (1H, ddd, J = 4.8, 5.4, 15.5 Hz, C-7H_β), 4.24 (1H, ddd, J = 4.8, 6.7, 6.7 Hz, C-6H), 4.28 (1H, ddd, J = 5.3, 5.4, 6.0 Hz, C-7aH), 4.37 (1H, ddd, J = 5.2, 5.3, 5.7 Hz, C-3aH), 4.45 (1H, ddd, J = 3.8, 6.7, 8.0 Hz, C-5H), 5.85 (1H, C-2H), 7.37 - 7.56 (5H, m); ^{13}C nmr ($CDCl_3$) δ: 34.4 (C-4), 35.5 (C-7), 48.3 (C-6), 50.8 (C-5), 73.0 (C-7a), 73.3 (C-3a), 103.8 (C-2), 126.4 (2 x ArC), 128.4 (1 x ArC), 129.3 (2 x ArC), 137.1 (1 x ArC); ms (GC-MS) *m/z* (%): 364 (3), 362 (6) and 360 (3) (all M^+), 363 (11), 361 (22) and 359 (12) (all M^+ - H), 159 (10), 157 (8), 105 (100), 79 (96), 78 (48), 77 (76), 67 (67), 51 (39). Exact mass calcd. for $C_{13}H_{13}{}^{79}Br_2O_2$ (M^+ - H): 358.9283; found: 358.9293.

For **131**: mp 125 - 127°C; ir (KBr) ν_{max}: 2903, 1459, 1362, 1219, 1107, 1069, 976 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.25 (1H, ddd, J = 4.7, 8.2, 15.1 Hz, C-4H_β), 2.46 (1H, ddd, J = 6.2, 8.0, 15.2 Hz, C-7H_α), 2.78 (1H, ddd, J = 4.5, 5.0, 15.2 Hz, C-7H_β), 2.84 (1H, ddd, J = 3.9, 5.5, 15.1 Hz, C-4H_α), 4.19 (1H, ddd, J = 4.5, 7.4, 7.8 Hz, C-6H), 4.33 (1H, m, C-7aH), 4.39 (1H, m, C-3aH), 4.47 (1H, ddd, J = 3.9, 7.4, 8.2 Hz, C-5H), 6.17 (1H, s, C-

2H), 7.31 - 7.45 (5H, m, ArH): ^{13}C nmr ($CDCl_3$) δ: 33.3 (C-4), 34.5 (C-7), 48.5 (C-6), 50.8 (C-5), 72.6 (C-7a), 72.9 (C-3a), 102.2 (C-2), 125.9 (2 x ArC), 128.3 (1 x ArC), 129.0 (2 x ArC), 138.9 (1 x ArC); ms (GC-MS) *m/z* (%): 363 (11), 361 (22), 359 (11), 287 (1), 285 (2), 283 (1), 201 (3), 159 (10), 105 (100), 79 (95), 67 (66), 51 (37), 41 (55). Exact mass calcd. for $C_{13}H_{14}{}^{81}Br_2O_2$ (M^+ - H): 362.9241; found: 362.9231.

(2α,3aβ,7aβ)-3a,7a-Dihydro-2-phenyl-1,3-benzodioxole (**132**)

From **121**

To a solution of **121** (77 mg, 0.67 mmol), and **129** (100 μL, 0.67 mmol) in $CDCl_3$ (*ca.* 0.5 ml), was added pTsOH (1.4 mg) in $CDCl_3$ (1 mL), and the mixture was stirred overnight. The analysis of the ^{1}H nmr spectrum revealed mainly signals for **132** (but no other derivative), benzaldehyde and a small amount of phenol. Compound **132** made in this way was purified by rotary thin-layer chromatography (20% CH_2Cl_2/hexane) in a yield of only 15%.

From **130**

To a solution of **130** (0.36 g, 0.98 mmol) in dry benzene (40 mL) was added DBU (0.60 g, 3.9 mmol) also in dry benzene (10 mL). This was refluxed for 16 h, after which the solution was cooled to room temperature and decanted from the white solid that had formed. The solid was extracted with more benzene (50 mL), and the combined solutions were washed with saturated $NaHCO_3$ (3 x 100 mL), water 100 mL and saturated NaCl (100 mL). Drying ($MgSO_4$), evaporation of the solvent, and chromatography (10% ethyl acetate/hexane) of the residue afforded **132** (0.106 g, 58%) as a colourless liquid; ir (film) ν_{max}: 3044, 2883, 1459, 1401, 1292, 1217, 1061, 697 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 4.66 (2H, t, J = 1.6 Hz, C-3aH and C-7aH), 5.64 (1H, C-2H), 5.96-6.00 (2H, m, C-4H and C-7H), 6.02-6.06 (2H, m, C-5H and C-6H), 7.32 - 7.36 (3H, m), 7.46 - 7.50 (2H, m); n.O.e. results

($CDCl_3$): δ 4.66: 5.64 (8.5%), 5.96 - 6.00 (4%); δ 5.64: 4.66 (4.0%), 7.46 - 7.50 (3.5%); ^{13}C nmr ($CDCl_3$) δ: 71.0 (C-3a and C-7a), 98.2 (C-2), 123.8 (C-5 and C-6), 124.1 (C-4 and C-7), 126.8 (2 x ArC), 128.2 (2 x ArC), 129.4 (1 x ArC), 136.5 (1 x ArC); ms *m/z* (%): 200 (4), 199 (3), 172 (6), 171 (2), 154 (39), 143 (4), 128 (8), 122 (4), 106 (35), 105 (90), 94 (100), 77 (86), 66 (99), 51 (50), 39 (51), 27 (9). Exact mass calcd. for $C_{13}H_{12}O_2$: 200.0837; found: 200.0836.

(2α,3aα,7aα)-3a,7a-Dihydro-2-phenyl-1,3-benzodioxole (**133**)

To a solution of **131** (1.23 g, 3.34 mmol) in dry benzene (40 mL) was added DBU (2.07 g, 13.4 mmol) as a solution in dry benzene (10 mL). This was refluxed for 16 h. After cooling, the benzene solution was decanted from the solid which had formed. The solid was extracted with benzene (50 mL), and the two organic extracts were washed with saturated $NaHCO_3$ (2 x 100 mL), H_2O (100 mL) and saturated NaCl (100 mL), dried ($MgSO_4$) and evaporated to give **133** as a yellow oil (0.490 g, 72%), containing negligible amounts of starting materials. Compound **133** was stable if refrigerated or in solution; ir (film) ν_{max}: 3043, 2927, 1641, 1217, 1068 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 4.86 (2H, narrow m, C-3aH and C-7aH), 5.83 (1H, s, C-2H), 5.88 - 5.93 (2H, m), 6.06 (2H, dd, *J* = 2.8, 7.9 Hz,), 7.34 - 7.38 (3H, m), 7.49 - 7.52 (2H, m); ^{13}C nmr ($CDCl_3$) δ: 70.6 (C-3a and C-7a), 100.2 (C-2), 124.7 (1), 124.9 (1), 126.3 (2 x ArC), 128.2 (2 x ArC), 129.0 (1 x ArC), 137.4 (1 x ArC); ms (GC-MS) *m/z* (%): 199 (M^+ - H, 1), 153 (1), 143 (1), 122 (4), 105 (46), 94 (58), 78 (100), 66 (54), 51 (28). Exact mass calcd. for $C_{13}H_{11}O_2$ (M^+ - H): 199.0758; found: 199.0749.

(2α,3aβ,5β,6α,7aβ)- (**135**) and (2α,3aα,5α,6β,7aα)-5,6-Dibromohexahydro-2-(4-nitrophenyl)-1,3-benzodioxole (**136**)

To a stirred solution of **128** (5.01 g, 18.3 mmol) in dry benzene (150 mL) was added *p*-nitrobenzaldehyde dimethyl acetal (**134**) (3.51 g, 17.8 mmol) as a solution in dry benzene (10 mL), followed by pre-dried *p*-tolulenesulfonic acid (250 mg). After refluxing for 16 h, the cooled solution was washed with 0.1M NaOH (100 mL), saturated $NaHCO_3$ (100 mL) and saturated NaCl (100 mL), dried ($MgSO_4$) and concentrated. Chromatography of the resulting solid (30% ethyl acetate/hexane) gave **135** (2.39 g, 32%) as lustrous plates, and **136** (2.10 g, 28%) as cubes.

For **135**: mp 152 - 154°C; ir (KBr) δ_{max}: 3074, 2967, 1611, 1518, 1345, 1084 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.31 (1H, ddd, *J* ~ 3.5, 6.7, 15.0 Hz, C-4Hβ), 2.53 (1H, ddd, *J* ~ 5.3, 5.3, 15.9 Hz, C-7Hα), 2.66 (1H, ddd, *J* ~ 3.5, 6.7, 15.0 Hz, C-4Hα), 2.92 (1H, ddd, *J* ~ 5.0, 5.0, 15.9 Hz, C-7Hβ), 4.33 (1H, m, C-6H), 4.38 (1H, m, C-7aH), 4.45 (1H, m, C-5H), 4.50 (1H, m, C-3aH), 5.95 (1H, s, C-2H), 7.74 (2H, d, *J* = 8.8 Hz), 8.27 (2H, d, *J* = 8.8 Hz); ^1H nmr (C_5D_5N) δ: 2.35 (1H, ddd, *J* = 4.6, 8.7, 15.0 Hz, C-4Hβ), 2.43 (1H, ddd, *J* = 5.9, 7.8, 15.0 Hz, C-7Hα), 2.79 - 2.92 (2H, m, C-4Hα and C-7Hβ), 4.35 - 4.43 (2H, m, C-3aH and C-7aH), 4.46 (1H, ddd, *J* = 4.6, 7.7, 7.8 Hz, C-6H), 4.65 (1H, ddd, *J* = 3.9, 7.7, 8.7 Hz, C-5H), 5.98 (1H, s, C-2H), 7.80 (2H, d, *J* = 8.7 Hz), 8.23 (2H, d, *J* = 8.7 Hz); n.O.e. results ($CDCl_3$): δ 4.38: 2.92 (6%), 5.95 (12%); δ 5.95: 4.38 (7%), 4.50 (6%), 7.74 (3%); ^{13}C nmr (C_5D_5N) δ: 35.2 (C-4), 36.9 (C-7), 50.0 (C-6), 52.0 (C-5), 73.7 and 74.8 (C-3a and C-7a), 102.4 (C-2), 124.0 (2 x ArC), 127.9 (2 x ArC), 145.3 (1 x ArC), 148.6 (1 x ArC); ms *m/z* (%): 408 (11), 406 (21), 404 (11), 392 (3), 390 (5), 388 (2), 246 (6), 218 (17), 193 (2), 172 (3), 159 (11), 150 (45), 135 (10), 107 (30), 95 (35), 79 (67), 67 (100), 41 (56). Exact mass calcd. for $C_{13}H_{12}{}^{79}Br^{81}BrNO_4$ (M^+ - H): 405.9112; found: 405.9119.

For **136**: mp 132 - 134°C; ir (KBr) ν_{max}: 3106, 2904, 1610, 1520, 1351 cm^{-1}; ^1H nmr ($CDCl_3$) δ : 2.32 (1H, ddd, *J* = 5.0, 7.6, 15.1 Hz, C-4Hβ), 2.52 (1H, ddd, *J* = 6.0, 6.8, 15.5 Hz, C-7Hα), 2.85 (2H, m, C-4Hα and C-7Hβ), 4.27 (1H, ddd, *J* = 4.7, 6.8, 6.9 Hz, C-6H), 4.35 (1H, ddd, *J* = 5.0, 5.1, 6.0 Hz, C-7aH), 4.44 (1H, ddd, *J* = 5.0, 5.0, 5.8 Hz, C-3aH), 4.51 (1H, ddd, *J* = 3.7, 6.9, 7.6 Hz, C-5H), 6.24 (1H, s, C-2H), 7.62 (2H, d, *J* = 8.7 Hz), 8.22 (2H, d, *J* = 8.7 Hz); ^1H nmr (C_5D_5N) δ: 2.35 (1H, ddd, *J* = 4.4, 9.3, 15.1 Hz, C-4Hβ), 2.47 (1H, ddd, *J* = 7.3, 9.2, 14.6 Hz, (C-7Hα), 2.81 (1H, ddd, *J* = 4.5, 5.8, 14.6 Hz, C-7Hβ), 2.92 (1H, ddd, *J* = 4.2, 4.4, 15.1 Hz, C-4Hα), 4.36 (1H, ddd, *J* = 4.4, 4.4, 4.8 Hz, C-3aH), 4.43 (1H, ddd, *J* = 4.5, 8.3, 9.2 Hz, C-6H), 4.48 (1H, ddd, *J* = 4.8, 5.8, 7.3 Hz, C-7aH), 4.63 (1H, ddd, *J* = 4.2, 8.3, 9.3 Hz, C-5H), 7.69 (2H, d, *J* = 8.7 Hz), 8.26 (2H, d, *J* = 8.7 Hz); n.O.e. results ($CDCl_3$): δ 4.27: 2.32 (1%), 2.52 (2%), 2.85 (5%); δ 4.35: 2.52 (1%), 2.85 (6%), 7.62 (1%); δ 4.44: 2.32 (5%), 2.85 (2%), 7.62 (1%); δ 4.51: 2.32 (1%), 2.52 (1%), 2.85 (5%); δ 6.24: 2.52 (5%), 2.85 (5%), 7.62 (3%); δ 7.62: 6.24 (4%), 8.22 (19%); ^{13}C nmr δ: 32.6 (C-4), 33.9 (C-7), 47.7 (C-6), 50.3 (C-5), 72.7 (C-7a), 73.1 (C-3a), 100.7 (C-2), 123.5 (2 x ArC), 126.9 (2 x ArC), 145.8 (1 x ArC), 148.1 (1 x ArC); ms *m/z* (%): 408 (13), 406 (24), 404 (13), 392 (2), 390 (6), 388 (2), 285 (5), 246 (5), 218 (11), 150 (83), 107 (29), 95 (41), 80 (82), 79 (73), 77 (40), 67 (100).

(2α,3aβ,7aβ)-3a,7a-Dihydro-2-(4-nitrophenyl)-1,3-benzodioxole (**137**)

To a solution of **135** (0.524 g, 1.29 mmol) in dry benzene (150 mL) was added DBU (0.78 g, 5.1 mmol) as a solution in dry benzene (10 mL). This was heated at reflux for 16 h. After cooling, the solution was decanted and the white solid remaining was extracted with benzene (20 mL). The combined benzene solutions were washed with saturated $NaHCO_3$ (2 x 100 mL) and saturated NaCl (100 mL), and dried ($MgSO_4$).

Evaporation of the solvent, followed by chromatography of the residue (30% ethyl acetate/hexane) afforded **137** (0.161 g, 51%) as lustrous light green plates: mp 141 - 142°C; ir (KBr) ν_{max}: 3047, 2914, 1611, 1519, 1349 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 4.73 (2H, t, J = 1.7 Hz), 5.74 (1H, s, C-2H), 5.94 - 6.00 (2H, m, C-4H and C-7H), 6.04 - 6.10 (2H, m, C-4H and C-5H), 7.64 (2H, d, J = 8.7 Hz), 8.19 (2H, d, J = 8.7 Hz); n.O.e. results: δ 4.73: 5.74 (8.5%), 5.94 - 6.00 (5%); δ 5.74: 4.73 (4.5%), 7.64 (3%); ^{13}C nmr ($CDCl_3$) δ: 71.3 (C-3a and C-7a), 96.8 (C-2), 123.4 (C-4 and C-7), 123.9 (C-5 and C-6), 124.1 (2 x ArC), 127.8 (2 x ArC), 143.8 (1 x ArC), 148.4 (1 x ArC); ms m/z (%): 244 (M^+ - 1, 1), 199 (2), 150 (15), 141 (2), 120 (3), 104 (7), 94 (98), 77 (24), 66 (100), 51 (19), 39 (29), 27 (5). Exact mass calcd. for $C_{13}H_{10}NO_4$ (M^+ - H): 244.0609; found: 244.0603.

(2α,3aα,7aα)-3a,7a-Dihydro-2-(4-nitrophenyl)-1,3-benzodioxole (**138**)

To a solution of dibromide **136** (2.08 g, 5.11 mmol) in dry benzene (100 mL) was added DBU (3.11 g, 20.4 mmol). This was heated for 16 h, and, after cooling, the benzene solution was decanted from a solid residue. Benzene (20 mL) was used to extract this residue, and the combined benzene solutions were washed with saturated $NaHCO_3$ (2 x 200 mL) and saturated NaCl (200 mL), dried ($MgSO_4$) and concentrated. Chromatography (20% ethyl acetate/hexane) of the residue provided **138** (0.526 g, 42%) as colourless crystals: mp 128-131°C, which formed a Diels-Alder dimer on melting; uv (CH_3OH) λ_{max} : 202 (ε = 10,200), 264 (13,300); ir (KBr) ν_{max}: 3046, 2881, 1640, 1525, 1355 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 5.24 (2H, t, J = 1.5 Hz, C-3aH and C-7aH), 6.23 (1H, s, C-2H), 6.27 - 6.31 (2H, m), 6.47 (2H, dd, J = 2.9, 7.9 Hz), 8.04 (2H, d, J = 8.7 Hz), 8.58 (2H, d, J = 8.7 Hz); ^{13}C nmr ($CDCl_3$) δ: 70.9 (C-3a and C-7a), 99.2 (C-2), 123.4 (2 x ArC), 124.2 (1), 125.2 (1), 127.4 (2 x ArC), 144.6 (1 x ArC), 148.2 (1 x ArC); ms m/z (%): 244

(M^+ - H, 1), 170 (1), 150 (24), 120 (5), 104 (10), 94 (87), 78 (100), 66 (92), 51 (26), 39 (36). Exact mass calcd. for $C_{13}H_{10}NO_4$ (M^+-H): 244.0609; found: 244.0589.

(2α,3aα,5aβ,6α,8β,9aβ,10α,10aβ,10bα)-3a,5a,6,6a,9a,10,10a,10b-Octahydro-2,8-diphenyl-6,10-ethenonaphtho[1,2-*d*: 6,7-*d*']bis[1,3]dioxole (**139**)

A crude, neat portion of **133** (98 mg, 0.49 mmol) was allowed to stand at room temperature overnight, giving a brown solid the next day. Chromatography (30% ethyl acetate/ hexane) gave **139** (83 mg) as the only product: mp 176 - 179°C; ir (KBr) ν_{max}: 3034, 2943, 1457, 1368, 1224, 1097 (strong), 1066 (strong), 751, 696 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.35 (1H, d, *J* = 9.0 Hz, C-10aH), 2.43 (1H, ddd, *J* = 1.8, 3.6, 9.0 Hz, C-5aH), 3.04 (2H, broad s, C-6H and C-10H), 4.25 (1H, d, *J* = 4.8 Hz, C-10bH), 4.41 (2H, s, C-6aH and C-10aH), 4.50 (1H, dd, *J* = 1.7, 4.7 Hz, C-3aH), 5.60 (1H, d, *J* = 10.1 Hz, C-4H), 5.80 (1H, ddd, *J* = 1.5, 3.9, 10.3 Hz, C-5H), 5.83 (1H, s, C-2H), 6.04 (1H, s, C-8H), 6.17 (1H, t, *J* = 3.2 Hz, C-11H and C-12H), 7.30 - 7.45 (10H, m, 10 x ArH); ^1H nmr (C_5D_5N) δ: 2.48 (2H, broad s, C-5aH and C-10aH), 3.03 (2H, m, C-6H and C-10H), 4.34 (1H, d, *J* = 4.7 Hz, C-10bH), 4.50 (2H, symmetrical m, C-6aH and C-9aH), 4.59 (1H, d, *J* = 4.2 Hz, C-3aH), 5.66 (1H, dd, *J* = 0.6, 10.4 Hz, C-4H), 5.80 (1H, dd, *J* = 2.7, 10.4 Hz, C-5H), 6.11 (1H, s, C-2H), 6.19 (2H, apparent t, *J* ≈ 3.8 Hz, C-11H and C-12H), 6.30 (1H, s, C-8H), 7.37 - 7.48 (6H, m, 6 x ArH), 7.60 (2H, d, *J* = 7.6 Hz, 2 x ArH), 7.70 (2H, d, *J* = 7.5 Hz, 2 x ArH); n.O.e. results (C_5D_5N): δ 2.48: 3.03 (2.5%), 4.34 (3.5%), 4.50 (13%), 5.80 (5%), 6.11 (3%); δ 4.34: 2.48 (1.5%), 3.03 (4%), 4.59 (8%), 7.70 (1.5%); δ 4.50: 2.48 (6.5%), 3.03 (2%), 6.30 (2%), 7.60 (2%); δ 4.59: 5.66 (1%); δ 5.66: 4.59 (3.5%), 5.80 (4.5%), 6.11 (2%); δ 5.80: 2.48 (1%), 3.03 (1.5%), 5.66 (4%); ^{13}C nmr ($CDCl_3$) δ: 33.0 (C-5a), 34.3 (C-10a), 40.9 and 41.3 (C-6 and C-10), 71.7 (C-3a), 77.2 (C-10b), 79.1 and

79.3 (C-6a and C-9a), 101.0 (C-2), 104.8 (C-8), 124.1 (C-4), 125.8 (2 x ArC), 126.2 (2 x ArC), 128.3 (2 x ArC), 128.7 (2 x ArC), 129.0 (2 x ArC), 129.7 (C-11 or C-12), 132.5 (C-5), 133.2 (C-11 or C-12), 138.7 (1 x ArC), 139.2 (1 x ArC); ms *m/z* (%): 400 (M^+, 1), 399 (3), 323 (2), 294 (12), 279 (2), 200 (1), 188 (18), 172 (17), 159 (16), 144 (13), 129 (16), 105 (100), 94 (27), 91 (36), 77 (34), 66 (12). Exact mass calcd. for $C_{19}H_{18}O_3$ (M^+ - C_7H_6O): 294.1255; found: 294.1250.

(2α,3aα,5aβ,6α,6aβ,8β,9aβ,10α,10aβ,10bα)-3a,5a,6,6a,9a,10,10a,10b-Octahydro-2,8-bis(4-nitrophenyl)-6,10-ethenonaphtho[1,2-*d*:6,7-*d*']bis[1,3]dioxole (**140**)

Compound **138** (60 mg, 0.12 mmol) was heated in a glass vial in an aluminum block under a stream of nitrogen. When the temperature had attained *ca.* 250°C (about 10 min), the glass vial was removed from the block to cool. The oil quickly solidified to a brown solid; ^{1}H nmr analysis of a sample clearly showed only one dimer present, which was purified by washing the solid with 50% $CHCl_3/CCl_4$ to give **140** (31 mg, 52%); mp 246 - 247°C; ir (KBr) ν_{max}: 3046, 2952, 1622, 1517, 1349, 1079, 729 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 2.38 (1H, d, *J* = 8.9 Hz, C-10aH), 2.47 (1H, broad m, C-5aH), 3.06 - 3.12 (2H, broad m, C-6H and C-10H), 4.23 (1H, d, *J* = 4.8 Hz, C-10bH), 4.45 (2H, narrow m, C-6aH and C-9aH), 4.53 (1H, dd, *J* = 1.6, 4.5 Hz, C-3aH), 5.63 (1H, d, *J* = 10.1 Hz, C-4H), 5.86 (1H, ddd, *J* = 1.4, 4.0, 10.4 Hz, C-5H), 5.90 (1H, s, C-2H), 6.06 (1H, s, C-8H), 6.20 (2H, broad m, C-11H and C-12H), 7.56 (2H, d, *J* = 8.7 Hz, 2 x ArH), 7.61 (2H, d, *J* = 8.7 Hz, 2 x ArH), 8.21 (2H, d, *J* = 8.7 Hz, 2 x ArH, overlapped with δ 8.23), 8.23 (2H, d, *J* = 8.7 Hz, 2 x ArH, overlapped with δ 8.21); ^{1}H nmr ($(CD_3)_2SO$) δ: 2.34 (1H, d, *J* = 8.9 Hz), 2.44 (1H, m), 3.04 (2H, m), 4.25 (1H, d, *J* = 4.8 Hz), 4.52 (3H, broad m), 5.52 (1H, d, *J* = 10.5 Hz), 5.84 (1H, ddd, *J* = 1.2, 3.9, 10.0 Hz), 5.86 (1H, s), 6.03 (1H, s), 6.11 (2H, m), 7.60

(2H, d, J = 8.7 Hz), 7.69 (2H, d, J = 8.8 Hz), 8.21 (2H, d, J = 8.7 Hz), 8.23 (2H, d, J = 8.8 Hz); n.O.e. results ($CDCl_3$): δ 2.38: 2.47 (2%), 4.45 (5.5%); δ 2.47: 3.06 - 3.12 (2.5%), 4.45 (4.5%), 5.86 (5%); δ 4.23: 2.38 (4%), 3.06 - 3.12 (5.5%), 4.53 (10%), 7.61 (1.5%); δ 4.45: 2.38 (16.5%), 2.47 (13%), 3.06 - 3.12 (5.5%), 6.06 (2%), 7.56 (3%); δ 4.53: 4.22 (5%), 5.63 (6.5%), 6.20 (1.5%); δ 5.63: 4.53 (4%), 5.86 and 5.90 (13%); δ 6.06: 7.56 (2.5%); δ 7.57 and 7.61: 5.90 (2%), 6.06 (1.5%), 8.21 and 8.23 (6.5%); ^{13}C nmr ($(CD_3)_2SO$) δ: 32.2, 33.2, 40.3, 40.7, 71.4, 77.0, 78.8, 78.9, 99.1, 102.7, 123.5 (3C), 127.4, 127.8, 130.0, 132.6, and 132.9 (4 quaternary aromatic signals too weak to be resolved); ms m/z (%): 489 (M^+ - 1, 2), 459 (1), 368 (2), 339 (5), 260 (3), 188 (26), 172 (23), 150 (92), 120 (47), 94 (90), 78 (100), 66 (65), 51 (29).

trans-4,5-Dibromocyclohexene oxide (**141**)

A solution of **127** (10.0 g, 4.17 mmol) and *meta*-chloroperoxybenzoic acid (10.0 g, 85%) in $CHCl_3$ (150 mL) was heated at reflux for 16 h. The mixture was cooled in ice, and the white solid which had formed was filtered and discarded. The filtrate was washed with 20% $NaHSO_3$ (100 mL), saturated $NaHCO_3$ (2 x 100 mL) and saturated NaCl (200 mL), and dried ($MgSO_4$). The solvent was evaporated to leave a viscous yellow oil. Recrystallization of this residue from cold hexane afforded **141** (6.97 g, 65%) as colourless crystals, mp 68-69°C; ir (KBr) ν_{max}: 3005, 1415, 1363, 1009 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.46 (1H, ddd, J = 3.2, 6.7, 16.0 Hz,), 2.65 (1H, dd, J = 6.3, 16.5 Hz,), 2.90 (1H, ddd, J = 3.5, 6.3, 16.5 Hz,), 2.99 (1H, dd, J = 4.5, 16.0 Hz,), 3.24 (2H, m), 4.20 (1H, ddd, J = 6.3, 6.3, 7.7 Hz,), 4.30 (1H, ddd, J = 4.6, 6.7, 7.7 Hz,); ^{13}C nmr ($CDCl_3$) δ: 32.3 and 33.3 (2 x CH_2), 47.3 and 48.7 (2 x CHBr), 50.2 and 50.7 (oxirane carbons); ms m/z (%): 177 (5) and 175 (5) both (M^+ - Br), 149 (3), 147 (5), 121 (5), 119 (5), 95 (18), 67

(100), 53 (5), 41 (48). Exact mass calcd. for $C_6H_8{}^{81}BrO$ and $C_6H_8{}^{79}BrO$ (both M^+ - Br): 176.9738 and 174.9759, respectively; found: 176.9742 and 174.9752.

1,3,5-Cyclohexatriene-1,2-oxide (**142**) / oxepin (**143**)

To a solution of **141** (1.07 g, 4.17 mmol) in ether (20 mL) was added DBU (2.50 g, 16.4 mmol) and this was stirred at room temperature for 24 h. The reaction mixture was poured over saturated $NaHCO_3$ (100 mL), and more ether was added (50 mL). The organic layer was washed successively with saturated $NaHCO_3$ (2 x 100 mL) and saturated NaCl (100 mL), and dried over anhydrous K_2CO_3. Evaporation of the solvent gave **142⇌143** (0.270 g, 67%) as a yellow liquid; ir (film) ν_{max}: 3028, 1609, 1431, 1072 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 5.12 (2H, d, J = 4.5 Hz), 5.88 (2H, m), 6.26 (2H, complex m); ^{13}C nmr ($CDCl_3$) δ: 107.5, 110.0, 120.2, 122.3, 128.6, 130.7; ms *m/z* (%): 94 (M^+, 61), 78 (7), 68 (35), 66 (100), 65 (68). Exact mass calcd. for C_6H_6O: 94.0418; found: 94.0420.

1,6-Dimethyl-7-oxabicyclo[4.1.0]hept-3-ene (**146a**)

To a solution of the magnesium salt of 80% monoperoxyphthalic acid hexahydrate (31.8 g) in 95% ethanol (500 mL) was added 1,2-dimethyl-1,4-cyclohexadiene (**145a**), (11.1 g, 103 mmol). After stirring at room temperature for 3 h, H_2O (1 L) was added. This was extracted with CH_2Cl_2 (300 mL). The organic layer was washed with H_2O (200 mL) and saturated NaCl (200 mL) and dried ($MgSO_4$). Evaporation of the solvent followed by chromatography (4% acetone/pentane) provided **146a** (5.4 g, 42%) as an oil; ^1H nmr (60 MHz, $CDCl_3$) δ: 1.3 (6H, s), 2.3 (4H, apparent s), 5.3 (2H, apparent s).

trans-4,5-Dibromo-1,2-dimethylcyclohexene oxide (**147a**)

To a solution of **146a** (5.4 g, 44 mmol) in $CHCl_3$ (100 mL) cooled to -50°C was added Br_2 (5.64 g, 35.2 mmol) in $CHCl_3$ (100 mL) at such a rate as to ensure the solution did not become orange (2 - 3 h). After addition was complete, the reaction was allowed to warm to room temperature overnight. Evaporation of the solvent, followed by crystallization of the residue from hexane, yielded **147a** (7.59 g, 76%) as fine colourless needles: mp 82-83°C; ir (KBr) ν_{max}: 1466, 1384, 1322, 1167, 847, 670 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.32 (3H, s, CH_3), 1.34 (3H, s, CH_3), 2.29 (1H, dd, J = 8.3, 15.4 Hz), 2.61 (1H, dd, J = 7.7, 16.1 Hz), 2.69 (1H, dd, J = 6.8, 16.1 Hz), 2.90 (1H, dd, J = 4.5, 15.4 Hz), 4.15 (1H, ddd, J = 6.8, 7.7, 9.1 Hz), 4.26 (1H, ddd, J = 4.5, 8.3, 9.1 Hz); ^{13}C nmr ($CDCl_3$) δ: 19.5 and 19.9 (2 x CH_3), 39.9 and 40.8 (2 x CH_2), 49.6 and 50.5 (2 x CHBr), 61.0 and 61.9 (oxirane carbons); ms *m/z* (%): 205 (50) and 203 (51) both M^+ - Br, 165 (4), 163 (5), 123 (67), 109 (5), 95 (12), 95 (12), 81 (49), 65 (8), 53 (24), 43 (100).

