TT-FACIAL DIASTEREOSELECTIVITY IN THE
DIELS-ALDER REACTIONS OF SUBSTITUTED
CYCLOHEXADIENES

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SUNNY M. OGBOMO
π-FACIAL DIASTEREOSELECTIVITY IN THE DIELS-ALDER REACTIONS OF SUBSTITUTED CYCLOHEXADIENES

by

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A thesis submitted to the School of Graduate Studies in partial fulfilment of the requirements for the degree of Master of Science

Department of Chemistry
Memorial University of Newfoundland

July 1995

St. John's Newfoundland
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ABSTRACT

The Diels-Alder reaction of cis-cyclohexa-3,5-diene-1,2-diol derivatives 50, 51, 40a, 41a and 42a with diethyl azodicarboxylate (DEAD) gave very predominantly products 56, 58, 59, 60 and 62, which arose by addition to the oxygen functions.

Similarly, cis-cyclohexa-3,5-diene-1,2-diol derivatives 50, 51, 40a, 41a, 42a, and benzene oxide-oxepin 48 reacted with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) 109 to afford anti adducts 70, 68, 70, 71 and 69 exclusively, and the anti adduct 66 was the predominant product in the case of diene 50. Moreover, there was a reversal of selectivity when the cis-diol 49 reacted with PTAD, the predominant product 64 arose by addition syn to the oxygen function. The structures of the adducts were determined by nmr, and X-ray crystallography in the cases of 72, 67, and 64. While the anti selectivity was rationalized in terms of electronic effects, hydrogen bonding explained the syn selectivity obtained with diene 49.

The acetonide 40a and its Diels-Alder reaction with dienophiles are described. The experiments indicated that the acetonide dimerized in a Diels-Alder manner affording two products in a ratio of 6:1. The major dimer was that in which addition occurred to the anti face of both reacting partners.

The results of Diels-Alder reactions of acetonide 40a with PTAD, DEAD, dimethyl acetylenedicarboxylate (DMAD), tetracyanoethylene (TCNE) and ethyl
propiolate (EP) afforded exclusively *anti* products 69, 59, 73, 81 and 86, respectively. When butenone, benzoquinone, maleimide and *N*-methylmaleimide were used, the predominant products were *anti* adducts, but selectivity was in favor of *syn* with vinylene carbonate and there was no selectivity when dimethyl maleate was used. Lone pair-lone pair i.e. electronic factor is invoked to explain these selectivities, an alternative rationalization is in terms of electron-donating and electron-withdrawing effects.

A study of the influence of solvent on facial selectivity was carried out using the acetonide 40a with maleimide. The kinetic results indicated that there was significant facial selectivity when water or a polar solvent was used but selectivity was less in a non-polar solvent. A 1M solution of LiCl in 100 mL water gave higher selectivity than a 5M solution of LiClO₄ in ether. However, selectivity was with LiClO₄ in water. Solubility and concentration phenomena are used to rationalize these selectivities.
Acknowledgements

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

Many thanks are given to every member of the Burnell group, in particular Messrs. Jim R. Gillard and Dean Strickland for their support.

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I thank my wife, Joan, and also Elizabeth Kamar for typing the manuscript.

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<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title</td>
<td></td>
</tr>
<tr>
<td>Abstract</td>
<td></td>
</tr>
<tr>
<td>Acknowledgements</td>
<td></td>
</tr>
<tr>
<td>Table of Contents</td>
<td>v</td>
</tr>
<tr>
<td>List of Figures</td>
<td>vii</td>
</tr>
<tr>
<td>List of Schemes</td>
<td>ix</td>
</tr>
<tr>
<td>List of Tables</td>
<td>xii</td>
</tr>
<tr>
<td>Glossary of Abbreviations</td>
<td>xiii</td>
</tr>
<tr>
<td>Dedication</td>
<td>xv</td>
</tr>
<tr>
<td>(1.0) Introduction</td>
<td>1</td>
</tr>
<tr>
<td>(2.0) Diels-Alder reaction</td>
<td>1</td>
</tr>
<tr>
<td>(2.1) Cis-trans conformation</td>
<td>5</td>
</tr>
<tr>
<td>(2.2) Stereospecificity of the Diels-Alder reaction</td>
<td>6</td>
</tr>
<tr>
<td>(2.2.1) Cis principle</td>
<td>6</td>
</tr>
<tr>
<td>(2.2.2) Endo-exo stereoselectivity</td>
<td>8</td>
</tr>
<tr>
<td>(2.3) Substituent effects</td>
<td>10</td>
</tr>
<tr>
<td>(2.4) Regioselectivity</td>
<td>12</td>
</tr>
<tr>
<td>(2.5) Rates</td>
<td>13</td>
</tr>
<tr>
<td>(2.5.1) Pressure</td>
<td>13</td>
</tr>
<tr>
<td>(2.5.2) Temperature</td>
<td>15</td>
</tr>
</tbody>
</table>
List of Figures

1. Frontier molecular orbital diagrams of both endo and exo transition states of the Diels-Alder reaction of cyclopentadiene with maleic anhydride . . . 9

2. Frontier orbital energy diagram for normal, neutral and inverse-electron demand Diels-Alder reactions
   R = electron-donating group and X = electron-withdrawing group . . . . 11

3. Orbital interactions in a 2-substituted diene case .......................... 13

4. Frontier molecular orbital control in regiochemistry ...................... 14

5. Secondary orbital interaction as stabilizing factor in regiocontrol of Diels-Alder reaction ...................................................... 15

6. Syn-anti stereoselectivity in the Diels-Alder reaction of 1,2,3,4,5-pentamethylcyclopentadiene with dienophiles .......................... 19

7. Transition state and propellane structures .................................. 31

8. Fukui's postulate of HOMO electron density distributions of 5-chloro- and 5-methylcyclopentadiene ........................................... 33

9. Kahn and Hehre's postulate of electrostatic interaction ................ 34

10. Anh's postulate ................................................................. 34

11. Cieplak's postulate of the favored axial attack of a nucleophile .... 35

12. Rationalization of the syn-adduct obtained in reaction of 1,2,3,4,5-pentachlorocyclopentadiene ................................................... 36

13. An extension of Cieplak's hyperconjugative α-bond assistance by Macaulay and Fallis ......................................................... 37

14. An extension of Cieplak's hyperconjugative α-bond by le Noble ....... 38

15. Four possible adducts in dimerization of the acetonide and benzylidene dienes ............................................................. 70
<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.</td>
<td>Perspective view of 67</td>
<td>57</td>
</tr>
<tr>
<td>17.</td>
<td>Perspective view of 64</td>
<td>58</td>
</tr>
<tr>
<td>18.</td>
<td>Perspective view of 72</td>
<td>62</td>
</tr>
<tr>
<td>19.</td>
<td>Perspective view of 87</td>
<td>73</td>
</tr>
<tr>
<td>20.</td>
<td>Perspective view of 88</td>
<td>73</td>
</tr>
<tr>
<td>21.</td>
<td>Possible orientation of nitrogen dienophiles with diol 49 and its</td>
<td>76</td>
</tr>
<tr>
<td></td>
<td>derivatives</td>
<td></td>
</tr>
<tr>
<td>22.</td>
<td>Highest occupied asymmetric molecular orbital's for the syn and anti</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>additions to the epoxide</td>
<td></td>
</tr>
<tr>
<td>23.</td>
<td>Hydrogen bond phenomenon as a stabilising factor for syn addition</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td>of diol</td>
<td></td>
</tr>
<tr>
<td>24.</td>
<td>Possible additions of acetylenic dienophiles with the acetonide</td>
<td>80</td>
</tr>
<tr>
<td>25.</td>
<td>Possible additions of ethylenic dienophiles with the acetonide</td>
<td>81</td>
</tr>
<tr>
<td>26.</td>
<td>Possible additions of the acetonide during dimerization</td>
<td>82</td>
</tr>
<tr>
<td>27.</td>
<td>Electron-donating and electron-withdrawing phenomenon in 5-</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td>acetoxyxyclopentadienes and diol 49 and its derivatives</td>
<td></td>
</tr>
<tr>
<td>28.</td>
<td>Conformations of cyclic dienes</td>
<td>85</td>
</tr>
</tbody>
</table>
**List of Schemes**

<table>
<thead>
<tr>
<th>No.</th>
<th>Scheme Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Diels-Alder reaction of 1,3-butadiene with ethylene</td>
<td>1</td>
</tr>
<tr>
<td>2.</td>
<td>Dimerization of 2-methyl-1,3-butadiene (isoprene)</td>
<td>2</td>
</tr>
<tr>
<td>3.</td>
<td>Dimerization of tetrachlorocyclopentadienone</td>
<td>3</td>
</tr>
<tr>
<td>4.</td>
<td>Reaction of cyclopentadiene with para-benzoquinone to afford 4</td>
<td>4</td>
</tr>
<tr>
<td>5.</td>
<td>Diels-Alder reaction of cyclopentadiene and diethyl azodicarboxylate</td>
<td>4</td>
</tr>
<tr>
<td>6.</td>
<td>1,3-Butadiene conformations</td>
<td>5</td>
</tr>
<tr>
<td>7.</td>
<td>Sequence of reactivity of dienes</td>
<td>6</td>
</tr>
<tr>
<td>8.</td>
<td>Cis principle</td>
<td>7</td>
</tr>
<tr>
<td>9.</td>
<td>Retention of stereochemical integrity in dienes</td>
<td>7</td>
</tr>
<tr>
<td>10.</td>
<td><em>Endo-exo</em> stereoselectivity</td>
<td>8</td>
</tr>
<tr>
<td>11.</td>
<td>Diels-Alder reaction of furan with maleic anhydride</td>
<td>10</td>
</tr>
<tr>
<td>12.</td>
<td>The regioselectivity of unsymmetrically substituted dienes and dienophiles</td>
<td>12</td>
</tr>
<tr>
<td>13.</td>
<td>Isomerization of dicyclopentadiene</td>
<td>16</td>
</tr>
<tr>
<td>14.</td>
<td>Diels-Alder reaction of 5-acetoxyhexadiene with ethylene</td>
<td>20</td>
</tr>
<tr>
<td>15.</td>
<td>Diels-Alder reaction of 5-methylcyclopentadiene 9 with maleic anhydride</td>
<td>21</td>
</tr>
<tr>
<td>16.</td>
<td>Diels-Alder reaction of 1,2,3,4,5-pentamethyl-cyclopentadiene 10 with maleic anhydride</td>
<td>21</td>
</tr>
<tr>
<td>17.</td>
<td>Diels-Alder reaction of heterosubstituted cyclopentadiene system with maleic anhydride</td>
<td>22</td>
</tr>
<tr>
<td>18.</td>
<td>Diels-Alder reaction of 14 with dienophiles</td>
<td>23</td>
</tr>
<tr>
<td>19.</td>
<td>Diels-Alder reaction of 2,5-dimethylthiophene s-oxide 15 with benzoquinone</td>
<td>23</td>
</tr>
<tr>
<td>20.</td>
<td>Diels-Alder reaction of 5-halocyclopentadienes with some dienophiles</td>
<td>25</td>
</tr>
<tr>
<td>21.</td>
<td>Diels-Alder reaction of 5-fluorocyclopentadiene 20 with ethylene</td>
<td>26</td>
</tr>
<tr>
<td>22.</td>
<td>Diels-Alder reaction of 1,2,3,4,5-pentachlorocyclopentadiene 21 with some dienophiles</td>
<td>27</td>
</tr>
<tr>
<td>23.</td>
<td>Diels-Alder reaction of diol derivative 22 with NPM</td>
<td>28</td>
</tr>
<tr>
<td>24.</td>
<td>Diels-Alder reaction of diene diacetate 23 with chiral heterodienophile 24</td>
<td>28</td>
</tr>
<tr>
<td>25.</td>
<td>Diels-Alder reaction of some substituted diol derivatives with dimethyl acetylenedicarboxylate (DMAD)</td>
<td>29</td>
</tr>
<tr>
<td>26.</td>
<td>Diels-Alder reactions of propellanes</td>
<td>30</td>
</tr>
<tr>
<td>27.</td>
<td>Diels-Alder reaction of 31 with benzoquinone</td>
<td>31</td>
</tr>
<tr>
<td>28.</td>
<td>Endo/exo stereoselectivity</td>
<td>40</td>
</tr>
<tr>
<td>29.</td>
<td>Dibromodiol 35 from benzene</td>
<td>42</td>
</tr>
<tr>
<td>30.</td>
<td>Derivatizations of dibromodiol 35</td>
<td>43</td>
</tr>
<tr>
<td>31.</td>
<td>Further derivatizations of dibromodiol 35</td>
<td>44</td>
</tr>
<tr>
<td>32.</td>
<td>Dienes from different derivatives of dibromodiol</td>
<td>45</td>
</tr>
<tr>
<td>33.</td>
<td>Method for the preparation of benzene oxide - oxepin</td>
<td>46</td>
</tr>
<tr>
<td>34.</td>
<td>Derivatization of cis-cyclohexa-3,5-diene-1,2-diol</td>
<td>47</td>
</tr>
<tr>
<td>35.</td>
<td>Diels-Alder reaction of derivatives of diol with DEAD</td>
<td>48</td>
</tr>
<tr>
<td>36.</td>
<td>Diels-Alder reaction 40a, 50 and 51 with DEAD</td>
<td>50</td>
</tr>
<tr>
<td>37.</td>
<td>Diels-Alder reaction of 41a and 42a with DEAD</td>
<td>52</td>
</tr>
<tr>
<td>38.</td>
<td>Diels-Alder reaction of diol 49 and its derivatives with PTAD 59</td>
<td>55</td>
</tr>
</tbody>
</table>
39. Diels-Alder reaction of dienes 49 and 50 with PTAD .......................... 56
40. Diels-Alder reaction of 40a, 41a and 51 with PTAD .......................... 59
41. Diels-Alder reaction of benzylidene diene 42a and benzene oxide 48 with PTAD ................................................................. 61
42. Diels-Alder reaction 40a with DMAD and butenone .......................... 67
43. Diels-Alder reaction of 40a with benzoquinone and vinylene carbonate 68
44. Diels-Alder reaction of 40a with TCNE, styrene and maleimide .......... 69
45. Diels-Alder reaction of 40a with cis-stilbene, DMM and EP ............ 70
46. Diels-Alder reaction of N-methylmaleimide and acetonide dimerization 71
47. Diels-Alder reaction of maleimide with acetonide 40a ....................... 73
List of Tables

1. Heteroatom directed n-facially selected adduct ratios ............... 22
2. Summary of the reaction of 21 with dienophiles ..................... 27
3. Relative amounts of adducts in % involved in reaction above ........ 28
4. Rates at different reaction conditions .................................... 39
5. Relative amounts of adducts of substituted diol 49 .................. 48
6. Relative amounts of adducts for the reaction of diol 49 and its derivatives with PTAD .................................................... 54
7. Results of cycloaddition of the acetonide 40a with different dienophiles 65
8. Diels-Alder reaction of the acetonide 40a with maleimide in different solvents ......................................................... 74
### 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>correlation spectrum</td>
</tr>
<tr>
<td>DBU</td>
<td>1,8-diazacyclo[5.4.0]undec-7-ene</td>
</tr>
<tr>
<td>DEAD</td>
<td>diethyl azodicarboxylate</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>dimethyl sulfoxide</td>
</tr>
<tr>
<td>EDG</td>
<td>electron-donating group</td>
</tr>
<tr>
<td>EP</td>
<td>ethyl propionate</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</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>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>
</tbody>
</table>
NMR  nuclear magnetic resonance [spectroscopy]
n.O.e.  nuclear Overhauser effect
NPM  N-phenylmaleimide
PTAD  4-phenyl-1,2,4-triazoline-3,5-dione
\(\rho\)TsOH  \(para\)-toluenesulfonic acid
TCNE  tetracyanoethylene
THF  tetrahydrofuran
TLC  thin layer chromatography
TMS  trimethylsilyl
UV  ultraviolet [spectroscopy]
Dedication

To my wife, Joan, and my children, Efosa and Iziegbe.
INTRODUCTION

The Diels-Alder Reaction

Cycloadditions are among the most widely-used reactions in organic synthesis, and their application to synthesis forms the basis of much research. Cycloadditions provide useful routes for the creation of a wide variety of rings. Important classes of cycloadditions include \([2+2]\) photophysical reactions of alkenes and alkynes, the \(1,3\)-dipolar addition and the \([4+2]\) thermal addition.

