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

CENTRE FOR NEWFOUNDLAND STUDIES

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JAMES R. GILLARD
\textbf{\pi-\textit{FACIAL SELECTIVITY IN THE}}

\textbf{\textit{DIELS-ALDER REACTIONS OF 1,3-CYCLOHEXADIENES}}

\textbf{BEARING ALLYLIC OXYGEN SUBSTITUTION}

\textit{by}

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B.Sc., Saint Francis Xavier University,

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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-phenylimaleimide 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,7aa)-3a,7a-dihydro-2-phenyl-1,3-benzodioxole (132) and (2α,3aα,7aa)-3a,7a-dihydro-2-phenyl-1,3-benzodioxole (133) also reacted with N-phenylimaleimide, 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[4.3.1.0^3.6]deca-2,4,6-diene (148b) reacted also with N-phenylimaleimide 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.
Acknowledgements

I would like to extend my sincerest appreciation to my supervisor, Dr. D. Jean Burnell, for his many hours of helpful instruction and discussion during the course of my research project.

Special thanks are given to Messrs. Tracy Jenkins and Dean Strickland, to Dr. Yong-Jin Wu, and to Ms. Pei-Ying Liu for their support, encouragement, and friendship.

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I am deeply grateful to my wife, Mrs. Ann Gillard, for her typing services, and for her love, support, and encouragement.

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INTRODUCTION TO THE DIELS-ALDER REACTION ............................................. 1

i) Diene conformation .................................................................................. 5

ii) Substitution patterns on diene/dienophile ................................................. 5

iii) Regioselectivity ....................................................................................... 9

iv) Stereoselectivity, the "cis principle", and the Alder "endo rule" ..................... 9

v) Lewis acid catalysis .................................................................................. 11

vi) Medium effects ....................................................................................... 12

vii) Syn-anti or \( \pi \)-facial selectivity ............................................................. 14

\( \text{syn/anti OR } \pi \text{-FACIAL SELECTIVITY} \) ..................................................... 16

Allylic Alkyl Substitution ........................................................................... 17
**List of Figures**

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1</td>
<td>Orbital energy diagram for neutral, normal and inverse electron demand Diels-Alder reactions</td>
<td>6</td>
</tr>
<tr>
<td>Figure 2a</td>
<td>The orientation of cyclopentadiene and maleic anhydride in the <em>endo</em> and <em>exo</em> transition states</td>
<td>10</td>
</tr>
<tr>
<td>Figure 2b</td>
<td>Frontier orbital picture of the <em>endo</em> (a) and <em>exo</em> (b) transition states in the Diels-Alder reaction of 1,3-butadiene and acrolein</td>
<td>10</td>
</tr>
<tr>
<td>Figure 3</td>
<td>The addition of a dienophile <em>syn</em> and <em>anti</em> to a plane-nonsymmetric diene</td>
<td>15</td>
</tr>
<tr>
<td>Figure 4</td>
<td>Orbital tilting postulate for the <em>n</em>-facial selectivity of isodicyclopentadienes</td>
<td>22</td>
</tr>
<tr>
<td>Figure 5</td>
<td>Secondary orbital overlap in the approach of an azo dienophile <em>syn</em> to an anhydride bridged propellane</td>
<td>24</td>
</tr>
<tr>
<td>Figure 6</td>
<td>Free rotation of the allylic center of acyclic 1,3-dienes</td>
<td>26</td>
</tr>
<tr>
<td>Figure 7</td>
<td>&quot;Like&quot; and &quot;unlike&quot; additions to acyclic 1,3-dienes</td>
<td>28</td>
</tr>
<tr>
<td>Figure 8</td>
<td>Approach of <em>N</em>-phenylmaleimide <em>syn</em> and <em>anti</em> to compound 56</td>
<td>28</td>
</tr>
<tr>
<td>Figure 9</td>
<td>Important conformations of the allylic center of acyclic 1,3-diene</td>
<td>34</td>
</tr>
</tbody>
</table>
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) ........................................ 36

Figure 11. Approach of an acetylenic dienophile to the Re (a) and Si (b) faces of an acyclic 1,3-diene ........................................ 36

Figure 12. Interactions postulated in the control of n-facial selectivity of vinyl cyclopentenenes ........................................ 38

Figure 13. Steric effects postulated in the control of n-facial selectivity of vinyl cyclohexenenes ........................................ 41

Figure 14. Postulated steric control in the n-facial selectivity of pyranose dienes ........................................ 48

Figure 15. Anh's postulate ........................................ 54

Figure 16. Fukui's postulate ........................................ 54

Figure 17. Hehre's postulate ........................................ 54

Figure 18. Cleplak's postulate for the preferred axial attack of nucleophiles to cyclohexanone ........................................ 56

Figure 19. α Bond donation model applied to the n-facial selectivity observed in the cycloaddition of adamantyl derivatives ........................................ 57

Figure 20. α Bond donation model applied to the n-facial selectivity observed in the Diels-Alder reactions of 5-hetero substituted cyclopentadienes ........................................ 57

Figure 21. Perspective view of 150 ........................................ 75
| Figure 22. | Perspective view of 151 | 75 |
| Figure 23. | Perspective view of 172 | 94 |
| Figure 24. | Perspective view of 176 | 94 |
| Figure 25. | Possible resonance forms of a boronate ester | 97 |
| Figure 26. | Important conformations of the acetonide and the benzylidene protected dienes | 99 |
| Figure 27. | σ Bond donation as a possible controlling mechanism for the n-facial selectivity observed for the Diels-Alder reactions of the benzene oxides 142, 148a and 148b | 101 |
| Figure 28. | Possible secondary orbital interactions that may promote syn addition | 104 |
| Figure 29. | Possible secondary orbital interactions that may promote anti addition | 105 |
List of Schemes

| Scheme 1. | The Diels-Alder reaction | 2 |
| Scheme 2. | The synthesis of perchloroisoidanone | 2 |
| Scheme 3. | The dimerization of isoprene | 2 |
| Scheme 4. | The s-cis and s-trans conformers of 1,3-butadiene | 2 |
| Scheme 5. | Regiochemical control of the Diels-Alder reaction | 8 |
| Scheme 6. | The Diels-Alder reaction of cyclopentadiene and maleic anhydride | 10 |
| Scheme 7. | Allylic alkyl group control of \( n \)-facial selectivity | 18 |
| Scheme 8. | Allylic alkyl group control of \( n \)-facial selectivity in the synthesis of prostaglandins | 18 |
| Scheme 9. | \( n \)-Facially selective Diels-Alder reactions of dienones | 18 |
| Scheme 10. | \( n \)-Facial selectivity in the Diels-Alder reaction of 5-alkyl substituted cyclopentadienes | 19 |
| Scheme 11. | Diels-Alder reaction of 5-(cyclopentadienyl)cyclopentadiene with dimethylacetylene dicarboxylate | 21 |
| Scheme 12. | \( n \)-Facial selectivity in the Diels-Alder reaction of isodicyclopentadienes | 21 |
| Scheme 13. | \( n \)-Facial selectivity in the Diels-Alder reactions of propellanes | 24 |
| Scheme 14. | Structural types of 1,3-dienes bearing allylic heteroatom substitution | 26 |
Scheme 27. n-Facial selectivity in the cycloaddition reactions of adamantyl derivatives

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, continued

Scheme 30. Microbial oxidation of benzene

Scheme 31. Derivatization of diol diene 121

Scheme 32. Synthesis of dibromo diol precursor 128

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

Scheme 34. Synthesis of cis benzyldiene diene directly from 121

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

Scheme 36. Dimerization of trans benzyldiene dienes 133 and 138

Scheme 37. The synthesis of benzene oxide 142

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

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

Scheme 40. Diels-Alder reaction of acetonide diene 114
Scheme 41. Hydrolysis of the anti acetonide adduct 153 to anti diol adduct 151 ........................................................................................................ 77

Scheme 42. Derivatization of syn diol adduct 150 ......................................................................................................................... 80

Scheme 43. Derivatization of anti adduct 151 .......................................................................................................................... 81

Scheme 44. Diels-Alder reaction of "siliconide" diene 123 ............................................................................................................. 84

Scheme 45. Diels-Alder reaction of boronate diene 125 ................................................................................................................ 84

Scheme 46. Diels-Alder reaction of cis benzylidene protected dienes 132 and 137 ........................................................................ 87

Scheme 47. Diels-Alder reaction of trans benzylidene protected dienes 133 and 138 ........................................................................... 88

Scheme 48. Derivatization of diol adducts 150 and 151 to the cis benzylidene protected adducts 164 and 165 ......................... 89

Scheme 49. Diels-Alder reactions of the benzene oxides 142, 148a and 148b ................................................................................ 93
List of Tables