1,2-Dimethyl-1,3,5-cyclohexatriene-1,2-oxide (**148a**) / 2,7-dimethyloxepin (**149a**)

Following the procedure by Paquette and Barrett,[101] to a solution of **147a** (2.14 g, 7.52 mmol) in anhydrous ether (50 mL) at 0°C was added potassium *tert*-butoxide (2.00 g) in 4 equal portions over 1 h. After stirring for an additional 1 h, the ether solution was poured over H_2O (75 mL), and more ether was added (25 mL). The organic layer was extracted and washed with H_2O (75 mL), saturated $NaHCO_3$ (75 mL) and saturated NaCl (75 mL) and dried ($MgSO_4$). Evaporation of the solvent provided **148a⇌149a** (0.754 g, 82%) as a yellow liquid; ir (film) ν_{max}: 3026, 1658, 1160, 1078, 743 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.91 (6H, s, 2 x CH_3), 5.44 (2H, complex m), 5.99 (2H, distorted t, J = 3 Hz); ^{13}C nmr ($CDCl_3$) δ: 21.1 (2 x CH_3), 112.2, 127.5, 149.9 (C-2 and C-7); ms *m/z* (%): 122

(M^+, 43), 107 (8), 91 (14), 79 (90), 77 (56), 43 (100). Exact mass calcd. for $C_8H_{10}O$: 122.0731; found: 122.0725.

10-Oxatricyclo[4.3.1.0]deca-3-ene (**146b**)

To a vigorously stirred solution of 5,8-dihydroindan (**145b**) (28.5 g, 0.237 mmol) in $CHCl_3$ (350 mL) was added Aliquat 336 (1.0 g), and over a 2 h period, a solution of 80% MMPP (88 g) in H_2O (450 mL). This was stirred for a further 2 h. The white solid which formed at the interface was dissolved by the addition of 1M NaOH (100 mL). The organic layer was separated, and the aqueous layer was extracted with $CHCl_3$ (2 x 50 mL). The organic extracts were combined and washed with H_2O (200 mL), saturated $NaHCO_3$ (200 mL) and saturated NaCl (400 mL), and dried ($MgSO_4$). Evaporation of the solvent, followed by chromatography (4% acetone/pentane) afforded **146b** (23.9 g, 74%), as a viscous, colourless liquid; ^1H nmr 60 MHz ($CDCl_3$) δ: 5.3 (2H, broad s), and 1.3 - 2.8 (10H, complex m) including a large narrow m at 2.4 (approx. 4H), 5.3 (2H, broad s).

trans-3,4-Dibromo-10-oxatricyclo[4.3.1.$0^{1,6}$]decane (**147b**)

In a manner similar to that for **146a**, **146b** (5.00 g, 36.7 mmol) and Br_2 (5.26 g, 32.9 mmol) were combined to yield **147b** (8.45 g, 87%) as a colourless solid: mp 87-88°C; ir (KBr) ν_{max}: 2955, 1415, 1163, 1069, 933, 656 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.42 (1H, m), 1.59 (3H, distorted septet), 2.04 (2H, distorted quintet), 2.42 (1H, dd, J = 5.4, 15.8 Hz), 2.67 (1H, dd, J = 4.9, 16.4 Hz), 2.82 (1H, dd, J = 4.2, 16.4 Hz), 3.01 (1H, dd, J = 4.3, 15.8 Hz), 4.30 (1H, ddd, J = 4.9, 6.2, 6.6 Hz), 4.41 (1H, ddd, J = 4.3, 5.4, 6.6 Hz); ^{13}C nmr ($CDCl_3$) δ: 19.6, 31.2 and 31.8 ($CH_2CH_2CH_2$ bridge), 33.5 and 34.6 (C-2 and C-5), 47.0 and 49.9 (C-3 and C-4), 64.6 and 65.5 (C-1 and C-6); ms m/z (%): 298 (0.3), 296

(0.7), and 294 (0.4) all M^+, 217 (2), 215 (2), 189 (2), 187 (2), 135 (100), 117 (9), 107 (19), 93 (40), 79 (51), 67 (12), 55 (36), 41 (23).

10-Oxatricyclo[4.3.1.0]deca-2,4-diene (**148b**)

In a similar manner to that for **147a, 147b** (1.20 g, 4.05 mmol) was doubly dehydrobrominated with potassium *tert*-butoxide (1.14 g) to afford **148b** (0.494 g, 91%) as a pale yellow liquid; ir (film) ν_{max}: 1437, 1271, 1187, 1055, 911, 868, 773 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.20-2.81 (6H, complex m, $CH_2CH_2CH_2$ bridge), 6.28 (2H, m), 6.46 (2H, m); ^{13}C nmr ($CDCl_3$) δ: 18.1 and 29.4 (3 x CH_2), 70.7 (C-1 and C-6), 126.9, 128.3; ms *m/z* (%): 134 (M^+, 67), 133 (21), 117 (17), 115 (18), 106 (21), 105 (38), 79 (43), 78 (100), 77 (39), 51 (48). Exact mass calcd. for $C_9H_{10}O$: 134.0731; found: 134.0737.

Diels-Alder reaction of **121**: (3aα,4α,7α,7aα,8*S**,9*R**)- (**150**) and (3aα,4α,7α, 7aα,8*R**,9*S**)-3a,4,7,7a-tetrahydro-8,9-dihydroxy-2-phenyl-4,7-ethano-1*H*-isoindole-1,3(2*H*)-dione (**151**)

To diene **121** (48 mg, 0.43 mmol) in $CHCl_3$ (5 mL) was added *N*-phenylmaleimide (75 mg, 0.43 mmol) in $CHCl_3$ (5 mL). This was refluxed for 16 h, after which time it was noted that a precipitate had formed. Evaporation of the solvent provided a colourless solid (115 mg, 93%). ^1H Nmr of a sample showed two adducts present in a ratio of 95:5. Repeated crystallization of the adduct mixture from 25% MeOH/EtOAc provided the pure major adduct **150**. The minor isomer was not isolated from the adduct mixture, but was conveniently prepared as follows: compound **153** (80 mg, 0.28 mmol) was suspended in 4M HCl (50 mL), and this was heated under reflux for 1 h. The material dissolved while being heated, but after cooling to room temperature, everything remained in solution. The

solution was extracted with CH_2Cl_2 (2 x 50 mL), and the organic layer was washed with saturated $NaHCO_3$ (25 mL) and saturated NaCl (25 mL), and dried ($MgSO_4$), and the solvent was evaporated to provide **151** as a colourless solid (37 mg, 53%). This was crystallized from 75% ethyl acetate/hexane.

For **150**: mp 218.5 - 220°C; ir (KBr) ν_{max}: 3423, 2960, 1768, 1693, 1502, 1392, 1184, 689 cm^{-1}; ^1H nmr (C_6D_6N) δ: 3.61 (2H, broad s), 3.88 (2H, s), 3.98 (2H, s), 5.14 (2H, broad s, 2 x OH), 6.26 (2H, dd, J = 3.2, 4.4 Hz, C-8H and C-9H), 7.31 - 7.36 (1H, m, ArH), 7.42 - 7.51 (4H, m, ArH); ^{13}C nmr (C_5D_5N) δ: 38.6 and 40.8 (C-3a and C-7a, and C-4 and C-7), 63.7 (C-8 and C-9), 127.5 (2 x ArC), 128.6 (1 x ArC), 129.3 (2 x ArC), 132.2 (C-5 and C-6), 133.6 (1 x ArC), 179.5 (C-1 and C-3); ms m/z (%): 285 (M^+, 26), 267 (4), 226 (89), 119 (83), 105 (17), 91 (26), 79 (100), 60 (28), 51 (10), 45 (23). Exact mass calcd. for $C_{16}H_{15}NO_4$: 285.1000; found: 285.0996.

For **151**: mp 260 - 261°C; ir (KBr) ν_{max}: 3450, 3382, 2901, 1775, 1705, 1393, 1200, 734 cm^{-1}; ^1H nmr (C_5D_5N) δ: 3.31 (2H, s), 3.71 (2H, broad s), 4.29 (2H, s), 5.01 (2H, broad s, 2 x OH), 6.45 (2H, t, J = 3.7 Hz, C-5H and C-6H), 7.30 - 7.33 (1H, m, ArH), 7.40 - 7.44 (4H, m, ArH); ^{13}C nmr (C_5D_5N) δ: 40.9 and 42.0 (C-3a and C-7a, and C-4 and C-7), 69.2 (C-8 and C-9), 127.4 (2 x ArC), 128.7 (1 x ArC), 129.3 (2 x ArC), 131.3 (C-5 and C-6), 133.4 (1 x ArC), 177.6 (C-1 and C-3); ms m/z (%): 285 (M^+, 12), 267 (3), 226 (73), 119 (100), 105 (11), 91 (25), 79 (70), 60 (31). Exact mass calcd. for $C_{16}H_{15}NO_4$: 285.1000; found 285.0993.

Diels-Alder reaction of **114**: (3aα,4α,4aα,7aβ,8α,8aα)- (**152**) and (3aα,4β,4aα, 7aα,8β,8aα)-4a,7a,8,8a-tetrahydro-2,2-dimethyl-6-phenyl-4,8-etheno-4*H*-1,3-dioxolo[4,5-*f*]isoindole-5,7-(3a*H*,6*H*)-dione (**153**)

To a solution of **114** (66 mg, 0.41 mmol) in $CHCl_3$ (1 mL), was added *N*-phenylmaleimide (77 mg, 0.44 mmol) in $CHCl_3$ (5 mL). This was stirred at room temperature for 24 h, followed by evaporation of the solvent. The ^1H nmr spectrum of the crude product showed a mixture of **152** and **153** in a 60:40 ratio, respectively. Separation of the of the adducts by preparative TLC afforded **152** (28 mg, 22%) and **153** (67 mg, 52%).

For **152**: mp 189 -190.5°C; ir (KBr) ν_{max}: 2981, 2913, 1773, 1501, 1397, 1187, 1047 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.35 (3H, s), 1.50 (3H, s), 3.48 (4H, s), 4.16 (2H, narrow m), 6.21 (2H, dd, *J* = 2.8, 4.3 Hz), 7.16 (2H, d, *J* = 7.1 Hz), 7.32 - 7.45 (3H, m); ^1H nmr (C_6D_6) δ: 1.10 (3H, s, β-CH_3), 1.35 (3H, s, α-CH_3), 3.19 (2H, t, *J* = 1.4 Hz, C-4aH and C-7aH), 3.29 (2H, broad m, C-4H and C-8H), 3.60 (2H, t, *J* = 1.9 Hz, C-3aH and C-8aH), 5.68 (2H, dd, *J* = 3.0, 4.4 Hz, C-9H and C-10H), 7.04 (1H, m, ArH), 7.18 (2H, m, ArH), 7.41 (2H, m, ArH); n.O.e. results (C_6D_6): δ 1.10: 1.35 (2%), 3.60 (7%); δ 1.35: 1.10 (1%), 3.19 (4%); δ 3.19: 1.35 (1%), 3.29 (5.5%); δ 3.29: 3.19 (4.5%), 3.60 (5.5%), 5.68 (5%); δ 3.60: 1.10 (1.5%), 3.29 (7%), 5.68 (1.5%); δ 5.68: 3.29 (4.5%), 3.60 (1.5%); ^{13}C nmr (C_6D_6) δ: 24.1 (β-CH_3), 26.4 (α-CH_3), 37.3 (C-4 and C-8), 37.9 (C-4a and C-7a), 74.0 (C-3a and C-8a), 112.2 (C-2), 126.6 (2 x ArC), 128.1 (1 x ArC), 128.9 (2 x ArC), 131.6 (C-9 and C-10), 133.1 (1 x ArC), 177.7 (C-5 and C-7); ms *m/z* (%): 325 (M^+, 8), 310 (17), 296 (7), 267 (22), 239 (17), 222 (31), 119 (55), 99 (47), 91 (100), 43 (45). Exact mass calcd. for $C_{19}H_{19}NO_4$: 325.1313; found: 325.1308.

For **153**: mp 263 -265°C; ir (KBr) ν_{max}: 2988, 2889, 1796, 1711, 1500, 1391, 1188 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.31 (3H, s, α-CH_3), 1.35 (3H, s, β-CH_3), 2.88 (2H, t, *J* = 1.4 Hz, C-4aH and C-7aH), 3.53 (2H, m, C-4H and C-8H), 4.32 (2H, s, C-3aH and C-8aH), 6.17 (2H, dd, *J* = 3.2, 4.3 Hz, C-9H and C-10H), 7.18 (2H, d, *J* = 7.0 Hz, ArH), 7.37-7.47 (3H, m, ArH); n.O.e. results: δ 1.31: 4.32 (6%); δ 1.35: 6.17 (2.5%); δ 2.88: 3.53 (7.5%), 4.32 (11%); δ 3.53: 2.88 (5%), 4.32 (2%), 6.17 (10%); δ 4.32: 1.31 (3%), 2.88 (13.5%), 3.53 (15.5%); δ 6.17: 3.53 (9.5%); ^{13}C nmr ($CDCl_3$) δ: 24.8 (α-CH_3), 25.2 (β-CH_3), 36.9 (C-4 and C-8), 40.3 (C-4a and C-7a), 77.1 (C-3a and C-8a), 109.6 (C-2), 126.3 (2 x ArC), 128.6 (1 x ArC), 129.0 (2 x ArC), 129.6 (C-9 and C-10), 131.6 (1 x ArC), 176.3 (C-5 and C-7); ms *m/z* (%): 325 (M^+, 2), 310 (24), 268 (23), 239 (19), 222 (28), 211 (9), 147 (14), 119 (100), 77 (18), 65 (16), 51 (7). Exact mass calcd. for $C_{19}H_{19}NO_4$: 325.1313; found: 325.1302.

Diels-Alder reaction of **109**: (3a*α*,4*α*,7*α*,7a*α*,8*S**,9*R**)- (**154**) and (3a*α*,4*α*,7*α*, 7a*α*,8*R**,9*S**)-8,9-bis(acetyloxy)-3a,4,7,7a-tetrahydro-2-phenyl-4,7-ethano-1*H*-isoindole-1,3(2*H*)-dione (**157**)

A solution of **109** (0.214 g, 1.09 mmol) in $CHCl_3$ (25 mL) was added to *N*-phenylmaleimide (0.190 g, 1.10 mmol) in $CHCl_3$ (5 mL). This solution was refluxed for 2 days, and then the solvent was evaporated to give a colourless solid (0.402 g, 99%). The ^1H nmr spectrum of the residue showed showed the signals for a trace amount of unreacted dienophile, and for adducts **154** and **157** in a ratio of 88:12, respectively. The two adducts were not separated. However, each was made in the following manner from the parent diol adducts **150** and **151**. To *syn* diol adduct **150** (71 mg, 0.25 mmol) in pyridine (2 mL) was added acetic anhydride (1 mL), and the mixture was stirred

overnight. Evaporation of all volatiles left a white powder (95 mg). Purified **154** was obtained by crystallization from ethyl acetate (41 mg, 45%). Likewise, to *anti* diol adduct **151** (43 mg, 0.15 mmol) in pyridine (5 mL) was added acetic anhydride (1 mL), and the mixture was stirred overnight. Evaporation of all volatiles left a white powder (56 mg), which was crystallized (60% ethyl acetate/hexane) to afford **157** (21 mg, 37%).

For **154**: mp 235-237°C; ir (film) ν_{max}: 2979, 1755, 1712, 1377, 1247, 1187, 1038 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.10 (6H, s, 2 x CH_3), 3.48 (4H, broad s, C-3aH and C-7aH, and C-4H and C-7H), 4.90 (2H, s, C-8H and C-9H), 6.30 (2H, dd, J = 3.0, 4.4 Hz, C-5H and C-6H), 7.17 (2H, d, J = 7.0 Hz, ArH), 7.36 - 7.48 (3H, m, ArH); ^{13}C nmr ($CDCl_3$) δ: 20.5 (2 x CH_3), 36.4 and 37.9 (C-3a and C-7a, and C-4 and C-7), 64.6 (C-8 and C-9), 126.2 (2 x ArC), 128.6 (1 x ArC), 128.9 (2 x ArC), 131.3 (C-5 and C-6), 131.5 (1 x ArC), 169.4 (2 x CH_3CO_2), 177.3 (C-1 and C-3); ms *m/z* (%): 369 (M^+, 10), 327 (24), 285 (5), 268 (2), 226 (29), 173 (3), 119 (15), 91 (13), 79 (18), 43 (100). Exact mass calcd. for $C_{18}H_{17}NO_5$ ($M^+ - C_2H_2O$): 327.1106; found: 327.1081.

For **157**: mp 235.5 - 237°C; ir (film) ν_{max}: 2963, 1738, 1711, 1376, 1191, 1062 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.04 (6H, s, 2 x CH_3), 3.12 (2H, s, C-3aH and C-7aH), 3.52 (2H, broad s, C-4H and C-7H), 5.15 (2H, s, C-8H and C-9H), 6.35 (2H, dd, J = 3.2, 4.2 Hz, C-5H and C-6H), 7.17 (2H, d, J = 7.0 Hz, ArH), 7.38 - 7.48 (3H, m, ArH); ^{13}C nmr ($CDCl_3$) δ: 20.5 (2 x CH_3), 36.5 (C-4 and C-7), 40.6 (C-3a and C-7a), 69.8 (C-8 and C-9), 126.3 (2 x ArC), 128.8 (1 x ArC), 129.2 (2 x ArC), 130.4 (C-5 and C-6), 131.5 (1 x ArC), 169.9 (2 x CH_3CO_2), 175.6 (C-1 and C-3); ms *m/z* (%): 369 (M^+, 10), 327 (40), 285 (7), 226 (43), 143 (10), 119 (22), 91 (14), 79 (25), 43 (100). Exact mass calcd. for $C_{20}H_{19}NO_6$: 369.1211; found: 369.1216.

Diels-Alder reaction of **122**: (3aα,4α,7α,7aα,8*S**,9*r**)-3a,4,7,7a-tetrahydro-2-phenyl-8,9-bis[(trimethylsilyl)oxy]-4,7-ethano-1*H*-isoindole-1,3(2*H*)-dione (**155**)

To a solution of diene **122** (92 mg, 0.36 mmol) in $CHCl_3$ (1 mL) was added *N*-phenylmaleimide (62 mg, 0.36 mmol) in $CHCl_3$ (5 mL). This was stirred at room temperature for 20 h, after which time the solvent was evaporated, and the residue was dried under vacuum for 1 h to yield a pale yellow solid (120 mg). The ^1H nmr spectrum of the product showed the presence of Diels-Alder adduct **155** and unreacted addends. The adduct was not isolated from the mixture. However, to diol adduct **150** (60 mg, 0.21 mmol) in dry pyridine (2 mL) was added chlorotrimethylsilane (1 mL) and this was stirred for 24 h. Carbon tetrachloride (10 mL) was added, and the resulting solid was removed by filtration through a Kimwipe plug in a Pasteur pipette. Concentration of the filtrate gave a colourless solid (75 mg, 83%). Crystallization from 25% hexane/CCl_4 provided **155**: mp 143 - 144°C; ir (KBr) ν_{max}: 3047, 2955, 2898, 1773, 1710, 1391, 1183, 898, 753 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 0.17 (18H, s, 6 x CH_3), 3.18 (2H, m, C-4H and C-7H), 3.54 (2H, t, J = 1.5 Hz, C-3aH and C-7aH), 3.72 (2H, t, J = 1.5 Hz, C-8H and C-9H), 6.17 (2H, dd, J = 3.3, 4.5 Hz, C-5H and C-6H), 7.17 (2H, d, J = 7.1 Hz, ArH), 7.35-7.46 (3H, m, ArH); ^{13}C nmr ($CDCl_3$) δ: 0.3 (6 x CH_3), 37.9 (C-3a and C-7a), 40.6 (C-4 and C-7), 65.3 (C-8 and C-9), 126.4 (2 x ArC), 128.4 (1 x ArC), 129.0 (2 x ArC), 131.4 (C-5 and C-6), 132.0 (1 x ArC), 179.1 (C-1 and C-3); ms *m/z* (%): 414 (M^+ - CH_3, 1), 324 (3), 204 (100), 147 (10), 119 (4), 73 (51), 45 (4). Exact mass calcd. for $C_{18}H_{18}NO_3Si$ (M^+ - $C_4H_{13}OSi$): 324.1055; found: 324.1066.

(3aα,4α,7α,7aα,8*R**,9*S**)-3a,4,7,7a-Tetrahydro-2-phenyl-8,9-bis[(trimethylsilyl)oxy]-4,7-ethano-1*H*-isoindole-1,3(2*H*)-dione (**158**)

To a solution of **151** (33.1 mg, 0.116 mmol) in pyridine (5 mL) was added chlorotrimethylsilane (1 mL). This was stirred at room temperature for 16 h, after which time carbon tetrachloride was added (10 mL), and the white solid which formed was removed by filtration through a Kimwipe plug in a Pasteur pipette and discarded. The filtrate was concentrated to yield a white residue (40.6 mg, 82%). Taking up a portion of this residue in carbon tetrachloride (2 mL) and then evaporating provided an impure sample of **158**: mp 166 - 171°C; ir (KBr) ν_{max}: 3055, 2962, 1778, 1718, 1499, 1385, 1109, 909, 843 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 0.16 (18H, s, 6 x CH_3), 2.93 (2H, t, *J* = 1.1 Hz, C-3aH and C-7aH), 3.26 (2H, broad m, C-4H and C-7H), 3.95 (2H, s, C-8H and C-9H), 6.32 (2H, dd, *J* = 3.1, 4.4 Hz, C-5H and C-6H), 7.160 (2H, d, *J* = 7.1 Hz, ArH), 7.36 - 7.46 (3H, m, ArH); ^{13}C nmr ($CDCl_3$) δ: 0.2 (6 x CH_3), 40.3 (C-4 and C-7), 41.2 (C-3a and C-7a), 70.9 (C-8 and C-9), 126.3 (2 x ArC), 128.6 (1 x ArC), 129.0 (2 x ArC), 130.3 (C-5 and C-6), 131.6 (1 x ArC), 176.7 (C-1 and C-3); ms *m/z* (%): 414 (M^+ - CH_3, 1), 324 (5), 298 (4), 204 (100), 189 (3), 147 (14), 132 (24), 116 (39), 101 (6), 73 (90), 45 (9). Exact mass calcd. for $C_{18}H_{18}NO_3Si$ (M^+ - $C_4H_{13}OSi$): 324.1055; found: 324.1078.

Diels-Alder reaction of **124**: (3aα,4α,7α,7aα,8*S**,9*R**)- (**156**) and (3aα,4α,7α,7aα,8*R**,9*S**)-3a,4,7,7a-tetrahydro-8,9-dimethoxy-2-phenyl-4,7-ethano-1*H*-isoindole-1,3(2*H*)-dione (**159**)

To a solution of **124** (67 mg, 0.48 mmol) in $CHCl_3$ (2 mL) was added *N*-phenylmaleimide (59 mg, 0.34 mmol) in $CHCl_3$ (3 mL). This was stirred at room temperature for 16 h, after which time the solvent was evaporated, and the residue

obtained was placed on a vacuum pump line for ca. 3 h to provide an orange-coloured solid (113 mg). The ^{1}H nmr spectrum of the residue indicated the presence of two adducts **156** and **159** (105 mg, 99%) in a ratio of 99:1, respectively, and unreacted dienophile (8 mg). This yield was based on the amount of unreacted dienophile in product mixture. Crystallization of the crude product from benzene gave **156** (28 mg); mp 195 - 196°C. The *anti* adduct **159** was not isolated from the crude product mixture, but it was made using the following procedure. To a solution of *anti* diol adduct **151** (30 mg, 0.11 mmol) in dry THF (10 mL) was added potassium hydride (50 mg, 0.42 mmol, 35% w/w dispersion in mineral oil; previously washed with hexane) as a suspension in THF (10 mL) and iodomethane (27 µL, 0.42 mmol). After stirring at room temperature for 2 h, 50 mL of CH_2Cl_2 was added and the organic layer washed with H_2O (100 mL), saturated $NaHCO_3$ (100 mL) and saturated NaCl (100 mL), and dried ($MgSO_4$) and the solvent was evaporated to provide **159** (31 mg, 94%), which was recrystallized from $CHCl_3/CCl_4$.

For **156**: 195 -196°C; ir (KBr) ν_{max}: 2966, 2891, 1767, 1709, 1497, 1371, 1177, 730 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 3.43 (4H, broad s), 3.51 (8H, broad s), 6.22 (2H, dd, J = 3.1, 4.5 Hz, C-5H and C-6H), 7.19 (2H, d, J = 7.1 Hz, ArH), 7.36 - 7.44 (3H, ArH); ^{1}H nmr (C_5D_5N) δ: 3.27 (2H, t, J = 1.5 Hz, C-8H and C-9H), 3.34 (6H, s, 2 x CH_3), 3.51 (2H, broad m, C-4H and C-7H), 3.62 (2H, t, J = 1.6 Hz, C-3aH and C-7aH), 6.20 (2H, dd, J = 3.2, 4.6 Hz, C-5H and C-6H), 7.30-7.33 (1H, m, ArH), 7.40-7.43 (4H, ArH); n.O.e. results (C_5D_5N): δ 3.27: 3.34 (2%), 3.51 (11%), 6.20 (2.5%); δ 3.34: 3.27 (3%), 3.51 (5.5%), 3.62 (2.5%); δ 3.51: 3.27 (6.5%), 3.34 (1%), 3.62 (6.5%), 6.20 (7.5%); δ 3.62: 3.34 (1%); δ 6.20: 3.27 (1%), 3.51 (6.5%); ^{13}C nmr (C_5D_5N) δ: 37.4 (C-4 and C-7), 38.7 (C-3a and C-7a), 58.0 (2 x CH_3), 73.9 (C-8 and C-9), 127.4 (2 x ArC), 128.6 (1 x ArC), 129.3 (2 x ArC), 131.9 (C-5 and C-6), 133.4 (1 x ArC), 179.0 (C-1 and C-3); ms m/z (%): 313 (M^+, 2), 282 (3), 225 (2),

173 (9), 165 (9), 151 (10), 134 (23), 119 (82), 103 (32), 88 (100), 73 (86), 65 (58), 51 (57), 45 (85). Exact mass calcd. for $C_{18}H_{19}NO_4$: 313.1313; found: 313.1322.

For **159**: 220 -223°C; ir (KBr) ν_{max}: 2956, 2876, 1777, 1708, 1498, 1385, 1180, 723 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.94 (2H, t, *J* = 1.4 Hz), 3.47 (6H, s, 2 x CH_3), 3.60 (2H, broad m, C-4H and C-7H), 3.69 (2H, broad s), 6.32 (2H, dd, *J* = 3.1, 4.6 Hz, C-5H and C-6H), 7.17 (2H, d, *J* = 7.0 Hz, ArH), 7.37-7.48 (3H, m, ArH); ^{13}C nmr ($CDCl_3$) δ: 36.1 and 40.9 (C-3a and C-7a, and C-4 and C-7), 58.5 (2 x CH_3), 79.2 (C-8 and C-9), 126.3 (2 x ArC), 128.8 (1 x ArC), 129.1 (2 x ArC), 130.2 (C-5 and C-6), 131.6 (1 x ArC), 176 (C-1 and C-2); ms *m/z* (%): 314 (M^+ + 1, 0.2), 313 (M^+, 0.05), 299 (0.6), 281 (0.6), 226 (11), 173 (1), 134 (4), 119 (22), 91 (26), 88 (100), 78 (27), 77 (24). Exact mass calcd. for $C_{14}H_{12}NO_2$ (M^+ - $C_4H_7O_2$ = loss of the C-8 and C-9 bridge with H transfer): 226.0867; found: 226.0862.

Diels-Alder reaction of **123**: (3aα,4α,4aβ,7aβ,8α,8aα)- (**160**) and (3aα,4β,4aα, 7aα,8β,8aα)-4a,7a,8,8a-tetrahydro-2,2-dimethyl-6-phenyl-4,8-etheno-4*H*-1,3,2-dioxasilolo[4,5-*f*]isoindole-5,7-(3a*H*,6*H*)-dione (**161**)

To a solution of *cis*-3,5-cyclohexadiene-1,2-diol (**121**) (0.141 g, 1.26 mmol) in $CDCl_3$ was added diacetoxydimethylsilane (222 μL, 1.26 mmol) and pyridine (10 μL). After 20 min ^1H nmr indicated a quantitative conversion of the starting diol to **123**. To this was then added *N*-phenylmaleimide (0.217 g, 1.25 mmol) dissolved in $CDCl_3$ (0.5 mL), and the mixture was stirred for 3 h at *ca.* 25°C. The ^1H nmr spectrum of the solution indicated that there was a quantitative conversion of the addends to adducts **160** and **161** in a ratio of 60:40, respectively. Column chromatography of the adducts resulted in the isolation of the diol adducts **150** (0.148 g, 41%) and **151** (54 mg, 15%).