The latter class of cycloadditions, known originally as the "diene synthesis", has become universally recognized as the Diels-Alder reaction (Scheme 1), although this reaction may have been known for quite a long time before the work of Diels and Alder. Its origin may be traced back to 1867 when Berthelot\(^6\) reportedly claimed a reaction of benzene with dienophiles. The first experimental dimerization of dienes utilizing 2-methyl-1,3-butadiene (isoprene)
to form (±)-limonene 1 (Scheme 2) was reported by Bouchardat in 1875. A couple of years later, Ipatieff synthesized isoprene and proposed a scheme which then became a useful guide to form other dimers. Worthy of note was how Zincke and his colleagues isolated perchloroindenone 3 by pyrolysis of 2,2,3,4,5,5-hexachloro-1-hydroxycyclopent-3-ene-1-carboxylic acid 2 with the elimination of carbon monoxide and a chlorine molecule from the tetrachlorocyclopentadienone dimer (Scheme 3).

Dimerization reactions proved to be of limited importance, and they were replaced by mixed reactions. The first reaction of this type was reported by Albrecht in 1906, and it involved reaction of cyclopentadiene with para-benzoquinone (Scheme 4) for which he erroneously assigned structures 5 and 6.
as the products. It was not until 1928 that Otto Diels and Kurt Alder clearly established the correct structure 4. They also presented structure 7 for the reaction of cyclopentadiene and diethyl azodicarboxylate (Scheme 5). The work of Diels and Alder opened a new, very promising page in the annals of organic chemistry, and they jointly received a Nobel Prize in 1950 for their work.

The Diels-Alder reaction has become one of the most important tools for the construction of six-membered carbocyclic and heterocyclic ring systems. The Diels-Alder reaction is a $[4_1+2_2]$ cycloaddition (Scheme 1) in which a
conjugated diene (1,3-diene) undergoes an addition to another component,

\[
\begin{align*}
\text{cyclopentadiene} & \quad \text{para-benzoquinone} \\
& \quad \text{ether} \\
& \quad 100\% \\
\end{align*}
\]

Scheme 4: Reaction of cyclopentadiene with para-benzoquinone to afford 4.

Scheme 5: Diels-Alder reaction of cyclopentadiene and diethyl azodicarboxylate
called the dienophile ("diene lover") via a highly ordered cyclic transition state. The product, which is a cyclohexene derivative, is called an adduct whereas the reactants are known as addends."

The Diels-Alder reaction is a thermally allowed, stereospecific, suprafacial process with a concerted, one-step synchronous or nearly synchronous mechanism. This is consistent with the low solvent and polarity effects on the reaction rate, which rules out zwitterionic intermediates. In support of the concerted mechanism is the cis-stereospecificity and by the principle of microscopic reversibility, secondary deuterium kinetic isotope measurements also led to the same mechanistic conclusion in terms of a concerted reaction.

**Cis-trans conformation**

1,3-Butadienes can exist in three types of conformations: s-cis, s-trans and skewed as shown in Scheme 6. In this case skewed refers to all non-planar forms, as opposed to the other two, which are planar. Molecular orbital calculations have shown that the s-trans conformer of 1,3-butadiene is 2-5
5 kcal/mol more stable than the other two. The skewed conformation is more stable than the planar s-cis, but the energy difference is very small.

Only dienes in the s-cis conformation can undergo a Diels-Alder reaction. This geometry is necessary to permit effective orbital overlap, electron delocalization and also formation of a double bond in a six-membered ring.

Dienes which are held in the s-cis conformation are consequently more reactive than those which are not. The reactivity of some dienes is as shown in Scheme 7. Cyclopentadiene is more reactive than cyclohexadiene because it is flat whereas the latter is puckered.

**Scheme 7: Sequence of reactivity of dienes**

Stereospecificity of the Diels-Alder reaction

The synthetic utility of the Diels-Alder reaction depends not only on the fact that it provides an easy access to a wide variety of cyclic compounds but also on its remarkable stereoselectivity.

**The cis-principle:** The relative stereochemistry of a Diels-Alder reaction adduct can be predicted based on empirical rules. The first was formulated by Alder and Stein in 1937. This is now known as the "cis-principle". The relative stereochemistry of addends is retained in the product. For examples, trans and cis dienophiles gives trans and cis adduct (scheme 8). Furthermore, a cis-
Scheme 8: Cis principle

Scheme 9: Retention of stereochemical integrity in dienes

trans-1,4-disubstituted diene gives an adduct with trans substituents, and a trans-trans-1,4-disubstituted diene gives an adduct with cis substituents (Scheme 9).
**Endo-exo stereoselectivity:** The second rule is the *endo*-addition rule, which states that addition proceeds preferentially via the orientation of the addends in which there is the maximum "accumulation of double bonds." Woodward and Hoffman\(^\text{15}\) and subsequently Houk,\(^\text{16}\) Salem\(^\text{17}\) and Alston\(^\text{18}\) explained *endo* selectivity by invoking frontier molecular orbital theory, i.e., by consideration of the highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO) of the addends.\(^\text{19}\) Consider the reaction of cyclopentadiene and maleic anhydride in Scheme 10. In Figure 1, the primary

![Scheme 10: Endo-exo stereoselectivity](image)

interaction (incipient σ-bonds) are indicated by solid lines (between HOMO and LUMO for both orientations) in the transition states. In the *endo* transition state, there is another stabilizing effect, shown by the broken lines, known as a symmetry-controlled secondary orbital interaction.\(^\text{15,20}\) The presence of the
secondary orbital interaction serves to lower the activation energy of the *endo* transition state. Clearly, this interaction is not present in the *exo* orientation.

![Frontier molecular orbital diagrams of both *endo* and *exo* transition states of the Diels-Alder reaction of cyclopentadiene with maleic anhydride.]

because the polar group is directed away from the diene's π-system. Dipole-dipole, charge transfer interactions between polar groups in the dienophile and an easily polarized diene, electrostatic, inductive, steric, and geometrical considerations have been suggested by others as responsible for the *endo* selectivity.

The reaction of cyclopentadiene and maleic anhydride gives a 99 : 1 ratio of the *endo* to *exo* adducts; however, the predominance of one isomer by a 99 : 1 ratio corresponds to a difference of less than 3 kcal/mol in the activation energy. The *endo* rule is violated by the reaction of furan with maleic anhydride (Scheme 11). The reason is that the initially formed *endo* adduct easily dissociates at moderate temperatures, allowing conversion of the kinetic product.
into the thermodynamically more stable \textit{exo} isomer.\textsuperscript{1,5,12} Indeed, in some other

\begin{center}
\begin{tikzpicture}
  \node at (0,0) {\text{Scheme 11: Diels-Alder reaction of furan with maleic anhydride}};
  \node at (0,-0.5) {\text{Diels-Alder reactions, prolonged reaction times may lead to the formation of some \textit{exo} isomer at the expense of the \textit{endo}.}^5,^{13}};
  \node at (0,-1.5) {\textit{Substituent effects}};
  \node at (0,-2) {\text{The success of the Diels-Alder reaction depends largely on structural features of the reacting components.}}^5 \text{ The Diels-Alder reaction is more rapid if the diene bears one or more electron-donating groups such as } \text{C}_6\text{H}_5, \text{OCH}_3, \text{CH}_3, \text{OAc, N(CH}_3)_2, \text{etc., and the dienophile bears electron-withdrawing substituents such as } \text{COR, CN, NO}_2, \text{CO}_2\text{CH}_3, \text{CHO.}^{13,5} \text{ In terms of frontier molecular orbital theory, the diene HOMO donates electron density to the dienophile LUMO. Electron-donating substituents on the diene raise the diene HOMO while electron-withdrawing groups lower the dienophile LUMO, resulting in a smaller energy difference, which in turn results in an increase in rate. This case is known as the normal Diels-Alder reaction (Figure 2). However, when the diene and dienophile have no substituents the difference in the orbital energies (HOMO and LUMO) of the diene and dienophile are similar, so both modes of addition can take place, albeit slowly. This type of reaction is known as the}\n\end{tikzpicture}
\end{center}
Figure 2: Frontier orbital energy diagram for normal, neutral and inverse-electron-demand Diels-Alder reactions
$R = \text{electron-donating group and } X = \text{electron-withdrawing group}$
diene may bear an electron-withdrawing group whereas the dienophile contains an electron-donating substituent. This type of cycloaddition is referred to as an inverse-electron-demand Diels-Alder reaction. In this case, the dienophile HOMO donates electron density to the diene LUMO.

**Regioselectivity**

The regioselectivity of reactions of unsymmetrically substituted dienes and dienophiles, such as 1-substituted dienes and 2-substituted dienes with methyl acrylate in Scheme 12, can be rationalized in terms of resonance contributors and perturbation molecular orbital theory (see Figures 3 and 4).

Secondary molecular orbital interactions have been considered as additional
modifying factors favoring the *ortho* and *para* isomers*\(^9\)* (Figure 5). This regioselectivity phenomenon is also referred to as the *ortho/para* rule.

Perturbation molecular orbital calculations on regioselectivity were carried out by Herndon and coworkers.*\(^{25}\)* Sustmann*\(^{26}\)* utilized the frontier orbital approach to account for reactivity phenomena, and a similar approach has been used by Houk*\(^{27}\)* and Anh*\(^{28}\)* to reveal the origin of regioselectivity. Hehre*\(^{29}\)* suggested that electrostatic potentials inherent to the reactants could explain the regioselectivity of disubstituted compounds.

**Rates**

Generally, rates have been known to be influenced by a number of factors. Some of the factors responsible for acceleration of the Diels-Alder reactions are:

**Pressure:** Pressure affects reactions that are sensitive to volume changes.*\(^9\)* Some reactions that are slower or do not occur under at normal conditions are
Figure 4: Frontier molecular orbital control in regiochemistry
accelerated by high or ultrahigh pressure conditions. An enormously high

![Diagram showing secondary orbital interaction as a stabilising factor in regiocontrol of a Diels-Alder reaction.]

Figure 5: Secondary orbital interaction as a stabilising factor in regiocontrol of a Diels-Alder reaction

pressure, e.g. 10 - 20 kbar, is always associated with a decrease of 26 - 40 cm$^3$/mol in the volume of activation.$^2$ An example of a reaction which has been influenced by pressure is the addition of maleic anhydride to naphthalene to afford an adduct in a yield of 78% at 10 kbar, whereas a yield of less than 1% was achieved at atmospheric pressure.$^3$ Some reactions which occur at about 100°C at atmospheric pressure can be realized at room temperature with a pressure of 9 - 10 kbar.$^2$

**Temperature:** Thermochemical measurements confirm that Diels-Alder reactions are exothermic, in the order of $\Delta H = 30 - 40$ kcal/mol, but many reactions do require drastic conditions.$^9$ It should be noted that raising the
temperature increases the rate of both the forward and the reverse reactions. While some addends react at room temperature or below, others require very high temperatures before they can undergo any transformation.

A change in reaction temperature affects the isomeric ratio of some Diels-Alder reactions. For example, isomerization of endo to exo forms of dicyclopentadiene have been reported. At a temperature of 160 - 180°C, endo dicyclopentadiene dissociates into the monomer cyclopentadiene, which can yield the thermodynamically more stable exo isomer (Scheme 13). Also,

\[
\text{endo} \quad \leftrightarrow \quad \text{exo}
\]

Scheme 13: Isomerization of dicyclopentadiene

the s-trans conformer of 1,3-butadiene is between 2-5 kcal/mol lower in energy than the s-cis conformer. Therefore, the s-trans conformation requires this energy in order to be isomerized into the s-cis conformation suitable for Diels-Alder reaction. Finally, prolonged exposure of adducts to heat or high temperatures usually leads to dissociation or decomposition (retro-Diels-Alder reaction).

Catalysis: Until Yates and Eaton in 1960 recognized that some Diels-Alder reactions proceed much more rapidly in the presence of AlCl₃ it was thought that the Diels-Alder reaction could be influenced only slightly by catalysis. It was
subsequently discovered that the reaction is also catalyzed by other Lewis acids such as (BF$_3$, SnCl$_4$, TiCl$_4$). Lewis acids not only accelerate the rate but also alter the isomer distribution (regiochemistry) when both addends are unsymmetrical. While cis stereospecificity is retained in catalysed reactions, the endo stereoselectivity increases, e.g. the proportion of the endo adduct rises from 80% without catalysis in the reaction of cyclopentadiene and methyl acrylate to 95% in the AlCl$_3$-catalysed reaction.

The explanation for these phenomena is contained in frontier molecular orbital changes. The Lewis acid catalyst lowers the dienophile LUMO energy. This then allows for a stronger interaction between the addends and lowers the activation energy. Complexation between the Lewis acid and the polar groups of the dienophile polarizes the dienophile LUMO (leading to a further reduction of the electron density at the double bond and increased dienophile character), which then increases the regioselectivity and the endo preference respectively. An earlier transition state for the catalysed reaction is known to increase diastereoselectivity as well as endo-exo ratios.