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td>$n$-Facially selective Diels-Alder reactions of acyclic dienes</td>
<td>29</td>
</tr>
<tr>
<td>Table 2</td>
<td>$r$-Facially selectivity in the Diels-Alder reactions of vinylcyclopentenes</td>
<td>39</td>
</tr>
<tr>
<td>Table 3</td>
<td>$r$-Facial selectivity in the Diels-Alder reactions of vinylcyclohexenes</td>
<td>42</td>
</tr>
<tr>
<td>Table 4</td>
<td>Anomeric versus allylic heteroatom control of $r$-facial selectivity of pyranose dienes</td>
<td>47</td>
</tr>
<tr>
<td>Table 5</td>
<td>Summary of the addition of various dienophiles to pentachloro 95</td>
<td>51</td>
</tr>
<tr>
<td>Table 6</td>
<td>Summary of the addition of maleic anhydride to dienes 102</td>
<td>52</td>
</tr>
<tr>
<td>Table 7</td>
<td>Reaction of diol diene 121 with N-phenylmaleimide in various solvents</td>
<td>74</td>
</tr>
<tr>
<td>Table 8</td>
<td>Relative amounts of syn and anti adducts obtained, and the relative rates, for the Diels-Alder reaction of 121 and derivatives of CHCl₃</td>
<td>79</td>
</tr>
<tr>
<td>Table 9</td>
<td>Relative amounts of syn and anti adducts obtained from the Diels-Alder reaction of various benzylidene protected derivatives of 121 with N-phenylmaleimide</td>
<td>86</td>
</tr>
</tbody>
</table>
Glossary of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ac</td>
<td>acetyl</td>
</tr>
<tr>
<td>APT</td>
<td>attached proton test</td>
</tr>
<tr>
<td>COSY</td>
<td>$^1$H-$^1$H correlation spectrum</td>
</tr>
<tr>
<td>DBU</td>
<td>1,8-diazabicyclo[5.4.0]undec-7-ene</td>
</tr>
<tr>
<td>DMAD</td>
<td>dimethyl acetylenedicarboxylate</td>
</tr>
<tr>
<td>DMF</td>
<td>N,N-dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
</tr>
<tr>
<td>EDG</td>
<td>electron-donating group</td>
</tr>
<tr>
<td>EWG</td>
<td>electron-withdrawing group</td>
</tr>
<tr>
<td>GC-MS</td>
<td>gas chromatography-mass spectrometry</td>
</tr>
<tr>
<td>HOMO</td>
<td>highest occupied molecular orbital</td>
</tr>
<tr>
<td>ir</td>
<td>infrared [spectroscopy]</td>
</tr>
<tr>
<td>LUMO</td>
<td>lowest unoccupied molecular orbital</td>
</tr>
<tr>
<td>MA</td>
<td>maleic anhydride</td>
</tr>
<tr>
<td>MMPP</td>
<td>magnesium mononaphtalene</td>
</tr>
<tr>
<td>mp</td>
<td>melting point</td>
</tr>
<tr>
<td>ms</td>
<td>mass spectrometry</td>
</tr>
<tr>
<td>mCPBA</td>
<td>meta-chloroperoxybenzoic acid</td>
</tr>
<tr>
<td>nmr</td>
<td>nuclear magnetic resonance [spectroscopy]</td>
</tr>
<tr>
<td>n.O.e.</td>
<td>nuclear Overhauser enhancement</td>
</tr>
<tr>
<td>n.O.e.d.</td>
<td>nuclear Overhauser enhancement difference [spectrum]</td>
</tr>
<tr>
<td>NPM</td>
<td>N-phenylmaleimide</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>PTAD</td>
<td>4-phenyl-1,2,4-triazoline-3,5-dione</td>
</tr>
<tr>
<td>pTsOH</td>
<td>para-toluenesulfonic acid</td>
</tr>
<tr>
<td>TCNE</td>
<td>tetracyanoethylene</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMS</td>
<td>trimethylsilyl</td>
</tr>
<tr>
<td>uv</td>
<td>ultraviolet [spectroscopy]</td>
</tr>
</tbody>
</table>
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-hexamethoxy-3-ene-1-carboxylic acid 5 occurred through the dimerization of perchlorocyclopentadiene 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 fourth Collective Index (1937-46) of *Chemical Abstracts* has 24 listings under the subject
Scheme 1. The Diels-Alder reaction

Scheme 2. The synthesis of perchloroisoiindanone

Scheme 3. The dimerization of isoprene
Scheme 4. The s- cis and s- trans conformers of 1,3-butadiene
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. Its importance rests with its ability to generate two carbon-carbon \( \sigma \) 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. These transformations are processes whereby two (or more) molecules condense to form a ring, with the formation of new \( \sigma \) bonds at the expense of the \( \pi \) 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 to pericyclic reactions (those reactions in which the bond-making and bond-breaking processes occur simultaneously, via a cyclic transition state) provided great insight into the mechanism of cycloadditions. The use of frontier orbital theory, 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, based on the conservation of orbital symmetry, 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. Although other directions of approach of the addends can be analyzed by the rules of orbital symmetry, i.e. \([4\pi_s + \]
2\pi), \; [4\pi + 2\pi_2] \; \text{and} \; [4\pi + 2\pi_2], \; \text{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. 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. 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, 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$_2$R, 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 $\text{HOMO}_{\text{dienophile}} - \text{LUMO}_{\text{dienophile}}$ as well as by $\text{HOMO}_{\text{dienophile}} - \text{LUMO}_{\text{dien}}$. 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 $\text{HOMO}_{\text{dien}} - \text{LUMO}_{\text{dienophile}}$ is less than the energy difference between $\text{HOMO}_{\text{dienophile}} - \text{LUMO}_{\text{dien}}$. 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 $\text{HOMO}_{\text{dienophile}} - \text{LUMO}_{\text{dien}}$ 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.\textsuperscript{11}
Scheme 5. Regiochemical control of the Diels-Alder reaction
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. 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 and others 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).

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". 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 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. 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, 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 AlCl₃ and SnCl₄, accelerate the rate of addition of addends in [4+2] cycloadditions 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\textsuperscript{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,\textsuperscript{11} in low melting fused salts,\textsuperscript{18} and under ultra-high pressures\textsuperscript{19} in conventional solvents. The most startling results, however, have come from Diels-Alder reactions performed in aqueous media\textsuperscript{20} and in solutions of LiClO\textsubscript{4}-diethyl ether.\textsuperscript{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.\textsuperscript{11} However, endo/exo ratios are both solvent and temperature dependent,\textsuperscript{11,22} and gas phase reactions seem to occur as fast as those in a nonpolar liquid phase.\textsuperscript{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\textsuperscript{23} (as opposed to those reactions performed in organic solvents). Grieco confirmed this unusual solvent effect with more complex substrates.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{24} Breslow discounted this idea based on additional experiments\textsuperscript{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\textsuperscript{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\textsubscript{4}-diethyl ether, a solvent medium that possesses a high internal solvent pressure. Shortly afterwards, however, Dailey\textsuperscript{24} provided evidence that suggests that the increases in rate in LiClO\textsubscript{4}-diethyl ether solutions are due to Lewis acid catalysis of the reaction by the Li\textsuperscript{+} ion, which may be the first example of catalysis of Diels-Alder reactions by a weak Lewis acid.

Syn-anti or \(\pi\)-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 \(\pi\)-system of the diene or dienophile are differentiated.\textsuperscript{73} An example of this \(\pi\)-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 \(\pi\)-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 \( \pi \)-FACIAL SELECTIVITY

\( \pi \)-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 \( \pi \)-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. \( \pi \)-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 \( \pi \)-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 \( \pi \)-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\textsuperscript{27,28} demonstrated complete \textit{n}-facial stereocontrol, as shown in Scheme 7, with dienes 32 and 33. Similarly, the prostaglandin synthesis by Corey\textsuperscript{29} utilized an alkyl substituent at the 5-position of a cyclopentadiene moiety 34 to control the Diels-Alder addition as shown in Scheme 8. In both instances, the adduct obtained was that arising from addition of the dienophile \textit{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 \textit{anti} to the dihalomethyl moiety.\textsuperscript{30}

More rigorous studies of the steric requirements of the Diels-Alder reaction have been reported by Burnell and Valenta\textsuperscript{31,33} and also by Paquette\textsuperscript{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\textsuperscript{35} supported this postulate. The possibility of some sort of $\sigma/\pi$ interaction (\textit{vide infra}) controlling the \textit{n}-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 $\pi$-facial selectivity

Scheme 8. Allylic alkyl group control of $\pi$-facial selectivity in the synthesis of prostaglandins

Scheme 9. $\pi$-Facially selective Diels-Alder reactions of dienones
Scheme 10. \( \pi \)-Facial selectivity in the Diels-Alder reaction of 5-alkyl substituted cyclopentadienes
from addition of the dienophile syn to the cyclopentadiene substituent to give intermediate 41.

The pioneer work of Paquette et al. on the isodicyclopentadiene systems 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 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 that these, and similar results, are due to mixing of the $\sigma$ orbitals of the norbornyl framework with the $\pi$ orbitals of the diene. This $\sigma/\pi$ interaction perturbs the $\pi_0$ of the diene unit, but not the $\pi_a$ (or HOMO). For both 43 and 44, this causes a disrotatory tilt of the terminal $\pi$ lobes towards the methano bridge, as shown in A (Figure 4). Conversely, the central $\pi$ lobes rotate in the opposite direction. The net effect is a minimization of closed-shell antibonding interaction between the $\pi_0$ 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 $\pi$ 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 suggested that the $\pi$-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\(_2\)CH\(_3\))

Scheme 12. \(\pi\)-Facial selectivity in the Diels-Alder reaction of isodicyclopentadienes
Figure 4. Orbital tilting postulate for the \( \pi \)-facial selectivity of isodicyclopentadienes.
the cycloaddition of dienophiles 49 and 50 with various dienes indicated that the $\pi$-facial selectivity displayed by these substrates was essentially due to steric effects.$^{38}$

Other examples of $\pi$-facial selectivity displayed by dienes with a carbon-based allylic substituent are the propellane systems investigated by Ginsburg et al.$^{49}$ 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 $\pi$ 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 $\pi^*$ orbitals of the carbonyls. This was predicted to occur at distances for which the HOMO$_{dien}$ - LUMO$_{dienophile}$ interaction leading to cycloaddition had not become significant.$^{40}$ 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 $\pi$-facial diastereoselectivity in the Diels-
Scheme 13. \( \pi \)-Facial selectivity in the Diels-Alder reactions of propellanes

Figure 5. Secondary orbital overlap in the approach of an azo dienophile \( \text{syn} \) 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 $\pi$-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 $\pi$-facial selectivity of acyclic dienes. For acyclic systems the general practice is to describe the mode of addition of dienophiles
Scheme 14. Structural types of 1,3-dienes bearing allylic heteroatom substitution

Figure 6. Free rotation of the allylic center of acyclic 1,3-dienes
in terms of "like" and "unlike". (This is based on the Seebach-Prelog\textsuperscript{41} convention for describing the relative topologies of approach to the faces of an enantiomer.) Reactant approach to the \textit{Re} face of a double bond with an adjacent \textit{R} allylic centre is termed "like" addition, and approach to the \textit{Si} face is termed "unlike" addition. Similarly, for an \textit{S} chiral centre, approach to the \textit{Re} face is "unlike", and approach to the \textit{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 \textit{R} or \textit{S} configuration of the chiral centre and the \textit{Re} and \textit{Si} assignments of the diene faces.\textsuperscript{42} For the purposes of the present discussion, "like" addition is termed \textit{syn}, and "unlike" is termed \textit{anti}. This convention is used by other authors.\textsuperscript{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 \textit{N}-phenylimaleimide to compound 56 resulted in the formation of diastereomers 57 and 58 (both by \textit{endo} addition) in a 83:17 ratio, respectively, in which the major adduct 57 arose from \textit{syn} addition, and the minor adduct 58 from \textit{anti} addition (Figure 8).