Adducts **160** and **161** could be synthesized independently in the following manner. To a solution of **150** (52 mg, 0.18 mmol) in C_5D_5N (*ca.* 0.5 mL) was added diacetoxydimethylsilane (32 μL, 0.18 mmol), to give a quantitative conversion to **160** after only 15 minutes. Evaporation of all volatiles yielded **160** as a white powder (63 mg, 100%). Likewise, to a warm solution of **151** (23 mg, 0.081 mmol) in C_5D_5N (*ca.* 0.5 mL) was added diacetoxydimethylsilane (15 μL, 0.085 mmol). After 25 minutes, **151** was cleanly converted to **161**. Evaporation of all volatiles left **161** as a white powder (28.0 mg, 100%).

For **160**: mp 200 - 205 °C; ^{1}H nmr ($CDCl_3$) δ: 0.26 (3H, s), 0.37 (3H, s), 3.37 (2H, t, J = 1.6 Hz, C-4aH and C-7aH), 3.49 (2H, m, C-4H and C-8H), 4.17 (2H, t, J = 1.8 Hz, C-3aH and C-8aH), 6.22 (2H, dd, J = 3.1, 4.5 Hz, C-9 and C-10), 7.17 - 7.21 (2H, m, ArH), 7.36 - 7.47 (3H, m, ArH); ^{1}H nmr (C_5D_5N) δ: 0.22 (3H, s), 0.32 (3H, s), 3.59 (2H, broad s, C-4H and C-8H), 3.65 (2H, t, J = 1.5 Hz, C-4aH and C-7aH), 4.21 (2H, t, J = 1.7 Hz, C-3aH and C-8aH), 6.22 (2H, dd, J = 3.1, 4.4 Hz, C-9H and C-10H), 7.29-7.34 (1H, m, ArH), 7.40 (4H, m, ArH); n.O.e. results ($CDCl_3$): δ 0.37: 3.37 (5.5%); δ 3.37: 0.37 (2.5%), 3.49 (6.5%); δ 3.49: 3.37 (3%), 4.17 (6.5%), 6.22 (7%); δ 4.17: 3.49 (10.5%), 6.22 (3%); δ 6.22: 3.49 (3.5%); ^{13}C nmr (C_5D_5N) δ: -1.0 (CH_3), -0.1 (CH_3), 38.5 (C-4 and C-8), 39.7 (C-4a and C-7a), 71.8 (C-3a and C-8a), 127.5 (2 x ArC), 128.8 (1 x ArC), 129.4 (2 x ArC), 132.2 (C-9 and C-10), 133.5 (1 x ArC), 178.9 (C-5 and C-7); ms *m/z* (%): 341 (M^+, 5), 326 (1), 193 (2), 179 (1), 129 (1), 116 (100), 101 (8), 91 (3), 84 (1), 78 (4), 75 (3). Exact mass calcd. for $C_{18}H_{19}NO_4Si$: 341.1082; found: 341.1071.

For **161**: mp 220 -225°C; ^{1}H nmr (C_5D_5N) δ: 0.16 (3H, s), 0.17 (3H, s), 3.22 (2H, s, C-4aH and C-7aH), 3.67 (2H, broad s, C-4H and C-8H), 4.46 (2H, s, C-3aH and C-8aH), 6.15 (2H, m, C-9H and C-10H), 7.29 - 7.35 (1H, m, ArH), 7.23 (4H, m, ArH); ^{1}H nmr

($CDCl_3$) δ: 0.19 (6H, s), 2.95 (2H, t, *J* = 1.3 Hz, C-4aH and C-7aH), 3.54 (2H, broad s, C-4H and C-8H), 4.36 (2H, s, C-3aH and C-8aH), 6.25 (2H, dd, *J* = 3.2, 4.4 Hz, C-9H and C-10H), 7.17 (2H, d, *J* = 7.0 Hz, ArH), 7.35 - 7.48 (3H, m, ArH); n.O.e. results ($CDCl_3$): δ 0.19: 4.36 (1.5%), 6.25 (3%); δ 2.95: 3.54 (13.5%), 4.36 (12.5%); δ 3.54: 2.95 (2.5%), 4.36 (2.5%), 6.25 (1.5%); δ 4.36: 2.95 (12.5%), 3.54 (14.5%); δ 6.25: 3.54 (3%); ^{13}C nmr (C_5D_5N) δ: -0.6 (CH_3), -0.1 (CH_3), 39.9 (C-4 and C-8), 41.3 (C-4a and C-7a), 76.3 (C-3a and C-8a), 127.4 (2 x ArC), 128.8 (1 x ArC), 129.3 (2 x ArC), 131.5 (C-9 and C-10), 133.3 (1 x ArC), 177.2 (C-5 and C-7); ms *m/z* (%): 341 (M^+, 2), 326 (1), 193 (2), 179 (1), 116 (100), 101 (8), 78 (4), 77 (2), 75 (3). Exact mass calcd. for $C_{18}H_{19}NO_4Si$: 341.1082; found: 341.1087.

cis-2-Ethyl-3a,7a-dihydro-2,1,3-benzoboradioxole (**125**) and its Diels-Alder reaction: (3aα,4α,4aβ,7aβ,8α,8aα)- (**162**) and (3aα,4β,4aα,7aα,8β,8aα)-2-ethyl-4a,7a,8,8a-tetrahydro-4,8-etheno-4*H*-2,1,3-boradioxolo[4,5-*f*]isoindole-5,7(3a*H*,6*H*)-dione (**163**)

To a solution of lithium triethylborohydride (0.6 mL, 1 M in THF) in dry THF (2 mL) chilled to 0°C was added **121** (60 mg, 0.54 mmol) in dry THF (5 mL), which was also chilled to 0°C. After stirring for 1 h, H_2O (6 drops) was added, and the solvent was evaporated under vacuum to leave a very viscous yellow oil. This was taken up in dry CH_2Cl_2 (10 mL) and 0.5 g of a 50/50 w/w mixture of $MgSO_4$/Celite was added, and then this was filtered through a sintered-glass funnel. Evaporation of the solvent left **125** (24 mg, 30%), which was immediately taken up in dry $CDCl_3$ (0.5 mL): ^1H nmr (60 MHz) δ: 1.0 (5H, m), 4.9 (2H, s), 5.8 (4H, m). To this material *N*-phenylmaleimide (34.5 mg, 0.20 mmol) was added in dry $CDCl_3$ (0.5 mL), and this solution was stirred at room temperature overnight. Afterwards, the ^1H nmr spectrum showed that the addends were

cleanly converted to the Diels-Alder adducts **162** and **163** in a ratio of 45:55, respectively. Evaporation of the solvent left a pale yellow powder (60 mg) containing, from ^{1}H nmr integration, unreacted dienophile (6 mg) and adducts (53 mg, 100%). The adducts could not be isolated chromatographically; ^{1}H nmr ($CDCl_3$) [resolved signals from **162** in the mixture] δ: 3.32 (2H, t, J = 1.5 Hz, C-4aH, C-7aH), 4.42 (2H, t, J = 1.9 Hz, C-3aH and C-8aH), 6.24 (2H, dd, J = 3.1, 4.5 Hz, C-9H and C-10H); ^{1}H nmr ($CDCl_3$) [resolved signals from **163** in the mixture] δ: 2.92 (2H, t, J = 1.4 Hz, C-3aH and C-7aH), 4.54 (2H, broad s, $W_{1/2}$ = 6.7 Hz, C-3aH and C-8aH), 6.21 (2H, dd, J = 3.1, 4.4 Hz, C-9H and C-10H); ^{1}H nmr ($CDCl_3$) [other unresolved signals from the mixture] δ: 0.75 - 1.00 (10H, complex m, CH_2CH_3), 3.57 (broad m, C-4H and C-8H for both **162** and **163**), 7.17 (4H, m, Ar), 7.39 - 7.47 (6H, m, ArH); n.O.e. results: δ 2.92: 3.57 (4%), 4.54 (11.5%); δ 3.32: 3.57 (3%); δ 3.57: 2.92 (5%), 3.32 (6.5%), 4.42 (8%), 4.54 (5%), 6.21 (3.5%), 6.24 (3.5%); δ 4.42: 3.57 (4.5%), 6.24 (1%); δ 4.54: 2.92 (12%), 3.57 (4.5%); δ 6.21: 3.57 (5.5%), 4.42 (1%); ^{13}C nmr ($CDCl_3$) [resolved signals from **162**] δ: 40.1 (C-4a and C-7a), 75.0 (C-3a and C-8a), 131.6 (C-9 and C-10); ^{13}C nmr ($CDCl_3$) [resolved signals of **163**] δ: 37.3 (C-4a and C-7a), 77.7 (C-3a and C-8a), 130.0 (C-9 and C-10); ^{13}C nmr ($CDCl_3$) [unresolved signals of mixture] δ: 2.2 (CH_2, m), 3.3 (CH_2, m), 7.5 (2 x CH_3), 37.0 (C-4 and C-8), 37.1 (C-4 and C-8), 126.0, 126.3, 127.9, 128.6, 128.7, 129.0; ms of the mixture m/z (%): 323 (M^+, 10), 294 (3), 225 (12), 145 (6), 129 (19), 119 (100), 103 (19), 78 (38), 64 (15), 54 (36), 28 (40). Exact mass calcd. for $C_{18}H_{18}{}^{11}BNO_4$: 323.1328; found 323.1310; calcd. for $C_{16}H_{13}{}^{11}BNO_4$ (M^+-C_2H_5): 294.0937; found: 294.0938; calcd. for $C_{14}H_{11}NO_2$ (M^+-$C_4H_7BO_2$): 225.0789; found: 225.0783.

Diels-Alder reaction of **132**: (2α,3aβ,4β,4aα,7aα,8β,8aβ)- (**164**) and (2α,3aβ,4α, 4aβ,7aβ,8α,8aβ)-4a,7a,8,8a-tetrahydro-2,6-diphenyl-4,8-etheno-4*H*-1,3,-dioxo[4,5-*f*]-isoindole-5,7-(3a*H*,6*H*)-dione (**165**)

To a solution of **132** (82 mg, 0.41 mmol) in $CHCl_3$ (5 mL) was added *N*-phenylmaleimide (71 mg, 0.36 mmol) in $CHCl_3$ (2 mL). This was stirred at room temperature for 16 h. Integration of the ^{1}H nmr spectrum of the crude product mixture gave a ratio of adducts of 28:72 for **164** to **165**, respectively. Chromatography (50% ethyl acetate/hexane) of the crude product mixture provided **165** (62 mg, 62%). Unfortunately, the minor isomer **164** and unreacted *N*-phenylmaleimide co-eluted, which gave a pale yellow solid (58 mg). Integration of the ^{1}H nmr spectrum of this mixture showed it to be comprised of **164** (33 mg, 33%) and *N*-phenylmaleimide (25 mg), which afforded a total yield of 95% yield for the adducts based on the amount of recovered dienophile. Pure **164** was obtained by careful crystallization of the adduct/*N*-phenylmaleimide mixture using 1:1:1 $CHCl_3$/ethyl acetate/hexane.

To **150** (64 mg, 0.22 mmol) in CH_2Cl_2 (15 mL) was added a small amount of *p*TsOH and benzaldehyde dimethyl acetal (**129**) (34 μL), and this was stirred for 14 h at room temperature. CH_2Cl_2 (*ca.* 50 mL) was added and the organic portion was washed with 10% NaOH (30 mL) and saturated NaCl (30 mL), dried ($MgSO_4$) and concentrated to provide **164** (78 mg, 93%).

Similarly, **151** (51 mg, 0.18 mmol) was suspended in CH_2Cl_2 (15 mL) and *p*TsOH was added, along with **129** (30 μL); the suspended solid dissolved within 15 minutes. This was stirred overnight at room temperature. Workup gave **165** as a colourless solid (66 mg, 99%).

For **164**: mp 210 - 211.5°C; ir (film) ν_{max}: 2922, 1774, 1712, 1500, 1384, 1182, 1053, 710 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 3.59 (2H, s, C-4aH and C-7aH), 3.66 (2H, broad s, C-4H and C-8H), 4.26 (2H, s, C-3aH and C-8aH), 5.94 (1H, s, C-2H), 6.31 (2H, dd, *J* = 3.1, 4.1 Hz, C-9H and C-10H), 7.18 (2H, d, *J* = 7.1 Hz, ArH), 7.34 - 7.51 (8H, m, ArH); ^1H nmr (C_6D_6) δ: 3.24 (2H, t, *J* = 1.6 Hz, C-4aH and C-7aH), 3.73 (2H, broad m, C-4H and C-8H), 3.60 (2H, t, *J* = 2.0 Hz, C-3aH and C-8aH), 5.61 (1H, s, C-2H), 5.67 (2H, dd, *J* = 3.0, 4.5 Hz, C-9H and C-10H), 7.02 (1H, d, *J* = 7.4 Hz, ArH), 7.12 - 7.24 (5H, m, ArH), 7.35 (2H, d, *J* = 7.3 Hz, ArH), 7.52 (2H, d, *J* = 6.5 Hz, ArH); n.O.e. results (C_6D_6): δ 3.24: 3.37 (5.5%), 7.52 (3%); δ 3.37: 3.24 (4%), 3.60 (4%), 5.67 (4.5%); δ 3.60: 3.37 (6%), 5.61 (12%), 5.67 (2%); δ 5.61: 3.60 (4.5%), 7.52 (1.5%); δ 5.67: 3.37 (6.5%), 3.60 (1%); ^{13}C nmr ($CDCl_3$) δ: 36.8 (C-4 and C-8), 37.9 (C-4a and C-7a), 74.8 (C-3a and C-8a), 105.8 (C-2), 126.3 (2 x ArC), 126.4, 128.6, 129.1, 131.8 (C-9 and C-10), 135.9 (1 x ArC), 178.1 (C-5 and C-7); ms *m/z* (%): 373 (M^+, 10), 372 (12), 344 (43), 326 (11), 298 (2), 267 (9), 239 (15), 222 (25), 211 (8), 194 (4), 147 (14), 119 (47), 105 (40), 91 (100), 77 (29), 65 (15), 51 (9). Exact mass calcd. for $C_{23}H_{19}NO_4$: 373.1313; found: 373.1312.

For **165**: mp 231 - 234.5°C; ir (film) ν_{max}: 2896, 1778, 1711, 1498, 1395, 1186, 1065, 745 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.95 (2H, s, C-4aH and C-7aH), 3.37 (2H, s, C-4H and C-8H), 4.64 (2H, s, C-3aH and C-8aH), 5.66 (1H, s, C-2H), 6.30 (2H, dd, *J* = 3.3, 4.1 Hz, C-9H and C-10H), 7.20 (2H, d, *J* = 7.0 Hz, ArH), 7.35-7.48(8H, m, ArH); n.O.e. results: δ 2.95: 3.70 (12%), 4.64 (15%); δ 3.70: 2.95 (11%), 4.37 (6%), 6.30 (11%); δ 4.37: 2.95 (16%), 3.70 (13%), 5.66 (18%); δ 5.66: 4.37 (2%); δ 6.30: 3.70 (12%); ^{13}C nmr ($CDCl_3$) δ: 36.6 (C-4 and C-8), 40.5 (C-4a and C-7a), 77.8 (C-3a and C-8a), 103.8 (C-2), 126.3 (2 x ArC), 127.2 (2 x ArC), 128.3 (2 x ArC), 128.8 (1 x ArC), 129.1 (2 x ArC), 129.9 (1 x ArC), 130.1 (C-9 and C-10), 131.6 (1 x ArC), 176.1 (C-5 and C-7); ms *m/z* (%): 373 (M^+, 7), 372

(11), 344 (5), 267 (15), 239 (21), 222 (25), 211 (8), 194 (3), 147 (15), 119 (50), 105 (76), 91 (100), 77 (29), 65 (13), and 51 (7). Exact mass calcd. for $C_{23}H_{19}NO_4$: 373.1313; found: 373.1276; calcd. for $C_{22}H_{18}NO_3$ (M^+-H-CO) 344.1287; found: 344.1280.

Diels-Alder reaction of **133**: (2α,3aα,4α,4aβ,7aβ,8α,8aα)- (**168**) and (2α,3aα, 4β,4aα,7aα,8β,8aα)-4a,7a,8,8a-tetrahydro-2,6-diphenyl-4,8-etheno-4*H*-1,3,-dioxo- [4,5-*f*]isoindole-5,7-(3a*H*,6*H*)-dione (**169**)

To crude **133** (0.392 g, 1.96 mmol) in $CHCl_3$ (5 mL) was added *N*-phenylmaleimide (0.337 g, 1.95 mmol) in $CHCl_3$ (5 mL), and this was stirred overnight. The ^1H nmr spectrum of the crude reaction mixture clearly showed the presence of two adducts in a ratio of 4:96. Careful and repeated chromatography (50% ethyl acetate/hexane, then 45% ethyl acetate/hexane) of the crude product gave the dimer **139** (31 mg), recovered *N*-phenylmaleimide (60 mg), adduct **168** (26 mg, 4%), and adduct **169** (0.520 g, 87%). Yields were based on recovered *N*-phenylmaleimide.

For **168**: mp 232 - 234°C; ir (KBr) ν_{max}: 3056, 2926, 1772, 1710, 1598, 1502, 1397, 1191, 1086, 745 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 3.62 (4H, broad s, C-4H, C-4aH, C-7aH and C-8H), 4.15 (2H, s, C-3aH and C-8aH), 6.24 (2H, dd, J = 2.9, 3.9 Hz, C-9H and C-10H), 6.47 (1H, s, C-2H), 7.19 (2H, d, J = 7.2 Hz, ArH), 7.35 - 7.47 (8H, m, ArH); ^1H nmr (10% $CDCl_3$ in CCl_4): 3.54 (2H, s, C-4aH and C-7aH), 3.57 (2H, broad m, C-4H and C-8H), 4.08 (2H, s, C-3aH and C-8aH), 6.21 (2H, dd, J = 3.1, 4.3 Hz, C-9H and C-10H), 6.41 (1H, s, C-2H), 7.16 (2H, d, J = 7.2 Hz, ArH), 7.24 - 7.42 (8H, m, ArH); n.O.e. results (10% $CDCl_3$ in CCl_4): δ 3.54: 6.41 (9%); δ 3.57: 4.08 (8%), 6.21 (6.5%); δ 4.08: 3.57 (11%), 6.21 (2.5%), 6.41 (2%); δ 6.21: 3.57 (7%), 4.08 (2%); δ 6.41: 3.54 (3%); ^{13}C nmr ($CDCl_3$) δ: 37.1 and 38.0 (C-4 and C-8, and C-4a and C-7a), 74.2 (C-3a and C-8a), 106.8 (C-2), 125.5

(2 x ArC), 126.4 (2 x ArC), 128.4 (2 x ArC), 128.6 (1 x ArC), 128.7 (1 x ArC), 129.1 (2 x ArC), 131.7 (C-9 and C-10), 134.2 (1 x ArC), 139.2 (1 x ArC), 178.2 (C-5 and C-7); ms *m/z* (%): 373 (M^+, 4), 372 (3), 344 (24), 326 (4), 267 (6), 239 (8), 222 (17), 211 (4), 147 (11), 119 (38), 105 (29), 91 (100), 77 (33), 65 (17), 51 (16).

For **169**: mp 269 - 270°C; ir (KBr) ν_{max}: 3064, 2969, 1777, 1712, 1595, 1497, 1455, 1386, 1187, 748 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.87 (2H, t, *J* = 1.2 Hz, C-4aH and C-7aH), 3.68 (2H, broad s, C-4H and C-8H), 4.41 (2H, s, C-3aH and C-8aH), 6.10 (1H, s, C-2H), 6.33 (2H, dd, *J* = 3.2, 4.3 Hz, C-9H and C-10H), 7.17 (2H, d, *J* = 7.0 Hz, 2ArH), 7.31 - 7.47 (8H broad m, ArH); n.O.e. results: δ 2.87: 3.68 (7%), 4.41 (5.5%); δ 3.68: 2.87 (5%), 4.41 (5.5%), 6.33 (8%); δ 4.41: 2.87 (14.5%), 3.68 (8.5%), 6.10 (2%); δ 6.10: 6.33 (1%); δ 6.33: 3.68 (7.5%), 6.10 (4%); ^{13}C nmr δ: 37.1 (C-4 and C-8), 40.3 (C-4a and C-7a), 77.9 (C-3a and C-8a), 105.4 (C-2), 125.8 (2 x ArC), 126.3 (2 x ArC), 128.4 (2 x ArC), 128.7 (1 x ArC), 128.9 (1 x ArC), 129.1 (2 x ArC), 130.6 (C-9 and C-10), 131.5 (1 x ArC), 138.7 (1 x ArC), 176.1 (C-5 and C-7); ms *m/z* (%): 373 (M^+, 4), 372 (2), 344 (2), 266 (4), 239 (7), 222 (17), 211 (4), 200 (11), 175 (19), 147 (11), 119 (39), 105 (91), 91 (100), 77 (39), 65 (20), 51 (15).

Diels-Alder reaction of **137**: (2α,3aβ,4β,4aα,7aα,8β,8aβ)- (**166**) and (2α,3aβ,4α,4aβ,7aβ,8α,8aβ)-4a,7a,8,8a-tetrahydro-2-(4-nitrophenyl)-6-phenyl-4,8-etheno-4*H*-1,3-dioxolo[4,5-*f*]isoindole-5,7-(3a*H*,6*H*)-dione (**167**)

To a solution of **137** (0.610 g, 2.49 mmol) in $CHCl_3$ (20 mL) was added *N*-phenylmaleimide (0.432 g, 2.49 mmol) in $CHCl_3$ (5 mL). This solution was stirred for 16 h, then concentrated. Integration of the ^1H nmr spectrum of the crude product mixture gave an adduct ratio of 27:73 for **166** to **167**, respectively. Chromatography (50% ethyl acetate/hexane) provided **166** (0.242 g, 23%) and **167** (0.665 g, 64%).

For **166**: mp 254 - 255°C; ir (KBr) ν_{max}: 3069, 2949, 1772, 1714, 1610, 1527, 1389, 1352, 1197, 745 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 3.46 (2H, t, *J* = 1.4 Hz, C-4aH and C-7aH), 3.67 (2H, broad m, C-4H and C-8H), 4.31 (2H, t, *J* = 1.9 Hz, C-3aH and C-8aH), 6.00 (1H, s, C-2H), 6.31 (2H, dd, *J* = 3.0, 4.5 Hz, C-9H and C-10H), 7.16 (2H, d, *J* = 7.0 Hz, ArH), 7.35 - 7.45 (3H, m, ArH), 7.69 (2H, d, *J* = 8.8 Hz, ArH), 8.26 (2H, d, *J* = 8.8 Hz, ArH); n.O.e. results: δ 3.46: 3.67 (9.5%), 7.69 (5%); δ 3.67: 3.46 (8.5%), 4.31 (8.5%), 6.31 (12.5%); δ 4.31: 3.67 (11%), 6.00 (24%), 6.31 (2.5%); δ 6.00: 4.31 (5%), 7.69 (2%); δ 6.31: 3.67 (10.5%), 4.31 (1.5%); δ 7.70: 3.46 (2%), 6.00 (3.5%), 8.26 (15.5%); ^{13}C nmr ($CDCl_3$) δ: 36.6 (C-4 and C-8), 37.7 (C-4a and C-7a), 75.0 (C-3a and C-8a), 104.0 (C-2), 123.6 (2 x ArC), 126.2 (2 x ArC), 127.1 (2 x ArC), 128.5 (1 x ArC), 148.4 (1 x ArC), 177.8 (C-5 and C-7); ms *m/z* (%): 418 (M^+, 19), 417 (3), 389 (77), 266 (9), 239 (11), 222 (31), 193 (19), 173 (9), 150 (17), 147 (15), 119 (52), 91 (100), 77 (20), 65 (15), 51 (8).

For **167**: mp 237 - 239°C; ir (KBr) ν_{max} : 3067, 2901, 1776, 1712, 1519 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 2.99 (2H, t, *J* = 1.2 Hz, C-3aH and C-7aH), 3.72 (2H, broad m, C-4H and C-8H), 4.44 (2H, s, C-3aH and C-8aH), 5.74 (1H, s, C-2H), 6.26 (2H, dd, *J* = 3.1, 4.3 Hz, C-9H and C-10H), 7.20 (2H, d, *J* = 7.0 Hz, ArH), 7.39 - 7.49 (3H, m, ArH), 7.62 (2H, d, *J* = 8.8 Hz, ArH), 8.21 (2H, d, *J* = 8.8 Hz, ArH); n.O.e. results: δ 2.99: 3.72 (10%), 4.44 (12.5%); δ 3.72: 2.99 (5.5%), 4.44 (4%), 6.26 (9%); δ 4.44: 2.99 (14%), 3.72 (8.5%), 5.74 (20.5%); δ 5.74: 4.44 (4%), 7.62 (6%); δ 6.26: 3.72 (9%), 7.62 (2.5%); ^{13}C nmr ($CDCl_3$) δ: 36.5 (C-8 and C-4), 40.3 (C-4a and C-7a), 78.1 (C-3a and C-8a), 102.1 (C-2), 123.5 (2 x ArC), 126.3 (2 x ArC), 128.2 (2 x ArC), 128.8 (1 x ArC), 129.1 (2 x ArC), 130.1 (C-9 and C-10), 131.5 (1 x ArC), 142.3 (1 x ArC), 148.6 (1 x ArC), 175.9 (C-5 and C-7); ms *m/z* (%): 418 (M^+, 4), 417 (2), 402 (3), 389 (9), 296 (2), 266 (5), 239 (11), 222 (21), 211 (6), 193 (11), 173 (8), 149 (14), 147 (10), 119 (47), 104 (10), 91 (100), 77 (28), 65 (18), 51 (13).

Diels-Alder reaction of **138**: (2α,3aα,4α,4aβ,7aβ,8α,8aβ)- (**170**) and (2α,3aα,4β, 4aα,7aα,8β,8aα)-4a,7a,8,8a-tetrahydro-2-(4-nitrophenyl)-6-phenyl-4,8-etheno-4*H*-1,3-dioxolo[4,5-*f*]isoindole-5,7-(3a*H*,6*H*)-dione (**171**)

To a solution of **138** (0.510 g, 2.08 mmol) in $CHCl_3$ (25 mL) was added *N*-phenylmaleimide (0.358 g, 2.07 mmol) This was stirred for 24 h at room temperature, and the solvent was evaporated. The ^1H nmr spectrum of the material displayed two sets of signals for adducts **170** and **171** in a ratio of 5:95, respectively. Chromatography (50% ethyl acetate/hexane) provided **171** (0.784 g, 95%), but the minor component co-eluted with unreacted *N*-phenylmaleimide, which gave a pale yellow solid (50 mg) consisting of **170** (33.0 mg, 4%) and unreacted dienophile (17 mg). Purified **170** was obtained by crystallization from $CHCl_3/CCl_4$.

For **170**: mp 253 - 254.5°C; ir (KBr) ν_{max}: 3068, 2921, 1776, 1713, 1517, 1347, 1196, 1085, 745 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 3.61 (2H, t, J = 1.6 Hz, C-4aH and C-7aH), 3.66 (2H, broad s, C-4H and C-8H), 4.12 (2H, t, J = 1.8 Hz, C-3aH and C-8aH), 6.26 (2H, dd, J = 4.5, 3.0 Hz, C-9H and C-10H), 6.50 (1H, s, C-2H), 7.19 (2H, d, J = 7.0 Hz, ArH), 7.26 - 7.51 (3H, m, ArH), 7.64 (2H, d, J = 8.7 Hz, ArH), 8.25 (2H, d, J = 8.7 Hz, ArH); n.O.e. results: δ 3.61: 6.50 (20.5%); δ 3.66: 4.12 (13%), 6.26 (11.5%); δ 4.12: 3.66 (20.5%), 6.26 (3.5%), 6.50 (2.5%), 7.64 (6%); δ 6.26: 3.66 (10%), 4.12 (2%); δ 6.50: 3.61 (3.5%), 7.64 (2.5%); δ 7.64: 4.12 (2%), 6.50 (5.5%), 8.25 (19.5%); ^{13}C nmr ($CDCl_3$) δ: 36.9 (C-4 and C-8), 37.8 (C-4a and C-7a), 74.4 (C-3a and C-8a), 105.5 (C-2), 123.7 (2 x ArC), 126.4 (2 x ArC), 126.7 (2 x ArC), 128.7 (1 x ArC), 129.1 (2 x ArC), 131.2 (C-9 and C-10), 134.1 (1 x ArC), 146.0 (1 x ArC), 148.2 (1 x ArC), 177.9 (C-5 and C-7); ms m/z (%): 418 (M^+, 10), 389 (65), 266 (7), 239 (8), 222 (25), 211 (6), 193 (15), 147 (12), 136 (10), 119 (52), 91 (100), 77 (20), 65 (5), 51 (8).

For **171**: mp 273 - 274°C; ir (KBr) ν_{max}: 3070, 2972, 1776, 1706, 1520, 1390 cm^{-1}; ^1H nmr ($(CD_3)_2SO$) δ: 3.12 (2H, s, C-4aH and C-7aH), 3.46 (2H, broad s, C-4H and C-8H), 4.56 (2H, s, C-3aH and C-8aH), 6.13 (1H, s, C-2H), 6.28 (2H, t, *J* = 3.8 Hz, C-9H and C-10H), 7.14 (2H, d, *J* = 7.2 Hz, ArH), 7.37 - 7.48 (3H, m, ArH), 7.63 (2H, d, *J* = 8.6 Hz, ArH), 8.23 (2H, d, *J* = 8.6 Hz, ArH); ^1H nmr ($CDCl_3$) δ: 2.96 (2H, s, C-4aH and C-7aH), 3.75 (2H, broad s, C-4H and C-8H), 4.46 (2H, s, C-3aH and C-8aH), 6.14 (1H, s, C-2H), 6.36 (2H, t, *J* = 3.7 Hz, C-9H and C-10H), 7.18 (2H, d, *J* = 7.5 Hz, ArH), 7.39 - 7.48 (3H, m, ArH), 7.58 (2H, d, *J* = 8.5 Hz, ArH), 8.23 (2H, d, *J* = 8.5 Hz, ArH); n.O.e. results ($CDCl_3$): δ 2.96: 3.75 (9%), 4.46 (16%); δ 3.75: 2.96 (5%), 4.46 (6%), 6.36 (11.5%); δ 4.46: 2.96 (17%), 3.75 (11.5%), 6.14 (4%), 7.58 (4%); δ 6.14: 6.36 (1.5%), 7.58 (2%); δ 6.36: 3.75 (9.5%), 6.14 (9%); δ 7.58: 6.14 (6.5%), 8.23 (20%); ^{13}C nmr ($(CD_3)_2SO$) δ : 36.9 (C-4 and C-8), 40.0 (C-4a and C-7a), 77.6 (C-3a and C-8a), 103.2 (C-2), 123.6 (2 x ArC), 126.9 (2 x ArC), 127.4 (2 x ArC), 128.5 (1 x ArC), 128.9 (2 x ArC), 130.5 (C-9 and C-10), 132.2 (1 x ArC), 146.4 (1 x ArC), 147.7 (1 x ArC), 176.7 (C-5 and C-7); ms *m/z* (%): 418 (M^+, 4), 389 (7), 296 (5), 268 (8), 222 (18), 174 (24), 150 (23), 120 (99), 91 (100), 77 (29), 65 (22), 51 (13).