**$n$-Facial Selectivity**

The stereochemistry of the Diels-Alder reaction has three controlling factors. They are the cis-principle, the endo-principle and the $n$-facial stereoselectivity. It is this last facet that decides the syn-anti isomerism.

The issue of facial stereoselectivity has attracted considerable attention in
recent years especially in the area of asymmetric organic synthesis.\textsuperscript{33} It is fascinating that a single allylic heteroatom substituent on the dienophile.\textsuperscript{34} or the diene,\textsuperscript{35} can control diastereofacial selectivity in Diels-Alder reactions. Studies of facial selectivity in dienes may be grouped into two main classes.\textsuperscript{36} The first one involves allylically substituted cyclic and multicyclic compounds, and the second is concerned with chiral acyclic dienes. This thesis will attempt to cover experimentally areas related to the former. In the latter, conformational ambiguities constitute a major area of dispute.

An example of n-facial selectivity is demonstrated in the reaction of 1,2,3,4,5-pentamethylycyclopentadiene with substituted ethylenic dienophiles (Figure 6).\textsuperscript{37} There are two possible modes of endo dienophile attack on the diene. The two possibilities depend on the approach of the dienophile with respect to the diene face, giving rise to syn-anti stereoselectivity. Syn is defined as dienophile addition to the same side as the plane-nonsymmetric allylic substituent and anti if it adds to the opposite side. Often both diastereomers are obtained.

The alternative approach to facial stereoselection is to incorporate a stereogenic center within the diene or dienophile, usually at an allylic position. The products of the cycloaddition are diastereomers because the stereogenic center is built into the product.\textsuperscript{38} There is no simple rule for predicting the effects of substituents on the facial selectivity of the Diels-Alder reaction. Considerable controversy exists in this area and there have been many attempts to rationalize
Figure 6: Syn-anti stereoselectivity in the Diels-Alder reaction of 1,2,3,4,5-pentamethylcyclopentadiene with ethylenic dienophiles.
Some of the factors considered have been: steric effects, van der Waals-London attraction, various orbital interactions, dipole-dipole, dipole-induced dipole, torsional effects (and secondary orbital interactions for conjugated dienophiles), electronic and electrostatic attractions, π-orbital distortion or tilting, hyperconjugative effects, polarizability, product stability and a host of others.

**Carbocyclic Five-Membered Ring Systems**

In 1955 Woodward and coworkers reported an exclusive syn-addition product 9 from the reaction of 5-acetoxy-cyclopentadiene 8 with ethylene (Scheme 14). However, no reason whatsoever was advanced for this selectivity. Since then there has been tremendous progress in both theoretical and experimental work into the possible factors responsible for facial selectivity.

The *syn-anti* stereoselection in the cycloadditions of 5-methylcyclopentadiene 10 was interesting. Minorov had reported high facial selectivity when 10 reacted with maleic anhydride to give as a predominant
product 11, which resulted by addition *anti* to the C-5 methyl group (Scheme 15). In a similar reaction involving 1,2,3,4,5-pentamethylcyclopentadiene 12

![Diels-Alder reaction of 5-methylcyclopentadiene 8 with maleic anhydride](image1)

Scheme 15: Diels-Alder reaction of 5-methylcyclopentadiene 8 with maleic anhydride

![Diels-Alder reaction of 1,2,3,4,5-pentamethylcyclopentadiene 10 with maleic anhydride](image2)

Scheme 16: Diels-Alder reaction of 1,2,3,4,5-pentamethylcyclopentadiene 10 with maleic anhydride

with dienophiles, selectivity also favored the *anti-endo* product 13 (Scheme 16).37

**Heterosubstituted Cyclopentadiene Systems**

A systematic study of heteroatom directed π-facial selectivity was
performed by Macaulay and Fallis,\textsuperscript{42} using different substituents at the 5-position

\[
\text{Me} - \text{Me} \quad \text{Me} - X
\]

\[
\text{Me} + \text{Me} \quad \text{Me} - H
\]

\[
\text{Me} - \text{Me} \quad \text{Me} - \text{Me}
\]

Scheme 17: Diels-Alder reaction of heterosubstituted cyclopentadiene system with maleic anhydride

<table>
<thead>
<tr>
<th>entry.</th>
<th>X</th>
<th>% endo-syn adduct</th>
<th>% endo-anti adduct</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cl</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>OH</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>OCH\textsubscript{3}</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>NH\textsubscript{2}</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>NHAc</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>SH</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>7</td>
<td>SMe</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>SCH\textsubscript{2}Ph</td>
<td>3</td>
<td>97</td>
</tr>
<tr>
<td>9</td>
<td>SOMe</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>10</td>
<td>SO\textsubscript{2}Me</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1. Heteroatom directed π-facially selected adduct ratios
as shown in Scheme 17. The diastereomeric ratios for the exclusively endo-additions of maleic anhydride are given in Table 1.

\[ \text{Scheme 18: Diels-Alder reaction of 14 with dienophiles} \]

\[ X = \text{SeR, TeR} \]

\[ \text{Scheme 19: Diels-Alder reaction of 2,5-dimethylthiophene s-oxide 16 with benzoquinone} \]
Orbital mixing rule arguments have been extended to the heteroatom directed n-facial stereoselectivity experienced with 5-substituted-1,3-cyclopentadienes 14 shown in Scheme 18 by invoking the mixing of \(\sigma\) orbitals of the carbon framework with that of the 5-substituents.\(^4\)

Naperstka and coworkers\(^4\) established that the 2,5-dimethylthiophene oxide 16 obtained \textit{in situ} by peracid oxidation of 2,5-dimethylthiophene 15 reacted with a number of dienophiles \textit{syn} to the sulfoxide oxygen of the diene, (Scheme 19). It was postulated that since there was a competition between the lone pair of the sulfur and sulfoxide oxygen, the interaction between the lone pair and the diene HOMO led to the observed selectivity.\(^4\) Products of the reactions of the (halo)dienes\(^4\) 17 with various dienophiles (Scheme 20) were exclusively \textit{anti}. The bromo derivative 18 reacted 100% \textit{anti} but DMAD gave both products, when it reacted with chloro derivatives 19.\(^{19,46}\)

More recently, McLinton reported a complete reversal of selectivity when 5-fluorocyclopentadiene 20 reacted with ethylene.\(^4\) The adduct obtained was 100% \textit{syn} as shown in Scheme 21. Williamson and others\(^3,46\) have observed that 1,2,3,4,5-pentachlorocyclopentadiene 21 reacted with some dienophiles to give mainly the \textit{syn-endo} adducts (Scheme 22 and Table 2).

\textbf{Substituted 1,3-Cyclohexadiene Systems}

Gillard and Burnell\(^4\) studied the cycloadditions of the plane-nonsymmetric six-membered diene system 22. They found that \textit{N}-phenylmaleimide added to the diene and many of its derivatives preferentially to the face \textit{syn} to the \textit{cis-
Scheme 20: Diels-Alder reaction of 5-halocyclopentadienes with some dienophiles
Scheme 21: Diels-Alder reaction of 5-fluorocyclopentadiene 20
with ethylene

The results demonstrated that
the syn-directing effect of some hetero atom12 is not restricted to
cyclopentadiene derivatives. The probable reason for the observed selectivity is
electronic, because there is no other reason to expect the dienophile to attack
the diene at the more sterically hindered syn face. Their results paralleled those
obtained from 5-acetoxy-cyclopentadiene by Woodward and coworkers,40 and
they are among the cases in which electronic factors override steric hindrance. In
a related reaction, Werbitzky and coworkers50 reported that diene 23 reacted
with the chiral dienophile 1-chloro-1-nitrosomannose 24, to give product 25
(Scheme 24) in very high optical yield.

Bio-oxidation of benzene derivatives such as toluene, chlorobenzene etc.,
with Pseudomonas putida have produced dienes of synthetic importance.51 For
example, compounds 26 and 27 in Scheme 25 are optically active, and
Hudlicky and Price52 utilized these for the preparation of enantiomERICally pure
Scheme 22: Diels-Alder reaction of 1,2,3,4,5-pentachlorocyclopentadiene 21 with some dienophiles

<table>
<thead>
<tr>
<th>entry</th>
<th>dienophile</th>
<th>endo-syn %</th>
<th>endo-anti %</th>
<th>exo-anti %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>maleic anhydride</td>
<td>91</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>acrylonitrile</td>
<td>72</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>methyl acrylate</td>
<td>53</td>
<td>37</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>vinyl acrylate</td>
<td>47</td>
<td>45</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>vinyl chloride</td>
<td>46</td>
<td>40</td>
<td>14</td>
</tr>
<tr>
<td>6</td>
<td>styrene</td>
<td>38</td>
<td>62</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>propene</td>
<td>31</td>
<td>12</td>
<td>57</td>
</tr>
</tbody>
</table>

Table 2: Summary of the reactions of 21 with dienophiles
Scheme 23: Diels-Alder reaction of diol derivatives 22 with NPM

Table 3: Relative amounts of adducts in % involved in reaction above

<table>
<thead>
<tr>
<th>entry</th>
<th>$R_1$</th>
<th>$R_2$</th>
<th>syn</th>
<th>anti</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H</td>
<td>H</td>
<td>94</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>Ac</td>
<td>Ac</td>
<td>88</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>Si(CH$_3$)$_3$</td>
<td>Si(CH$_3$)$_3$</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>-Si(CH$_3$)$_2$-</td>
<td>-Si(CH$_3$)$_2$-</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>5</td>
<td>-C(CH$_3$)$_2$-</td>
<td>-C(CH$_3$)$_2$-</td>
<td>60</td>
<td>40</td>
</tr>
</tbody>
</table>

Scheme 24: Diels-Alder reaction of diene diacetate 23 with chiral heterodienophile 24
prostaglandins and sugar derivatives.

Pittol et al.\textsuperscript{53} and Mahon et al.\textsuperscript{54} treated the four dienes 27 in Scheme 25

\begin{equation}
\begin{aligned}
\text{26} \\
R = \text{Me, Cl}
\end{aligned}
\end{equation}

Scheme 25: Diels-Alder reactions of some substituted diol derivatives with dimethyl acetylenedicarboxylate (DMAD)

with DMAD, and they proposed that steric reasons were responsible for the exclusively \textit{anti} adducts observed in all cases.

\textbf{Multicyclic Systems}

Ginsburg and Gleiter\textsuperscript{55} demonstrated how subtle effects can exert a major impact on the course of the Diels-Alder reaction by modulating the bridgehead substituent of the propellanes. They observed that in the reaction of propellanes 28 in Scheme 26 with \textit{N}-phenyltriazolinedione, selectivity was in favor of the \textit{syn-syn-bis} adduct 29. An explanation for this was advanced by Gleiter\textsuperscript{55} who
invoked a secondary orbital interaction as shown in Figure 7. He stated that the interaction between the N=N lone pairs and the antisymmetric π' orbital of the CO-X-CO bridge of the propellane stabilized the syn-transition state. For propellanes 30 with X = SO, SO$_2$ treated with $N$-phenytriazolinedione attack was 97% syn (Figure 7). This selectivity could not be explained by a secondary orbital interaction, but rather it was explained in terms of a polar group effect in which there was an attraction between the strongly electron deficient S atom in the SO and SO$_2$ groups and the electron rich -N=N- group in the dienophile, with the resulting stabilization of the syn transition state.$^{56}$ We must consider the area
Scheme 27: Diels-Alder reaction of 31 with benzoquinone

Figure 7: Transition state and propellane structures
of high electron density around the oxygen centers of the $\text{SO}_2$ group and the charge deficient region on either side of the $\pi$-plane of the dienophile. However, Macaulay and Fallis\(^{37}\) stated that the results obtained were cases of how neighbouring double-bonds could influence selectivity.

Burnell et al\(^{68}\) asserted that the syn-anti stereoselectivity experienced in spiro(bicyclo[2.2.1]-heptane-2,1'-[2,4]cyclopentadiene)\(^{31}\) was due to a steric interaction between the incoming dienophile and hydrogens on the diene moiety (Scheme 27). The more favorable approach was that in which the dienophile approached the diene moiety syn to the C-3 methylene of diene \(^{31,59}\). The other adduct was the result of endo addition to the face of the diene moiety syn to the C-1 methine. Calculations verified this result.\(^{66}\)

**Theories**

Attempts to probe the origin of facial selectivity have culminated in several interesting rationalizations. In early work by Fukui\(^{61}\) (Figure 8), he stated that the HOMO of 5-chlorocyclopentadiene was biased towards the syn surface. This presented two unequal electron surfaces to an incoming dienophile. In other words, the non-bonding orbital of the 5-substituent perturbed the HOMO of the diene and allowed low lying $\sigma$-orbitals of the carbon skeleton to mix into the HOMO.

Fukui's calculations indicated that the HOMO of 5-chlorocyclopentadiene was biased in the region syn to the chlorine atom, thereby the syn adduct would
be obtained. He also indicated that since a 5-methyl substituent does not have
lone-pair electrons, the HOMO electron density distribution above and below the
diene would be the same. The implication of this was that the addition would be
expected to be governed by steric control. Experimentally, what was obtained
was the anti adduct, which inferred that the addition was indeed governed by
steric effects: the dienophile would avoid the sterically hindered syn face and
attack from the anti face. The model failed to account for the anti adducts
obtained in 5-bromo- and 5-iodocyclopentadiene systems.

Kahn and Hehre\textsuperscript{62} concluded from an electrostatic point of view that there
was an inherent preference for the addition of electrophilic dienophiles to the
more nucleophilic face of the diene syn to "lone-pair-containing allylic
substituent" (Figure 9). This simple model cannot be extended to sulfur
systems.