Table 1 does not include all of the many examples of the \textit{n}-facial selectivity observed in acyclic dienes. It is only meant as an overview (see Ref. 44\textsuperscript{b} 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
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2. Even highly substituted acyclics are able to display high levels of selectivity (entries 6, 7, 11-12, 15).

3. Allylic heteroatoms 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 \( \pi \)-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 \( \text{syn} \) addition occurs from the \( \text{Re} \) 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 \( \text{anti} \) conformation (Scheme 16). This was termed the "Inside alkoxy" effect. Houk argued that when bond formation occurs during electrophilic attack, the \( \pi \)-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 CHOR' 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, Franck126 argued that this would predict the Si facial attack of dienophiles to conformer E (or anti addition), the opposite of that observed126 by Franck and others (see references in Table 1). Franck reasoned instead that Re face addition to conformer B should be preferred. MacDougall45 also favored this conformation, based on arguments put forward by McGarvey54 and Fleming55 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). Kozlowski57 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 coworkers57 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).

Figure 11. 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.  

Type II dienes

Only two reports have been published to date with the semicyclic dienes of type II. Overman and coworkers 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 n-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. \( \pi \)-Facial selectivity in the Diels-Alder reaction of vinyl cyclopentenes

Figure 12. Interactions postulated in the control the \( \pi \)-facial selectivity of vinyl cyclopentenes
Table 2. π-Facial selectivity in the Diels-Alder reactions of vinylcyclopentenes (reactions performed in toluene, except where indicated)

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<td>NPM</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>61a</td>
<td>NPM</td>
<td>64</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>61a</td>
<td>NPM</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>61a</td>
<td>TCNE</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>5</td>
<td>61b</td>
<td>NPM</td>
<td>3</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>61b</td>
<td>TCNE</td>
<td>3</td>
<td>97</td>
</tr>
<tr>
<td>7</td>
<td>61c</td>
<td>NPM</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>8</td>
<td>61c</td>
<td>TCNE</td>
<td>31</td>
<td>69</td>
</tr>
</tbody>
</table>

* 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.\textsuperscript{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\textsuperscript{56} 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-
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)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Dienophile</th>
<th>% syn to OR</th>
<th>% anti to OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64a</td>
<td>NPM</td>
<td>63</td>
<td>37</td>
</tr>
<tr>
<td>2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>64a</td>
<td>NPM</td>
<td>17</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>64b</td>
<td>NPM</td>
<td>11</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>64c</td>
<td>NPM</td>
<td>9</td>
<td>91</td>
</tr>
<tr>
<td>5</td>
<td>65a</td>
<td>NPM</td>
<td>92</td>
<td>8</td>
</tr>
<tr>
<td>6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>65a</td>
<td>NPM</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>7</td>
<td>65b</td>
<td>NPM</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>8</td>
<td>65c</td>
<td>NPM</td>
<td>23</td>
<td>77</td>
</tr>
<tr>
<td>9</td>
<td>64a</td>
<td>DMAD</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>10</td>
<td>64c</td>
<td>DMAD</td>
<td>8</td>
<td>92</td>
</tr>
<tr>
<td>11&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64a</td>
<td>PTAD</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

<sup>a</sup> DMF  
<sup>b</sup> CH<sub>2</sub>Cl<sub>2</sub> / 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 CH₃ 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 OCH₃ and H versus OTMS) the facial selectivity was dependent on the size of the substituent on the oxygen. When H was replaced by CH₃ in 65b and 65c (CH₃ versus OCH₃ and CH₃ 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-Forster²⁰ model of determining group volume, OCH₃ is a larger group than CH₃.

Type III dienes

These carbohydrate-derived dienes have only recently received attention. Fraser-Reid and coworkers had reported that furanose derivatives 70a₆¹,a and 70b₆¹,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.
Scheme 19. Addition of maleic anhydride to furanose dienes

Scheme 20. Addition of maleic anhydride to pyranose dienes
In two more recent and concurrent publications,\textsuperscript{62,63} pyranose derivative 72 was found to add maleic anhydride,\textsuperscript{62,63} DMAD,\textsuperscript{62,63} dimethyl fumarate,\textsuperscript{63} benzoquinone\textsuperscript{63} and naphthoquinone\textsuperscript{63} exclusively from the face of the diene \textit{anti} to the anomic methoxyl group (i.e., 73, Scheme 20). The isomeric diene 74\textsuperscript{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 \textit{anti} to the axially oriented allylic methoxyl group.\textsuperscript{62} This seemed to override any \textit{syn}-directing effect of the allylic oxygen at C-5 in both 72 and 74.

In an effort to determine the extent of anomic versus allylic directing ability for \pi-facial selectivity, a number of pyranose dienes 76-79 (Scheme 21) were synthesized and their Diels-Alder reactions with maleimide were examined.\textsuperscript{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 \textit{anti} to both the C-1 anomic and the C-3 allylic oxygens. Reversing the configurations at C-1 and at C-3 for 77 also afforded the \textit{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 (\textit{syn} to allylic OMe) and 85 (\textit{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 \textit{syn}/\textit{anti} ratio obtained with 79.

The adducts from the Diels-Alder reactions of dienes 76-79 indicated a strong tendency for dienophiles to react \textit{anti} to the anomic substituent. In light of the previously discussed results obtained by Franck\textsuperscript{59} with dienes 64a-c and 65a-c, the formation of only \textit{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 $\pi$-facial selectivity of pyranose dienes

Figure 14. Postulated steric control in the $\pi$-facial selectivity of pyranose dienes
Table 4. Anomeric versus allylic heteroatom control of $\pi$-facial selectivity of pyranose dienes

<table>
<thead>
<tr>
<th>Diene</th>
<th>$\text{Syn}$ to allylic $\text{O}$</th>
<th>$\text{Anti}$ to allylic $\text{O}$</th>
<th>% $\text{Syn}$ / % $\text{Anti}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td>$\text{H}_3\text{CO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>$\text{H}_3\text{CO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>0 / 100</td>
</tr>
<tr>
<td>77</td>
<td>$\text{H}_3\text{CO}$ - $\text{BnO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>$\text{H}_3\text{CO}$ - $\text{BnO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>0 / 100</td>
</tr>
<tr>
<td>78</td>
<td>$\text{H}_3\text{CO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>$\text{H}_3\text{CO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>81 / 19</td>
</tr>
<tr>
<td>79</td>
<td>$\text{H}_3\text{CO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>$\text{H}_3\text{CO}$ - $\text{O}$ - $\text{H}$ - $\text{C}$ - $\text{O}$ - $\text{N}$ - $\text{H}$</td>
<td>75 / 25</td>
</tr>
</tbody>
</table>
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 \( \pi \)-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\(^5\)). 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 than 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 \( \pi \)-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 \(\pi\)-facial selectivity of these dienes is quite apparent from the results obtained by Burnell and Valenta\(^{53}\) 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 \(\pi\)-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 \(\pi\)-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 \textit{anti} to the metal;\(^{66}\) however, the modes of cycloaddition to mercury and platinum dienes have not been elucidated.\(^{65}\) 5-(Trimethylsilyl)cyclopentadiene reacted \textit{anti}.\(^{67}\) 5-Bromopenta-
Scheme 22. $\pi$-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

<table>
<thead>
<tr>
<th>XCH=CHY</th>
<th>96 % endo-Syn</th>
<th>97 % endo-Anti</th>
</tr>
</thead>
<tbody>
<tr>
<td>maleic anhydride</td>
<td>91</td>
<td>9</td>
</tr>
<tr>
<td>benzoquinone</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>acrylonitrile</td>
<td>83</td>
<td>17</td>
</tr>
<tr>
<td>methyl acrylate</td>
<td>59</td>
<td>41</td>
</tr>
<tr>
<td>vinyl acetate</td>
<td>51</td>
<td>49</td>
</tr>
<tr>
<td>vinyl bromide</td>
<td>58</td>
<td>42</td>
</tr>
<tr>
<td>vinyl chloride</td>
<td>53</td>
<td>47</td>
</tr>
<tr>
<td>styrene</td>
<td>38</td>
<td>62</td>
</tr>
<tr>
<td>propene</td>
<td>31</td>
<td>69</td>
</tr>
</tbody>
</table>

Scheme 24. The Diels-Alder reactions of a 5-hydroxycyclopentadiene derivative
Scheme 25. The Diels-Alder reaction of a thiophene oxide derivative with various dienophiles

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

<table>
<thead>
<tr>
<th>X</th>
<th>% 103</th>
<th>% 104</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>OH</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>OCH₃</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>NH₂</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>NHAc</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>SH</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>SMe</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>SCH₂Ph</td>
<td>3</td>
<td>97</td>
</tr>
<tr>
<td>SOMe</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>SO₂Me</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>
chlorocyclopentadiene reacted with a number of dienophiles, but the configuration at the 7-position of the adducts was not determined. 5-Acetoxy-2-cyclopentadiene with ethylene gave only the adduct arising from addition to the face syn to the oxygen (Scheme 22). Also, the 5-halo derivatives reacted with PTAD to provide anti addition products, while gave both syn and anti adducts and respectively. DMAD gave more of the anti isomer, but provided only with DMAD (Scheme 22).

Williamson et al. established that 1,2,3,4,5-pentachlorocyclopentadiene 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 (Scheme 23 and Table 5). Jones found that diene also gave only the syn addition adduct with several dienophiles (Scheme 24).

Much more recently, Naperstkov et al. determined that 2,5-dimethylthiophene oxide reacted with a number of dienophiles to give only adducts 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. Selected results are summarized in Table 6, and Scheme 26. Substitution of the 5-position of with chlorine, oxygen or nitrogen directed addition of maleic anhydride to the face of the diene syn to the heteroatom, to give only while sulfur substitution clearly favored addition to the anti face to give mainly.

What factors determine whether a dienophile will add syn or anti to 5-heteroatom substituted cyclopentadienes? With 1,2,3,4,5-pentachlorocyclopentadiene, Williamson 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\textsuperscript{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 \textit{syn} face of the diene (Figure 15). An alternative view from Fukui's group,\textsuperscript{76a} more recently expanded upon,\textsuperscript{76b} invoked the mixing of low lying \(\sigma\) orbitals into the \(\pi\)-HOMO, thereby causing a perturbation of the electron density distribution on the two faces of the diene. Figure 16 shows the \(\pi\)-electron density distribution on the \textit{syn} and \textit{anti} faces of 5-chloro- and 5-methylcyclopentadiene.\textsuperscript{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 \(\pi\)-electron density biased in favor of the face \textit{syn} to the chlorine. A highly electron poor dienophile would then prefer addition \textit{syn} to the chlorine, whereas more electron rich dienophiles would be directed \textit{anti}.