Diels-Alder reaction of **142**: (1a*R**,2α,2aα,5aα,6α,6a*S**)-1a,2a,5a,6,6a-pentahydro-2,6-etheno-4-phenyl-2*H*-oxireno[*f*]isoindole-3,5(4*H*)-dione (**172**)

To a solution of **141** (0.838 g, 3.27 mmol) in dry ether (10 mL) was added DBU (2.0 g, 13 mmol) in dry ether (5 mL). This was stirred at room temperature for 24 h, after which workup of the **142/143** mixture was carried out as previously described. *N*-Phenylmaleimide (0.584 g, 3.37 mmol) was added in $CHCl_3$ (25 mL), and this solution was stirred for a further 16 h. Evaporation of the solvent left a yellow residue, whose ^1H

nmr spectrum showed signals for only one adduct. Chromatography (30% EtOAC/hexane) followed by crystallization ($CHCl_3$-C_6H_6) afforded **172** (0.274 g, 31% from **141**) as a colourless solid: mp 218-219°C; ir (KBr) ν_{max}: 3035, 1709, 1498, 1385, 1195, 726 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 3.05 (2H, t, *J* = 1.8 Hz, C-2aH and C-5aH), 3.27 (2H, m, C-1aH and C-6aH), 3.65 (2H, m, C-2H and C-6H), 5.91 (2H, dd, *J* = 3.6, 4.6 Hz, C-7H and C-8H), 7.15 (2H, d, *J* = 7.0 Hz, ArH), 7.34 - 7.46 (3H, m, ArH); n.O.e. results: δ 3.05: 3.37 (6%), 3.65 (6%); δ 3.37: 3.05 (5%), 3.65 (7%); δ 3.65: 3.05 (5%), 3.37 (6%), 5.91 (6%); δ 5.91: 3.65 (6%); ^{13}C nmr ($CDCl_3$) δ: 35.6 (C-2 and C-6), 41.9 (C-2a and C-5a), 47.1 (C-1a and C-6a), 126.3 (2 x ArC), 126.5 (C-7 and C-8), 128.6 (1 x ArC), 128.9 (2 x ArC), 131.4 (1 x ArC), 176.0 (C-3 and C-5); ms *m/z* (%): 267 (M^+, 35), 239 (2), 222 (5), 173 (22), 147 (4), 119 (32), 91 (100), 65 (23), 51 (11). Exact mass calcd. for $C_{16}H_{13}NO_3$: 267.0895; found: 267.0892.

Diels-Alder reaction of **148a**: (1a*R**,2α,2aα,5aα,6α,6a*S**)-2a,5a,6,-trihydro-1a,6a-dimethyl-2,6-etheno-4-phenyl-2*H*-oxireno[*f*]isoindole-3,5(1a*H*,4*H*,6a*H*)-dione (**173**)

To a solution of **148a/149a** (0.129 g, 1.05 mmol) in $CHCl_3$ (50 mL) was added *N*-phenylmaleimide (0.166 g, 0.958 mmol). This was heated at reflux for 10 h. Evaporation of the solvent provided a residue whose ^1H nmr spectrum showed signals for only one adduct. Chromatography (30% ethyl/acetate) afforded **173** (0.154 g, 83% from recovered dienophile) as a colourless solid: mp 261-262°C; ir (KBr) ν_{max}: 3020, 1709, 1498, 1388, 1195, 726 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.44 (6H, s, 2 x CH_3), 3.13 (2H, t, *J* = 1.6 Hz, C-2aH and C-5aH), 3.38 (2H, m, C-2H and C-6H), 5.97 (2H, dd, *J* = 3.6, 4.5 Hz, C-7H and C-8H), 7.15 (2H, d, *J* = 7.0 Hz, ArH), 7.37 - 7.47 (3H, m, ArH); n.O.e. results: δ 1.44: 3.13 (10.5%), 3.38 (12%); δ 3.13: 1.44 (2.5%), 3.38 (9.5%); δ 3.38: 1.44 (1%), 3.13 (5%), 5.97

(8.5%); δ 5.97: 3.38 (7.5%); ^{13}C nmr ($CDCl_3$) δ: 13.8 (2 x CH_3), 41.7 (C-2 and C-6), 42.2 (C-2a and C-5a), 57.6 (C-1a and C-6a), 126.3 (C-7 and C-8), 127.5 (2 x ArC), 128.7 (1 x ArC), 129.0 (2 x ArC), 131.5 (1 x ArC), 176.5 (C-3 and C-5); ms *m/z* (%): 295 (M^+, 7), 253 (29), 244 (2), 175 (10), 161 (9), 148 (8), 133 (8), 118 (11), 106 (77), 105 (76), 93 (19), 77 (28), 43 (100). Exact mass calcd for $C_{18}H_{17}NO_3$: 295.1207; found: 295.1209.

Diels-Alder reaction of **148b** with *N*-phenylmaleimide: (3aα,4α,4a*R**,7a*S**,8α,8aα)-3a,4,5,6,7,8,8a-heptahydro-2-phenyl-4a,7a-epoxy-4,8-ethenocyclopent[*f*]isoindole-1,3(2*H*,4a*H*,7a*H*)-dione (**174**)

A solution of **148b** (95 mg, 0.71 mmol) and *N*-phenylmaleimide (120 mg, 0.71 mmol) in $CHCl_3$ (1 mL) was stirred at room temperature for 16 h, and the solvent was evaporated. The ^{1}H nmr spectrum of the residue showed signals for only one adduct. Chromatography (30% ethyl acetate/hexane) provided **174** (157 mg, 72%) as a colourless solid: mp 261-262°C; ir (KBr) ν_{max}: 2967, 1713, 1384, 1185 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 1.74 - 1.88 (4H, m,), 2.03 (2H, m), 3.26 (2H, t, *J* = 1.7 Hz, C-3aH and C-8aH), 3.65 (2H, m, C-4H and C-8H), 6.03 (2H, dd, *J* = 3.3, 4.7 Hz), 7.16 (2H, d, *J* = 7.0 Hz, ArH), 7.38 - 7.48 (3H, m, ArH); n.O.e. results: δ 1.75: 2.03 (30%), 3.26 (13.5%); δ 2.03: 1.75 (10.5%), 3.65 (3%); δ 3.26: 1.75 (4%), 3.65 (12%); δ 3.65: 3.26 (5.5%), 6.03 (11%); δ 6.03: 3.65 (10.5%); ^{13}C nmr ($CDCl_3$) δ: 25.0 (1 x CH_2), 25.3 (2 x CH_2), 37.4 (C-4 and C-8), 42.2 (C-3a and C-8a), 64.2 (C-4a and C-7a), 126.3 (2 x ArC), 127.9 (C-10 and C-11), 128.6 (1 x ArC), 129.0 (2 x ArC), 131.4 (1 x ArC), 176.3 (C-1 and C-3); ms *m/z* (%): 307 (M^+, 74), 279 (5), 262 (5), 251 (3), 224 (3), 187 (12), 173 (33), 160 (17), 134 (100), 117 (31), 106 (28), 91 (47), 78 (42), 65 (17), 51 (17). Exact mass calcd. for $C_{19}H_{17}NO_3$: 307.1207; found: 307.1193.

Diels-Alder reaction of **148b** with *N*-methylmaleimide: (3aα,4α,4a*R**,7a*S**,8α,8aα)-3a,4,5,6,7,8,8a-heptahydro-2-methyl-4a,7a-epoxy-4,8-ethenocyclopent[*f*]isoindole-1,3(2*H*,4a*H*,7a*H*)-dione (**175**)

A solution of **148b** (0.231 mg, 1.72 mmol) and *N*-methylmaleimide (0.192 g, 1.72 mmol) in $CHCl_3$ (2 mL) was stirred at room temperature for 16 h. The ^1H nmr spectrum of the residue obtained after evaporation of the solvent showed signals for only one adduct. Chromatography (50% ethyl acetate /hexane) of the residue gave **175** (0.327 mg, 77%) as a colourless solid: mp 151-153°C; ir (KBr) ν_{max}: 2942, 1771, 1702, 1435 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.62 - 2.05 (6H, m, 3 x CH_2), 2.89 (3H, s, CH_3), 3.06 (2H, m, C-3a and C-8a), 3.52 (2H, m, C-4H and C-8H), 5.88 (2H, dd, J = 3.3, 4.6 Hz, C-10 and C-11); n.O.e. results: approx. δ 2.75: approx. 2.00 (35%), 3.52 (8%); ^{13}C nmr ($CDCl_3$) δ: 24.4 (CH_3), 24.8 (C-6), 25.2 (C-5 and C-7), 36.9 (C-4 and C-8), 42.0 (C-3a and C-8a), 64.0 (C-4a and C-7a), 127.6 (C-10 and C-11), 177.2 (C-1 and C-3); ms *m/z* (%): 245 (M^+, 16), 217 (29), 200 (6), 186 (32), 173 (2), 160 (21), 134 (100), 117 (56), 104 (86), 91 (66), 78 (88), 65 (31), 51 (43), 39 (52). Exact mass calcd. for $C_{14}H_{15}NO_3$: 245.1051; found: 245.1056.

Diels-Alder reaction of **148b** with dimethylacetylenedicarboxylate: (3a*R**,4α,7α,7a*S**)-2,3,4,7-tetrahydro-5,6-bis[carbomethoxy]-3a,7a-epoxy-4,7-etheno-1*H*-indene (**176**)

To a solution of **148b** (0.166 g, 1.24 mmol) in $CHCl_3$ (5 mL) was added DMAD (150 μL, 1.24 mmol). This solution was stirred for 16 h at room temperature, after which evaporation of the solvent provided an orange oil, whose ^1H nmr spectrum showed signals for only one adduct. Chromatography (20% acetone/hexane) yielded a pale yellow oil that crystallized on standing (0.344 g, 84%): mp 72-75°C; ir (film) ν_{max}: 2954, 1717, 1635, 1435, 1329, 1270, 1055 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.60-1.98 (6H, m, 3 x CH_2),

3.80 (6H, s, 2 x OCH_3), 4.16 (2H, t, J = 3.7 Hz, C-4H and C-7H), 6.32 (2H, dd, J = 3.5, 4.2 Hz, C-9H and C-10H); ^{13}C nmr ($CDCl_3$) δ: 25.9 (1 x CH_2), 27.2 (2 x CH_2), 44.9 (C-9 and C-10), 52.3 (2 x OCH_3), 70.9 (C-3a and C-7a), 131.3 (C-9 and C-10), 147.2 (C-5 and C-6), 166.2 (2 x C=O); ms *m/z* (%): 276 (15), 244 (93), 219 (34), 217 (50), 205 (53), 189 (77), 185 (76), 173 (18), 157 (50), 145 (12), 129 (100), 115 (49), 102 (35), 91 (30), 77 (60), 65 (15), 59 (56).

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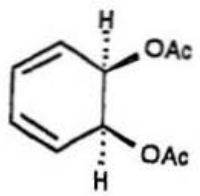
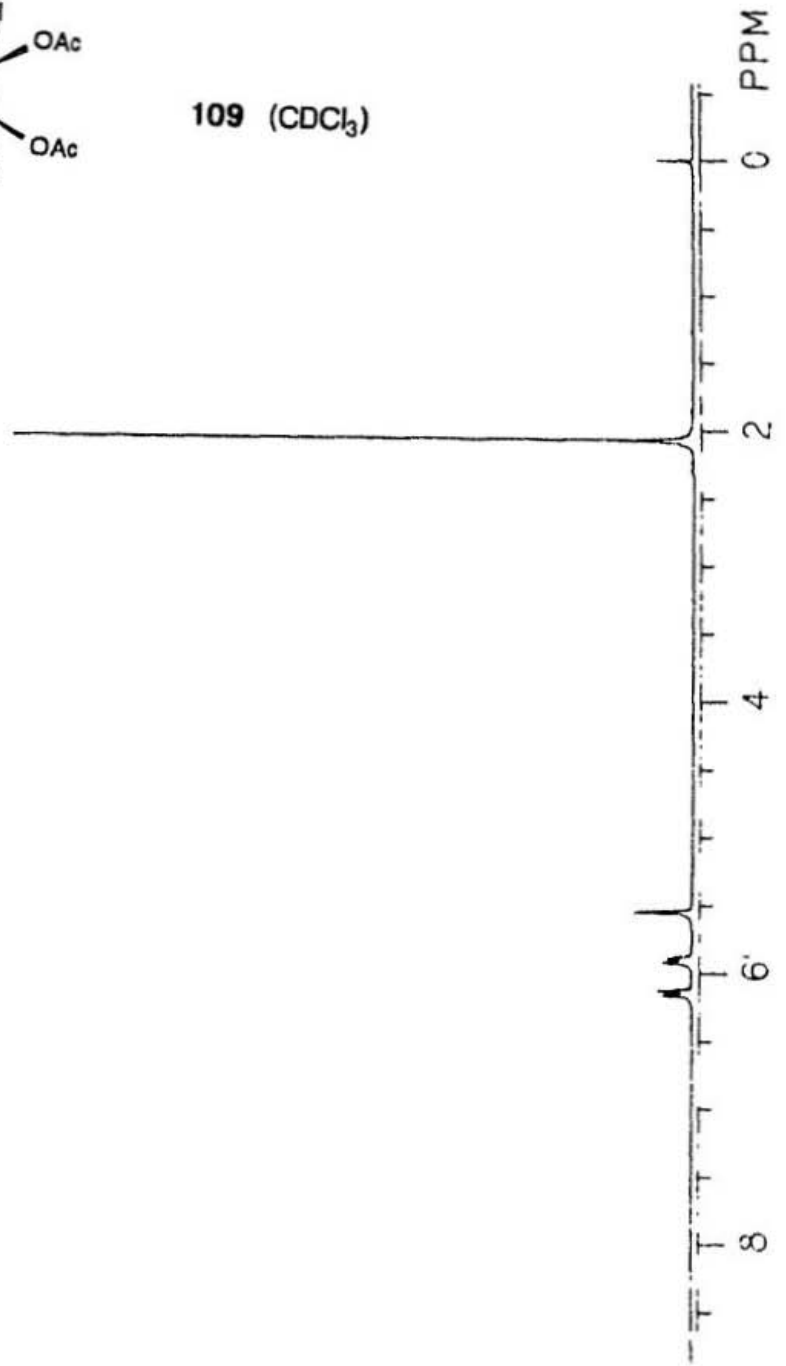
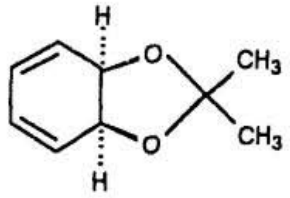
Appendix

The selected ^{1}H nmr spectra and the ^{1}H nmr n.O.e.d. spectra of dienes and adducts were arranged according to the order in which they appear in the text. For the instrument employed, see **Experimental, General.**

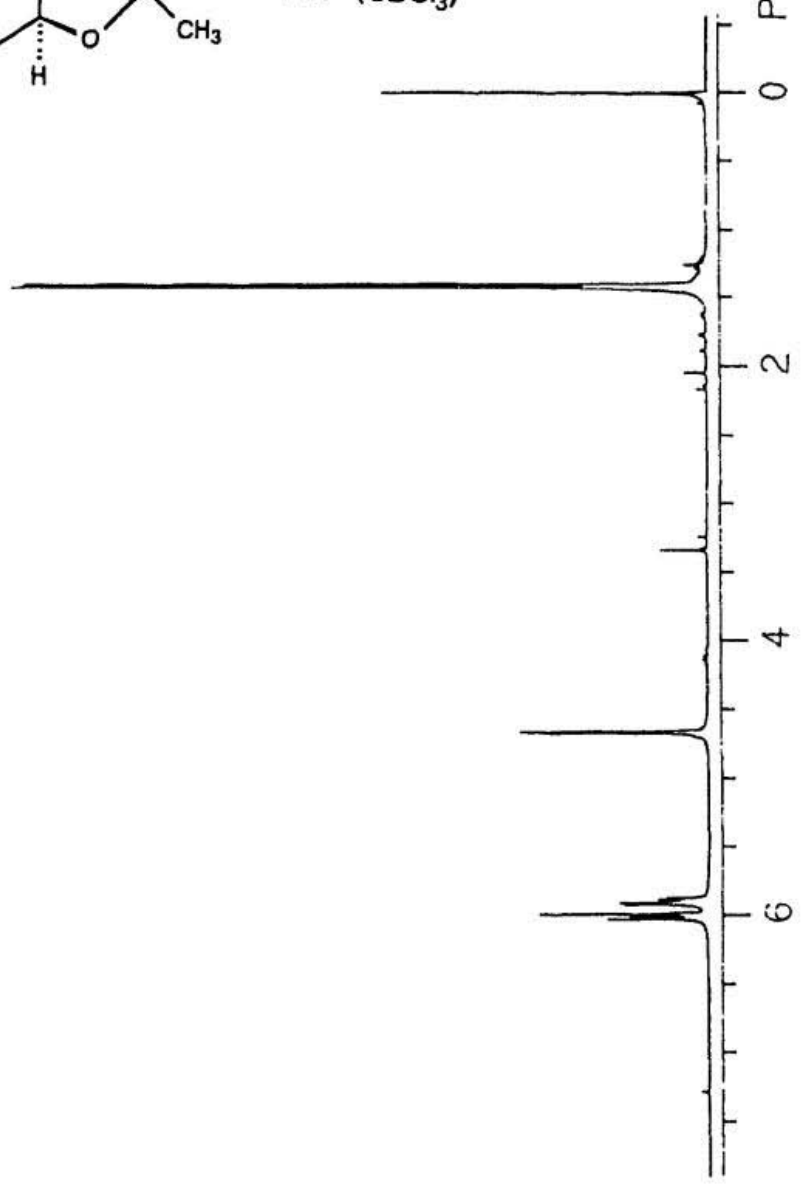


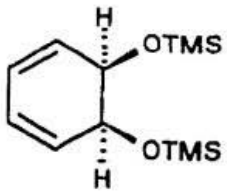
109 ($CDCl_3$)



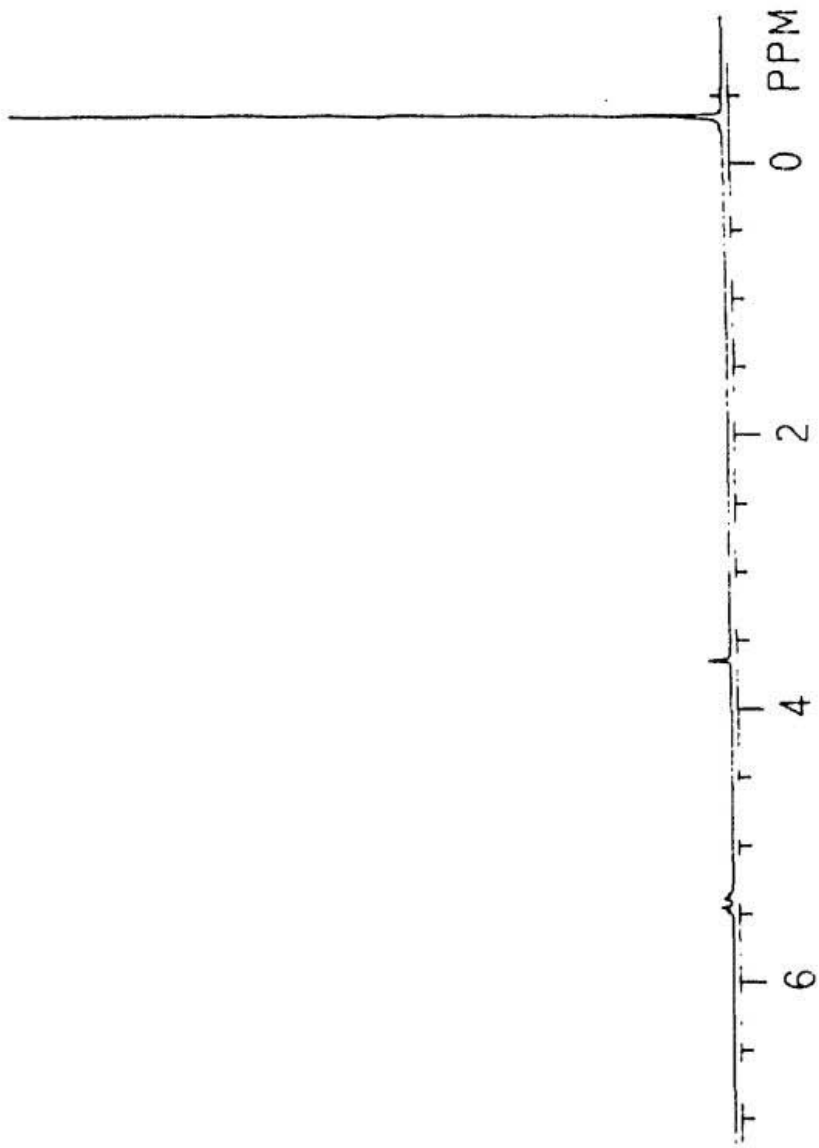


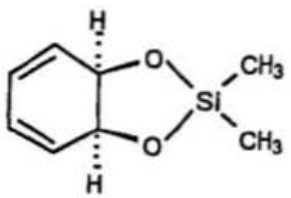
114 ($CDCl_3$)



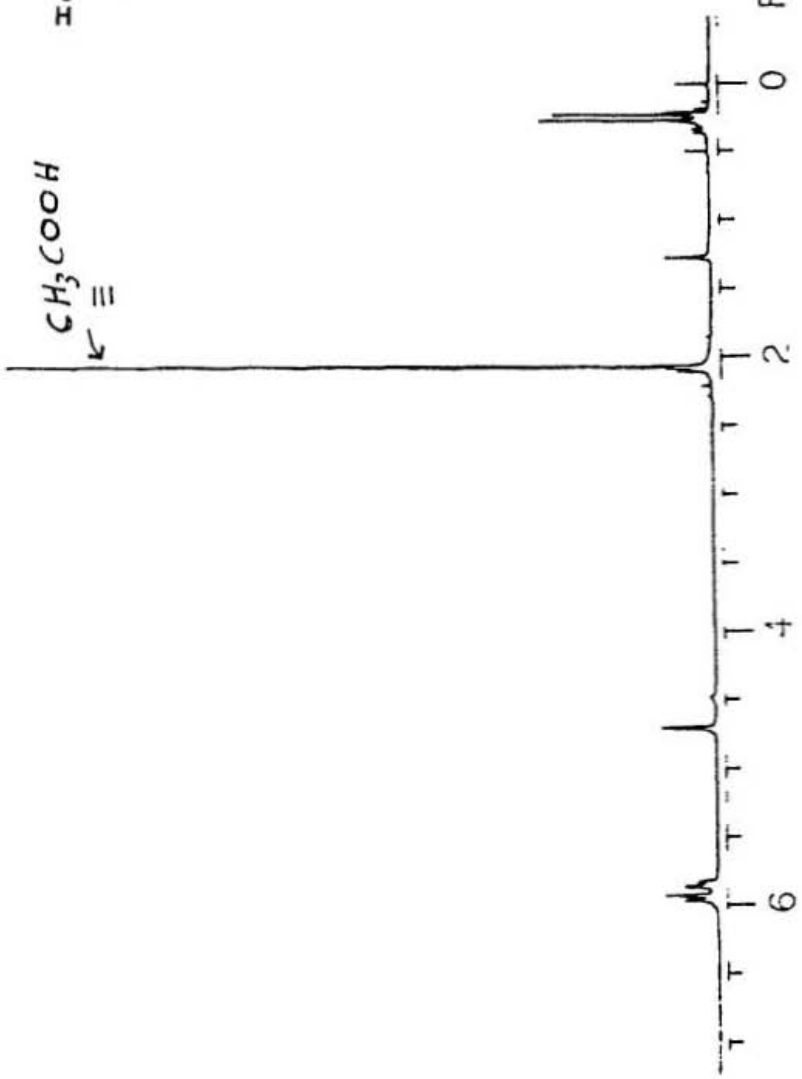


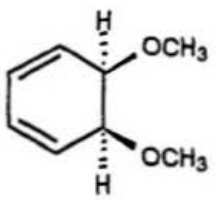
122 ($CDCl_3$)



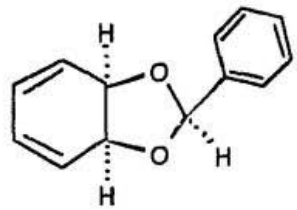


123 ($CDCl_3$)



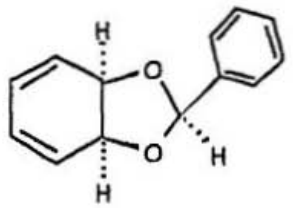


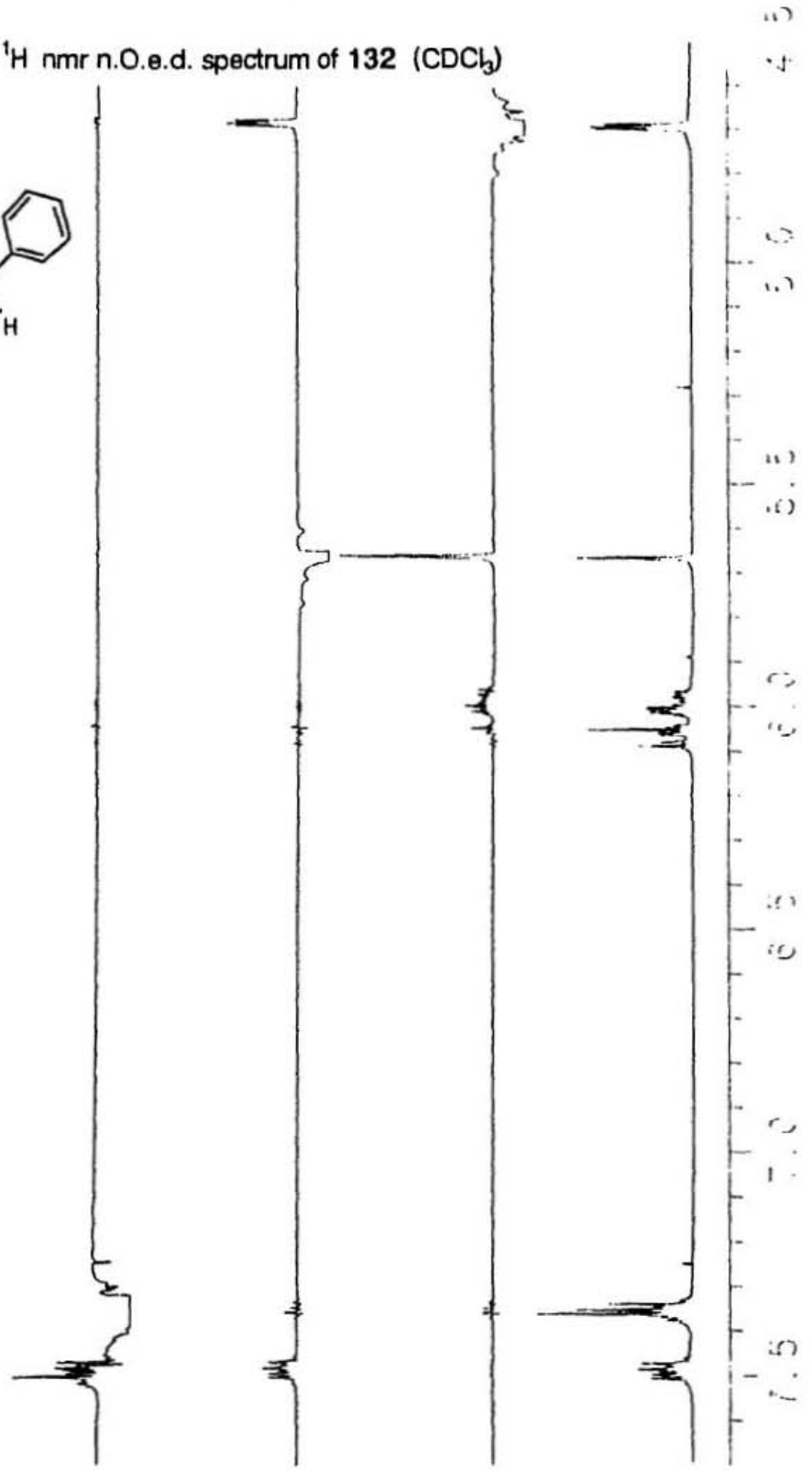
124 ($CDCl_3$)

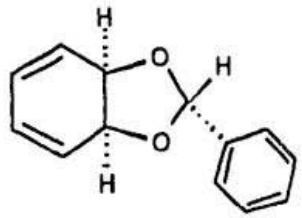


132 ($CDCl_3$)

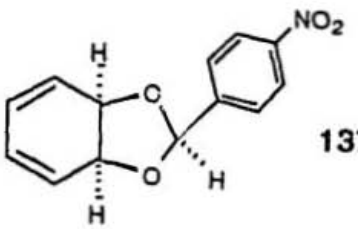
^{1}H nmr n.O.e.d. spectrum of **132** ($CDCl_3$)