The Anh\textsuperscript{63} model was based on the assumption that there might be an
attractive interaction between the lone pair orbitals of the allylic heteroatom and

\[ X = \text{electron-donating group} \]
\[ Y = \text{electron-withdrawing group} \]

Figure 9: Kahn and Hehre's postulate of electrostatic interaction

the LUMO of the incoming dienophile (Figure 10). This secondary orbital

Figure 10: Anh's postulate

interaction stabilized the syn transition state leading to syn adduct. Thus, Anh's model could be used to rationalize the syn adduct obtained in the 5-
acetoxycyclopentadiene reaction, but it failed to explain the anti adducts observed in many reactions, for example, the reaction of benzene oxide/oxepin with dienophiles.63

An analysis of π-facialy selective reactions which invokes the interaction of the incipient bond with the two nonequivalent faces was put forward by Cieplak39 (Figure 11). He stated that the hyperconjugation of the antiperiplanar

\[ \text{Nu} \quad \text{vacant orbital} \]

favored \[ \sigma_{\text{CH}} > \sigma_{\text{CC}} \]

\[ \text{Figure 11: Cieplak's postulate of the favored axial attack of a nucleophile} \]

\sigma\text{-bond gives rise to transition state stabilization by }\sigma\text{-electron donation into the vacant }\sigma\text{ orbital associated with the incipient bond. Macaulay57 gave Epitols list of order of increasing }\sigma\text{-donor ability as }\sigma_{\text{CS}} > \sigma_{\text{CH}} > \sigma_{\text{CC}} > \sigma_{\text{CCI}} > \sigma_{\text{CN}} > \sigma_{\text{CO}}. \text{ The Cieplak model could be used to rationalize syn attack to chlorine in the reaction of }1,2,3,4,5\text{-pentachlorocyclopentadiene (Figure 12). This was because }\sigma_{\text{CH}} \text{ is a better donor than }\sigma_{\text{CCI}}.
Macaulay and Fallis\textsuperscript{57} supported and extended the Cieplak model. This extension of the Cieplak theory correctly explained the anti selectivity observed in sulfur systems. As in the example, in Figure 13, the better $\sigma$-donor is the CC bond compared to the CO bond, therefore addition should occur anti to CC bond hence syn to CO was formed. In the same fashion, the CS bond is a better $\sigma$-donor than the CC bond, therefore addition should occur anti to the CS bond, hence the anti adduct was formed.

Le Noble and coworkers\textsuperscript{39} studied the reaction of butadiene with 5-fluoroadamantane-2-thione (Figure 14). They could not account for the syn attack of its reaction based on the electrostatic model. However by an extension of the Cieplak model to this system, Le Noble was able to explain this selectivity. The thermal and photochemical reactions of bond formation were demonstrated to occur on the face anti to the more electron-rich $\sigma$-bond.
Figure 13: An extension of Cieplak's hyperconjugative \( \sigma \)-bond assistance by Macaulay and Fallis
Figure 14: An extension of Cieplak's hyperconjugative 
\( \sigma \)-bond or assistance by le Noble

![Diagram of molecular structures](image)

\[ X = \text{electron-donating group} \quad X = \text{electron-withdrawing group} \]

**Water and Selectivity**

Hopff and Rautenstrauch\(^6\) in 1942 reported the first Diels-Alder reaction conducted in water. Sauer\(^6\) showed that for a wide range of solvent systems, the rate of reaction is only slightly affected by a change in medium. Although water has been considered as a possible solvent in Diels-Alder reactions ever since it was first used by Hopff,\(^6\) its poor solvent properties for dienes made it look unfavourable. Consequently, in numerous papers on the subject, water is absent from the list of solvents under investigation, a fact which undoubtedly discouraged its utilization.\(^6\)

However, in 1980 Breslow and his coworker\(^8\) reopened the use of water and reported remarkable acceleration both in rate and *endo/exo* stereoselectivity. They attributed this intriguing result to a hydrophobic effect.
Table 4 shows the dramatic rate change in switching from the use of isoctane to water as solvent.

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>additional component</th>
<th>rate $(k_2 \times 10^5, \text{m}^{-1}\text{s}^{-1})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>isoctane</td>
<td>-</td>
<td>5.94±0.3</td>
</tr>
<tr>
<td>2</td>
<td>MeOH</td>
<td>-</td>
<td>75.5</td>
</tr>
<tr>
<td>3</td>
<td>H$_2$O</td>
<td>-</td>
<td>4000±70</td>
</tr>
<tr>
<td>4</td>
<td>H$_2$O</td>
<td>LiCl</td>
<td>10800</td>
</tr>
<tr>
<td>5</td>
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<td>C(NH$_2$)$_3^+$Cl$^-$</td>
<td>4300</td>
</tr>
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<td>6</td>
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<td>β-cyclodextrin</td>
<td>10900</td>
</tr>
<tr>
<td>7</td>
<td>H$_2$O</td>
<td>α-cyclodextrin</td>
<td>2610</td>
</tr>
</tbody>
</table>

Table 4. Rates at different reaction conditions

with an improved rate.$^{68}$ Breslow and his coworker$^{68}$ also reported that lithium chloride when added to the water enhanced the rate even more, and they contrasted this with guanidium chloride, which has a surface-tension-reducing properties and decreased the rate. More evidence for the hydrophobic effect came from the use of β-cyclodextrin, which is known to have a hydrophobic cavity. Reactions conducted with β-cyclodextrin gave dramatic results, which paralleled rate enhancement by hydrophobic binding of the molecules. The reason for the small rate acceleration in α-cyclodextrin was ascribed to the
smaller cavity, which would be unable to accommodate both addends.$^{68}$

In spite of the evidence for the hydrophobic effect, Grieco et al.$^{69}$ in 1983 argued that the increased rate was due to micellar aggregation. Further experiments conducted by Breslow and his coworkers$^{70}$ and others$^{71}$ showed that the hydrophobic effect was indeed the phenomenon responsible. Ever since, there has been remarkable improvement in utility of aqueous media in the form of microemulsion and aqueous surfactant-based media.$^{72}$ Grieco and his coworkers$^{73}$ reported a dramatic rate acceleration of Diels-Alder reactions using lithium perchlorate in diethyl ether (LPDE). They proposed that a "high" internal solvent pressure present in water was equally present in this reagent. It was concluded that Diels-Alder adducts that could not be accessible through conventional means would now be possible. In one of their studies using LPDE a 93% yield with an endo:exo ratio of 8:1 was realized when ethyl acrylate and cyclopentadiene was reacted, whereas a similar reaction in water afforded only a 73% yield and an endo:exo ratio of 4:1 (Scheme 28).

\[
\text{Scheme 28: Endo/exo stereoselectivity}
\]
As an alternative explanation, Forman and his coworkers\textsuperscript{74} claimed that the rate enhancement by LPDE was not due to internal pressure but to Lewis acid catalysis with the lithium ion functioning as the Lewis acid. It is important to note that LPDE should be handled with care because a recent report by Silva\textsuperscript{75} indicated that it has an explosive character.

From the work of Gillard and Burnell\textsuperscript{49} two things were remarkable: (a) that the Diels-Alder reaction of \textit{cis}-cyclohexa-3,5-diene-1,2-diol and its derivatives with N-phenylmaleimide afforded adducts whose addition occurred from the more sterically hindered face of the diene, \textit{syn} to the oxygen functions, and (b) that the facial selectivity was less pronounced with cyclic derivatives of this diol. The research described in this thesis was geared towards examining \textit{syn-anti} stereoselectivity of the same substrates but with different dienophiles. Also, for the first time, the effect of water on facial selectivity using the cyclic derivatives has been examined.
RESULTS

Synthesis of the dienes

The dibromodiol 35 appeared to be an efficient common precursor to many dienes. Benzene 32 was reduced under Birch conditions\(^{76}\) to give 1,4-cyclohexadiene 33. Addition of one molar equivalent of bromine in the cold using the procedure by Wibaut and Hauk\(^{77}\) afforded 34, which was purified by vacuum distillation. Following an established procedure by Yang and co-workers,\(^{78}\) cis-hydroxylation of 34 by potassium permanganate solution\(^{79}\) gave dibromodiol 35 in 40-45\% yield (Scheme 29). Treatment of 35 with acetic anhydride in pyridine provided compound 36 (90\%). When compound 35 was treated with chlorotrimethylsilane in pyridine, 37 was obtained in 72\% yield along with a small amount of 38 (Scheme 30). A phase-transfer reaction utilizing a
procedure by Merz\textsuperscript{89} with dimethylsulfate as the methylating agent resulted in

![Chemical structure](image)

**Scheme 30: Derivatization of dibromodiol 35**
dibromo derivatives 43 (60%) and 44 (10%) in Scheme 31. Compound 40 was

[Diagram of chemical reactions]

Scheme 31. Further derivatizations of dibromodiol 35
obtained as a yellow oil in good yield by acetonization of 35 with 2,2-dimethoxypropane and a catalytic amount of pTsOH (Scheme 30). The benzylidene derivatives 41 and 42 were obtained by acid-catalysed acetalization of 35 with a large excess of benzaldehyde dimethylacetal followed by chromatography. The dibromo monoTMS 38 (Scheme 30) and dibromo monomethyl 44 compounds (Scheme 31) were acetylated to provide corresponding acetylated compounds 39 and 45. In the same fashion, silylation of 44 afforded 46 (Scheme 31).

Double dehydrobromination of 40, 41, and 42 with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in boiling benzene yielded dienes 40a, 41a, and 42a (Scheme 32). These dienes were chromatographed on silica gel to afford pure compounds. Dienes 40a, 41a, and 42a have a tendency to dimerize, even in the cold, so they were used immediately.
The benzene oxide 48 was synthesized in a few steps starting from 37 (Scheme 33). Epoxidation of 34 with meta-chloroperoxybenzoic acid gave 47 and double dehydrobromination with DBU afforded 48 as a mixture of benzene oxide and oxepin, its valence tautomer. The $^1$H nmr spectrum of this product displayed a single set of signals, which according to Vogel and coworkers, resulted from averaging of the signals of both tautomers.

Dienes 50, 51, 52 and 53 were obtained in good yields from commercially available cis-cyclohexa-3,5-diene-1,2-diol 49 by derivatization in a straightforward manner (chlorotrimethylsilane/pyridine or acetic anhydride/pyridine or dimethyrsulfate) as shown in Scheme 34. Diol 49 has been produced by stereospecific microbial oxidation of benzene by mutants of
Pseudomonas putida, a soil bacterium.\textsuperscript{62}

\begin{center}
\includegraphics[width=0.5\textwidth]{Scheme_34.png}
\end{center}

Scheme 34: Derivatization of \textit{cis}-cyclohexa-3,5-diene-1,2-diol

\textbf{Diels-Alder reactions}

The Diels-Alder reactions of dienes 50 and 51 with diethyl azodicarboxylate (DEAD) 55 were conducted in chloroform (Scheme 35). The
Scheme 35. Diels-Alder reaction of derivatives of diol with DEAD

Table 5. Relative amounts of adducts of substituted diol 49
reaction mixture containing 50 was stirred for about 72 hours at room
temperature while that for 51 was stirred for 24 hours. Thin layer
chromatography (TLC) of the reaction with 50 indicated two new spots along with
some unreacted starting materials. The solvent was evaporated and analysis of
the crude sample by $^1$H nmr spectroscopy revealed considerable broadening of
the signals of the putative adducts in the region $\sigma$ 5.0 - 7.0 so their ratio could
not be measured. Flash column chromatography of the sample resulted in the
isolation of 56a and 56b as colorless oils. Their $^1$H nmr spectra were still
unclear.

Similarly, the $^1$H nmr spectrum of the crude sample after evaporating the
solvent from the reaction of 51 indicated the presence of anti adducts.
Subsequent chromatography was problematic as the material proved unstable
towards the chromatographic system. However, a light pink oil was collected
and a small amount of the starting materials was recovered. Rerunning the
spectrum of compound 56a at 50°C led to simplification of the spectrum, but at
70°C more signals were discerned. Nevertheless, there was still ambiguity
regarding the number of different adducts each crude product contained.

A benzene solution of the acetonide 40a with DEAD was stirred at room
temperature, and subsequent analysis of the crude sample revealed only one
adduct (Scheme 36). Purification of this sample afforded a colorless oil 58 in
good yield. The complete assignment of the $^1$H nmr spectrum of the adduct was
done on the basis of chemical shift and nuclear Overhauser effect (nOe)
Scheme 36. Diels-Alder reaction 40a, 50 and 51 with DEAD
experiments. Signals at δ 6.50 and 5.15 were assigned to the olefinic and the bridgehead protons, respectively, whereas that at δ 4.46 was that for the acetoxy protons. Multiplets at δ 4.26 and δ 1.28 arose from the methylene and methyl portions of the molecule. Saturation of the olefinic signal at δ 6.50 enhanced the intensity of the bridgehead protons at δ 5.15 ppm. Conversely, saturation of the methyl signal gave enhancement of the olefinic signal. These results showed the proximity of the olefinic hydrogens to a methyl group and clearly showed the adduct was 58 (Scheme 36).

The benzylidene dienes 41a or 42a reacted with DEAD (Scheme 37). The 1H nmr analysis of the two crude samples showed signals for a dimer which completely masked the signals for the DEAD adducts in the downfield region of the spectrum. Chromatography of each crude sample afforded an oily adducts 60 and 62 and dimers 61 and 63. Assignments of the signals in 1H nmr spectra were carried out in a fashion analogous with that previously used for adduct 58. Moreover, correlation spectroscopy (COSY) confirmed these assignments. Nuclear Overhauser enhancements (nOe) established the stereochemistry of 60. Similar nOe experiments were performed on 62 (Scheme 37). Saturation of the olefinic signal gave an enhancement of 0.6% for the phenyl signal. This result confirmed the stereochemistry in which the phenyl ring was closer to the olefinic hydrogens i.e., an anti adduct.

There were four possible modes of dimerization of dienes 40a, 41a and 42a (Figure 15). The predominant product in all cases of dienes was the one in
Scheme 37. Diels-Alder reaction of 41a and 42a with DEAD

which both the diene and the dienophile partners were anti. In the case of the acetonide diene 40a, the selectivity was 6:1 in favor of this dimer. Rigorous
Dimerization → 4 possible adducts:

Figure 15: Four possible adducts in dimerization of the acetonide and benzylidene dienes
assignment of the stereochemistry of the two dimers 61 and 63 was obtained spectroscopically. Results of NOe experiments with dimer 61 showed that it resulted from anti-anti endo addition of the diene (Scheme 37) because saturation of the signal for the hydrogen at C-12 gave an enhancement of C-8 (6%), C-3a (5%) and C-6 (6%) hydrogens whereas saturation of the singlet signal at C-8 gave enhancement of 0.35% for the phenyl group. In the case of dimer 63 (Scheme 37), enhancements of 0.8% and 1%, respectively, of the phenyl signal of C-8 and C-3a hydrogen was observed when hydrogens on C-11 and C-12 were saturated. Moreover, saturation of hydrogen on C-3a resulted in significant enhancement of 1% of olefinic hydrogens on C-11 and C-12.

4-Phenyl-1,2,4-triazoline-3,5-dione 59 is one of the most reactive dienophiles known. It was prepared from 4-pheny lurazole by the action of t-buty lhypochlorite as the oxidizing agent. Sublimation was used to purify this dienophile, which is intensely red.