Kahn and Hehre\textsuperscript{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, semicyclic or cyclic) the face of the diene bearing a lone pair-containing substituent, i.e., the \textit{syn} face, should have a higher nucleophilicity than the \textit{anti} face. Thus, "Additions, involving ... electron-poor dienophile should occur onto the diene face which is the more nucleophilic".\textsuperscript{43} It was predicted that electrophiles should prefer addition \textit{syn} to a lone pair-containing allylic substituent, and \textit{anti} to an electropositive allylic substituent. These generalizations did not take into account any overriding steric effects that might control the \(\pi\)-facial selectivity,\textsuperscript{58,59} nor could it account for the \textit{anti} facial selectivity displayed by sulfur substitution on cyclopentadienes (\textit{vide supra}).
Figure 18. Cieplak's postulate for the preferred axial attack of nucleophiles to cyclohexanone.

Scheme 27. π-Facial selectivity in the cycloaddition reactions of adamantyl derivatives.
Figure 19. $\sigma$ Bond donation model applied to the $\pi$-facial selectivity observed in the cycloaddition of adamantyl derivatives

$X = \text{OH, Br, Cl, F}$ \quad $\sigma C_1C_8, \sigma C_3C_{10} > \sigma C_3C_4, \sigma C_1C_9$

Figure 20. $\sigma$ Bond donation model applied to the $\pi$-facial selectivity observed in the Diels-Alder reactions of 5-hetero substituted cyclopentadienes

$\sigma_{CC} > \sigma_{CO}$

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

This proposal correctly accounted for the $\pi$-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 $\sigma$ bonds to become better donors than the C3-C4 and C1-C9 $\sigma$ bonds. Accordingly, the more reactive face should be the one anti to the better $\sigma$ 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 $\sigma$ bond that is the better donor.”\textsuperscript{44} The common atom combinations, listed in order of their $\sigma$ donor ability are as follows: $\sigma$CO < $\sigma$CN < $\sigma$CCI < $\sigma$CC < $\sigma$CH < $\sigma$CS.\textsuperscript{79} Thus, in transition state A (Figure 20), in which a $\sigma$CO bond is pitted against a $\sigma$CC bond, addition would be expected to occur on the face of the diene anti to the better donor, i.e., the $\sigma$CC, to give the syn adduct 103 (Scheme 26). For a $\sigma$CC bond versus a $\sigma$CS 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 o donor ability has CH > CCl, 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 and 107b 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; 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, Yates and Auks.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. 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 \(\pi\)-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 *Pseudomonas 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 \(^1\)H 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

* 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 Br₂ in the cold to 126, followed by cis-hydroxylation 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.

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 (pTsOH) as a catalyst in CDCl₃. 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 pTsOH 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) 
*ρ*-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 1H 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 ¹H 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-chloroperbenzoic 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 ¹H nmr spectrum. Vogel and Gunther⁹⁹ 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

* 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 monoperxyphthalic acid (MMPP) 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 Br₂ in the cold, gave the dibromides 147a and 147b, respectively. Following the procedure by Paquette and Barrett, 147a and 147b were doubly dehydrobrominated in ether with potassium tert-butoxide, which provided 148a and 148b, respectively.

Vogel 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.
Scheme 37. The synthesis of benzene oxide 142

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

<table>
<thead>
<tr>
<th>Solvent</th>
<th>ε</th>
<th>% syn 150</th>
<th>% anti 151</th>
<th>% yield a</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyridine</td>
<td>12</td>
<td>95</td>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>acetone</td>
<td>21</td>
<td>95</td>
<td>5</td>
<td>93</td>
</tr>
<tr>
<td>chloroform</td>
<td>5</td>
<td>95</td>
<td>5</td>
<td>93</td>
</tr>
<tr>
<td>methanol</td>
<td>33</td>
<td>93</td>
<td>7</td>
<td>80</td>
</tr>
<tr>
<td>benzene</td>
<td>2</td>
<td>92</td>
<td>8</td>
<td>91</td>
</tr>
<tr>
<td>DMSO b</td>
<td>47</td>
<td>92</td>
<td>8</td>
<td>87</td>
</tr>
<tr>
<td>acetonitrile</td>
<td>38</td>
<td>88</td>
<td>12</td>
<td>94</td>
</tr>
</tbody>
</table>

a Based on mass recovery of adducts, and sample purity as determined by 1H 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 $\delta$ 7.35 - 7.18 and $\delta$ 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 $\delta$ 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 $\delta$ 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 $\delta$ 6.17, $\delta$ 4.32 and $\delta$ 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 $\delta$ 2.88 was therefore due to those hydrogens at C-4a and C-7a, $\alpha$ to the carbonyls of the maleimide function. The high field signals at $\delta$ 1.35 and $\delta$ 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 diane 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 \(^{13}\text{C}\) nmr spectrum of \(153\) was aided considerably by the use of \(^1\text{H} - ^{13}\text{C}\) heteronuclear correlation experiments (HET-CORR). The carbon signals appearing at \(\delta 129.6, 77.1, 40.3\) and \(36.9\) were found to be one-bond coupled to the hydrogen signals at \(\delta 6.17, 64.32, 63.53\) and \(\delta 2.88\), respectively. Nearly all adducts synthesized gave \(^1\text{H}\) nmr and \(^{13}\text{C}\) 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 \(\alpha\)-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 \(\beta\)-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 \(\beta\)-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 \(^1\text{H}\) 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 CHCl₃ (reactions stirred at room temperature except where indicated)

<table>
<thead>
<tr>
<th>Diene</th>
<th>X</th>
<th>% syn</th>
<th>% anti</th>
<th>Rate a</th>
</tr>
</thead>
<tbody>
<tr>
<td>109 b</td>
<td>COCH₃</td>
<td>88</td>
<td>12</td>
<td>0.002</td>
</tr>
<tr>
<td>122</td>
<td>Si(CH₃)₃</td>
<td>100</td>
<td>0</td>
<td>0.03</td>
</tr>
<tr>
<td>121 b</td>
<td>H</td>
<td>95</td>
<td>5</td>
<td>0.1</td>
</tr>
<tr>
<td>124</td>
<td>CH₃</td>
<td>99</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>123</td>
<td>-Si(CH₃)₂⁻</td>
<td>60</td>
<td>40</td>
<td>2.7</td>
</tr>
<tr>
<td>114</td>
<td>-C(CH₃)₂⁻</td>
<td>60</td>
<td>40</td>
<td>&gt; 100</td>
</tr>
<tr>
<td>125</td>
<td>-B(CH₂CH₂)⁻</td>
<td>45</td>
<td>55</td>
<td></td>
</tr>
</tbody>
</table>

a Rate relative to 1,3-cyclohexadiene (rate = 1)
b Heated under reflux
Scheme 42. Derivatization of syn diol adduct 150

 retrosynthetic analysis:

\[ \text{160} \xrightarrow{[\text{C}_5\text{D}_5\text{N}]} \text{150} \]

\[ \text{150} \xrightarrow{[\text{CH}_3\text{I}, \text{KH}]} \text{155} \]

\[ \text{155} \xrightarrow{[\text{TMSCl, py}]} \text{154} \]

\[ \text{154} \xrightarrow{[\text{Ac}_2\text{O, py}]} \]
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 CDCl₃ 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 ¹³C nmr spectrum, of the adduct mixture were entirely consistent with the spectral data reported for other ethyl boronate esters.⁴⁰² 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-benzylidene dienes 132 and 137 were studied. In contrast, the epimeric trans-benzylidene 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 n-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 CHCl₃ at room temperature)

<table>
<thead>
<tr>
<th>Diene</th>
<th>X</th>
<th>Y</th>
<th>% syn</th>
<th>% anti</th>
</tr>
</thead>
<tbody>
<tr>
<td>132</td>
<td>Ph</td>
<td>H</td>
<td>28</td>
<td>72</td>
</tr>
<tr>
<td>137</td>
<td>Ph-pNO₂</td>
<td>H</td>
<td>27</td>
<td>73</td>
</tr>
<tr>
<td>133</td>
<td>H</td>
<td>Ph</td>
<td>4</td>
<td>96</td>
</tr>
<tr>
<td>138</td>
<td>H</td>
<td>Ph-pNO₂</td>
<td>5</td>
<td>95</td>
</tr>
</tbody>
</table>
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 CDCl₃ (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:¹⁰₂

\[
\frac{k_A}{k_B} = \frac{\log [A] - \log ([A] - [Ax])}{\log [B] - \log ([B] - [Bx])}
\]

in which \((k_A/k_B)\) 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 CHCl₃ 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.
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 con
tactronic 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.68 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 n-facial selectivity.69 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 and Inagaki. 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 (CH₃ 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 and by leNoble 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 Cleplak model 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
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 acetalone 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 $n$-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\cite{143} stating that dienophiles add preferentially to the face syn to a lone-pair-bearing substituent. \textit{Ab initio} calculations on 142 have shown that the $n$-electron density is only slightly biased in favor of the face syn to the oxygen.\cite{103}

Therefore, it is unlikely that the exclusive anti facial attachment of dienophiles arose by "orbital mixing" as described by Fukui and Inagaki.\cite{78}

The anti-additions of dienophiles to the benzene oxides were, however, not really inconsistent with the model proposed by Macaulay and Fallis.\cite{144} This model would predict syn-addition since the $\sigma$CH bonds and the $\sigma$CC bonds are better donors than the $\sigma$CO bond. But this model also requires that the $\sigma$ 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 $\sigma$CH and $\sigma$CC bonds are better electron-donors, only the $\sigma$CO bond possesses the proper orientation to enable it to hyperconjugate with the $\sigma^*$ of the incipient bond. The $\sigma$CH(R) bond is not far enough out-of-plane to interact properly in this manner to stabilize effectively a syn transition state.
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 $\pi$-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. 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\textsuperscript{72} 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,\textsuperscript{74} 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 planar-nonsymmetric cyclopentadienes and cyclohexadienes.