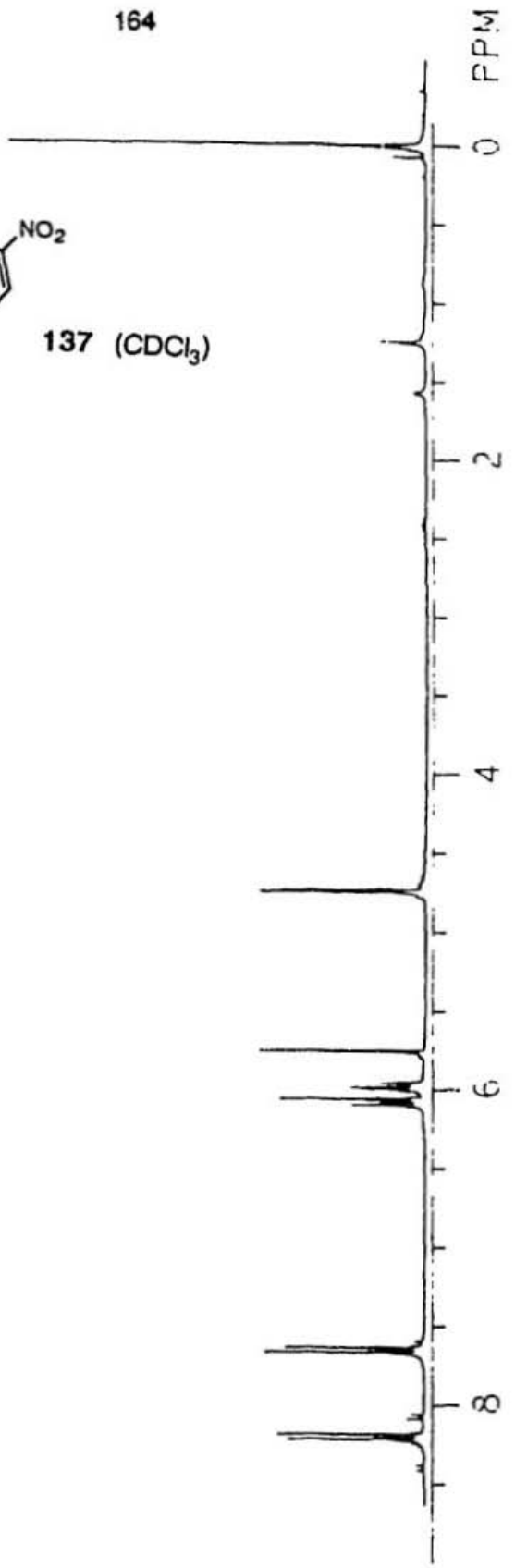




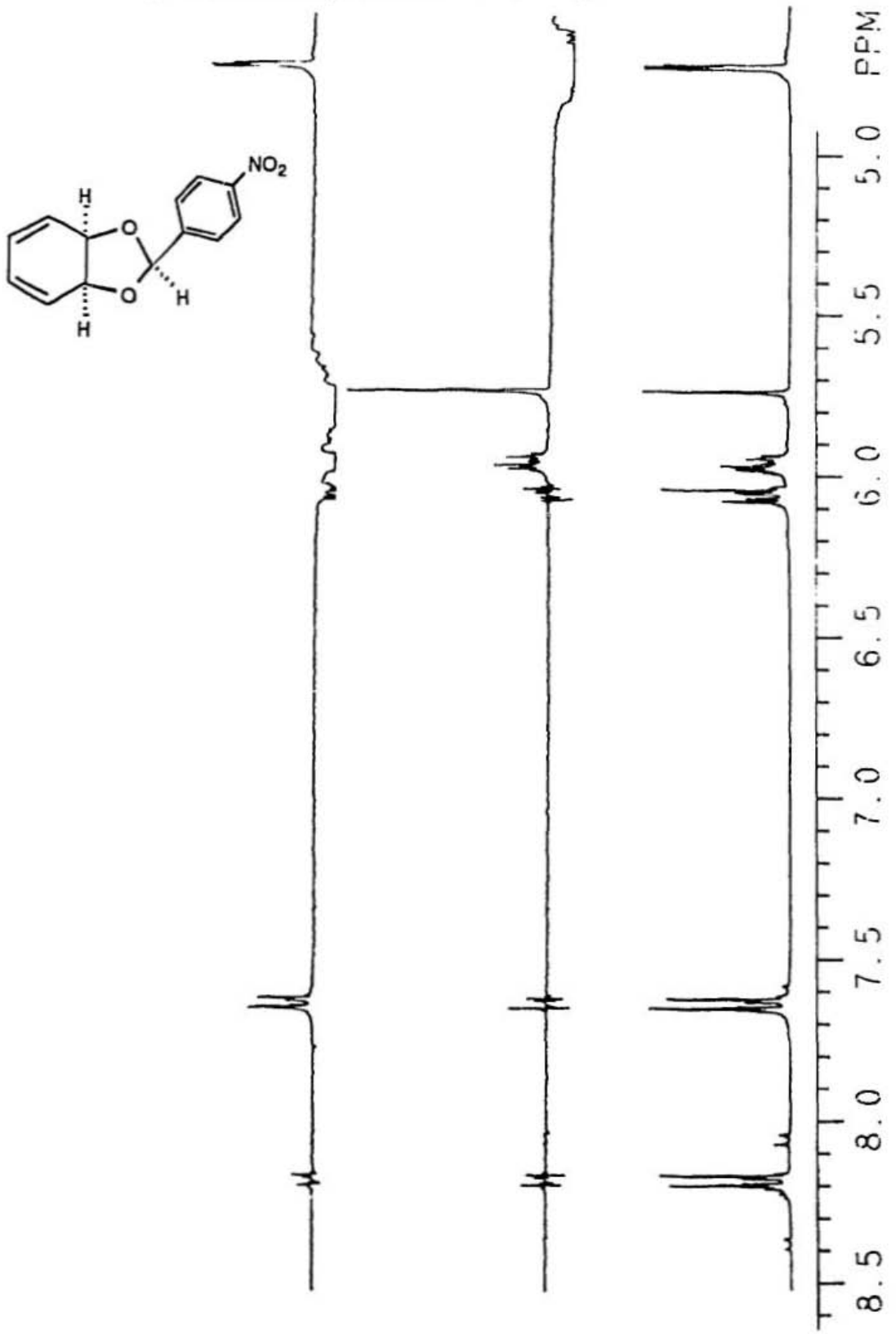
133 ($CDCl_3$)

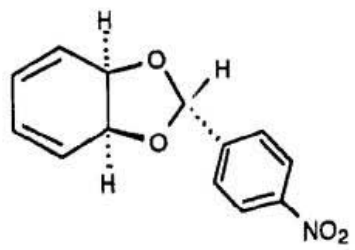


137 ($CDCl_3$)

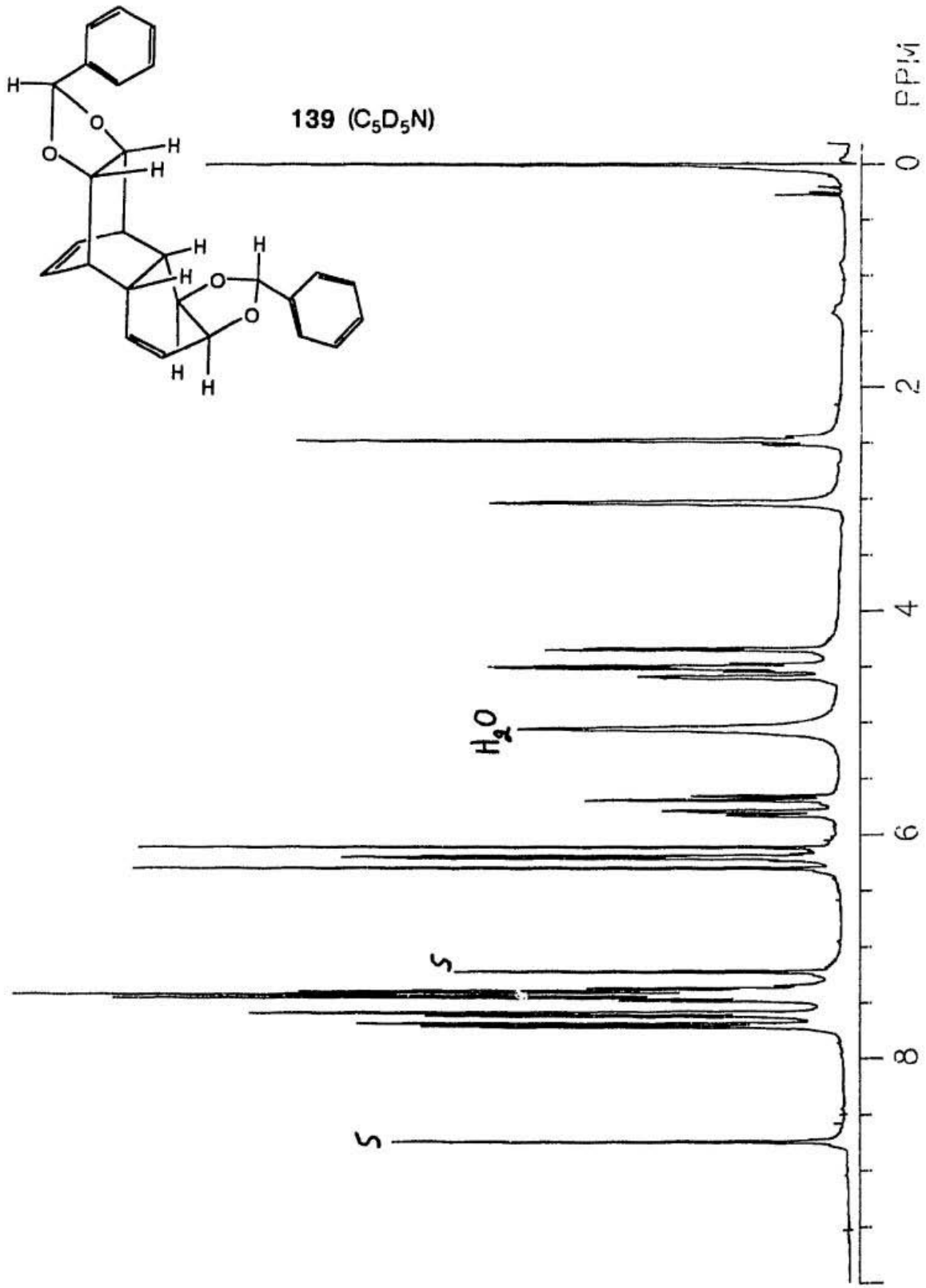


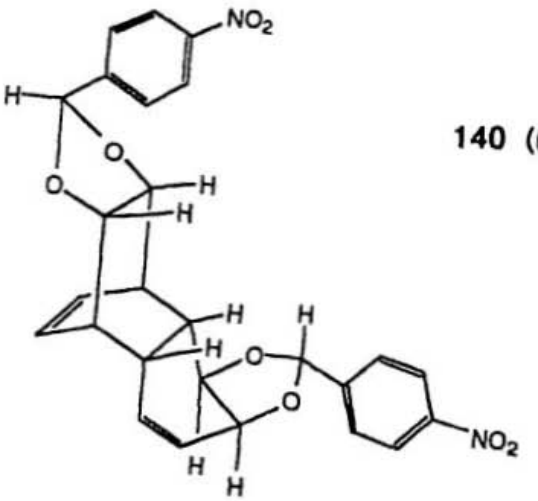
^{1}H nmr n.O.e.d. spectrum of **137** ($CDCl_3$)



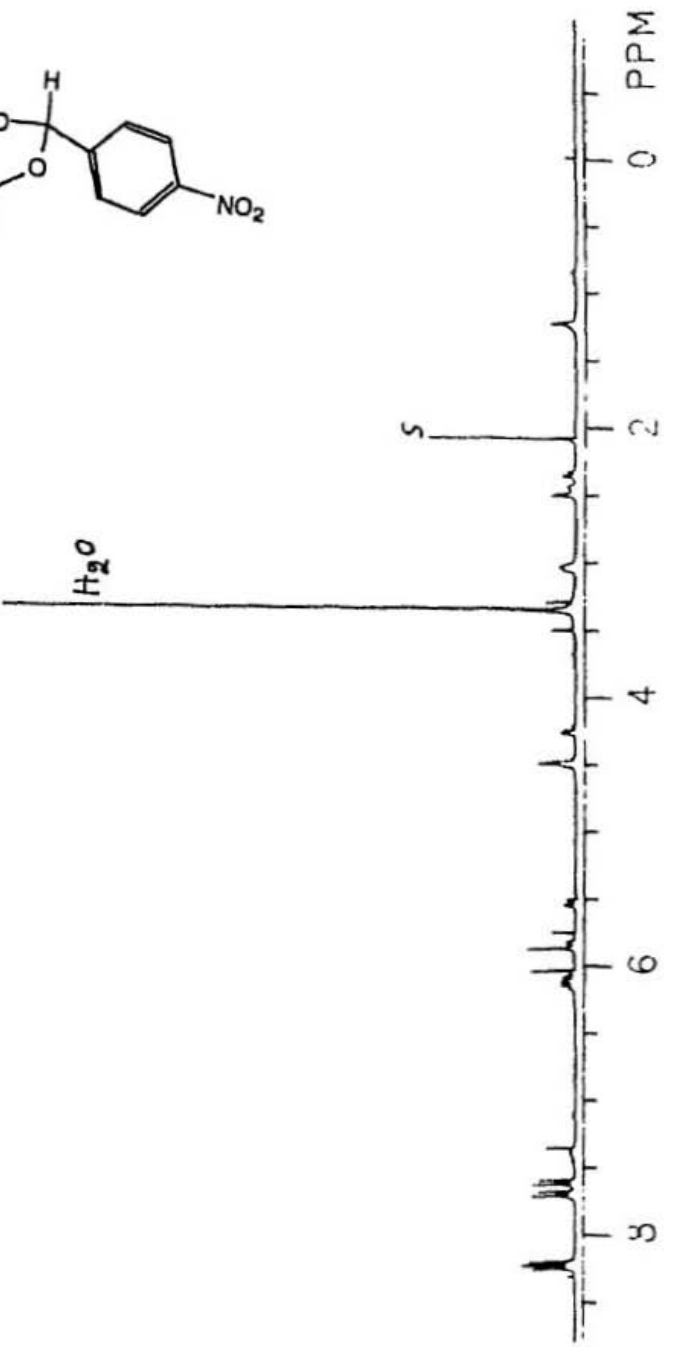


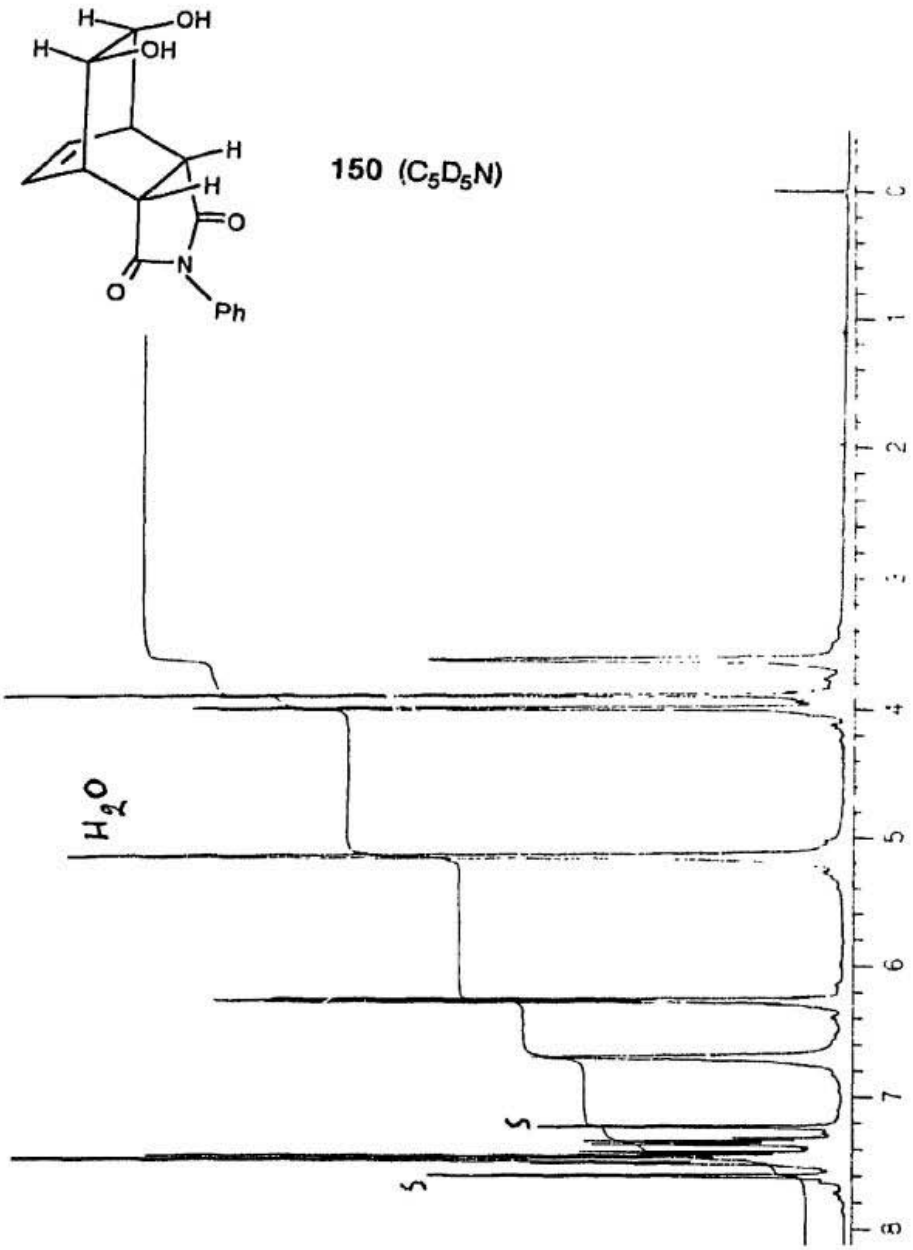
138 ($CDCl_3$)


139 (C_5D_5N)
H
O
H
H
H
H
O
H
O
H
H
TMS
H_2O
S
S
PPM
0
2
4
6
8



140 ($(CD_3)_2SO$)




H
OH
H
OH
H
H
O
N
O
Ph
150 (C5D5N)
H2O
S
S
0
1
2
3
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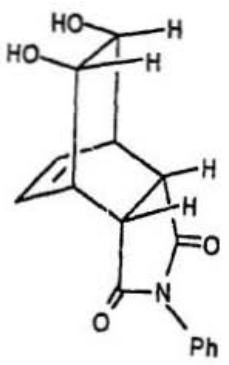
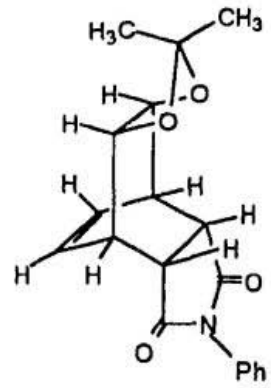
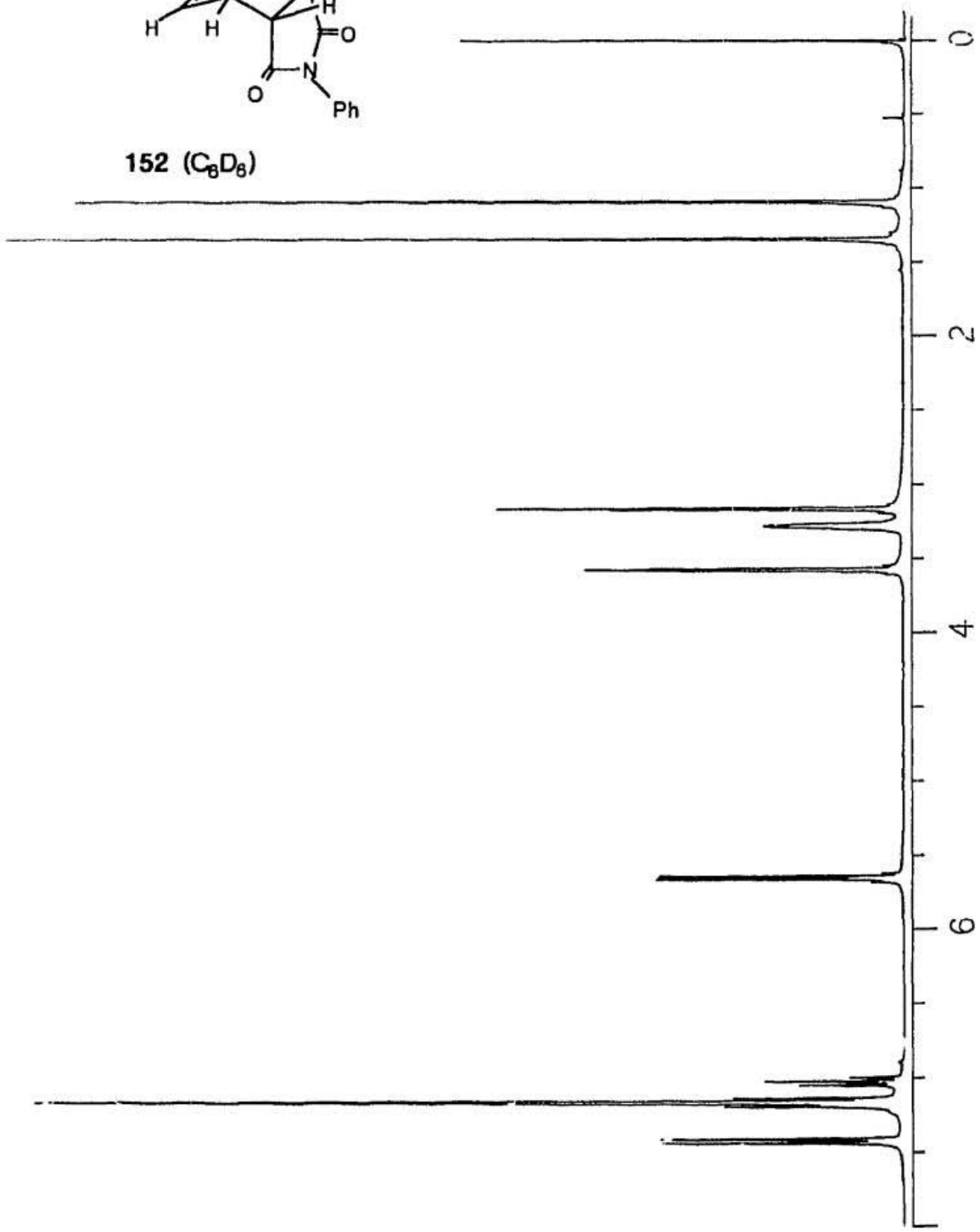
5
6
7
8

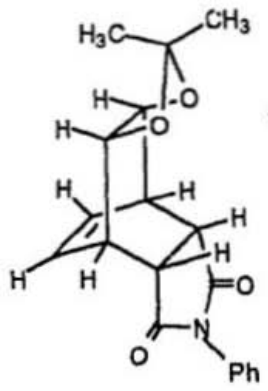


151 (C_5D_5N)

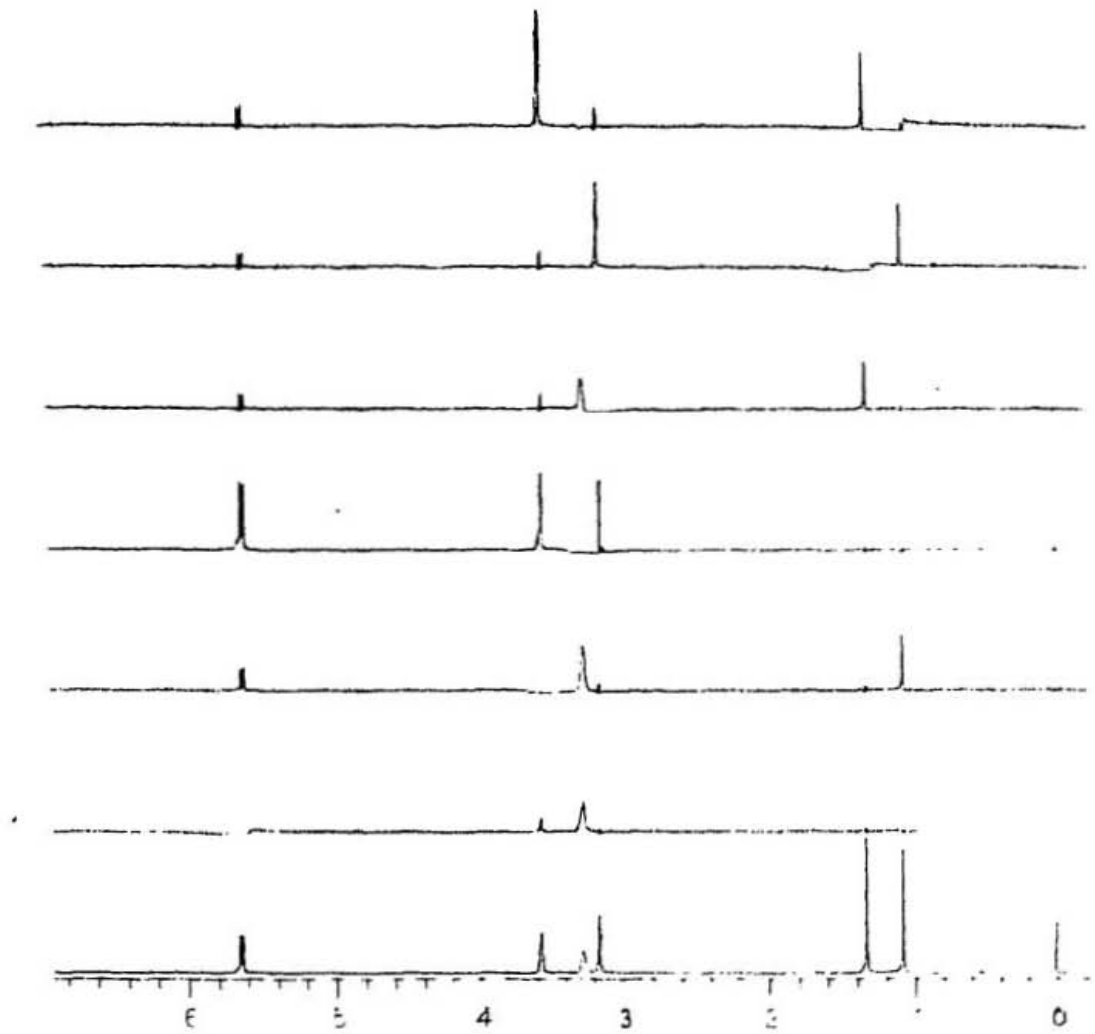


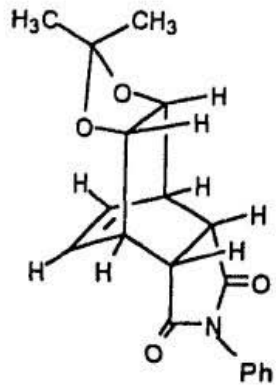
152 (C_6D_6)



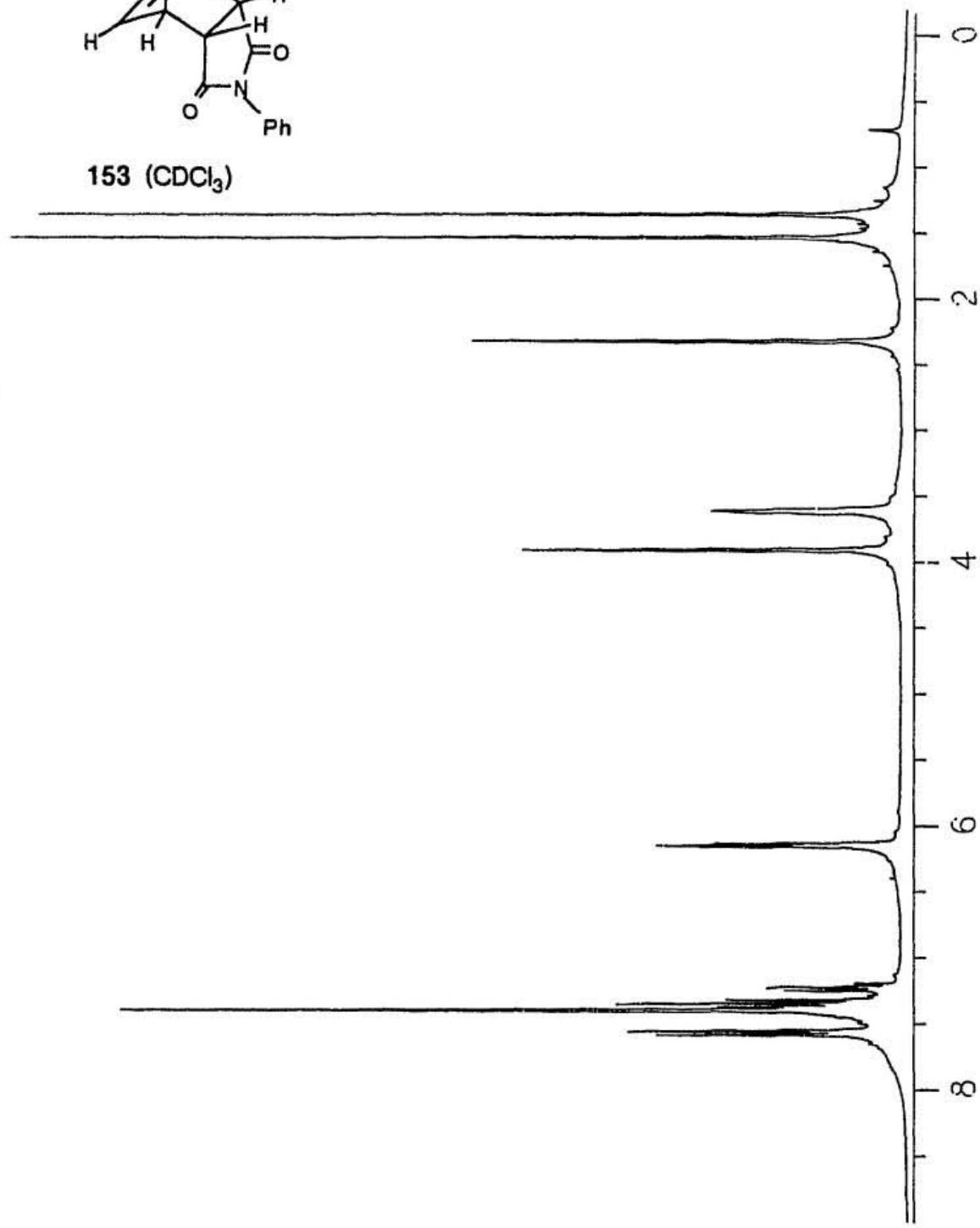


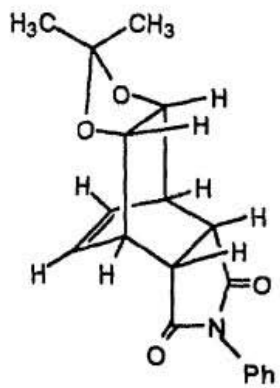
^{1}H nmr n.O.e.d. spectrum of **152** (C_6D_6)
aromatic signals not shown