Slow addition of the requisite amount of a solution of 59 in acetone into a solution of diene 50 led to instantaneous discharge of the red colour. The mixture was nevertheless stirred for 16 hours after which TLC indicated two spots. The $^1\text{H}$ nmr spectrum of the crude sample indicated signals for two adducts in a ratio of 9:1. Flash column chromatography yielded both adducts as colorless solids. The major one (66) was isolated in 77% yield and the minor one (67) in 13% yield (Schemes 38 and 39). Analysis of the $^1\text{H}$ nmr and COSY spectra of the two adducts showed that the olefinic hydrogen was coupled to the
Scheme 38: Diels-Alder reaction of diol 49 and its derivatives with PTAD 59

Table 6: Relative amounts of adducts for the reaction of diol 49 and its derivatives with PTAD
Scheme 39: Diels-Alder reaction of dienes 49 and 50 with PTAD
bridgehead hydrogen, and this in turn was coupled to the acetoxy protons. Irradiation of the olefinic hydrogen gave an enhancement of 0.2% of the acetate group. This showed conclusively that the major adduct was anti 66, i.e., the result of anti addition. The opposite stereochemical assignment was made for 67 which showed that the minor adduct resulted from syn attack of the diene to the dienophile. An X-ray crystallographic study of the minor adduct 67 revealed unambiguously the stereochemistry to be that of a syn adduct (Figure 16).

Figure 16: Perspective view of 67

Following a similar procedure as that used above, slow addition of the requisite amount of PTAD into diene 49 and stirring for 16 hours followed by subsequent spectroscopic analysis revealed two adducts 64 and 65 as shown in
Scheme 39. An X-ray crystal structure (Figure 17) proved that the major adduct was 64. Also, the assignment of the major adduct 64 was confirmed by chemical correlation with the adduct 67 by a straightforward transformation of the adduct 64 to the corresponding ester 67 whose structure had been elucidated unambiguously both by nOe experiments and X-ray crystallography.

The Diels-Alder reaction of diene 51 was performed by slow addition of the requisite amount of a solution of 59 in acetone into a solution of diene 51, and this was stirred at room temperature for 16 hours (Scheme 40). Analysis of
Scheme 40: Diels-Alder reactions of 40a, 41a and 51 with PTAD
the reaction mixture revealed a component with a molecular ion at m/z 416, corresponding to the mass of the new adduct. The $^1$H nmr spectrum of the resultant crude sample showed signals for a single adduct. Flash column chromatography afforded the product 68 as a colorless solid. There was evidence from nOe experiments that the stereochemistry of 68 resulted from addition to the anti face of the diene.

The Diels-Alder reactions of the benzyldiene dienes 41a and 42a were conducted in a similar manner with the 4-phenyltriazolinedione (PTAD) (Schemes 40 and 41). The $^1$H nmr spectrum of each crude reaction product showed signals for only one adduct (and a dimer). Purification of the adduct from the benzyldiene diene 41a afforded a colorless solid 70 and a dimer 61. Likewise 71 was isolated as a colorless solid from the reaction mixture from 42a (Scheme 41). The stereochemistry of both 70 and 71 was established unequivocally by nOe experiments. For compound 70 (Scheme 40) saturation of the olefinic hydrogen on C-10 gave an enhancement of the singlet for the hydrogen on C-2. Conversely, irradiation of this singlet gave an nOe of 3% for the olefinic hydrogen on C-10. Results of experiments with 71 indicated that saturation of the C-10 hydrogen only led to an nOe of 1% of the phenyl group, but not to the C-2 hydrogen, which meant that this hydrogen was farther from the olefinic hydrogen on C-10 than was the phenyl group on C-2 (Scheme 41). These results for both adducts indicated that both adducts were formed by addition to the face of the diene anti to the oxygen functions. The relative
the olefinic hydrogen on C-10 than was the phenyl group on C-2 (Scheme 41).

Scheme 41: Diels-Alder reaction of benzylidene diene 42a and benzene oxide 48 with PTAD
stereochemistry of the two dimers obtained from reactions involving \(41a\) and \(42a\) were found to be the same as those of \(61\) and \(63\), respectively, in Scheme 37.

The acetonide diene \(40a\) reacted with PTAD after about 16 hours to give a single adduct \(69\) (from the \(^1\)H nmr spectrum of the crude product). Measurements of nOe's in its \(^1\)H nmr spectrum established the proximity of the olefinic hydrogens to one of the acetonide methyl groups, i.e., this was an antil adduct.

The addition of PTAD to the tautomeric mixture of benzene oxide-oxepin resulted in the formation a single adduct (Scheme 41). Analysis of the nmr data showed that the adduct was symmetrical, i.e., the result of reaction of the

![Figure 18: Perspective view of 72](image-url)
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<th>entry</th>
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<th>anti-endo</th>
<th>syn-endo</th>
<th>% yield</th>
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<td>18&lt;sup&gt;a&lt;/sup&gt;</td>
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Table 7: Results of cycloaddition of the acetonide 40a with different dienophiles
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<th>syn-endo</th>
<th>% yield</th>
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<td>65</td>
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<td>41</td>
<td>83</td>
</tr>
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<td></td>
<td></td>
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<td>entry</td>
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<td>syn-endo</td>
<td>% yield</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
<td>-----------</td>
<td>----------</td>
<td>---------</td>
</tr>
<tr>
<td>12</td>
<td>COOC₂H₅</td>
<td>100</td>
<td>0</td>
<td>61</td>
</tr>
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<td>N-Me</td>
<td>53</td>
<td>47</td>
<td>77</td>
</tr>
</tbody>
</table>

a contained a lesser amount of the exo adduct  
b no reaction

Table 7: Results of cycloaddition of the acetonide 40a with different dienophiles
benzene oxide form only. Unambiguous structure determination was performed by X-ray crystallography, and the structure of the adduct 72 proved to be the result of addition anti to the oxygen function (Figure 18).

Following the same method of reaction of the acetonide with the nitrogen dienophiles, the Diels-Alder reactions of acetonide 40a with a wide variety of dienophiles were conducted (Table 7). An anti-addition product was observed exclusively in the cases involving the acetylenic dienophiles. Tetracyanoethylene also gave an anti adduct exclusively. An anti adduct was the predominant, but not the exclusive product when butenone, maleimide, N-methylmaleimide (NMM), para-benzoquinone (BQ) were treated with the acetonide diene. Moreover, the 1H nmr spectrum of the syn addition product with butenone revealed that the sample was accompanied by a small amount of exo adduct. There was, however, no facial selectivity with dimethyl maleate (DMM). Selectivity favored the syn-endo mode of addition with vinylene carbonate (Schemes 42-45).

A neat liquid sample of the acetonide diene 40a stored at room temperature dimerized in a Diels-Alder manner to afford two isomers 89 and 90 (Scheme 46 and Figure 15). Results of nmr data and X-ray crystallography for both dimers showed that the predominant adduct resulted from addition anti to the oxygen functions of both reacting partners (Figures 19 and 20).

The Diels-Alder reactions of the acetonide diene 40a with maleimide in various solvents were performed (Scheme 47). Results revealed a steady
Scheme 42: Diels-Alder reactions of 40a with DMAD and butenone
Scheme 43: Diels-Alder reaction of 40a with benzoquinone and vinylene carbonate
Scheme 44: Diels-Alder reaction of 40a with TCNE, styrene and maleimide
Scheme 45: Diels-Alder reaction of 40a with cis-stilbene, DMM and EP
Scheme 46: Diels-Alder reaction of N-methylmaleimide and acetonide dimerization
Figure 19: Perspective view of 89

Figure 20: Perspective view of 90
Scheme 47: Diels-Alder reaction of maleimide with acetonide 40a

<table>
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<th>ratio of adduct ( anti : syn )</th>
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<td>83</td>
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<tr>
<td>2</td>
<td>dichloromethane</td>
<td>1.6 : 1</td>
<td>99</td>
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<tr>
<td>3</td>
<td>pyridine</td>
<td>2.5 : 1</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>methanol</td>
<td>2.7 : 1</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>acetonitrile</td>
<td>3.7 : 1</td>
<td>99</td>
</tr>
<tr>
<td>6</td>
<td>dimethyl sulfoxide</td>
<td>6.1 : 1</td>
<td>97</td>
</tr>
<tr>
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<td>neat</td>
<td>2.7 : 1</td>
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</tr>
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<td>8</td>
<td>chloroform</td>
<td>1 : 1</td>
<td>99</td>
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<tr>
<td>9</td>
<td>ether</td>
<td>1.2 : 1</td>
<td>90</td>
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<td>4.2 : 1</td>
<td>94</td>
</tr>
<tr>
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<td>water (100 mL)</td>
<td>9.4 : 1</td>
<td>89</td>
</tr>
<tr>
<td>12</td>
<td>water (1000 mL)</td>
<td>4.5 : 1</td>
<td>86</td>
</tr>
<tr>
<td>13</td>
<td>1M LiCl (100 mL water)</td>
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<td>14</td>
<td>1M LiClO₄ (100 mL water)</td>
<td>4.4 : 1</td>
<td>85</td>
</tr>
<tr>
<td>15</td>
<td>5M LiClO₄ (2.0 mL ether)</td>
<td>2.1 : 1</td>
<td>92</td>
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</table>

Table 8: Diels-Alder reactions of the acetonide 40a with maleimide in different solvents
Preference for adduct ratio in favour of anti 1:4:1 from benzene to acetonitrile (Table 8), but this preference was more in dimethylsulfoxide (6:1) and low in the case of a neat sample. There was no facial selectivity in chloroform. There was a similar rise in selectivity from ether (1.2:1) to use of water as solvent (9.4:1). Lithium perchlorate (1M LiClO₄) only led to a selectivity of 4.4:1 when it was added to the mixture in 100 mL of water while a 5M concentration of the same compound in ether produced just a 2.1:1 selectively in favor of anti.
DISCUSSION

cis-Cyclohexa-3,5-diene-1,2-diol 49 and many of its derivatives added to
$N$-phenylmaleimide predominantly syn to the oxygen functions.\textsuperscript{49} In a similar
fashion, the syn-anti stereoselectivity of Diels-Alder reactions involving some 5-
heterosubstituted cyclopentadienes led predominantly to products that have
been concluded to be formed by addition to the face of the diene syn to the
heteroatom, i.e., to the more substituted face.\textsuperscript{49} Other heteroatoms in a similar
position direct addition mainly anti to the heteroatoms.\textsuperscript{42,45} We have observed
that derivatization of 49 and subsequent Diels-Alder reactions with nitrogen
dienophiles afforded exclusively, or very predominantly, anti adducts. These
results are consistent with the anti adduct observed when 4-(p-bromophenyl)-
1,2,4-triazoline-3,5-dione was used with 3-methylsubstituted diacetate.\textsuperscript{84} The
reaction of diol 49 itself with the nitrogen dienophile, 4-phenyl-1,2,4-triazoline-
3,5-dione (PTAD) reversed the selectivity largely in favor of syn. Benzene oxide
48 with PTAD afforded exclusively the anti adduct. Earlier studies of this same
diene with $N$-phenylmaleimide also resulted in anti adduct exclusively.\textsuperscript{85} In
contrast to this result, the cyclopentadienyl and cyclohexadienyl dienes that
possess allylic oxygen functions all give syn adducts.

Many theories have been forwarded to explain facial selectivity in Diels-
Alder reactions.\textsuperscript{39,42} Many of these are not consistent with our results. For
example, an extension of the proposals of Anh\textsuperscript{86} and of Kahn and Hehre\textsuperscript{87} to our
results with our dienes 40a, 41a, 42a, and 48-51 would indicate that the

Figure 21: Possible orientation of nitrogen dienophiles with diol 49 and its derivatives
major adducts would be expected to arise by addition to the more nucleophilic face of the diene, i.e., the syn face, but this was not the case with the nitrogen dienophiles. Apparently, however, the selectivity observed in our earlier studies of 49 and its derivatives with the ethylenic dienophiles is in favor of this idea. While the Cieplak model\textsuperscript{39} accounted for the syn approach of ethylenic dienophiles to 49 and its derivatives, it failed to account for our results observed in the reaction of dienes 40a, 41a, 42a and 48 - 52 with nitrogen dienophiles.

An explanation why an anti adduct was observed either predominantly or exclusively with dienes 40a, 41a, 42a, and 48 - 52 with diethylazodicarboxylate (DEAD) and with PTAD is an electrostatic repulsion in the syn transition state due to the lone pairs of the oxygen atoms of the diene and the lone pairs on the nitrogens of the incoming dienophile.\textsuperscript{55,56} The anti face, which is relatively unencumbered both electronically and sterically, is the face on which addition takes place (Figure 21). Benzene oxide 48 produced anti adducts exclusively, irrespective of the dienophile. This indicated that electronic features are less important and steric or torsional interactions within the diene play a major role. Indeed, results of \textit{ab initio} calculations on the syn and anti transition states of benzene oxide have revealed that all of the difference in energy between the transition states is due to very unfavorable deformation of the epoxide part of the molecule in the syn transition state (Figure 22). Thus the anti transition state is 11.4 kcal/mol more stable than the syn.\textsuperscript{68}

Whereas Anh's theory was not consistent with our results with the
nitrogen dienophile and derivatives of diol 49, the diol itself with PTAD gave

\[ \text{syn} \]

\[ \text{anti} \]

\[ \text{anti} > \text{syn} \ (11.4 \text{ kcal/mol}) \]

Figure 22: Highest occupied asymmetric MO’s for the syn and anti additions to the epoxide

predominantly the syn adduct. However, the reason for this is unlikely to be due to a HOMO-LUMO interaction of the type that Anh described. We rationalize that in this case only, hydrogen bonding controls the facial selectivity, as shown in Figure 23.

Our idea of lone pair-lone pair repulsion can be extended to rationalize
the results obtained in the Diels-Alder reactions of the acetonide diene 40a with a number of dienophiles, as shown in Figures 24, 25 and 26. The acetylenic dienophiles have π-electrons similar to the lone pair electrons in the nitrogen

![Hydrogen bond phenomenon as a stabilising factor for syn addition of diol](image)

Figure 23: Hydrogen bond phenomenon as a stabilising factor for syn addition of diol

nitrogen dienophiles (Figure 24). Further support of this lone pair-lone pair repulsion theory is exhibited in the anti result reported in the [4+2] cycloaddition of singlet oxygen.\(^{27}\) Earlier studies of the same acetonide diene 40a with N-phenylmaleimide (NPM) in our laboratory revealed a slight preference for syn addition.\(^{49}\) Since the difference in energy between syn and anti addition in this
reaction is very small, then very slight differences in electronic or steric effects will manifest themselves in a measurable manner. Thus, it is interesting to note the difference in facial selectivity between N-phenylmaleimide, N-methylmaleimide, and maleimide itself, which showed a preference, albeit modest, for anti addition. The more important lesson from Table 7 was that

![Diagram of possible additions of acetylenic dienophiles with the acetonide](image)

\[
R_1 = \text{CO}_2\text{Me}, \ R_2 = \text{CO}_2\text{Me} \quad R_1 = \text{H}, \ R_2 = \text{CO}_2\text{CH}_2\text{CH}_3
\]

Figure 24: Possible additions of acetylenic dienophiles with the acetonide
with the acetonide diene, the facial selectivity was a function of the dienophile. Therefore, hypotheses such as those of Hehre and Kahn and of Fukui and Cieplak, which are based on properties residing solely with the plane-nonsymmetric diene molecules, are unquestionably refuted by our data.