In retrospect, the postulate that is most similar with the above proposal was that extended by Anh. 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 23. 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 (CaH₂). 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 CaH₂. 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
$^1$H 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$_6$D$_6$ = δ 128.0, C$_5$D$_3$N = δ 149.5 and (CH$_3$)$_2$SO = 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 $^1$H - $^1$H correlation (COSY) and $^1$H - $^{13}$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 $^1$H 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
diphactometer, 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, 86%) as a clear, colourless oil; uv (CH₃OH) λ<sub>max</sub>: 256 nm (ε = 3900); ir (film) ν<sub>max</sub>: 3054, 1740, 1371, 1241 cm<sup>-1</sup>; <sup>1</sup>H nmr (CDCl₃) δ: 2.07 (6H, s), 5.54 (2H, t, J = 1.2 Hz), 5.87 - 5.93 (2H, m), 6.14 (2H, m); <sup>13</sup>C nmr (CDCl₃) δ: 20.7 (3), 26.6 (3), 70.2

Excess mass calcd. for C₁₀H₁₂O₄: 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 pTsOH (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 NaHCO₃ (50 mL) and saturated NaCl (100 mL), dried (MgSO₄) and the solvent evaporated. Chromatography of the residue (30% ethyl acetate/hexane) gave 114 as a colourless liquid (0.226 g, 83%); uv (CH₃OH) λ<sub>max</sub>: 257 nm (ε = 3500); ir (film) ν<sub>max</sub>: 2987, 1379, 1209, 1032 cm<sup>-1</sup>; <sup>1</sup>H nmr (CDCl₃) 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); <sup>13</sup>C nmr (CDCl₃) 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 C₁₂H₇O₂ (M⁺ -CH₃): 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 CCl₄ (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 (CH₃OH) λ max: 259 nm (ε = 4000); ir (film) ν max: 2958, 1412, 1252, 1119, 840 cm⁻¹; ¹H nmr (CDCl₃) 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); ¹³C nmr (CDCl₃) 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 C₁₂H₂₄O₂Si₂: 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 CDCl₃ (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 (CH₃OH) λ max: 260 nm (ε = 3600); ir (film) ν max: 3044, 2962, 2902, 1413, 1258 cm⁻¹; ¹H nmr (CDCl₃) 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); ¹³C nmr (CDCl₃) δ: -1.9
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/H₂O (50 mL) and CH₂Cl₂ (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 H₂O (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 NaHCO₃ (100 mL) and saturated NaCl (100 mL). The organic layer was dried over MgSO₄ and concentrated under vacuum. Chromatography of the residue (30% ethyl acetate/hexane) provided 124 (0.296 g, 76%) as a colourless liquid; IR (film) νmax: 2929, 1464, 1122 cm⁻¹; UV (CH₃OH) λmax (ε): 262 nm (ε = 2500); "H nmr (CDCl₃) δ: 3.44 (6H, s), 3.81 (2H, s), 5.99 - 6.08 (4H, m); "C nmr (CDCl₃) 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 C₉H₁₂O₂Si: 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 MgSO₄ (60 g), was cooled to -5 to -10°C with the aid of a Dry Ice/isopropanol bath. To this stirred mixture, 127¹⁰⁰ (30.1 g, 0.125 mol) in acetone (10 mL) was added dropwise over 5 minutes. To this solution was added KMnO₄ (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 KMnO₄ addition was complete, the reaction was stirred overnight (ca. 16 h). The brown precipitate of MnO₂ was discharged by bubbling SO₂ 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 CH₂Cl₂ (10 x 100 mL), and the combined organic layers were washed with saturated NaCl (200 mL), dried over MgSO₄ and filtered. Evaporation of the solvent and crystallization of the residue from hot CHCl₃ afforded 128 (15.1 g, 44%) as an off-white powder: mp 103-105°C; ir (KBr) v max: 3380, 2910, 1445, 1285, 1060, 990 cm⁻¹; ¹H nmr (CD₂D₂N) δ: 2.16 (1H, ddd, J = 2.2, 12.0, 13.8 Hz, C-6H₂), 2.70 (1H, ddd, J = 4.2, 4.5, 12.5 Hz, C-3H₂), 2.82 (1H, ddd, J = 2.9, 4.5, 13.8 Hz, C-6H₂), 2.92 (1H, ddd, J = 11.3, 12.0, 12.5 Hz, C-3H₂), 3.98 (1H, ddd, J = 2.8, 4.2, 11.3 Hz, C-2H), 4.25 (1H, m, W₁/₂ = 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); ¹³C nmr (CDCl₃) 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⁺ - Br, 14), 193 (M⁺ - Br, 14), 177 (20), 175 (21), 165 (4), 163 (5), 147 (23), 121 (6), 119 (5), 113 (13), 95 (67), 83 (14), 87 (100), 55 (79), 41 (82). Exact mass calcd. for C₂H₅BrO (M⁺ - Br - H₂O): 176.9734; found: 176.9728.

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

To a solution of 128 (5.88 g, 21.5 mmol) in dry CH₂Cl₂ (150 mL) was added pTsOH (1.03 g) and benzaldehyde dimethylacetal (129) (16.3 g, 107 mmol) as a solution in dry CH₂Cl₂ (10 mL). This was stirred at room temperature for 2 days, after which the solution was washed with 20% NaHSO₃ (50 mL), 1M NaOH (100 mL), saturated NaHCO₃
(100 mL) and saturated NaCl (100 mL). After drying (MgSO₄) 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; 1H nmr (CDCl₃) δ: 2.28 (1H, ddd, J = 5.2, 8.0, 15.0 Hz, C-4H₆), 2.49 (1H, ddd, J = 6.0, 6.7, 15.5 Hz, C-7H₆), 2.79 (1H, ddd, J = 3.8, 5.7, 15.0 Hz, C-4H₆), 2.84 (1H, ddd, J = 4.8, 5.4, 15.5 Hz, C-7H₆), 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); 13C nmr (CDCl₃) 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), 381 (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 C₁₃H₁₃Br₂O₂ (M⁺ - H): 358.9283; found: 358.9293.

For 131: mp 125 - 127°C; 1H nmr (CDCl₃) δ: 2.25 (1H, ddd, J = 4.7, 8.2, 15.1 Hz, C-4H₆), 2.46 (1H, ddd, J = 6.2, 8.0, 15.2 Hz, C-7H₆), 2.78 (1H, ddd, J = 4.5, 5.0, 15.2 Hz, C-7H₆), 2.84 (1H, ddd, J = 3.9, 5.5, 15.1 Hz, C-4H₆), 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-
(2α,3αβ,7αβ)-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 CDCl₃ (ca. 0.5 ml), was added pTsOH (1.4 mg) in CDCl₃ (1 mL), and the mixture was stirred overnight. The analysis of the ¹H 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% CH₂Cl₂/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 NaHCO₃ (3 x 100 mL), water 100 mL and saturated NaCl (100 mL). Drying (MgSO₄), 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) \( \nu_{\text{max}} \): 3044, 2883, 1459, 1401, 1292, 1217, 1061, 697 cm⁻¹; ¹H nmr (CDCl₃) 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
(2α,3αa,7αα)-3α,7α-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 NaHCO₃ (2 x 100 mL), H₂O (100 mL) and saturated NaCl (100 mL), dried (MgSO₄) 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 (CDCl₃) 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); ¹³C nmr (CDCl₃) 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 C₁₃H₁₁O₂ (M⁺ - H): 199.0758; found: 199.0749.
(2α,3αβ,5β,6α,7αβ)- (135) and (2α,3αα,5α,6β,7αβ)-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-toluenesulfonic acid (250 mg). After refluxing for 16 h, the cooled solution was washed with 0.1 M NaOH (100 mL), saturated NaHCO₃ (100 mL) and saturated NaCl (100 mL), dried (MgSO₄) 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 (CDCl₃) δ: 2.31 (1H, ddd, J = 3.5, 8.7, 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 (C₅D₅N) 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 (CDCl₃): δ 4.38: 2.92 (6%), 5.95 (12%); δ 5.95: 4.38 (7%), 4.50 (6%), 7.74 (3%); ¹³C nmr (C₅D₅N) 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 C₁₅H₁₂⁷⁶Br₁⁴¹BrNO₄ (M⁺ - H): 405.9112; found: 405.9119.
For 136: mp 132 - 134°C; ir (KBr) v max: 3106, 2904, 1610, 1520, 1351 cm⁻¹; ¹H nmr (CDCl₃) 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-5H), 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 (C₆D₆N) 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 (CDCl₃): δ 4.27: 2.32 (1%), 2.52 (2%), 2.85 (5%); δ 4.35: 2.52 (1%), 2.85 (6%), 7.82 (1%); δ 4.44: 2.32 (5%), 2.85 (2%), 7.82 (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%); ¹³C 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,3αβ,7αβ)-3α,7α-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 NaHCO₃ (2 x 100 mL) and saturated NaCl (100 mL), and dried (MgSO₄).
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) \( \nu_{\text{max}} \): 3047, 2914, 1611, 1519, 1349 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 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: \( \delta \) 4.73: 5.74 (8.5%), 5.94 - 6.00 (5%); \( \delta \) 5.74: 4.73 (4.5%), 7.64 (3%); \(^{13}\)C nmr (CDCl\(_3\)) \( \delta \): 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\(_{10}\)N\(_2\)O\(_4\) (M\(^+\) - H): 244.0609; found: 244.0603.

(2\(\alpha\),3\(\alpha\),7\(\alpha\))-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\(_3\)OH) \( \lambda_{\text{max}} \): 202 (\( \epsilon = 10,200 \)), 264 (13,300); ir (KBr) \( \nu_{\text{max}} \): 3046, 2881, 1640, 1525, 1355 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 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\(_3\)) \( \delta \): 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 (28), 39 (36). Exact mass calcd. for C_{15}H_{19}NO_{4} (M+H): 244.0609; found: 244.0589.