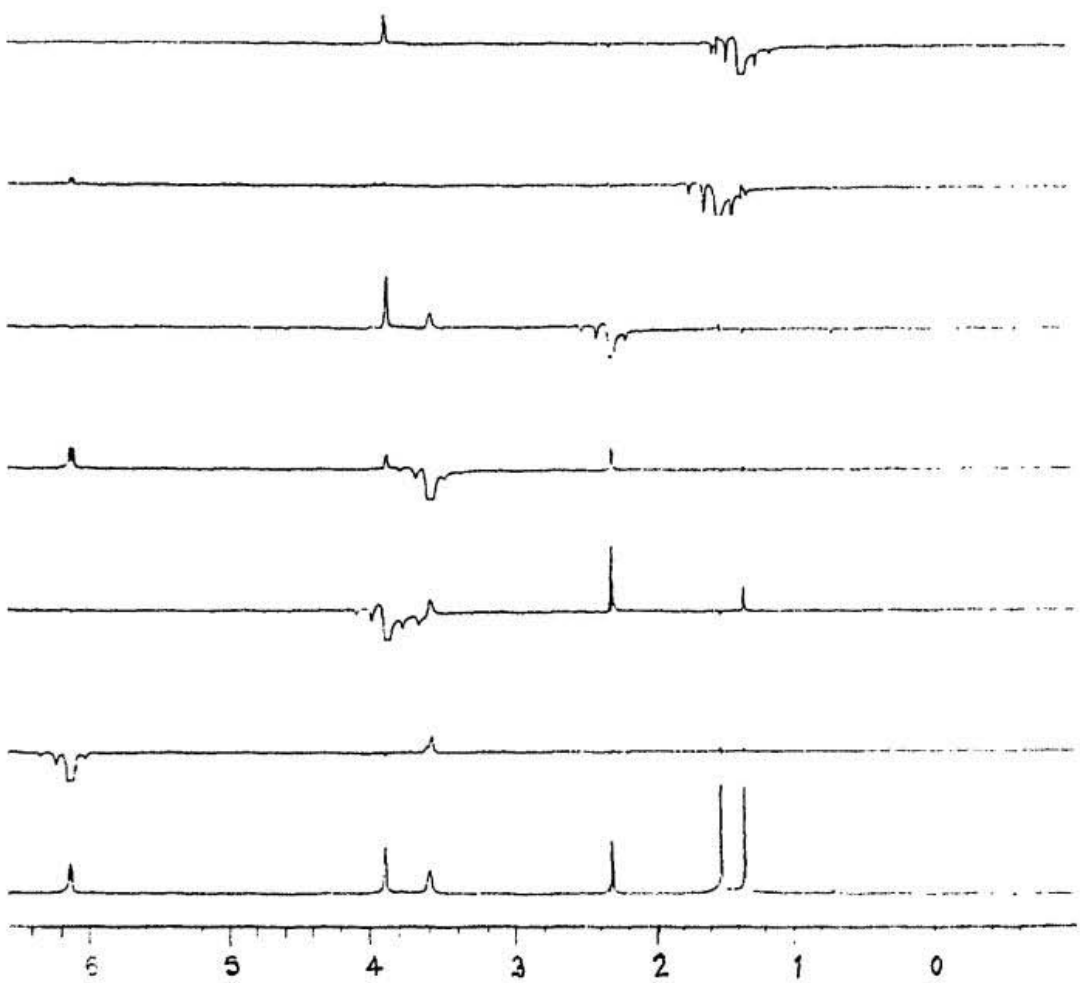


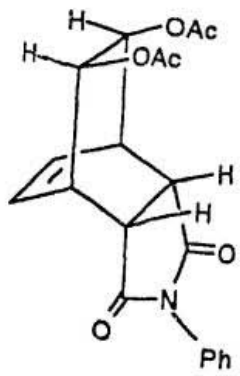
153 ($CDCl_3$)



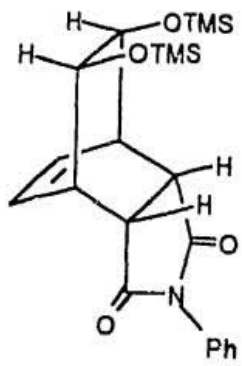


^{1}H nmr n.O.e.d. spectrum of **153** ($CDCl_3$)
aromatic signals not shown

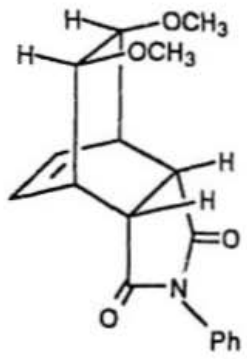




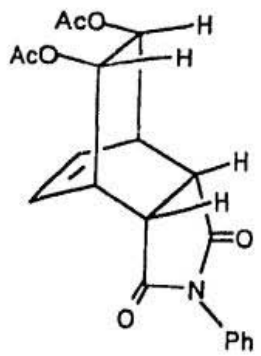
154 ($CDCl_3$)



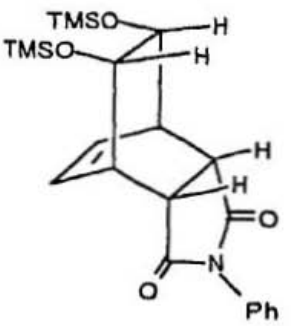
155 ($CDCl_3$)



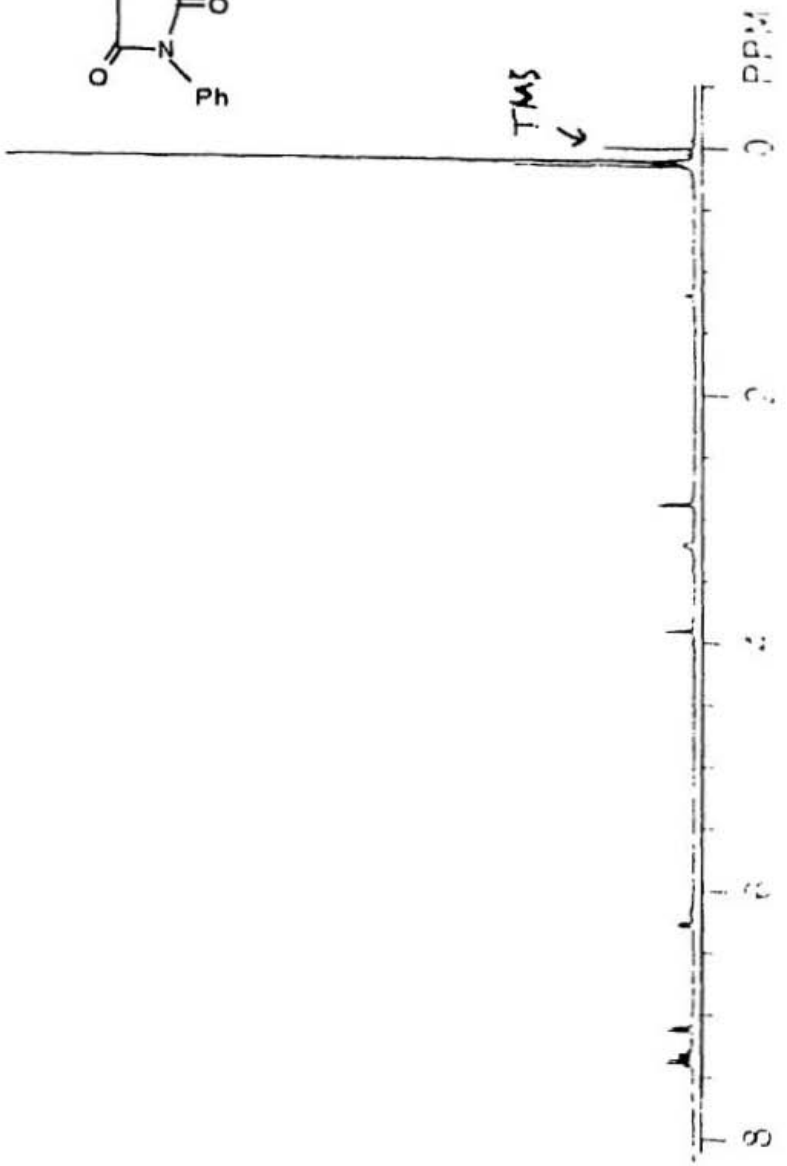
156 (C_5D_5N)

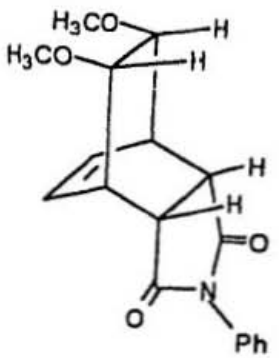


157 ($CDCl_3$)

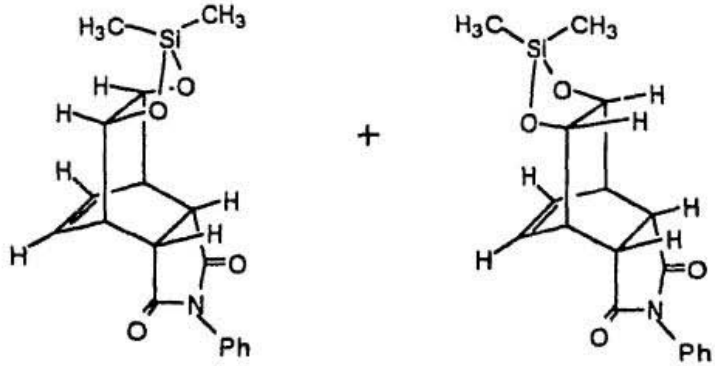


158 ($CDCl_3$)



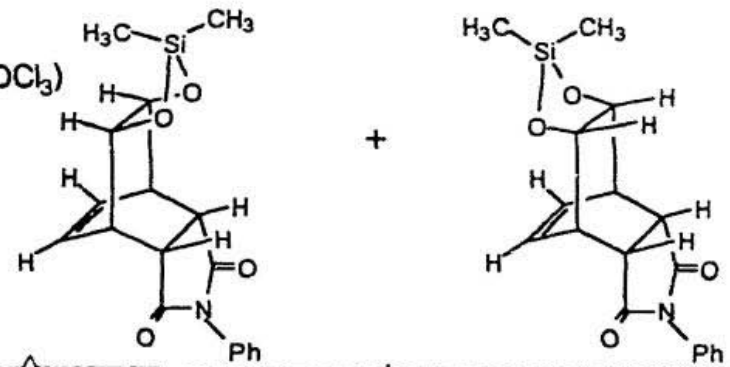


159 ($CDCl_3$)

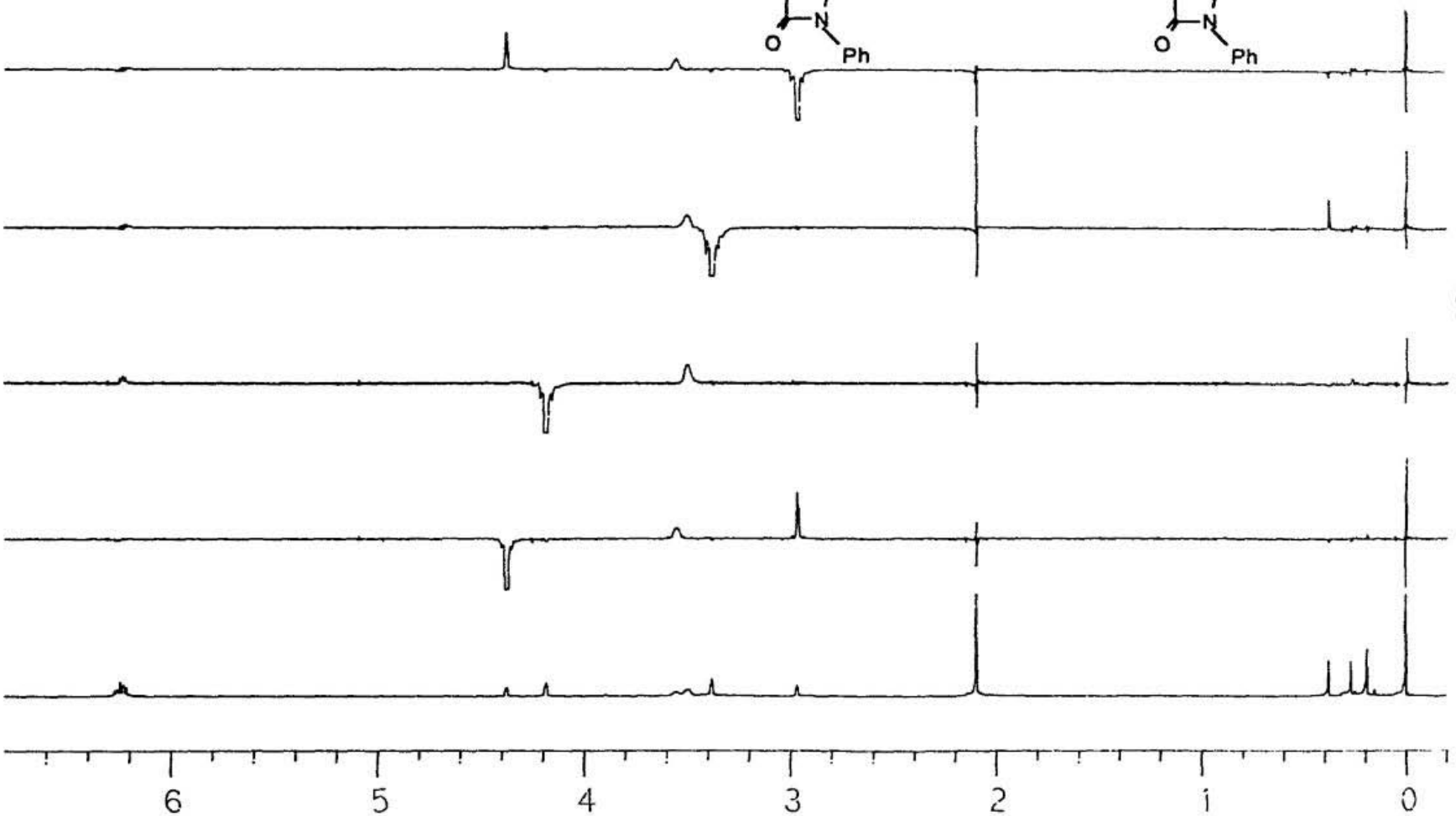


Mixture of **160** and **161** ($CDCl_3$)

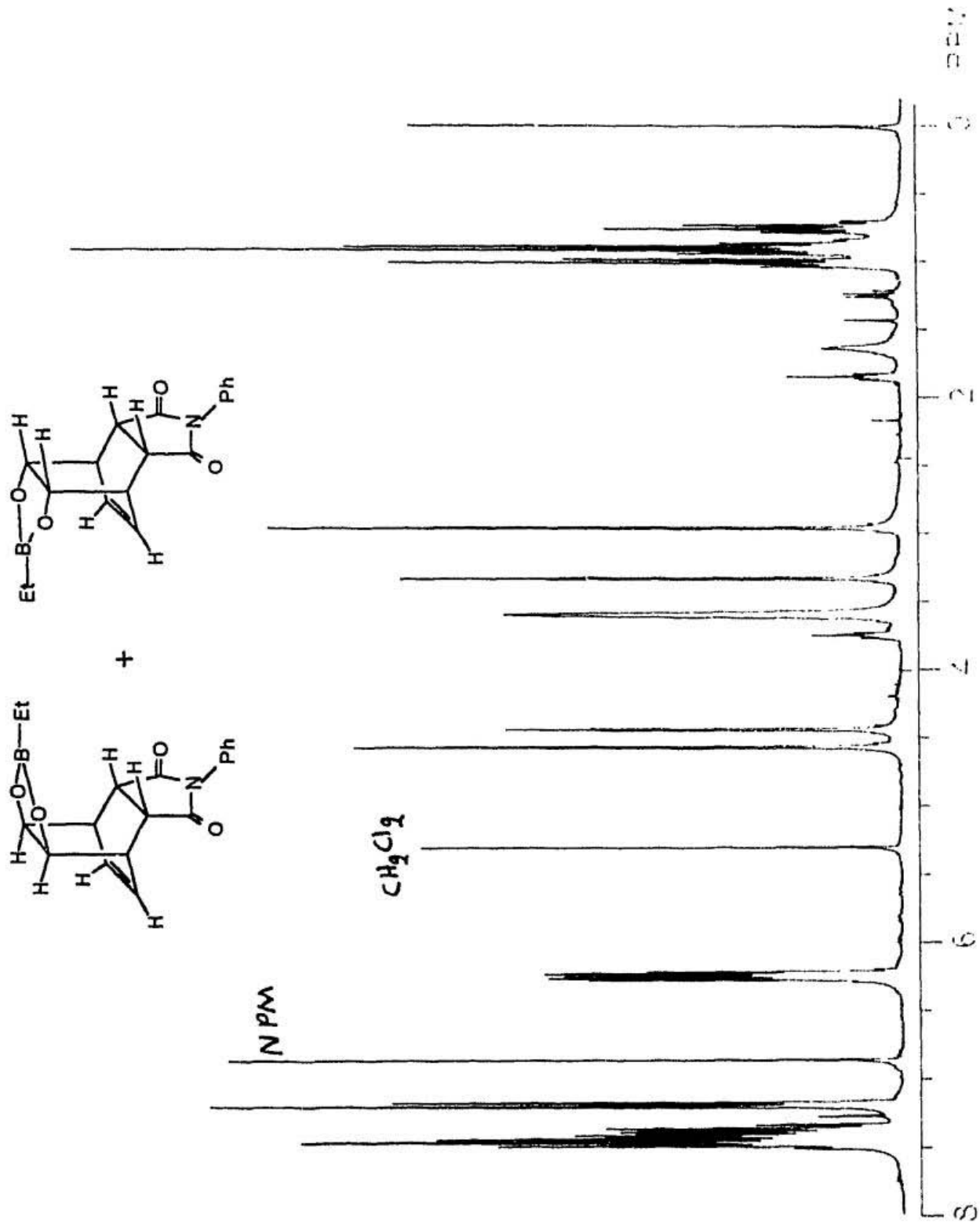
^{1}H nmr n.O.e.d. spectrum of mixture of **160** and **161** ($CDCl_3$)
aromatic signals not shown

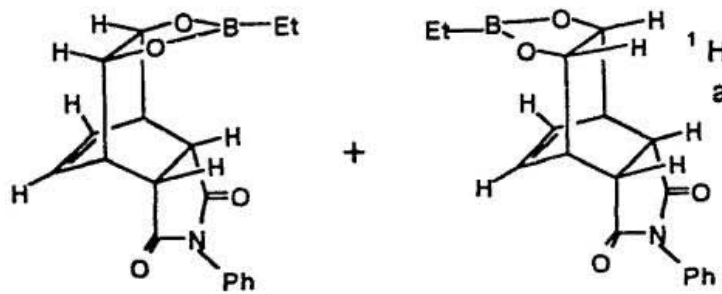


+



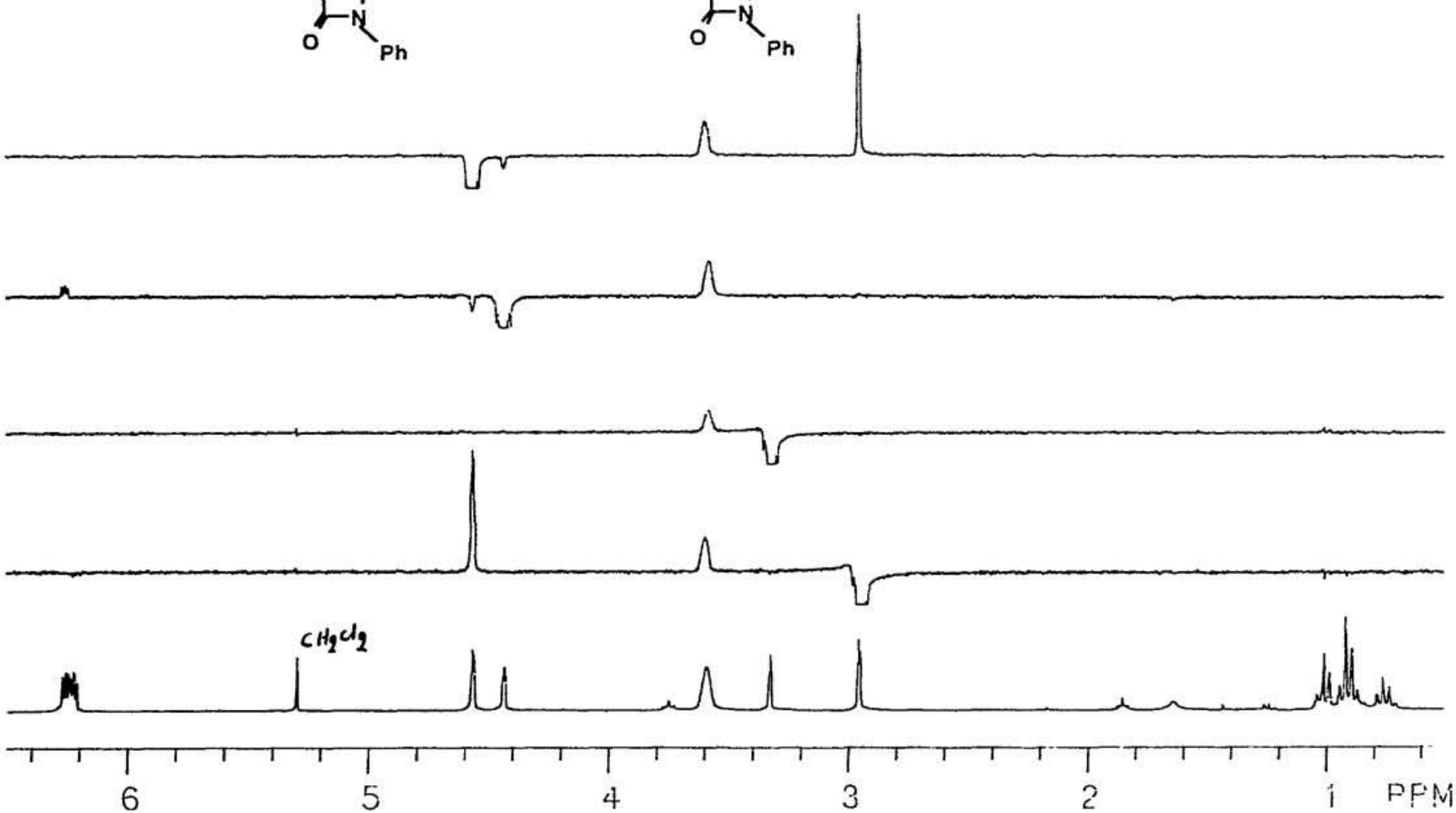
Mixture of **162** and **163** ($CDCl_3$)

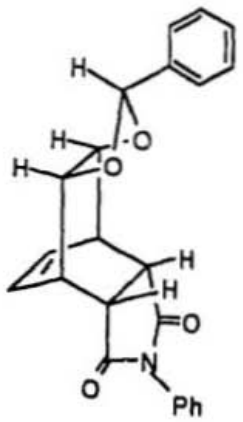




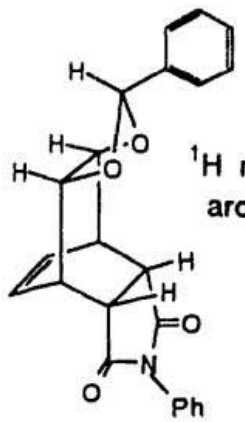
+

^{1}H nmr n.O.e.d. spectrum of mixture of **162** and **163** ($CDCl_3$)
aromatic signals not shown

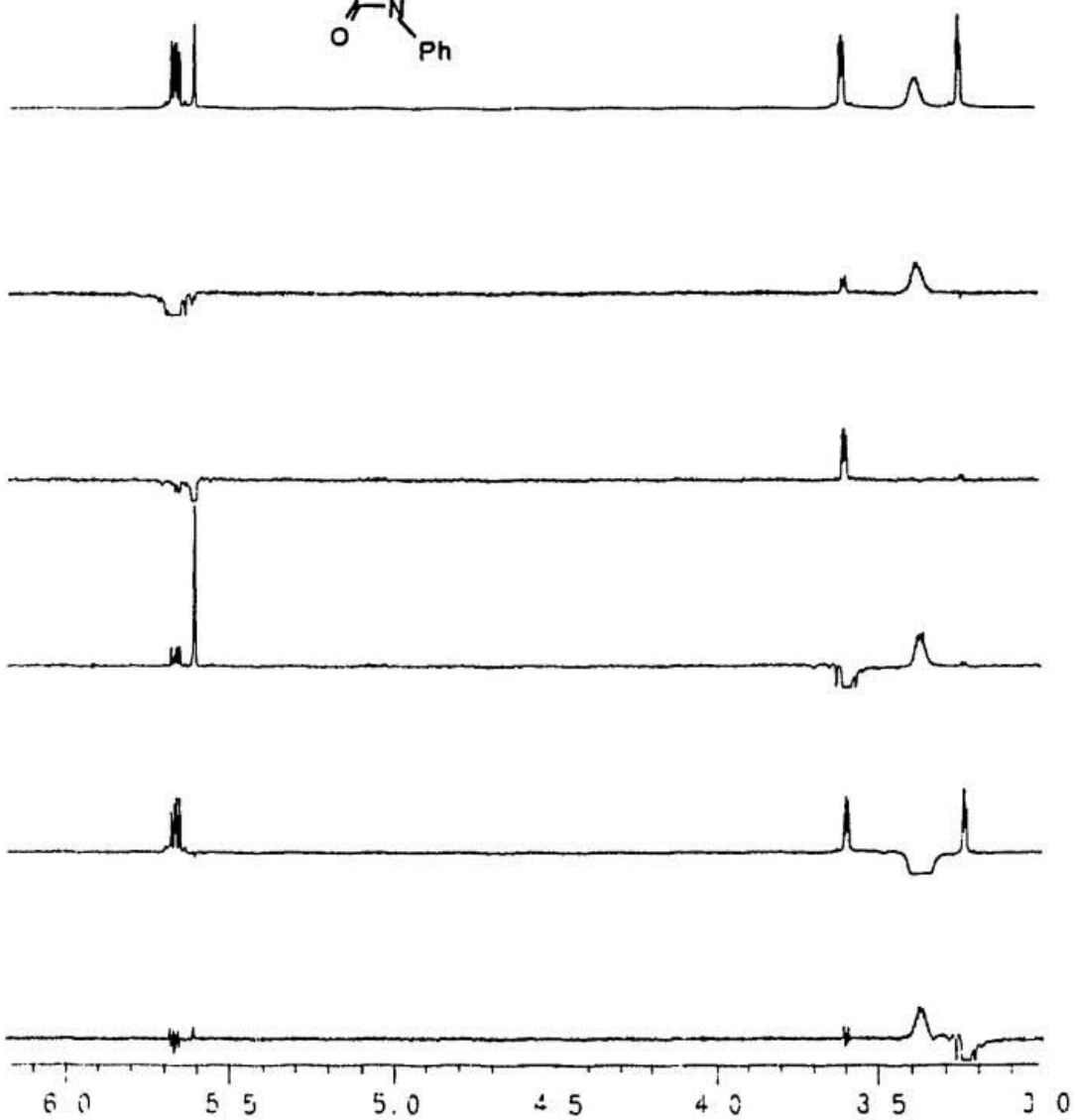


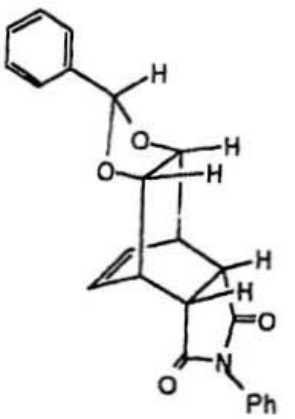


164 (C_6D_6)