An alternative approach to rationalizing the facial selectivity of systems such as 5-heterosubstituted cyclopentadienes and 1,3-cyclohexadiene

\[ R_1 \] and \[ R_2 \] are substituents in
- (i) butenone
- (ii) para-benzoquinone
- (iii) vinylene carbonate
- (iv) tetracyanoethylene
- (v) maleimide
- (vi) \( N \)-methylmaleimide and
- (vii) dimethyl acetylenedicarboxylate

Figure 25: Possible additions of ethylenic dienophiles with the acetonide
Figure 26: Possible additions of the acetonide during dimerization
derivatives with allylic heteroatom substitution is in terms of electron-donation and electron-withdrawal. In normal Diels-Alder reactions the HOMO donates electron density to the LUMO of the dienophile. Therefore, the direction of electron donation is from the diene toward the dienophile. The allylic heteroatom substituent must play a major role in polarizing the transition state. Oxygen is a \( \alpha \)-withdrawing group to carbon. In the \textit{anti} transition state (Figure 27), the oxygen substituents must withdraw electron density in a direction opposite to the direction required for electrons to flow in order to establish the incipient C-C bonds. Thus, the \textit{syn} addition, in which both the electron withdrawal by the oxygens and the incipient C-C bond formation are roughly in the same direction, appears more favorable. Reactions of diene 49 and its derivatives with \( N \)-phenylmaleimide generally took place by \textit{syn} addition as did addition to oxygen-substituted cyclopentadienes.

Opposing this \textit{syn}-directing phenomenon is the sort of \textit{anti}-directing interaction that was described with triazolinedione and acetylenic dienophiles. Even with alkene dienophiles, some unfavorable repulsive interaction must be present between the \( \pi \)-electrons of the dienophile and the lone pairs on the oxygens of the diene. In many instances with the acetonide diene this latter effect was more than sufficient to overcome the inherent \textit{syn}-directing tendency, but, except with the nitrogen dienophiles and the acetylenic dienophiles, the two effects are nearly balanced and both \textit{syn} and \textit{anti} addition were observed.

It was noted that diene 41a showed high facial selectivity both in its
Diels-Alder reaction with DEAD and PTAD and in its involvement in dimerization.

The apparent reason for these selectivities has been suggested as being due to steric versus conformational effects since both dienes could assume either conformations shown in Figure 28. It is possible that the phenyl group orients itself pseudo-equatorially or pseudo-axially with respect to the 1,3-dioxolane.

Figure 27: Electron-donating and electron-withdrawing phenomenon in 5-acetoxycclopentadienes and diol 49 and its derivatives

\[ R = H, OAc, OTMS, C(CH_3), etc \]
Therefore, diene 41a prefers conformation A ($R_1 = H, R_2 = C_6H_5$), i.e.,

![Diagram of conformations A and B](image)

<table>
<thead>
<tr>
<th>$R_1$</th>
<th>$R_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$</td>
<td>CH$_3$</td>
</tr>
<tr>
<td>Ph</td>
<td>H</td>
</tr>
<tr>
<td>H</td>
<td>Ph</td>
</tr>
</tbody>
</table>

Figure 28: Conformations of cyclic dienes

in which the phenyl group adopts a pseudo-equatorial position, whereas the preferred conformation for diene 42a is B ($R_1 = C_6H_5, R_2 = H$), because in A the syn face is encumbered. Stereoelectronically, even in the preferred conformation B in the case of diene 42a, the oxygen and nitrogen lone pairs interact to destabilize the syn transition state, hence the anti adduct is formed.

For diene 41a, both steric and electronic factors should be considered. There is no reason to believe that this diene would favor syn addition because of the unfavorable interaction between the acetal hydrogen and incoming dienophile at the syn face in conformation A. Even if diene 41a existed in conformation B, the electrostatic effect between the oxygen lone pairs and that of the nitrogens is stronger than any apparently unfavorable interaction between the phenyl group.
and the hydrogens on C-3a and C-7a on the incoming dienophile. This electrostatic reason is likely responsible for the anti-anti addition observed in the dimers of these dienes.

A study of the relative rates in the endo/exo selectivities in the Diels-Alder reaction of cyclopentadiene with butenone (Table 4) has been investigated in a polar solvent, e.g. water, and the results indicated an increase in endo selectivity.\textsuperscript{68,70} Earlier results of studies of 49 and its derivatives with dienophiles in our laboratory similarly established that the various adducts obtained arose from endo addition.\textsuperscript{49} An extension of this selectivity in terms of facial selectivity was carried out in a study of acetonide diene 40a with maleimide in various solvents (Table 8). Anti addition was observed, but the facial selectivity increased steadily from non-polar solvent to polar solvent such as dimethylsulfoxide and highest in water. Rationalizations offered for the endo selectivities obtained in reaction of cyclopentadiene with butenone, range from micellar aggregation to the hydrophobic effect.\textsuperscript{68,69} It seems probable in our systems that the increase in facial selectivity correlated loosely with concentration and solubility phenomenon. In organic solvents the addends dissolved and their effective distribution between the two faces, i.e., the syn and anti faces, were evenly spread, clearly, there is no discrimination of any part of the addends which would be more polar or non-polar that would present or demand beneficial coordination with the solvent. However, in a polar solvent, such as water, the addends were much less soluble, and it is conceivable that
the water molecules were more crowded at the syn face due to hydrogen bonding with the oxygen thus encumbering this syn face. This therefore induced the dienophile to undergo addition from the opposite side, i.e., the anti face. This syn-face crowding proposal diminishes upon decreasing the concentration of the polar solvent used. For example, very dilute solutions in water the facial selectivity was low. The probable rationalization is that at this very small concentration the addends become diluted such that the water molecules become available at both faces just as in organic solvents. When LiCl, LiClO₄ in ether were used⁷⁰ (Scheme 28) in the Diels-Alder reaction of cyclopentadiene with ethyl acrylate, the hydrophobic effect was advanced to account for the remarkable rate acceleration. Recently, catalysis has been argued as being responsible for the acceleration.⁷³ We similarly investigated the effect on facial selectivity using the same media, i.e., LiCl, and LiClO₄ in ether. The effect on our additions was that it decreased the proportion of the anti adduct. The reason for these selectivities with LiCl, LiClO₄ in ether in our system stems from the fact that this compound behaves as organic molecules which affect the effective polarity of the polar molecule, e.g. water, therefore what is expected is an effect which invariably affected the resultant selectivity.

Finally, the synthetic utility of adducts obtained is that they may serve as precursors for the synthesis of natural products and novel compounds of biological interest.
EXPERIMENTAL

Melting points (mp) were determined on a Fisher-Johns apparatus and are uncorrected. Infrared (ir) spectra were recorded on a Mattson Polaris FT instrument. Mass spectral (ms) data were from a V.G. Micromass 7070 HS instrument, or from the model 5970 mass selective detector that is part of a Hewlett-Packard gas chromatograph - mass spectrometer (gc / ms) system.

The ms data have this format: m/z (% of base peak). Nuclear magnetic resonance (nmr) spectra were obtained on a General Electric GE 300-NB (300 MHz) instrument, except in some few instances in which a Varian EM -360 (60 MHz) instrument was employed. The ¹H shifts of CDCl₃ solutions were measured relative to tetramethylsilane, but in other solvents shifts were calibrated to a solvent resonance. Standard abbreviations apply: br = broad, s = singlet, d = doublet, t = triplet and q = quartet. All ¹³C nmr chemical shifts were calibrated to a solvent resonance. For some carbons for which rigorous assignments are not provided the number of attached protons (APT) may be indicated in parentheses after the chemical shift. Unambiguous assignments were aided by correlation spectroscopy (COSY), heteronuclear 2-D spectra (HETCOR) and by nuclear Overhauser effect (nOe) measurements, which also led to the assignment of stereochemistry. The nOe measurements were made from sets of interleaved ¹H experiments (16k) of 8 transients cycled 12 to 16 times through the list of frequencies to be saturated. The decoupler was gated
on in CW 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 seconds 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 nOe difference spectra were obtained from zero-filled 32k data tables to which a 1-2 Hz exponential line-broadening function had been applied. The nOe data are reported in this format: irradiated signal (enhanced signal, enhancement).

Solvants such as chloroform, dichloromethane, and carbon tetrachloride were purified by distillation from calcium hydride (CaH₂). Methanol, acetone, benzene and diethyl ether of A.C.S. reagent grade quality were used. Pyridine was stored over anhydrous potassium hydroxide (KOH), after distillation from KOH. Reactions were run under an atmosphere of dry nitrogen. The progress of reactions was monitored by thin layer chromatography (TLC) using commercial plates of silica gel 60 (0.2 mm; F-254, E. Merck). Spots of components were detected by observation under short-wavelength ultraviolet light or by spraying with a solution of phosphomolybdic acid and ceric sulfate in 10% sulfuric acid, followed by heating. Ethyl acetate and hexane was the solvent system used during flash column chromatography using a Merck Type 60 silica gel (230-400 mesh).
trans-4,5-Dibromo-1-cyclohexene (34)

To a solution of 1,4-cyclohexadiene 33 (34.0 g, 0.425 mol) chilled to -60°C was added bromine (67.9 g) in CHCl₃ (130 mL, i.e.; about 5 g of Br₂ to 10 mL of CHCl₃) dropwise while stirring slowly so that the temperature did not rise above -60°C. CHCl₃ (100 mL) was added to increase the proportion of solvent until a yellow colour persisted. The dibromo compound was insoluble in cold solvent and this precipitated. After obtaining a persistent yellow colour, the solution was warmed, which caused the dissolution of the precipitate. The solvent was evaporated under reduced pressure to about 10 mL and the product was vacuum distilled at 78 - 79°C (0.9 mm Hg) to afford 34 (93.0 g, 91%): mp 33 - 34.5°C; ir ν_max: 3036, 2955, 2899, 1655, 1427, 1339, 1253, 1170, 851 cm⁻¹. ¹H nmr (CDCl₃) δ: 5.66 (dd, J = 0.7, 1.5 Hz, 2H), 4.52 (t, J = 1.5 Hz, 2H), 3.20 (dt, J = 1.4, 14 Hz, 2H), 2.60 (dt, J = 2.0, 19.1 Hz, 2H); ¹³C nmr (CDCl₃) δ: 121.9 (1), 48.3 (1), 30.9 (2); gc / ms: 242 (3), 240 (4), 238 (2) (all M⁺), 161 (2), 159 (3), 81 (3), 79 (100), 77 (33), 51 (18), 43 (3).

(1R',2S',4R',5R')-4,5-Dibromocyclohexane-1,2-diol (35)

In a 5-litre, 3-necked flask was placed 95% (2-litres) of ethanol and water (1 L). Into this was added MgSO₄, fitted with a stirring motor and chilled to between (-5 to -10°C). The dibromocyclohexene (30.0 g, 0.125 mol) was added as a liquid (melted before hand, mp 33-34.5°C) mixed with a small amount of acetone (10 mL) to lower its viscosity and prevent freezing. KMnO₄ (20.0 g,
0.125 mol) was dissolved in \( \text{H}_2\text{O} \) (1 L) was added for over 5 hours, and the mixture was stirred for another 16 hours after which time reaction has warmed up to room temperature. The resulting MnO\(_2\) was dissolved with \( \text{SO}_2 \) gas until the muddy color became light brown. The solid was filtered, and the filtrate was reduced to 1 Litre using vacuum distillation, and the concentrate was extracted with \( \text{CH}_2\text{Cl}_2 \) (100 mL x 10). The combined organic layers were washed with saturated NaCl (200 mL x 2) and dried over MgSO\(_4\). This was followed by filtration of the MgSO\(_4\) and recrystallization from CHCl\(_3\) (50 mL) to afford a white powder 35 (13.0 g, 38\%): mp 103 - 105\(^\circ\)C; \( \nu_{\text{max}} \): 3380, 2910, 1445, 1295, 1060, 990 cm\(^{-1}\); \(^1\)H nmr (C\(_6\)D\(_5\)N) \( \delta \): 6.60 (br s, 2H), 4.84 (ddd, \( J = 4.5, 10.7, 12.0 \) Hz, 1H), 4.39 (ddd, \( J = 4.5, 10.7, 12.0 \) Hz, 1H), 4.26 (m, 1H), 3.98 (ddd, \( J = 2.8, 4.2, 11.3 \) Hz, 1H), 2.92 (ddd, \( J = 11.3, 12.0, 12.5 \) Hz, 1H), 2.82 (ddd, \( J = 2.9, 4.5, 13.8 \) Hz, 1H), 2.70 (ddd, \( J = 4.2, 4.5, 12.5 \) Hz, 1H), 2.16 (ddd, \( J = 2.2, 12.0, 13.8 \) Hz, 1H); \(^{13}\)C nmr (C\(_6\)D\(_5\)N) \( \delta \): 70.7 (1), 70.2 (1), 55.6 (1), 54.8 (1), 42.9 (2), 41.2 (2); ms: 195 (M\(^+\) - \(^{79}\)Br, 14), 193 (14), 177 (20), 175 (21), 113 (13), 95 (67), 67 (100), 55 (79). Exact Mass calcld. for C\(_8\)H\(_8\)\(^{81}\)BrO (M\(^+\) - \(^{79}\)Br - H\(_2\)O): 176.9734; found: 176.9728.

(1\(R'\),2\(S'\),4\(R'\),5\(R'\))-4,5-Dibromo-1,2-bis(trimethylsilyloxy)cyclohexane (37) and (1\(R'\),2\(S'\),4\(R'\),5\(R'\))-4,5-Dibromo-2-hydroxy-1-trimethylsilyloxy cyclohexane (38)

To 366 mg (1.33 mmol) of the dibromodiol 35 in pyridine (5.0 mL) was added chlorotrimethylsilane (TMSCl) (1.69 mL, 0.013 mmol) at 0\(^\circ\)C, and the
mixture was allowed to warm up for 1 hour. Carbon tetrachloride (10 mL) was added, and the resultant solid was filtered off with a Kimwipe plug in a Pasteur pipette. TLC indicated two spots, one for compound 37, the other for 38. The filtrate was evaporated and flash chromatography on silica gel (10% ethyl acetate in hexane) gave two products 37 (0.404 g, 72%) and 38 (0.020 g, 4%).