(2α,3α,5αβ,6αβ,9aβ,10α,10αβ,10bα)-3a,5a,6,6a,9a,10,10a,10b-Octahydro-2,8-diphenyl-6,10-ethanonaphtho[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; \textit{IR} (KBr) \nu_{max}: 3034, 2943, 1457, 1368, 1224, 1097 (strong), 1086 (strong), 751, 696 cm\(^{-1}\); \textit{\textit{\textit{1H nmr}} \textit{\textit{\textit{(CDCl}_3)}} \delta: 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); \textit{1H nmr} \textit{(CsD}_8N) \delta: 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 (CsD\(_8\)N): \delta 2.48: 3.03 (2.5%), 4.34 (3.5%), 4.50 (13%), 5.80 (5%), 6.11 (3%); \delta 4.34: 2.48 (1.5%), 3.03 (4%), 4.59 (8%), 7.70 (1.5%); \delta 4.50: 2.48 (6.5%), 3.03 (2%), 6.30 (2%), 7.60 (2%); \delta 4.59: 5.66 (1%); \delta 5.66: 4.59 (3.5%), 5.80 (4.5%), 6.11 (2%); \delta 5.80: 2.48 (1%), 3.03 (1.5%), 5.66 (4%); \textit{13C nmr} \textit{(CDCl}_3) \delta: 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
(2α,3α,5αβ,6α,6αβ,8β,9αβ,10α,10αβ,10bα)-3α,5α,6α,9α,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; 1H nmr analysis of a sample clearly showed only one dimer present, which was purified by washing the solid with 50% CHCl₃/CCl₄ to give 140 (31 mg, 52%); mp 246 - 247°C; Ir (KBr) νmax: 3046, 2952, 1622, 1517, 1349, 1079, 729 cm⁻¹; 1H nmr (CDCl₃) 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); 1H nmr ((CD₂)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 (CDCl₃): 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%), 7.81 (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%); ¹³C nmr (CD₂SO) 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 CHCl₃ (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% NaHSO₃ (100 mL), saturated NaHCO₃ (2 x 100 mL) and saturated NaCl (200 mL), and dried (MgSO₄). 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) νₘₚₓ: 3005, 1415, 1363, 1009 cm⁻¹; ¹H nmr (CDCl₃) 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); ¹³C nmr (CDCl₃) δ: 32.3 and 33.3 (2 x CH₂), 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 C₆H₈⁶¹BrO and C₆H₈⁷⁹BrO (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 NaHCO₃ (100 mL), and more ether was added (50 mL). The organic layer was washed successively with saturated NaHCO₃ (2 x 100 mL) and saturated NaCl (100 mL), and dried over anhydrous K₂CO₃. Evaporation of the solvent gave 142~143 (0.270 g, 67%) as a yellow liquid; IR (film) vₘₐₓ: 3028, 1609, 1431, 1072 cm⁻¹; ¹H nmr (CDCl₃) δ: 5.12 (2H, d, J = 4.5 Hz), 5.88 (2H, m), 6.26 (2H, complex m); ¹³C nmr (CDCl₃) 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 C₆H₈O: 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, H₂O (1 L) was added. This was extracted with CH₂Cl₂ (300 mL). The organic layer was washed with H₂O (200 mL) and saturated NaCl (200 mL) and dried (MgSO₄). Evaporation of the solvent followed by chromatography (4% acetone/pentane) provided 146a (5.4 g, 42%) as an oil; ¹H nmr (60 MHz, CDCl₃) 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 CHCl₃ (100 mL) cooled to -50°C was added Br₂ (5.64 g, 35.2 mmol) in CHCl₃ (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) v max: 1466, 1384, 1322, 1167, 847, 670 cm⁻¹; ¹H nmr (CDCl₃) δ: 1.32 (3H, s, CH₃), 1.34 (3H, s, CH₃), 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, 15.1 Hz), 2.90 (1H, dd, J = 4.5, 15.4 Hz), 4.15 (1H, ddd, J = 6.8, 7.7, 9.1 Hz), 4.28 (1H, ddd, J = 4.5, 8.3, 9.1 Hz); ¹³C nmr (CDCl₃) δ: 19.5 and 19.9 (2xCH₃), 39.9 and 40.8 (2xCH₃), 49.6 and 50.5 (2xCHBr), 61.0 and 61.9 (oxirane carbons); ms m/z (%): 205 (50) and 203 (51) both M⁺ - Br, 165 (4), 163 (5), 123 (57), 109 (5), 95 (12), 95 (12), 81 (49), 65 (6), 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 H₂O (75 mL), and more ether was added (25 mL). The organic layer was extracted and washed with H₂O (75 mL), saturated NaHCO₃ (75 mL) and saturated NaCl (75 mL) and dried (MgSO₄). Evaporation of the solvent provided 148a~149a (0.754 g, 82%) as a yellow liquid; ir (film) v max: 3026, 1658, 1160, 1078, 743 cm⁻¹; ¹H nmr (CDCl₃) δ: 1.91 (6H, s, 2xCH₃), 5.44 (2H, complex m), 5.99 (2H, distorted t, J = 3 Hz); ¹³C nmr (CDCl₃) δ: 21.1 (2xCH₃), 112.2, 127.5, 149.9 (C-2 and C-7); ms m/z (%): 122
10-Oxatricyclo[4.3.1.0^3.8]deca-3-ene (146b)

To a vigorously stirred solution of 5,8-dihydropindan (145b) (28.5 g, 0.237 mmol) in CHCl₃ (350 mL) was added Aliquat 336 (1.0 g), and over a 2 h period, a solution of 80% MMPP (88 g) in H₂O (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 CHCl₃ (2 x 50 mL). The organic extracts were combined and washed with H₂O (200 mL), saturated NaHCO₃ (200 mL) and saturated NaCl (400 mL), and dried (MgSO₄). Evaporation of the solvent, followed by chromatography (4% acetone/pentane) afforded 146b (23.9 g, 74%), as a viscous, colourless liquid; 'H nmr 60 MHz (CDCl₃) 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[4.3.1.0^3.8]deca-3-ene (147b)

In a manner similar to that for 146a, 146b (5.00 g, 36.7 mmol) and Br₂ (5.26 g, 32.9 mmol) were combined to yield 147b (3.45 g, 87%) as a colourless solid: mp 87 - 88°C; ir (KBr) ν max: 2955, 1415, 1163, 1069, 933, 656 cm⁻¹; 'H nmr (CDCl₃) 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, 6.8 Hz), 4.41 (1H, ddd, J = 4.3, 5.4, 6.8 Hz); ¹³C nmr (CDCl₃) δ: 19.6, 31.2 and 31.3 (CH₂CH₂CH₂bridge), 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
10-Oxatriocyclo[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\text{max}: 1437, 1271, 1187, 1055, 911, 868, 773 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) δ: 1.20-2.81 (6H, complex m, CH\(_2\)CH\(_2\)CH\(_2\) bridge), 6.28 (2H, m), 6.46 (2H, m); \(^13\)C nmr (CDCl\(_3\)) δ: 18.1 and 29.4 (3 x CH\(_3\)), 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 (39), 79 (43), 78 (100), 77 (39), 51 (48). Exact mass calc. for C\(_9\)H\(_{10}\)O: 134.0731; found: 134.0737.

Diels-Alder reaction of 121: (3α\(_a\),4α\(_a\),7α\(_a\),7α\(_a\),8S\(_a\),9R\(_a\)) - (150) and (3α\(_a\),4α\(_a\),7α\(_a\),7α\(_a\),8R\(_a\),9S\(_a\)) - 3a,4,7a-tetrahydro-8,9-dihydroxy-2-phenyl-4,7-ethano-1H-isoindole-1,3(2H)-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%). \(^1\)H 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 CH₂Cl₂ (2 x 50 mL), and the organic layer was washed with saturated NaHCO₃ (25 mL) and saturated NaCl (25 mL), and dried (MgSO₄), 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) vₘₐₓ: 3423, 2960, 1768, 1693, 1502, 1392, 1184, 689 cm⁻¹; ¹H nmr (C₆D₆N) 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 - 7.38 (1H, m, ArH), 7.42 - 7.51 (4H, m, ArH); ¹³C nmr (C₆D₆N) 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 C₁₆H₁₅NO₄: 285.1000; found: 285.0996.

For 151: mp 260 - 261°C; ir (KBr) vₘₐₓ: 3450, 3382, 2901, 1775, 1705, 1393, 1200, 734 cm⁻¹; ¹H nmr (C₆D₆N) 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); ¹³C nmr (C₆D₆N) 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 C₁₅H₁₆NO₄: 285.1000; found 285.0993.
Diels-Alder reaction of 114: (3α,4α,4α,7αβ,8α,8αα,7αα,8β,8α)-4a,7a,8,8a-tetrahydro-2,2-dimethyl-6-phenyl-4,8-ethano-4H-1,3-dioxolo[4,5-
7]isindole-5,7-(3αH,8H)-dione (153)

To a solution of 114 (66 mg, 0.41 mmol) in CHCl₃ (1 mL), was added N-
phenylmaleimide (77 mg, 0.44 mmol) in CHCl₃ (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) νmax: 2981, 2913, 1773, 1501, 1397, 1187, 1047

1H nmr (CDCl₃) 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 (C₆D₆)
δ: 1.10 (3H, s, β-CH₃), 1.35 (3H, s, α-CH₃), 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 (C₆D₆): 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%); ¹³C nmr (C₆D₆) δ:
24.1 (β-CH₃), 26.4 (α-CH₃), 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), 257
(22), 239 (17), 222 (31), 119 (55), 99 (47), 91 (100), 43 (45). Exact mass calcd. for
C₁₉H₁₉NO₄: 325.1313; found: 325.1308.
For 153: mp 263-265°C; ir (KBr) \( v_{\text{max}}\): 2988, 2889, 1796, 1711, 1500, 1391, 1188 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 1.31 (3H, s, \( \alpha\)-CH\(_3\)), 1.35 (3H, s, \( \beta\)-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: \( \delta \): 1.31: 4.32 (6%); \( \delta \): 1.35: 6.17 (2.5%); \( \delta \): 2.88: 3.53 (7.5%), 4.32 (11%); \( \delta \): 3.53: 2.88 (5%), 4.32 (2%), 6.17 (10%); \( \delta \): 4.32: 1.31 (3%), 2.88 (13.5%), 3.53 (15.5%); \( \delta \): 6.17: 3.53 (9.5%); \(^13\)C nmr (CDCl\(_3\)) \( \delta \): 24.8 (\( \alpha\)-CH\(_3\)), 25.2 (\( \beta\)-CH\(_3\)), 38.9 (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), 288 (23), 239 (19), 222 (28), 211 (9), 147 (14), 119 (100), 77 (18), 65 (16), 51 (7). Exact mass calcd. for C\(_{18}\)H\(_{18}\)N\(_2\)O\(_4\): 325.1313; found: 325.1302.