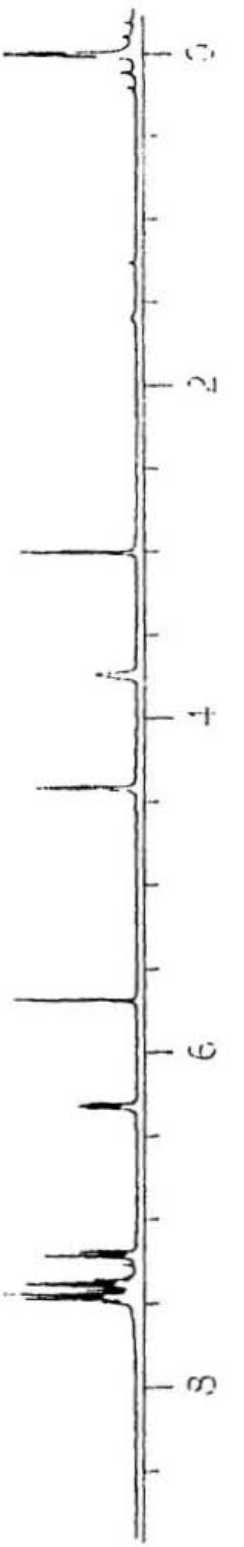


^{1}H nmr n.O.e.d. spectrum of **164** (C_6D_6)
aromatic signals not shown

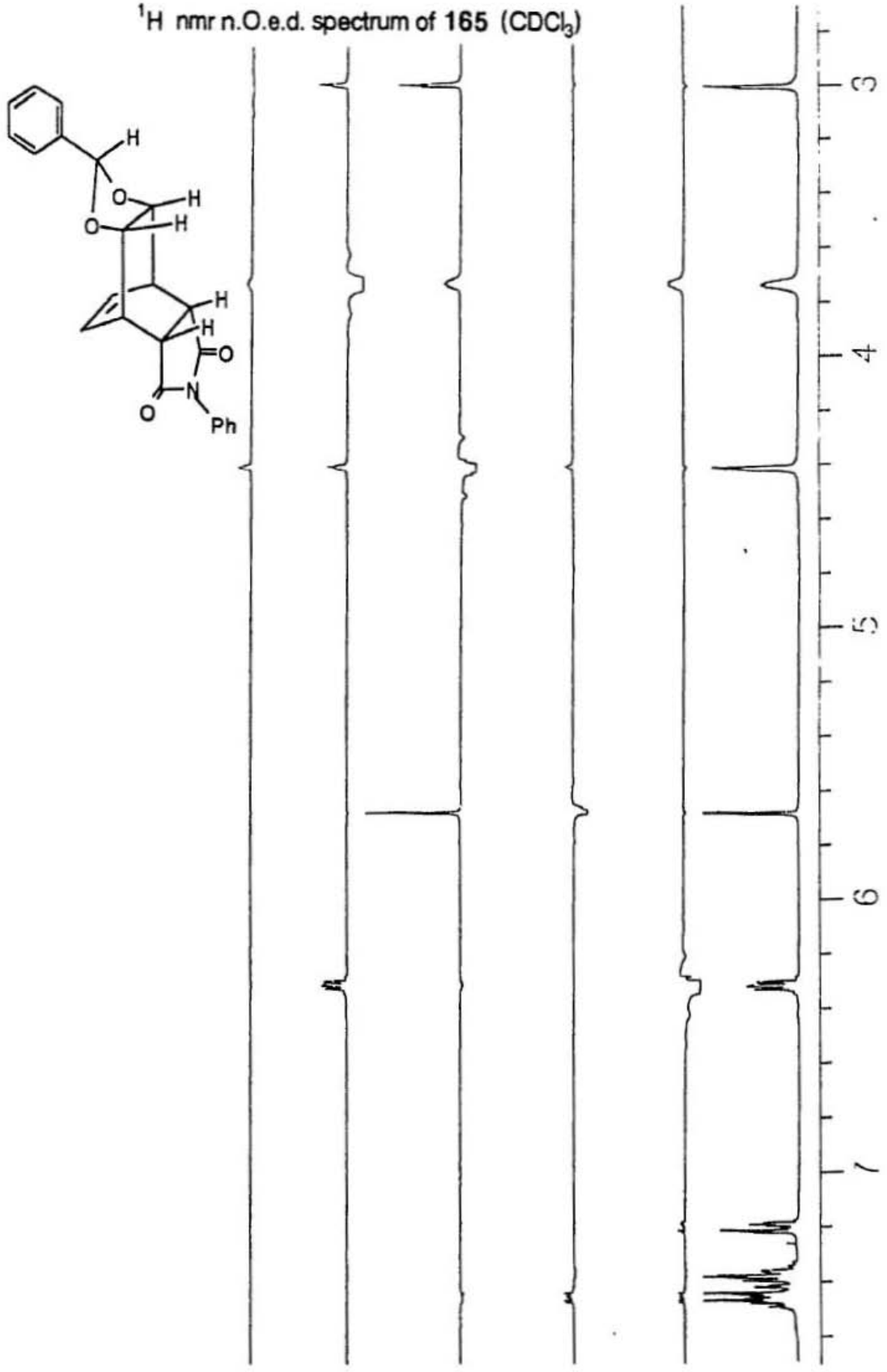


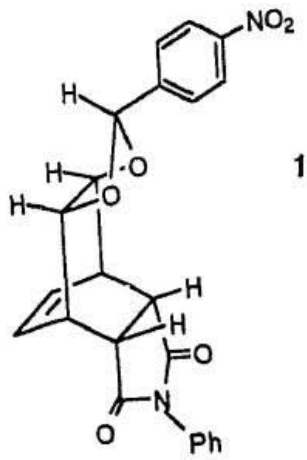


165 ($CDCl_3$)



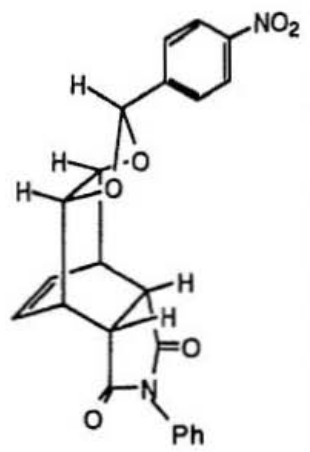
^{1}H nmr n.O.e.d. spectrum of **165** ($CDCl_3$)

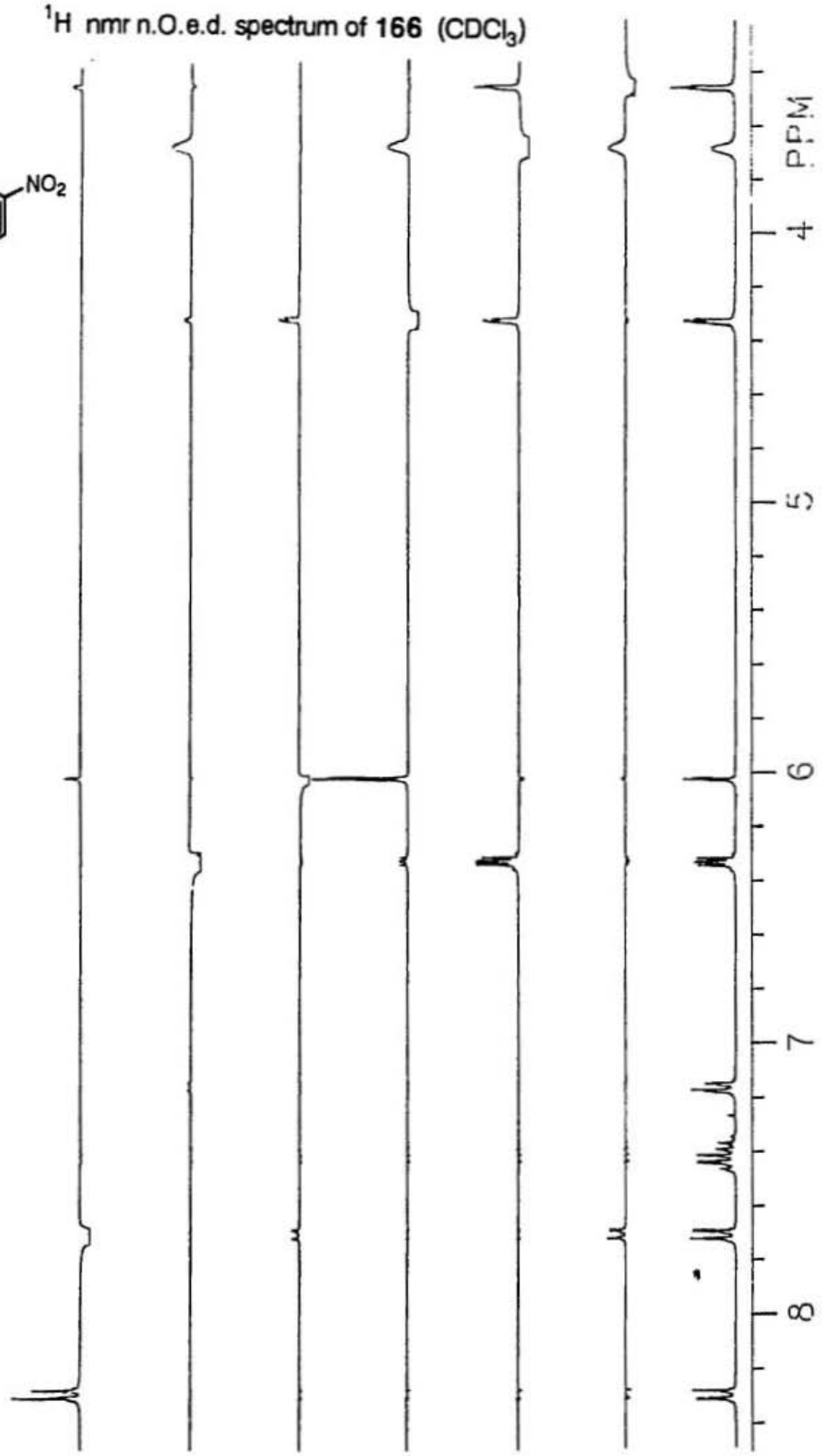


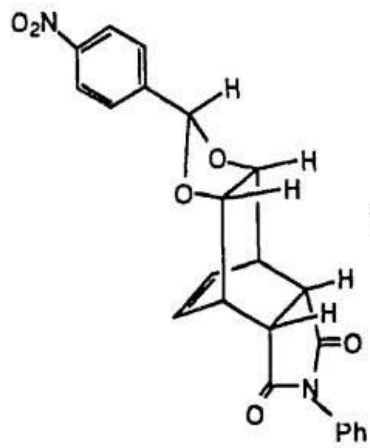


166 ($CDCl_3$)

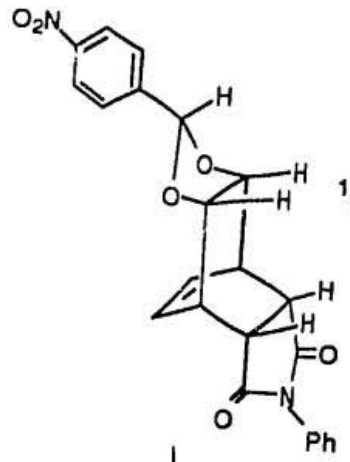
^{1}H nmr n.O.e.d. spectrum of **166** ($CDCl_3$)



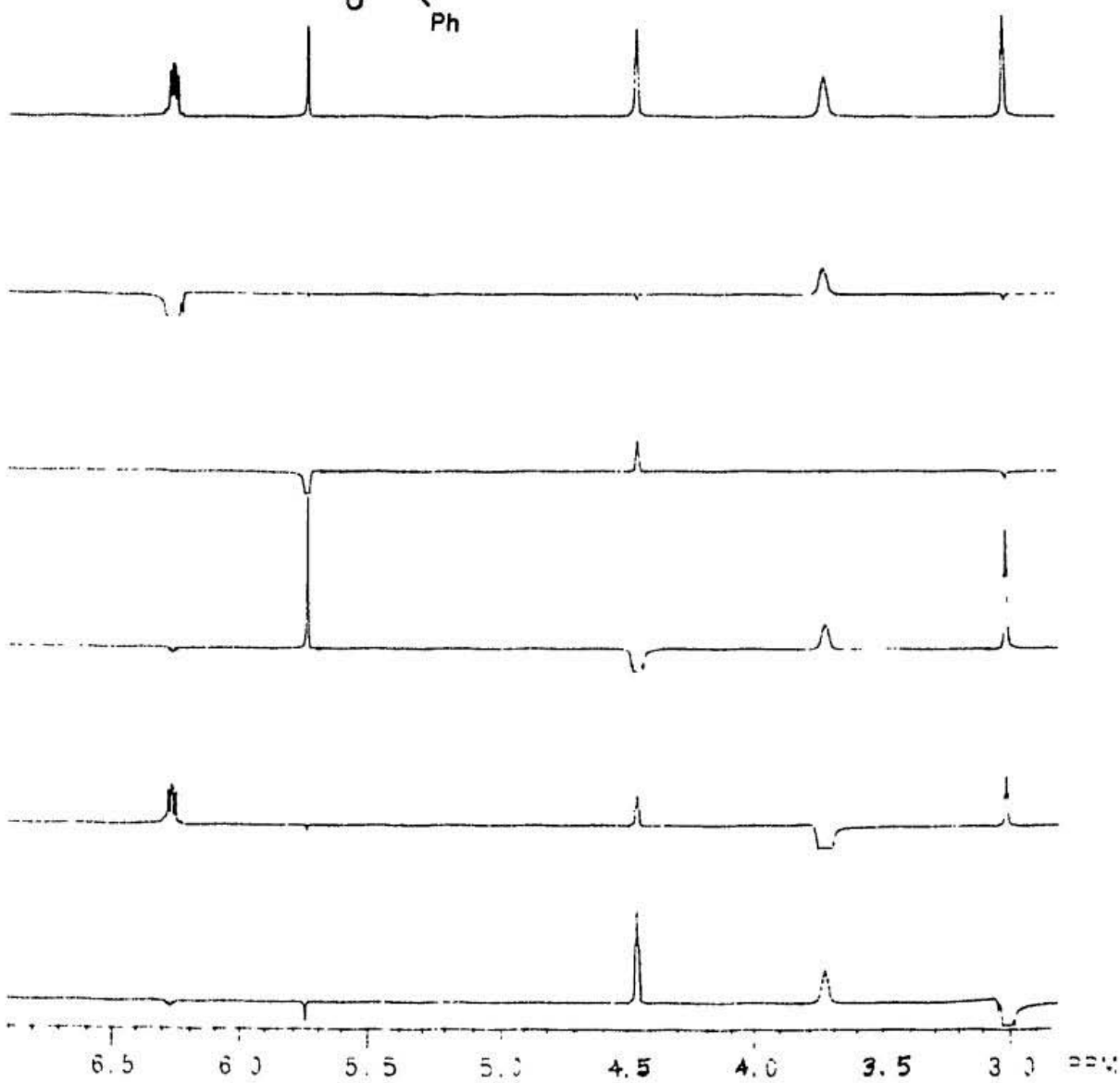




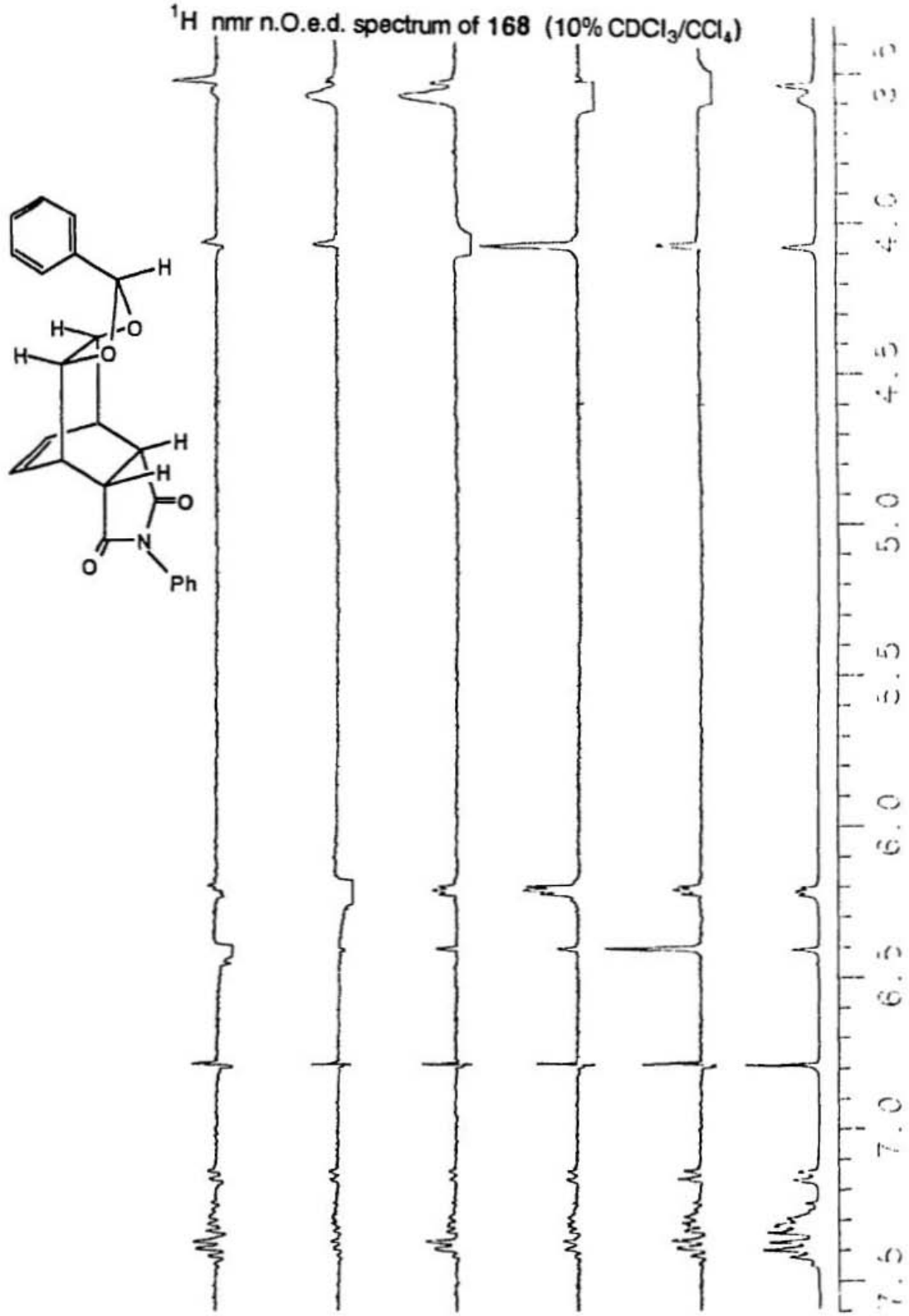
167 ($CDCl_3$)

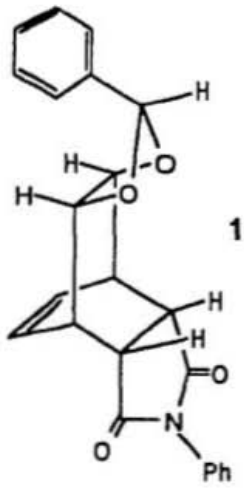


^1H nmr n.O.e.d. spectrum of 167 ($CDCl_3$)
aromatic signals not shown

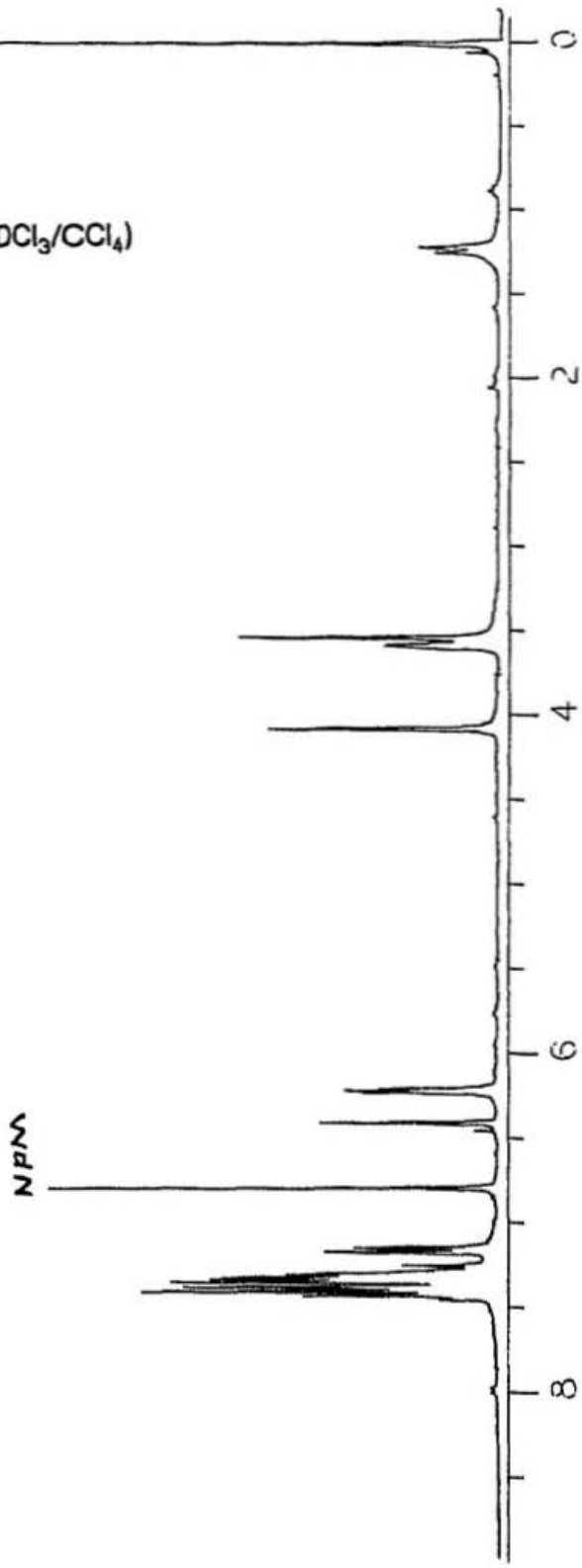


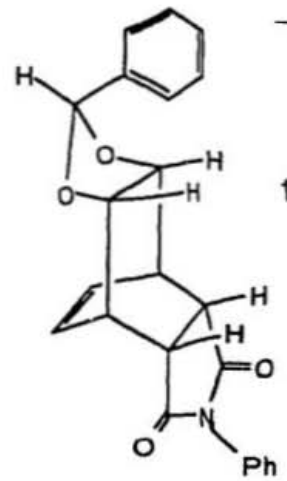
^{1}H nmr n.O.e.d. spectrum of **168** (10% $CDCl_3/CCl_4$)





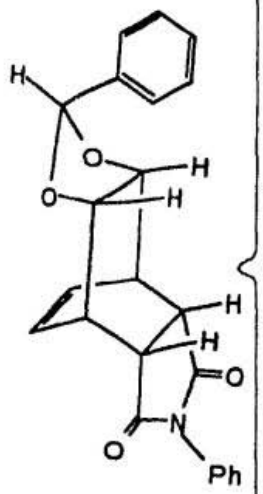
168 (10% $CDCl_3/CCl_4$)

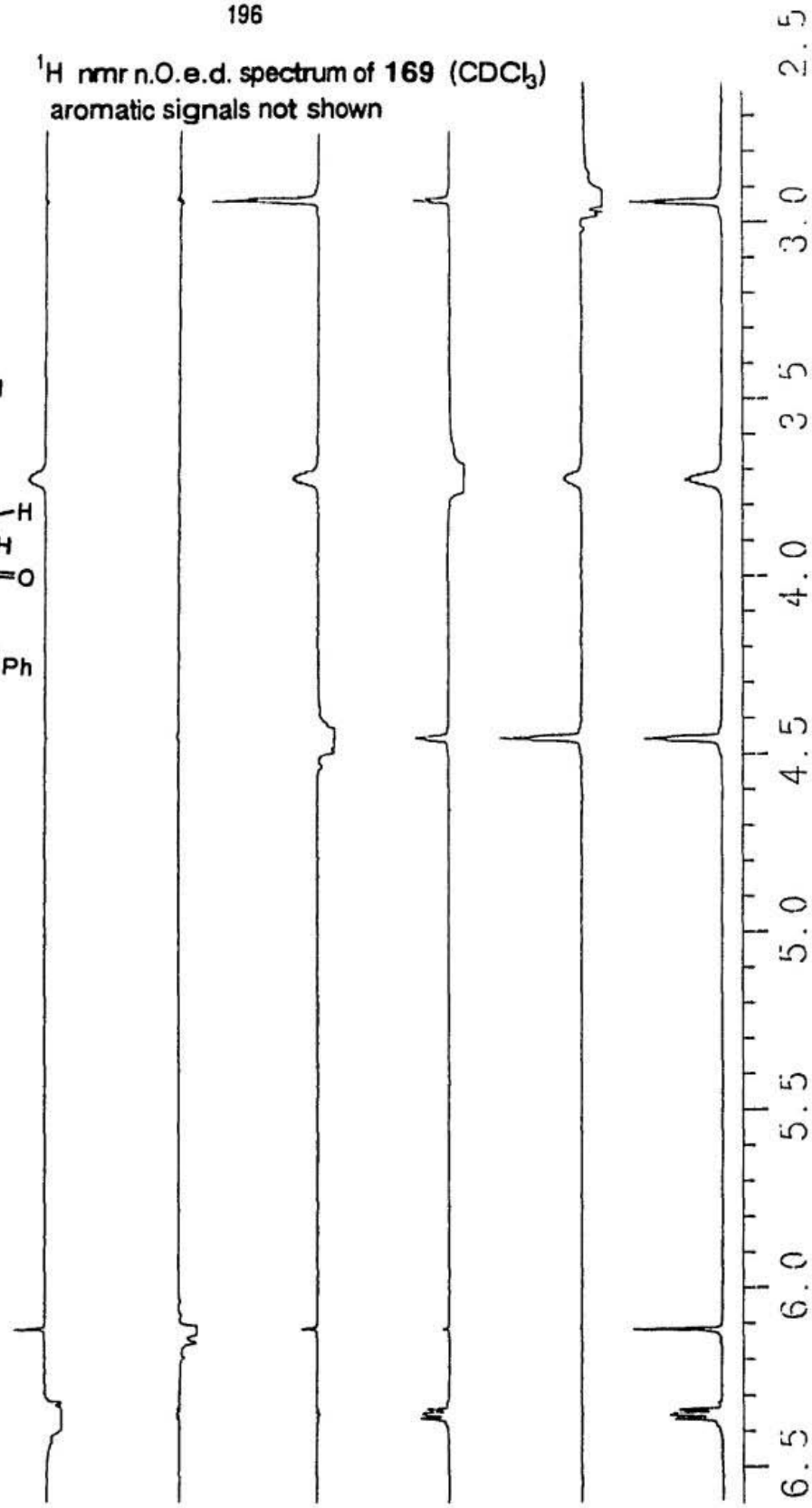


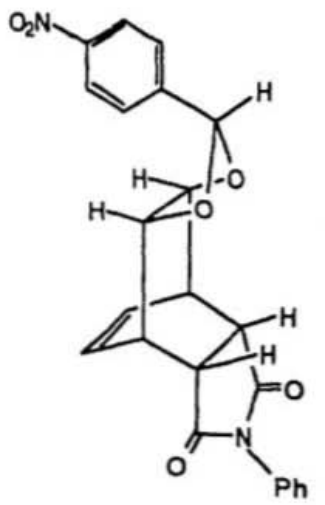


169 ($CDCl_3$)

^{1}H nmr n.O.e.d. spectrum of **169** ($CDCl_3$)
aromatic signals not shown

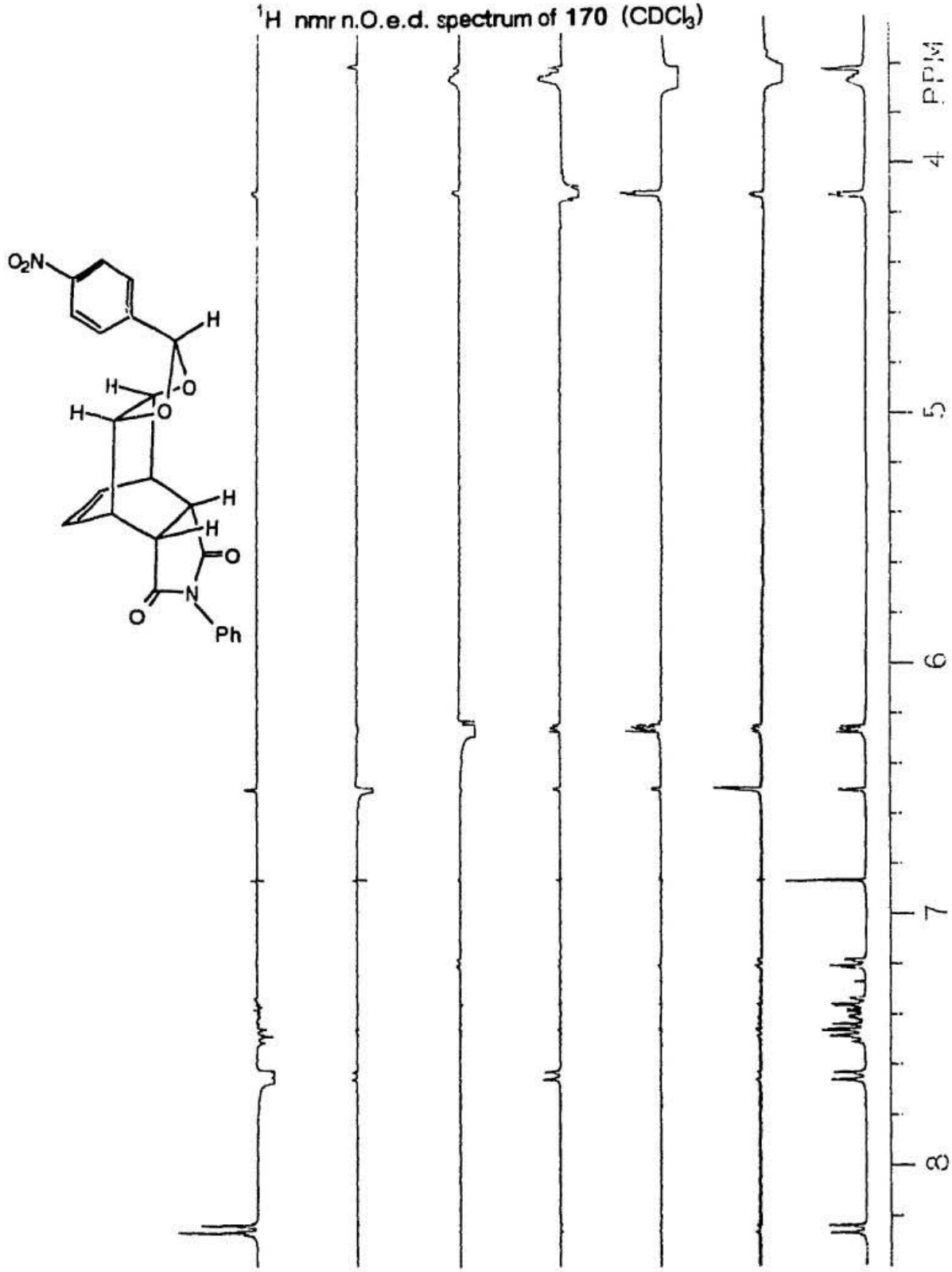


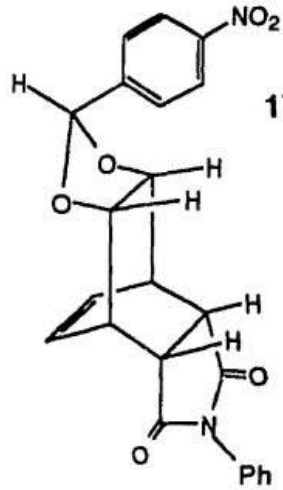




170 ($CDCl_3$)