For 37: mp 42 - 43°C; IR ν\textsubscript{max}: 2956, 1251, 840 cm\textsuperscript{-1}; \textsuperscript{1}H nmr (CD\textsubscript{3}Cl) δ: 4.32 (t, J = 11.4, 1H), 3.98 (t, J = 12.7 Hz, 1H), 3.79 (s, 1H), 3.52 (dd, J = 2.1, 11.1 Hz, 1H), 2.47 - 2.35 (m, 2H), 2.17 (t, J = 6.4 Hz, 1H), 1.89 (t, J = 13.0 Hz, 1H), 0.08 (s, 18H); \textsuperscript{13}C nmr (CD\textsubscript{3}Cl) δ: 71.1 (1), 71.0 (1), 53.4 (1), 52.7 (1), 42.7 (2), 39.8 (2), 0.4 (3), 0.01 (3); MS: 405 (8), 403 (14), 401 (7) (all M\textsuperscript{+} - CH\textsubscript{3}), 339 (7), 257 (3), 249 (12), 191 (8), 176 (7), 167 (4), 156 (3), 147 (80), 136 (7), 103 (18), 95 (16), 73 (100), 67 (32), 45 (19). Exact Mass calcd. for C\textsubscript{11}H\textsubscript{23}\textsuperscript{81}Br\textsuperscript{79}BrSi\textsubscript{2}O\textsubscript{2} (M\textsuperscript{+} - CH\textsubscript{3}): 402.9582; found: 402.9585.

For 38: mp 92 - 92.5°C; IR ν\textsubscript{max}: 3498, 2933, 1489, 1251, 1111, 862 cm\textsuperscript{-1}; \textsuperscript{1}H nmr (CD\textsubscript{3}Cl) δ: 4.31 (ddd, J = 4.4, 8.8, 13.3 Hz, 1H), 3.97 (ddd, J = 5.1, 5.2, 15.3 Hz, 1H), 3.76 (d, J = 3.3 Hz, 1H), 3.66 (ddd, J = 2.9, 3.3, 12.6 Hz, 1H), 2.68 (ddd, J = 4.2, 4.2, 14.5 Hz, 1H), 2.39 - 2.83 (m, 2H), 1.92 (ddd, J = 2.3, 7.2, 14.5 Hz, 1H), 0.01 (s, 9H); \textsuperscript{13}C nmr (CD\textsubscript{3}Cl) δ: 70.3 (1), 69.8 (1), 52.6 (1), 51.6 (1), 39.9 (2), 39.6 (2), 0.05 (3); MS: 333 (7), 331 (14), 329 (7) (all M\textsuperscript{+} - CH\textsubscript{3}), 267 (14), 265 (14), 176 (15), 174 (16), 151 (6), 138 (6), 95 (29), 77 (10), 75 (100), 73 (80), 67 (59), 45 (12), 40 (12). Exact Mass calcd. for C\textsubscript{9}H\textsubscript{14}O\textsubscript{2}Si\textsuperscript{81}Br\textsuperscript{79}Br (M\textsuperscript{+} - CH\textsubscript{3}): 330.9187; found: 330.9185.
(1R',2S',4R',5R')-2-Acetoxy-4,5-dibromo-1-trimethylsilyloxy-3-cyclohexane (39)

To 0.378 g (1.09 mmol) of the mono-TMS derivative 38 dissolved in pyridine (2.0 mL) was added acetic anhydride (0.6 mL) at room temperature under N\textsubscript{2} and the solution was stirred for 18 hours. TLC indicated three spots. The solvent was evaporated, and the residue was chromatographed on silica gel (30% ethyl acetate in hexane) to afford 39 as white solid (0.156 g, 37%), starting material 38 and dibromodiacetate 36. For 39: mp 103 - 104°C; ir \( \nu_{\text{max}} \): 2959, 1738, 1438, 1376, 1188, 1078 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 5.10 (t, \( J = 2.3\) Hz, 1H), 4.24 (ddd, \( J = 4.1, 4.3, 16.2\) Hz, 1H), 4.08 (ddd, \( J = 4.8, 4.9, 14.1\) Hz, 1H), 3.78 (ddd, \( J = 3.0, 3.0, 11.1\) Hz, 1H), 2.66 (ddd, \( J = 4.6, 4.6, 14.7\) Hz, 1H), 2.44 - 2.33 (m, 2H), 2.12 (s, 3H), 2.03 (ddd, \( J = 1.3, 2.2, 3.1, 3.1\) Hz, 1H), 0.01 (s, 9H); \(^{13}\)C nmr (CDCl\(_3\)) \( \delta \): 170.1 (0), 71.1 (1), 68.6 (1), 51.6 (1), 51.4 (1), 40.0 (2), 39.9 (2), 21.1 (3), - 0.14 (3); ms: 258 (2), 256 (4), 254 (2) (all M\(^\pm\) = C\(_9\)H\(_{15}\)O\(_2\)Si), 169 (1), 132 (2), 117 (100), 95 (5), 79 (2), 55 (5), 45 (17), 43 (87).

(1R',2S',4R',5R')-1,2-Diacetoxy-4,5-dibromocyclohexane (36)

To dibromodiol 35 (138 mg, 0.50 mmol) dissolved in pyridine (2.0 mL) was added acetic anhydride (1.0 mL), and this was stirred for 18 hours. The solvent was evaporated, and flash column chromatography of the residue on silica gel (30% ethyl acetate in hexane) gave 36 (0.163 g, 90%) as a white solid: mp 72 - 74°C; ir \( \nu_{\text{max}} \): 1741, 1596, 1365, 1224 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 5.31 (t, \( J = 2.4\) Hz, 1H), 4.92 (dd, \( J = 3.2, 6.5\) Hz, 1H), 4.35 - 4.28 (m, 1H), 4.18 - 4.12 (m,
(1R', 2S', 4R', 5R')-4,5-Dibromo-1,2-dimethoxycyclohexane (43) and
(1R', 2S', 4R', 5R')-4,5-Dibromo-2-hydroxy-1-methoxycyclohexane (44)

To a stirred solution of dibromodiol 35 (2.00 g, 7.30 mmol) in CH₂Cl₂ (75 mL) was added 50% NaOH/H₂O (50 mL), followed by dimethylsulfate (1 mL), and tetra-n-butylammonium iodide (1.0 g), which had already been dissolved in CH₂Cl₂ (1 mL). The mixture was stirred for 24 hours, and CH₂Cl₂ (50 mL) was added, and the organic layer was separated. This was washed with H₂O (50 mL) and dried over MgSO₄. Flash column chromatography afforded 43 as an oil (0.843 g, 41%) and 44 (0.729 g, 35%), also as an oil. For 44: ir νₘₐₓ: 3427, 2985, 2944, 2897, 1636, 1439, 1196, 1104, 1030, 932 cm⁻¹; ¹H nmr (CDCl₃) δ: 4.68 (br d, J = 6.6 Hz, 2H), 3.92 (dd, J = 2.9, 7.3 Hz, 1H), 3.44 - 3.36 (m, 2H), 3.29 (br s, 3H), 2.18 (dq, J = 2.9, 6.5 Hz, 1H), 2.07 (dq, J = 7.3, 14.2 Hz, 1H), 1.81 (dq, J =
(1'R',2'S',4'R',5'R')-4,5-Dibromo-1-methoxy-2-trimethylsilyloxy cyclohexane (46)

To a solution of 44 (2.06 g, 7.17 mmol) and pyridine (5.0 mL) was added TMSCI (2.0 mL, 14.3 mmol) at 0°C, and the solution was stirred at room temperature for 2 hours. The solution was extracted with CCl₄ (10 mL), and filtered to remove pyridinium chloride, and flash column chromatography yielded 46 (0.901 g, 35%) and unreacted starting materials. For 46: ir νₘₐₓ: 3434, 2987, 1652, 1445, 1380, 1265 cm⁻¹; ¹H nmr (CDCl₃) δ: 4.36 (ddd, J = 4.5, 4.5, 17.7 Hz, 1H), 4.13 - 3.96 (m, 2H), 3.32 (br s, 3H), 3.11 (ddd, J = 2.3, 4.5, 10.8 Hz, 1H), 2.53 - 2.31 (m, 3H), 1.90 (ddd, J = 1.8, 2.1, 24.0 Hz, 1H); ms: 346 (3), 344 (6), 342 (3) (all M⁺-CH₃), 280 (22), 278 (22), 264 (12), 242 (11), 246 (4), 176 (7), 150 (6), 108 (7), 95 (24), 88 (100), 82 (14), 75 (18), 73 (87), 67 (52), 58 (27), 45 (32),
40 (13). Exact Mass calcd. for C_{27}H_{27}Si^{81}Br^{79}BrO_{2} (M^{+} - CH_{3}): 344.9343; found: 344.9352.

(1'R',2'S',4'R',5'R')-2-Acetoxy-4,5-Dibromo-1-methoxycyclohexane (45)

To a solution of 44 (1.09 g, 3.80 mmol) in pyridine (1.0 mL) was added acetic anhydride (1.0 mL), and the solution was stirred at room temperature for 24 hours. Concentration of the mixture and flash column chromatography in silica gel (20% ethyl acetate in hexane) afforded 45 (1.09 g, 87%) as a colorless oil and unreacted starting material. For 45: ir ν_{max}: 2962, 2831, 1740, 1439, 1375, 1291, 1236, 1189, 1168, 1111, 1023 cm^{-1}; ^{1}H\ nmr (CDCl_{3}) δ: 5.36 (dd, J = 1.7, 4.3 Hz, 1H), 4.23 (ddd, J = 4.5, 6.0, 17.2 Hz, 1H), 4.05 (ddd, J = 4.5, 4.8, 16.8 Hz, 1H), 3.34 (br s, 3H), 3.29 (dd, J = 2.9, 3.9 Hz, 1H), 2.68 (ddd, J = 4.5, 14.7 Hz, 1H), 2.55 (ddd, J = 1.4, 4.4, 8.8 Hz, 1H), 2.33 (ddd, J = 11.2, 11.3, 13.3 Hz, 1H), 2.13 (br s, 3H), 2.01 (ddd, J = 2.5, 2.5, 2.8 Hz, 1H); ^{13}C\ nmr (CDCl_{3}) δ: 170.1 (0), 77.4 (1), 67.5 (1), 56.9 (1), 51.8 (1), 51.3 (2), 38.2 (2), 37.1 (3), 21.1 (3); ms: 272 (7), 270 (14), 268 (7) (all M^{+} - C_{3}H_{4}O_{2}), 250 (6), 190 (25), 188 (26), 127 (7), 108 (15), 95 (9), 67 (21), 60 (13), 45 (26), 43 (100), 40 (13), 38 (10). Exact Mass calcd. for (C_{7}H_{10}^{81}Br^{79}BrO): 269.9078; found: 269.9065.

(3αα,5α,6β,7αα)-5,6-Dibromo-3α,7α-hexahydro-2,2-dimethyl-1,3-benzodioxole (40)
To the dibromodiol 35 (4.28 g, 0.015 mol) in CH₂Cl₂ (50 mL) was added
para-toluenesulfonic acid (pTsOH) (1.39 g, 0.007 mol). To these was added 2,2-
dimethoxypropane (8.14 g, 9.61 mL) and mixture was stirred at room
temperature for 3 hours. TLC showed a product at Rᵢ = 0.46 (20% ethyl acetate
/ hexane). The solution was washed with 1M NaOH (100 mL x 2), saturated
NaCl (100 ml x 2), and dried over MgSO₄. The solvent was evaporated, and
flash column chromatography afforded 40 as an oil (4.68 g, 96%), which
solidified during storage: mp 107 - 108°C; ir νₘₐₓ: 2940, 2906, 1439, 1364, 1289,
1182, 1117, 1062 and 1062 cm⁻¹; ¹H nmr (CDCl₃) δ: 4.44 (ddd, J = 3.8, 4.1, 7.6
Hz, 1H), 4.30 (dd, J = 5.0, 10.1 Hz, 1H), 4.20 (t, J = 12.3 Hz, 2H), 2.75 (t, J = 4.6
Hz, 2H), 2.37 (dd, J = 7.6, 14.9 Hz, 1H), 2.82 - 2.17 (m, 1H), 1.53 (s, 3H), 1.33
(s, 3H); ¹³C nmr (CDCl₃) δ: 108.7 (0), 72.4 (1), 71.9 (1), 51.0 (1), 45.8 (1), 35.9
(2), 34.4 (2), 28.1 (3), 25.9 (3).

cis-3a,7a-Dihydro-2,2-dimethyl-1,3-benzodioxole (40a)

According to the method of Yang,⁷⁸ to the dibromo compound 40 (4.68 g,
0.015 mol) in benzene (35 mL) was added DBU (8.97 mL, 0.060 mol) as a
solution in benzene (10 mL), and the mixture was heated at reflux for 3 hours,
after which time TLC showed a UV active spot for the diene Rᵢ = 0.68. A white
curdy precipitate was found deposited at the sides of the reaction flask. The
reaction mixture was cooled and filtered, and this was extracted into benzene
(50 mL). The benzene solution was washed with NaHCO₃ (50 mL x 2) and dried
over MgSO₄. The solvent was evaporated to afford an oil, which was flash chromatographed on silica gel (20% ethyl acetate / hexane) to afford 40a as a colorless oil (2.09 g, 92%): \( \nu_{\text{max}} \): 2987, 1379, 1209, 1032 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 6.00 (m, 2H), 5.93 - 5.87 (m, 2H), 4.66 (t, \( J = 1.7 \text{ Hz} \), 2H), 1.43 (s, 3H), 1.40 (s, 3H); \(^1\)C nmr (CDCl\(_3\)) \( \delta \): 125.1 (1), 123.6 (1), 104.4 (0), 70.2 (1), 26.6 (3), 24.6 (3); ms: 152 (M\(^+\), 1), 137 (42), 109 (3), 95 (100), 94 (96), 77 (53), 66 (94), 65 (50), 43 (87). Exact Mass calc. for C\(_9\)H\(_9\)O\(_2\) (M\(^+\) - CH\(_3\)): 137.0680; found: 137.0599.