Diels-Alder reaction of 109: (3a\(\alpha\),4\(\alpha\),7\(\alpha\),7a\(\alpha\),8\(S\)\(^\ast\),9\(R\)\(^\ast\))- (154) and (3a\(\alpha\),4\(\alpha\),7\(\alpha\),7a\(\alpha\),8\(R\)\(^\ast\),9\(S\)\(^\ast\))-8,9-bis(acetyloxy)-3a,4,7\(\alpha\)-tetrahydro-2-phenyl-4,7-ethano-1H-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 \(^1\)H nmr spectrum of the residue 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 (CDCl₃) δ: 2.10 (6H, s, 2 × CH₃), 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); ¹³C nmr (CDCl₃) δ: 20.5 (2 × CH₃), 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 × ArC), 128.6 (1 × ArC), 128.9 (2 × ArC), 131.3 (C-5 and C-6), 131.5 (1 × ArC), 169.4 (2 × CH₃CO), 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 C₁₈H₁₇NO₆ (M⁺ - C₂H₅O): 327.1066; found: 327.1081.

For 157: mp 235.5 - 237°C; ir (film) ν max: 2963, 1738, 1711, 1376, 1191, 1062 cm⁻¹; ¹H nmr (CDCl₃) δ: 2.04 (6H, s, 2 × CH₃), 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); ¹²C nmr (CDCl₃) δ: 20.5 (2 × CH₃), 36.5 (C-4 and C-7), 40.6 (C-3a and C-7a), 59.8 (C-8 and C-9), 126.3 (2 × ArC), 128.8 (1 × ArC), 129.2 (2 × ArC), 130.4 (C-5 and C-6), 131.5 (1 × ArC), 169.9 (2 × CH₃CO), 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 C₂₀H₁₅NO₆: 369.1211; found: 369.1216.
Diels-Alder reaction of 122: (3α,4α,7α,7aa,8S*-9α)-3α,4,7,7a-tetrahydro-2-phenyl-8,9-bis[(trimethylsilyl)oxy]-4,7-ethano-1H-isoindole-1,3(2H)-dione (155)

To a solution of diene 122 (92 mg, 0.36 mmol) in CHCl₃ (1 mL) was added N-phenylmaleimide (62 mg, 0.36 mmol) in CHCl₃ (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/CHCl₃ provided 155: mp 143 - 144°C; ir (KBr) v max: 3047, 2955, 2898, 1773, 1710, 1391, 1183, 898, 753 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.17 (18H, s, 6xCH₃), 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); ¹³C nmr (CDCl₃) δ: 0.3 (6 x CH₃), 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⁺ - CH₃, 1), 324 (3), 204 (100), 147 (10), 119 (4), 73 (51), 45 (4). Exact mass calcd. for C₁₆H₁₆NO₅Si (M⁺ - C₆H₁₃OSi): 324.1055; found: 324.1066.
(3α,4α,7α,7αα,8R*,9S*)-3a,4,7,7a-Tetrahydro-2-phenyl-8,9-bis[(trimethylsilyl)oxy]-4,7-ethano-1H-isooindole-1,3(2H)-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 (CDCl₃) δ: 0.16 (18H, s, 6 x CH₃), 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); ¹³C nmr (CDCl₃) δ: 0.2 (6 x CH₃), 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), 178.7 (C-1 and C-3); ms m/z (%): 414 (M⁺ - CH₃, 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 C₁₈H₁₃NO₃Si (M⁺ - C₄H₅O₃Si): 324.1055; found: 324.1078.

Diels-Alder reaction of 124: (3α,4α,7α,7αα,8R*,9R*)- (158) and (3αα,4α,7α,7αα,8R*,9R*)-3a,4,7,7a-tetrahydro-8,9-dimethoxy-2-phenyl-4,7-ethano-1H-isooindole-1,3(2H)-dione (159)

To a solution of 124 (67 mg, 0.48 mmol) in CHCl₃ (2 mL) was added N-phenylmaleimide (59 mg, 0.34 mmol) in CHCl₃ (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$_2$Cl$_2$ was added and the organic layer washed with H$_2$O (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 158: 195 -196°C; ir (KBr) $\nu_{\text{max}}$: 2966, 2891, 1767, 1709, 1497, 1371, 1177, 730 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 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 (CsD$_3$N) $\delta$: 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 (CsD$_3$N): $\delta$ 3.27: 3.34 (2%), 3.51 (11%), 6.20 (2.5%); $\delta$ 3.34: 3.27 (3%), 3.51 (5.5%), 3.62 (2.5%); $\delta$ 3.51: 3.27 (6.5%), 3.34 (1%), 3.62 (6.5%), 6.20 (7.5%); $\delta$ 3.62: 3.34 (1%); $\delta$ 6.20: 3.27 (1%), 3.51 (6.5%); $^{13}$C nmr (CsD$_3$N) $\delta$: 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),...
Diels-Alder reaction of 123: (3α,4α,4αβ,7αβ,8α,8αα)- (160) and (3α,4β,4αα, 7αα,8β,8αα)-4a,7α,8,8α-tetrahydro-2,2-dimethyl-6-phenyl-4H-1,3,2-dioxasilolo[4,5-f]isooindole-5,7-(3aH,6H)-dione (161)

To a solution of cis-3,5-cyclohexadiene-1,2-diol (121) (0.141 g, 1.26 mmol) in CDCl₃ 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-phenylimaleimide (0.217 g, 1.25 mmol) dissolved in CDCl₃ (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 CsD$_5$N (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 CsD$_5$N (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 (CsD$_5$N) 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 (CsD$_5$N) 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$_{15}$H$_{19}$NO$_5$Si: 341.1082; found: 341.1071.

For 161: mp 220 -225 °C; $^1$H nmr (CsD$_5$N) 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
cis-2-Ethyl-3a,7a-dihydro-2,1,3-benzoboradlo xo (125) and its Diels-Alder reaction:

(3α,4α,4αβ,7αβ,8α,8αα) - (162) and (3αα,4ββ,4αα,7αα,8ββ,8αα)-2-ethyl-4α,7a,8,8a-tetrahydro-4,8-etheno-4H-2,1,3-boradioxolo[4,5-f]isoindo le-5,7(3aH,6aH)-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, H₂O (6 drops) was added, and the solvent was evaporated under vacuum to leave a very viscous yellow oil. This was taken up in dry CH₂Cl₂ (10 mL) and 0.5 g of a 50/50 w/w mixture of MgSO₄/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 CDCl₃ (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 CDCl₃ (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] \(\delta\): 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] \(\delta\): 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] \(\delta\): 0.75 - 1.00 (10H, complex m, CH\(_2\)CH\(_2\)), 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: \(\delta\): 2.92: 3.57 (4%), 4.54 (11.5%); \(\delta\): 3.32: 3.57 (3%); \(\delta\): 3.57: 2.92 (6%), 3.32 (6.5%), 4.42 (8%), 4.54 (5%), 6.21 (3.5%), 6.24 (3.5%); \(\delta\): 4.42: 3.57 (4.5%), 6.24 (1%); \(\delta\): 4.54: 2.92 (12%), 3.57 (4.5%); \(\delta\): 6.21: 3.57 (5.5%), 4.42 (1%); \(^{13}\)C nmr (CDCl\(_3\)) [resolved signals from 162] \(\delta\): 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] \(\delta\): 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] \(\delta\): 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\(_{18}\)H\(_{13}\)\(^{11}\)BNO\(_4\) (M\(^+\)-C\(_2\)H\(_4\)): 294.0937; found: 294.0938; calcd. for C\(_{14}\)H\(_{11}\)NO\(_2\) (M\(^+\)-C\(_4\)H\(_7\)BO\(_2\)) 225.0789; found: 225.0783.
Diels-Alder reaction of 132: \((2\alpha,3\alpha,4\beta,4\alpha,7\alpha,8\beta,8\alpha\beta)\) (164) and \((2\alpha,3\alpha,4\alpha,4\alpha,7\alpha,8\alpha,8\alpha\beta)\)-tetrahydro-2,6-diphenyl-4,8-etheno-4H-1,3-dioxo[4,5-f]-isoindole-5,7-(3aH,6H)-dione (165).

To a solution of 132 (82 mg, 0.41 mmol) in CHCl₃ (5 mL) was added N-phenylmaleimide (71 mg, 0.36 mmol) in CHCl₃ (2 mL). This was stirred at room temperature for 16 h. Integration of the '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 '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 CHCl₃/ethyl acetate/hexane.

To 150 (64 mg, 0.22 mmol) in CH₂Cl₂ (15 mL) was added a small amount of pTsOH and benzaldehyde dimethyl acetal (129) (34 μL), and this was stirred for 14 h at room temperature. CH₂Cl₂ (ca. 50 mL) was added and the organic portion was washed with 10% NaOH (30 mL) and saturated NaCl (30 mL), dried (MgSO₄) and concentrated to provide 164 (78 mg, 93%).

Similarly, 151 (51 mg, 0.18 mmol) was suspended in CH₂Cl₂ (15 mL) and pTsOH 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) v_max: 2922, 1774, 1712, 1500, 1384, 1182, 1053, 710 cm⁻¹; ¹H nmr (CDCl₃) 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 (C₆D₆) 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 = 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: 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%); ¹³C nmr (CDCl₃): 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 C₂₃H₁₈NO₄: 373.1313; found: 373.1312.