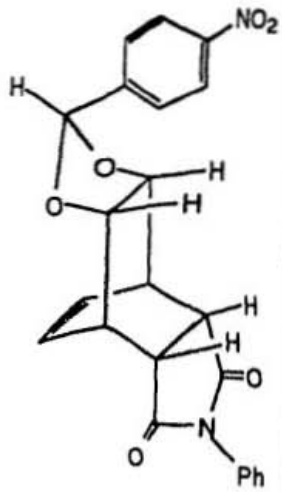
^{1}H nmr n.O.e.d. spectrum of **170** ($CDCl_3$)

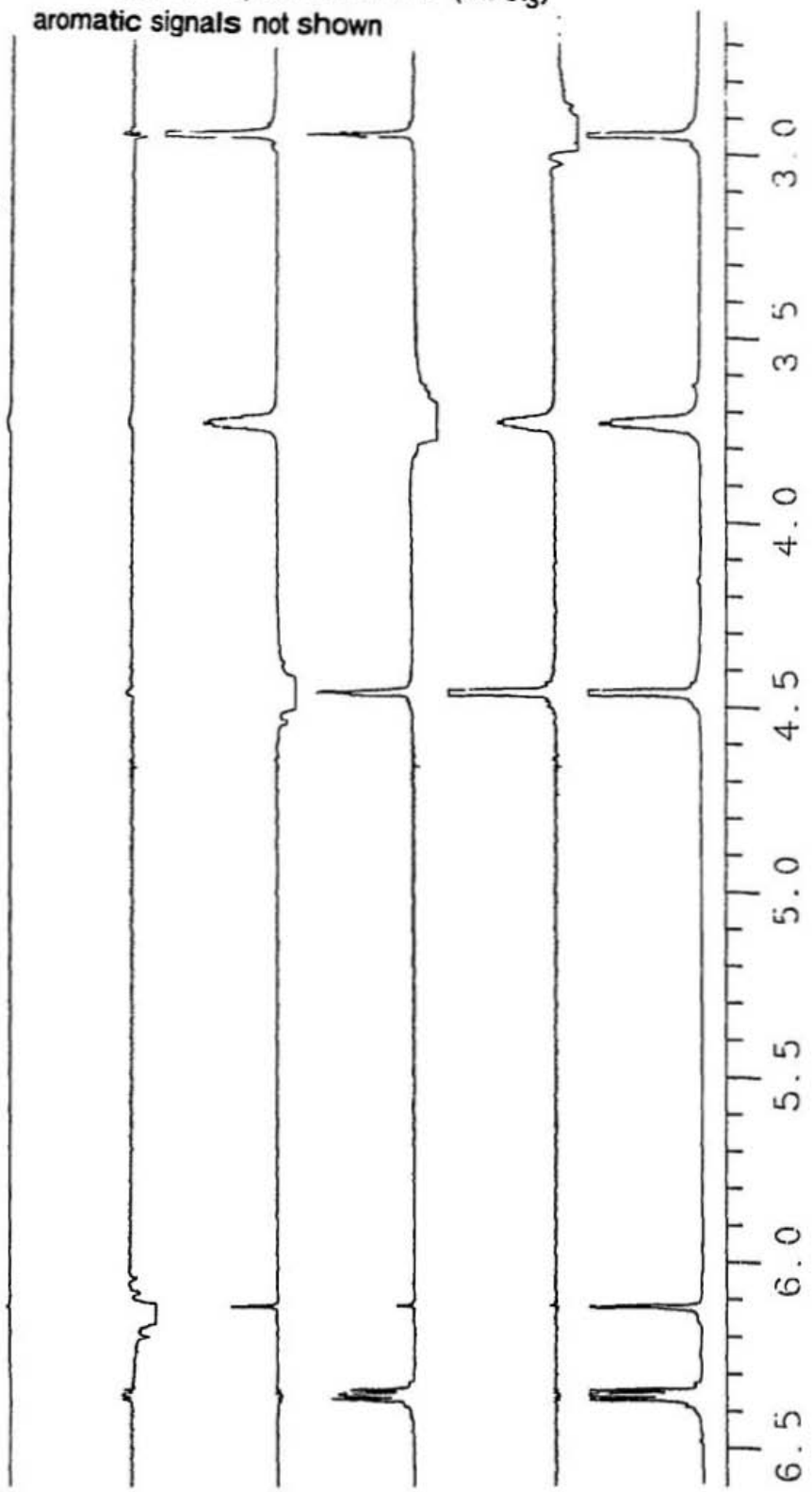


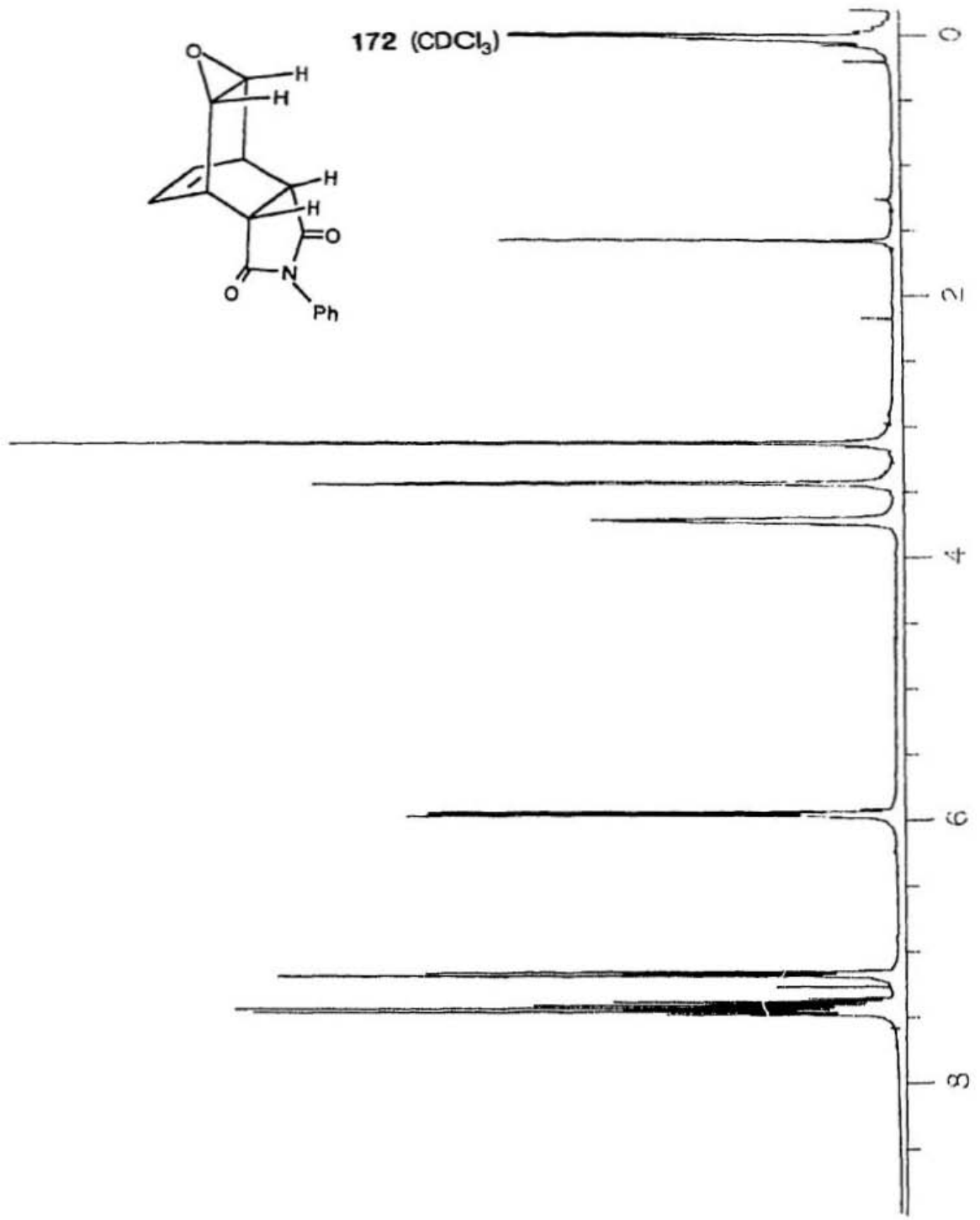


171 ($CDCl_3$)

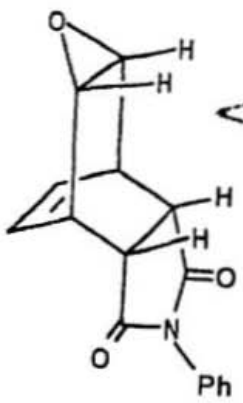
^{1}H nmr n.O.e.d. spectrum of **171** ($CDCl_3$)
aromatic signals not shown

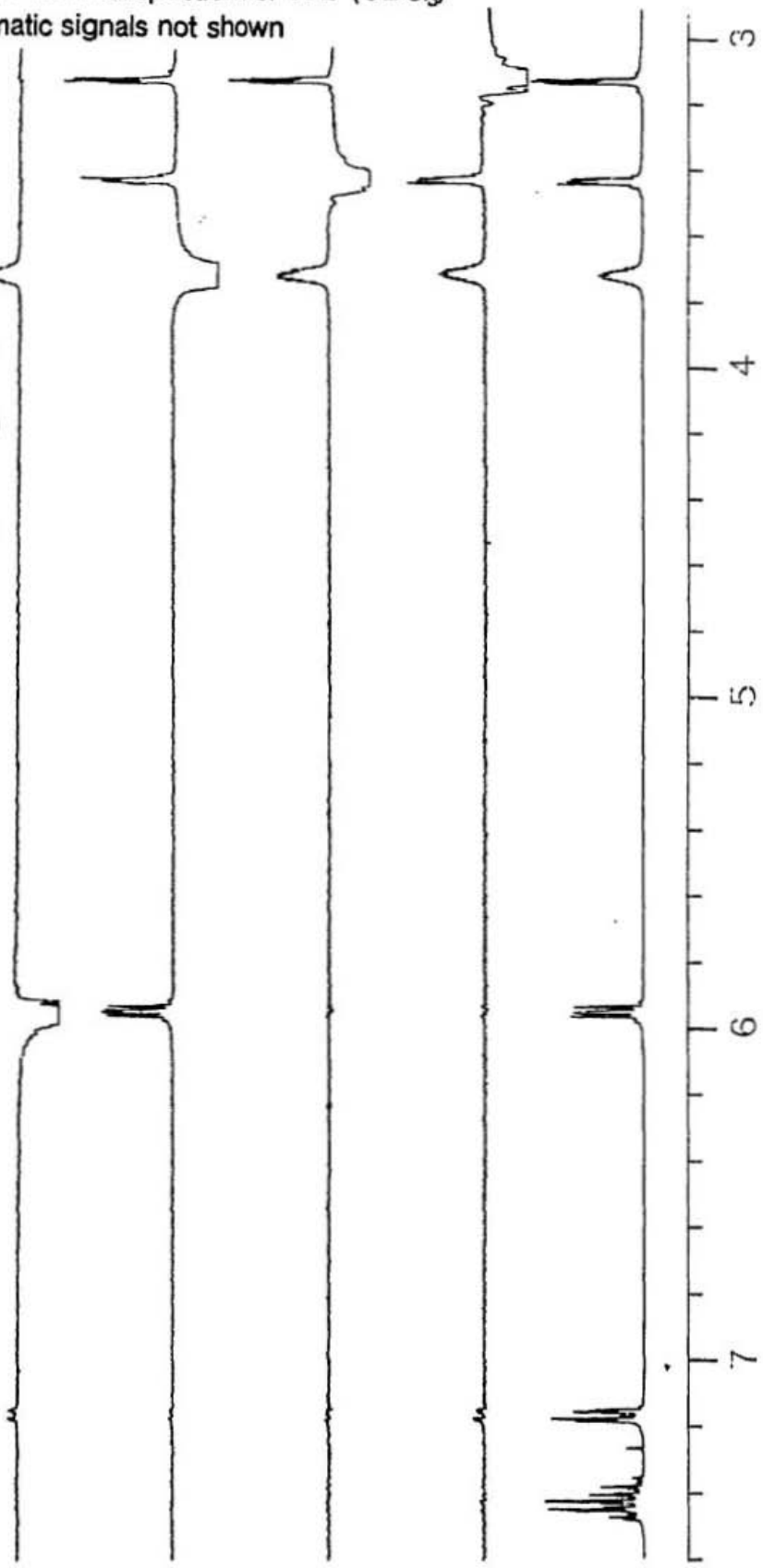


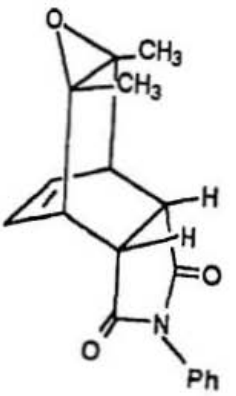



172 (CDCl3)
O
H
H
H
H
O
O
N
Ph
0
2
4
6
8

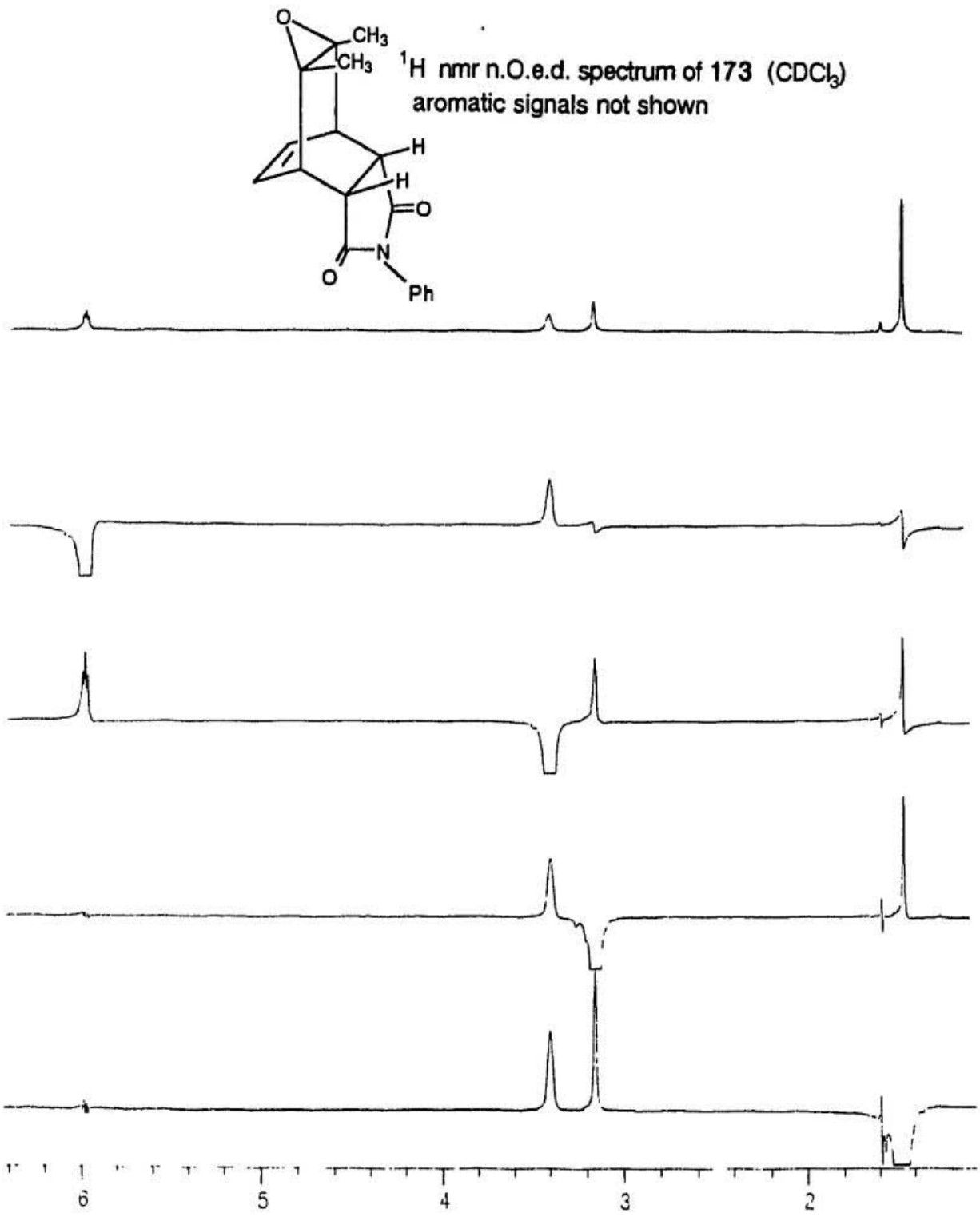
^{1}H nmr n.O.e.d. spectrum of **172** ($CDCl_3$)
aromatic signals not shown



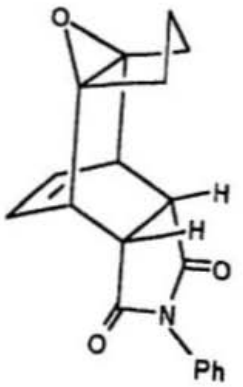




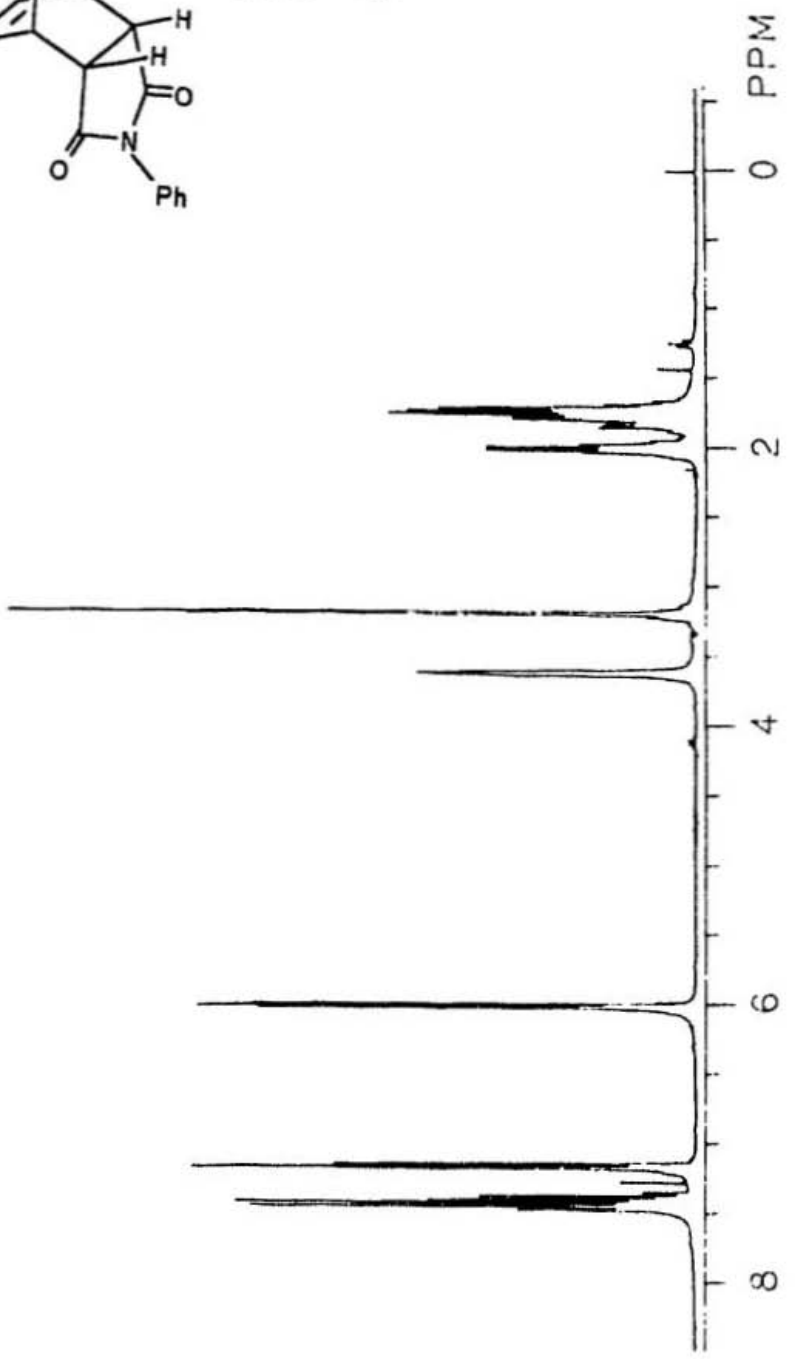
173 ($CDCl_3$)

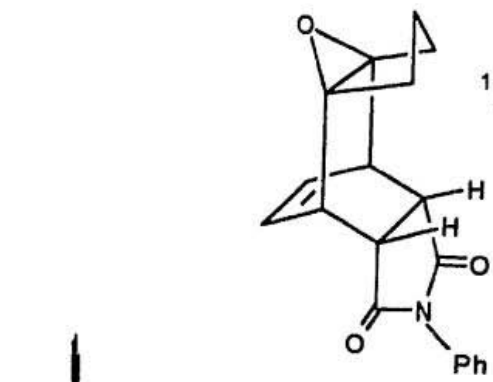


^{1}H nmr n.O.e.d. spectrum of **173** ($CDCl_3$)
aromatic signals not shown

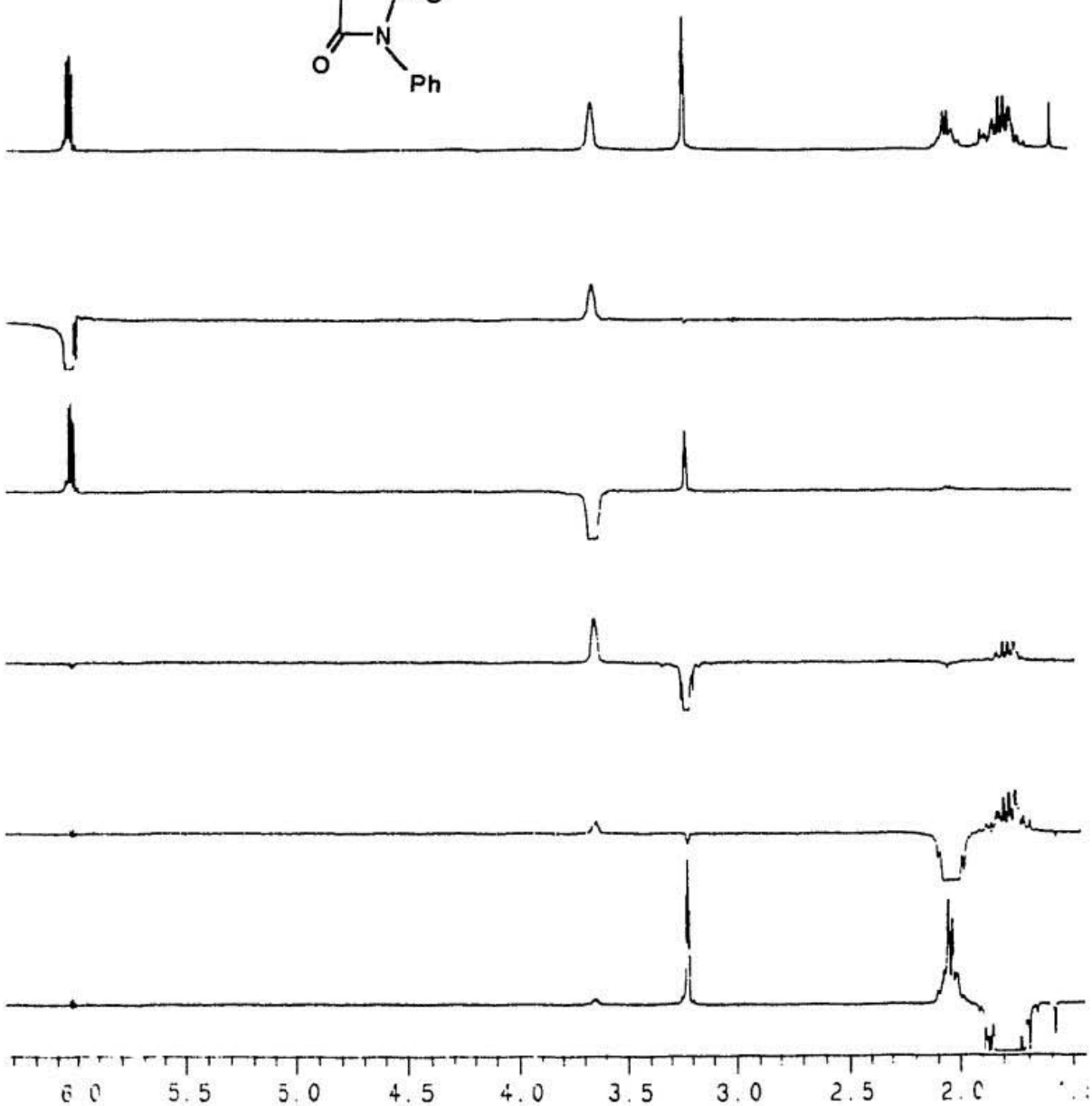


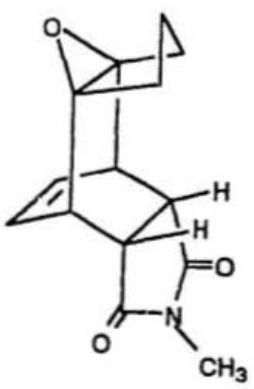
174 ($CDCl_3$)





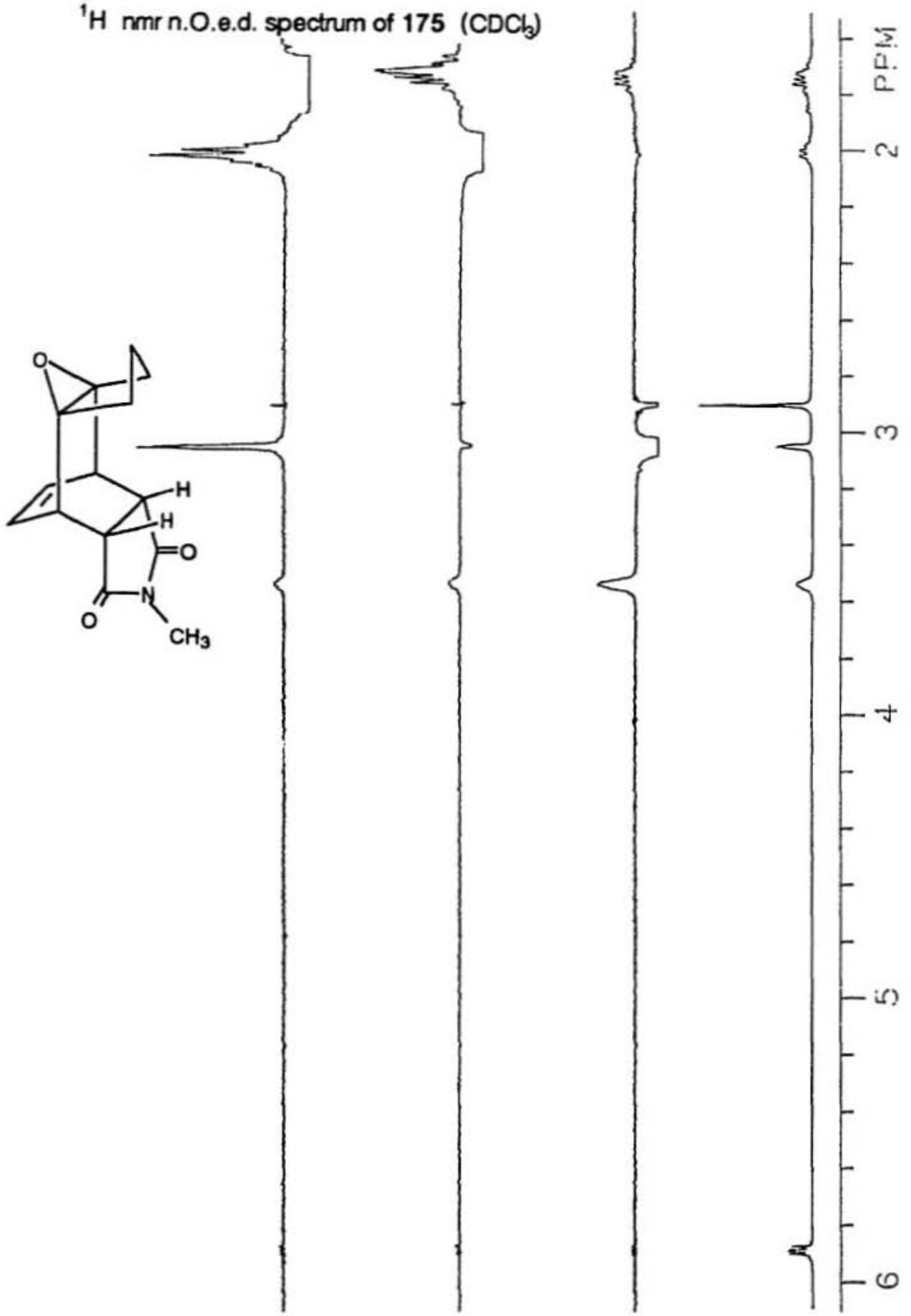
^{1}H nmr n.O.e.d. spectrum of **174** ($CDCl_3$)
aromatic signals not shown

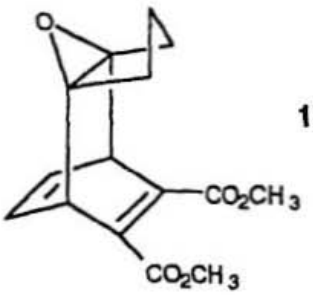




175 ($CDCl_3$)

^{1}H nmr n.O.e.d. spectrum of **175** ($CDCl_3$)





176 ($CDCl_3$)