For 165: mp 231 - 234.5°C; ir (film) v_max: 2896, 1778, 1711, 1498, 1395, 1186, 1065, 745 cm⁻¹; ¹H nmr (CDCl₃) 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%); ¹³C nmr (CDCl₃) 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
Diels-Alder reaction of 133: $(2\alpha, 3a\alpha, 4\alpha, 4a\beta, 7a\beta, 8\alpha, 8a\alpha)$- (168) and $(2\alpha, 3a\alpha, 4\beta, 4a\alpha, 7a\alpha, 8\beta, 8a\alpha)$-4a, 7a, 8a-tetrahydro-2,6-diphenyl-4,8-etheno-4H-1,3-dioxo- [4,5-f]isoindole-5,7-(3aH, 6H)-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 $^1$H 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) $\nu_{max}$: 3056, 2926, 1772, 1710, 1598, 1502, 1397, 1191, 1086, 745 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 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); $^1$H 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$_4$): $\delta$ 3.54: 6.41 (9%); $\delta$ 3.57: 4.08 (8%), 6.21 (6.5%); $\delta$ 4.08: 3.57 (11%), 6.21 (2.5%), 6.41 (2%); $\delta$ 6.21: 3.57 (7%), 4.08 (2%); $\delta$ 6.41: 3.54 (3%); $^{13}$C nmr (CDCl$_3$) $\delta$: 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 (CDCl₃) 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%); 13C 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,3αβ,4β,4αα,7αα,8β,8αβ)- (166) and (2α,3αβ,4α, 4αβ,7αβ,8α,8αβ)-4a,7α,8α-tetrahydro-2-(4-nitrophenyl)-6-phenyl-4,8-etheno-4H-1,3- dioxolo[4,5-f]isoindole-5,7-(3αH,6H)-dione (167)

To a solution of 137 (0.610 g, 2.49 mmol) in CHCl₃ (20 mL) was added N-phenylmaleimide (0.432 g, 2.49 mmol) in CHCl₃ (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) \( \nu_{max} \): 3089, 2949, 1772, 1714, 1610, 1527, 1389, 1352, 1197, 745 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 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: \( \delta \) 3.46: 3.67 (9.5%), 7.69 (5%); \( \delta \) 3.67: 3.46 (8.5%), 4.31 (8.5%), 6.31 (12.5%); \( \delta \) 4.31: 3.67 (11%), 6.00 (24%), 6.31 (2.5%); \( \delta \) 6.00: 4.31 (5%), 7.69 (2%); \( \delta \) 6.31: 3.67 (10.5%), 4.31 (1.5%); \( \delta \) 7.70: 3.46 (2%), 6.00 (3.5%), 8.26 (15.5%); \(^{13}\)C nmr (CDCl\(_3\)) \( \delta \): 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 (2x ArC), 126.2 (2x ArC), 127.1 (2x ArC), 128.5 (1x ArC), 148.4 (1x ArC), 177.8 (C-5 and C-7); ms m/z (%): 418 (M\(^+\), 19), 417 (3), 389 (77), 268 (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) \( \nu_{max} \): 3067, 2901, 1776, 1712, 1519 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 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: \( \delta \) 2.99: 3.72 (10%), 4.44 (12.5%); \( \delta \) 3.72: 2.99 (5.5%), 4.44 (4%), 6.26 (9%); \( \delta \) 4.44: 2.99 (14%), 3.72 (8.5%), 5.74 (20.5%); \( \delta \) 5.74: 4.44 (4%), 7.62 (6%); \( \delta \) 6.26: 3.72 (9%), 7.62 (2.5%); \(^{13}\)C nmr (CDCl\(_3\)) \( \delta \): 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 (2x ArC), 126.3 (2x ArC), 128.2 (2x ArC), 128.8 (1x ArC), 129.1 (2x ArC), 130.1 (C-9 and C-10), 131.5 (1x ArC), 142.3 (1x ArC), 148.6 (1x 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: 

\[ (2\alpha,3\alpha,4\alpha,4\alpha,7\alpha\beta,8\alpha,8\alpha\beta) - (170) \] and 

\[ (2\alpha,3\alpha,4\beta,4\alpha,7\alpha\alpha,8\beta,8\alpha\alpha) - 4a,7a,8,8a-tetrahydro-2-(4-nitrophenyl)-6-phenyl-4,8-etheno-4H-1,3-dioxolo[4,5-f]isoindole-5,7-(3aH,6H)-dione (171) \]

To a solution of 138 (0.510 g, 2.08 mmol) in CHCl₃ (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 CHCl₃/CCl₄.

For 170: mp 253 - 254.5°C; ir (KBr) νₘₐₓ: 3068, 2921, 1776, 1713, 1517, 1347, 1196, 1085, 745 cm⁻¹; ¹H nmr (CDCl₃) δ: 3.61 (2H, t, J = 1.8 Hz, C-4αH and C-7αH), 3.66 (2H, broad s, C-4H and C-8H), 4.12 (2H, t, J = 1.8 Hz, C-3αH and C-8αH), 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%), 8.26 (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%); ¹³C nmr (CDCl₃) δ: 36.9 (C-4 and C-8), 37.8 (C-4α and C-7α), 74.4 (C-3α and C-8α), 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 (CD₂SO) 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 (CDCl₃) 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 (CDCl₃): 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%); ¹³C nmr ((CD₂SO) 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: (1αR*,2α,2aα,5αα,6α,6αE)-1a,2a,5a,6,6a-pentahydro-2,6-etheno-4-phenyl-2H-oxireno[f]isoindole-3,5(4H)-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 CHCl₃ (25 mL), and this solution was stirred for a further 16 h. Evaporation of the solvent left a yellow residue, whose ¹H
The nmr spectrum showed signals for only one adduct. Chromatography (30% EtOAC/hexane) followed by crystallization (CHCl₃-C₆H₆) afforded 172 (0.274 g, 31% from 141) as a colourless solid: mp 218-219°C; ir (KBr) νmax: 3035, 1709, 1498, 1385, 1195, 726 cm⁻¹; ¹H nmr (CDCl₃) 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%); ¹³C nmr (CDCl₃) 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 C₁₆H₁₃NO₃: 267.0895; found: 267.0892.

Diels-Alder reaction of 148a: (1aR*,2α,2α,5α,6α,6aS*)-2a,5a,6,-trihydro-1a,6a-dimethyl-2,6-etheno-4-phenyl-2H-oxireno[3,5(1aH,4H,6aH)-dione (173)

To a solution of 148a/149a (0.129 g, 1.05 mmol) in CHCl₃ (50 mL) was added N-phenylimaleimide (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) νmax: 3020, 1709, 1498, 1388, 1195, 726 cm⁻¹; ¹H nmr (CDCl₃) δ: 1.44 (6H, s, 2 x CH₂), 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\(_{19}\)H\(_{17}\)NO\(_3\): 295.1207; found: 295.1209.

Diels-Alder reaction of 148b with N-phenylmaleimide: (3\(\alpha\),4\(\alpha\),4\(\alpha\)R\(^{\star}\),7\(\alpha\)S\(^{\star}\),8\(\alpha\),8\(\alpha\))-3a,4,5,6,7,8,8a-heptahydro-2-phenyl-4a,7a-epoxy-4,8-ethenocyclopent[f]isoindole-1,3(2H,4aH,7aH)-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) \(v_{\text{max}}\): 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\(_3\)), 25.3 (2 x CH\(_3\)), 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: (3α,4α,4aR*,7αS*,8α,8αa)-3a,4,5,6,7,8,8a-heptahydro-2-methyl-4a,7α-epoxy-4,8-ethenocyclopent[f]isoindole-1,3(2H,4aH,7aH)-dione (175)

A solution of 148b (0.231 mg, 1.72 mmol) and N-methylmaleimide (0.192 g, 1.72 mmol) in CHCl₃ (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) v max: 2942, 1771, 1702, 1435 cm⁻¹; ¹H nmr (CDCl₃) δ: 1.62 - 2.05 (6H, m, 3 x CH,J, 2.89 (3H, s, CH₃), 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, 4.8 Hz, C-10 and C-11); n.O.e. results: approx. 8 2.75: approx. 2.00 (35%), 3.52 (8%); ¹³C nmr (CDCl₃) δ: 24.4 (CH₃), 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 (69), 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 C₁₄H₁₂NO₃: 245.1051; found: 245.1056.

Diels-Alder reaction of 148b with dimethylacetylenedicarboxylate: (3αR*,4α,7α,7αS*)-2,3,4,7-tetrahydro-5,6-bis[carbomethoxy]-3a,7α-epoxy-4,7-etheno-1H-indene (178)

To a solution of 148b (0.166 g, 1.24 mmol) in CHCl₃ (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) v max: 2954, 1717, 1635, 1435, 1329, 1270, 1055 cm⁻¹; ¹H nmr (CDCl₃) δ: 1.60-1.98 (6H, m, 3 x CH₃),
3.80 (6H, s, 2 x OCH₃), 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); ¹³C nmr (CDCl₃) δ: 25.9 (1 x CH₃), 27.2 (2 x CH₃), 44.9 (C-9 and C-10), 52.3 (2 x OCH₃), 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 (CDCl₃)
122 (CDC$_3$)
123 (CDCl₃)
132 (CDCl₃)
$^{1}H$ nmr n.O.e.d. spectrum of 132 (CDCl$_3$)
$^1$H nmr n.O.e.d. spectrum of 137 (CDCl$_3$)
168

140 $(\text{CD}_3)_2\text{SO}$
150 (C₆D₆N)
151 (C₅D₃N)
\[ ^{1}H \text{ nmr n.O.e.d. spectrum of 152 (C}_6\text{D}_6) \]

aromatic signals not shown
153 (CDCl₃)
$^1$H nmr n.O.e.d. spectrum of 153 (CDCl$_3$)

aromatic signals not shown
158 (CDCl₃)
Mixture of 160 and 161 (CDCl₃)
Mixture of 162 and 163 (CDCl₃)
$^1$H nmr n.O.e.d. spectrum of mixture of 162 and 163 (CDCl$_3$)
aromatic signals not shown
$^1$H nmr n.O.e.d. spectrum of 164 ($C_6D_6$)

aromatic signals not shown
$^1\text{H nmr n.O.e.d. spectrum of 165 (CDCl}_3$}
$^1$H nmr n.O.e.d. spectrum of 166 (CDCl$_3$)
\( ^1 \text{H nmr n.O.e.d. spectrum of 167 (CDCl}_3 \text{)} \)

aromatic signals not shown
$\text{H nmr n.O.e.d. spectrum of 168 (10\% CDCl}_3/\text{CCl}_4$}
168 (10% CDCl$_3$/CCl$_4$)
$^1$H nmr n.O.e.d. spectrum of 169 (CDCl$_3$)
aromatic signals not shown
$^1$H nmr n.O.e.d. spectrum of 170 (CDCl$_3$)
$^1$H nmr n.O.e.d. spectrum of 171 (CDCl$_3$)

aromatic signals not shown
172 (CDCl₃)
'$^1$H nmr n.O.e.d. spectrum of 172 (CDCl$_3$)

aromatic signals not shown
173 (CDCl₃)
\(^1\)H nmr n.O.e.d. spectrum of 173 (CDCl\(_3\))

aromatic signals not shown
$^1$H nmr n.O.e.d. spectrum of 174 (CDCl$_3$) 
aromatic signals not shown
175 (CDCl₃)
\textsuperscript{1}H nmr n.O.e.d. spectrum of 175 (CDCl\textsubscript{3})