(2a,3\(\alpha\),5\(a\),6\(\beta\),7\(\alpha\)\(\alpha\))- (41) and (2a,3\(\alpha\),5\(\beta\),6\(a\),7\(\alpha\)\(\alpha\))-5,6-Dibromohexahydro-2-phenyl-1,3-benzodioxole (42)

To a solution of the cis-diol 35 (6.39 g, 23.3 mmol) in dry CH\(_2\)Cl\(_2\) (15 mL) was added pTsOH (1.05 g) and benzaldehyde dimethyl acetal (17.7 g, 116 mmol) as a solution in dry CH\(_2\)Cl\(_2\) (10 mL), and the mixture was stirred at room temperature for 24 hours after which time the solution was washed with 20% NaHSO\(_3\) (100 mL), 1M NaOH (100 mL), NaHCO\(_3\) (100 mL) and saturated NaCl (100 mL). After drying over MgSO\(_4\), the solvent was evaporated, hexane (50 mL) was added to the residue, and the solution was refrigerated at 0 to -5°C for 2 - 3 days. White crystals were filtered off and washed several times with hexane. The combined hexane solutions were evaporated and concentrated to about 5 mL by vacuum distillation. The residue was chromatographed on silica gel (10% ethyl acetate / hexane). The total yield of 41 was 30% (2.39 g) while
that of isomer 42 was 23% (1.85 g). For 41: mp 125 - 127°C; ir $v_{\text{max}}$: 2903, 1459, 1362, 1219, 1107, 1069, 976 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 7.51 - 7.34 (m, 5H), 6.17 (s, 1H), 4.47 (ddd, $J$ = 3.9, 7.4, 8.2 Hz, 1H), 4.39 (m, 1H), 4.33 (m, 1H), 4.19 (ddd, $J$ = 4.5, 7.4, 7.8 Hz, 1H), 2.84 (ddd, $J$ = 3.9, 5.5, 15.1 Hz, 1H), 2.78 (ddd, $J$ = 4.5, 5.0, 15.2 Hz, 1H), 2.46 (ddd, $J$ = 6.2, 7.8, 15.2 Hz, 1H), 2.25 (ddd, $J$ = 4.7, 8.2, 15.1 Hz, 1H); $^{13}$C nmr (CDCl$_3$) $\delta$: 138.9 (0), 129.0 (1), 128.3 (1), 125.9 (1), 102.2 (1), 72.9 (1), 72.6 (1), 50.8 (1), 48.5 (1), 34.5 (1), 33.3 (1); ms: 364 (3), 362 (6), 360 (3) (all M$^+$), 363 (11), 361 (22), 359 (11) (all M$^+$ - H), 159 (12), 157 (10), 105 (100), 79 (96), 78 (49), 77 (71), 67 (59), 51 (35). Exact Mass calcd. for C$_{13}$H$_{13}$Br$_2$O$_2$(M$^+$ - H): 362.9241; found: 362.9231. For 42: mp 63 - 65°C; ir $v_{\text{max}}$: 1412, 1173, 1069, 1011 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 7.58 - 7.56 (m, 5H), 5.85 (s, 1H), 4.45 (ddd, $J$ = 3.8, 6.7, 8.0 Hz, 1H), 4.37 (ddd, $J$ = 5.2, 5.3, 5.7 Hz, 1H), 4.28 (ddd, $J$ = 5.3, 5.4, 6.0 Hz, 1H), 4.24 (ddd, $J$ = 4.8, 6.7, 6.7 Hz, 1H), 2.79 (ddd, $J$ = 3.8, 5.7, 15.0 Hz, 1H), 2.49 (ddd, $J$ = 4.8, 5.4, 15.5 Hz, 1H), 2.28 (ddd, $J$ = 5.2, 8.0, 15.0 Hz, 1H); $^{13}$C nmr (CDCl$_3$) $\delta$: 137.1 (0), 129.3 (1) 128.4 (1), 126.4 (1) 103.8 (1), 73.3 (1), 73.0 (1), 50.8 (1), 48.3 (1), 35.5 (2), 34.4 (2); ms: 364 (3), 362 (6), 360 (3) (all M$^+$), 363 (11), 361 (22), 359 (12) (all M$^+$ - H), 159 (10), 157 (8), 105 (100), 79 (96), 78 (48), 77 (76), 67 (67), 51 (39). Exact Mass calcd. for C$_{13}$H$_{13}$Br$_2$O$_2$ (M$^+$ - H): 358.9283; found: 358.9293.

(2$\alpha$,3$\alpha$,7$\alpha$)-3a,7a-Dihydro-2-phenyl-1,3-benzodioxole (41a)
To the dibromoacetald 41 (1.88 g, 5.20 mmol) in benzene (35 mL) was added DBU (3.11 mL, 0.02 mmol) as a solution in benzene (10 mL), and this was stirred at reflux for 8 hours. The HBr salt was filtered from the benzene solution, and it was re-extracted with benzene (50 mL). The combined benzene solution was washed with NaHCO₃ (100 mL x 2), H₂O (100 mL x 2), and saturated NaCl (100 mL x 2) followed by drying over MgSO₄. The solvent was carefully removed to give 41a (0.679 g, 64%) as a light yellow cloudy oil: \( \nu_{\text{max}} \) 3043, 2927, 1641, 1217, 1068 cm\(^{-1}\); \(^1\)H nmr (CDCl₃) δ: 7.55 - 7.45 (m, 2H), 7.40 - 7.32 (m, 3H), 6.05 (m, 2H), 5.91 (m, 2H), 5.83 (s, 1H), 4.86 (m, 2H); \(^{13}\)C nmr (CDCl₃) δ: 137.4 (0), 129.0 (1), 128.2 (2), 126.3 (2), 124.9 (2), 124.6 (2) 100.7 (1) 70.6 (2); gc / ms: 199 (M⁺ - H, 0.4), 153 (0.5), 128 (3), 122 (4), 105 (46), 96 (59), 78 (100), 77 (46), 66 (54), 51 (28). Exact Mass calc'd. for C₁₇H₁₀O₂: 200.0837; found: 200.0828.

\((2\alpha,3\alpha,7\alpha\beta)-3\alpha,7\alpha\)-Dihydro-2-phenyl-1,3-benzodioxole (42a)

The same procedure for 41a was used. To the dibromo compound 42 (1.66 g, 4.59 mmol) in benzene (35 mL) was added DBU (2.79 g, 0.073 mol) as a solution in benzene (10 mL), and the mixture was heated at reflux for 7 hours. The solution was allowed to cool and filtered. The benzene solution was washed with NaHCO₃ (100 mL x 2), H₂O (100 mL x 2), and saturated NaCl (100 mL x 2) followed by drying over MgSO₄. The solvent was evaporated to give 42a as a light yellow oil (0.549 g, 60%): \( \nu_{\text{max}} \) 3044, 2883, 1459, 1401, 1217, 1061 cm\(^{-1}\);
cis-1,2-Diacetoxyl-3,5-cyclohexadiene (50)

To a solution of the cis-cyclohexa-3,5-diene-1,2-diol 49 from Aldrich (0.310 g, 3.34 mmol) in dry pyridine (2.0 mL) was added acetic anhydride (1.5 mL), and the mixture was stirred for 16 hours. Evaporation of the solvent followed by chromatography afforded 50 (0.210 g, 92%) as a colorless oil: \( v_{\text{max}} \): 3054, 1740, 1371, 1241 cm\(^{-1} \); \(^1\)H nmr (CDCl\(_3\)) \( \delta \): 6.14 (m, 2H), 5.93 - 5.87 (m, 2H), 5.54 (t, \(J = 1.2\) Hz, 2H), 2.07 (s, 6H); \(^13\)C nmr (CDCl\(_3\)) \( \delta \): 170.1 (0), 126.1 (1), 125.1 (1), 66.8 (1), 20.7 (3); ms: 196 (M\(^+\), 1), 154 (3), 136 (13), 112 (60), 95 (98), 94 (100), 78 (33), 77 (24), 66 (66), 43 (100). Exact Mass calcd. for C\(_{10}\)H\(_{12}\)O\(_2\): 196.0735; found 196.0725.

cis-1,2-Bis(trimethylsilyloxy)-3,5-cyclohexadiene (51) and cis-2-Hydroxy-1-trimethylsilyloxy-3,5-cyclohexadiene (52)

To cis-diol 49 (0.305 g, 2.72 mmol) in dry pyridine (3.0 mL) was added
TMSCI (2.8 mL) at 0°C. The solution was allowed to warm up to room
temperature for 1 hour before CCl₄ (10 mL) was added, and the solution was
filtered. The filtrate was evaporated and flash chromatography on silica gel
(10% ethyl acetate / hexane) afforded 51 (0.403 g, 60%) as a colorless oil, and
22.6 mg of the mono TMSdiene 52 was also obtained. For 51: \( \text{ir } v_{\text{max}}: 2958, \)
14 12, 1252, 1119, 840 cm⁻¹; \( \text{¹H nmr (CDCl₃)} \) \( \delta: 5.99 - 5.94 (m, 2H), 5.89 - 5.84 \)
(m, 2H), 4.14 (t, \( J = 1.1 \text{ Hz}, 2H), 0.15 (s, 18 H) ; \text{¹³C nmr (CDCl₃)} \) \( \delta: 130.4 (1) \)
124.0 (1), 68.9 (1), 0.2 (3); \text{ms: 256 (M⁺, 21), 191 (10), 167 (2), 147 (17), 73 \)
(100), 45 (17). Exact Mass calc'd for C₁₂H₂₄O₂S: 256.1314; found: 256.1314.
For 52: \( \text{¹H nmr (CDCl₃)} \) \( \delta: 6.015 - 5.89 (m, 3H), 5.18 - 5.76 (m, 1H), 4.34 - 4.30 \)
(m, 1H), 4.25 (s, 1H), 4.15 - 4.12 (m, 1H), 0.17 (s, 9H); \( \text{¹³C nmr (CDCl₃)} \) \( \delta: 129.4 \)
(1), 124.6 (1), 124.5 (1), 68.2 (1), 67.5 (1), 67.0 (1), 0.2 (9).

cis-1,2-Dimethoxy-3,5-cyclohexadiene (53) and cis-2 Hydroxy-1-methoxy-3,5-
cyclohexadiene (54)
To a 50% NaOH/H₂O (50 mL) solution was added CH₂Cl₂ (75 mL), the diol
49 (0.344 mL, 2.77 mmol), dimethylsulfate (1.59 mL, 16.6 mmol), and tetra-\text{-n-}
butylammonium iodide 40% w/w (0.6 g), which had been dissolved in CH₂Cl₂ (1.0
mL). This was stirred at room temperature for 16 hours. More CH₂Cl₂ (50 mL)
was added to the mixture, and the organic extract was washed with H₂O (50
mL), saturated NaHCO₃ solution (50 mL), H₂O (50 mL), and saturated NaCl (50
mL), and dried over MgSO₄. Filtration and concentration of the sample afforded
53 (0.711 g, 20%) as colorless oil as well as the monomethylated derivative 54 (0.049 g, 14%). For 53: ir \( \nu_{\text{max}} \): 2929, 1464, 1122 cm\(^{-1}\); \( ^1\)H nmr (CDCl\(_3\)) 6: 6.04 - 6.03 (m, 4H), 4.00 - 3.99 (m, 1H), 3.81 (s, 1H), 3.44 (s, 6H); \( ^{13}\)C nmr (CDCl\(_3\)) 6: 126.9 (1), 124.8 (1), 73.9 (1), 56.2 (3). For 54: \( ^1\)H nmr (CDCl\(_3\)) 6: 6.04 - 5.97 (m, 4H); 4.36 (dd, \( J = 1.8, 6.1 \) Hz, 1H), 3.86 (dd, \( J = 3.6, 6.3 \) Hz, 1H), 3.45 (s, 3H), 2.47 (d, \( J = 7.8 \) Hz, 1H); \( ^{13}\)C nmr (CDCl\(_3\)) 6: 130.3 (1), 125.9 (1), 125.7 (1), 124.3 (1), 65.9 (1), 60.3 (1), 56.8 (3).

**Diels-Alder reaction of 50 with diethyl azodicarboxylate (DEAD) (55):**

Diethyl(3\(\alpha\),6\(\alpha\),7\(\alpha\),8\(\alpha\),7\(R\),8\(S\)) (56a) and (3\(\alpha\),6\(\alpha\),7\(\beta\),8\(\beta\),7\(R\),8\(R\))-3\(\alpha\),6,7,8-tetrahydro-3,6-etheno-1,3-diacetyloxypyridazine-1,2-dicarboxylate (56b)

To a solution of cis-cyclohexa-3,5-diene-1,2-diacetate 50 (0.288 g, 1.47 mmol) in chloroform (2.0 mL) was added diethyl azodicarboxylate (0.231 mL, 1.47 mmol) and the solution was stirred at room temperature for 72 hours. TLC indicated two new spots along with some unreacted starting materials. The solvent was evaporated, but \( ^1\)H nmr analysis of the crude adduct mixture revealed broadening of the proton signals in the methine region so that adduct ratios could not be taken. Chromatography (30% ethyl acetate / hexane) gave 56 (0.316 g, 58%) as pink oil along with another diastereomer 57 (0.080 g, 15%).

For 56a: ir \( \nu_{\text{max}} \): 2984, 1736, 1607, 1480, 1406, 1405, 1300, 1233, 1060 cm\(^{-1}\); \( ^1\)H nmr (CDCl\(_3\)) 6: 7.00 - 5.00 (br, 4H, methine and bridgehead H's), 4.26 (m, 4H), 2.03 (m, 6H), 1.27 (m, 6H); ms: 370 (M\(^+\), 0.03), 237 (4), 196 (8), 176 (19), 151
(3), 58 (19), 28 (100), 27 (27). For 56b: $\nu_{\text{max}}$: 2984, 1727, 1606, 1489, 1373, 1324, 1236, 1203 and 1061 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 7.00 - 5.00 (br, olefinic protons), 4.33 - 4.19 (m, 2H), 2.13 - 2.01 (m, 3H), 1.36 - 1.25 (m, 3H).

Diels-Alder reaction of 51 with DEAD: $(3\alpha, 6\alpha, 7\alpha, 8\alpha, 7R', 8S')$-1,2-dicarboethoxy-3,6,7,8-tetrahydro-7,8-bis(trimethylsilyloxy)-3,6-ethenopyridazine (57)

To a solution of cis-1,2-bis(trimethylsilyloxy)-3,5-cyclohexadiene 51 (0.155 g, 0.603 mmol) in chloroform (1.0 mL) was added DEAD (0.095 mL, 0.603 mmol), and the solution was stirred at room temperature for 24 hours. The solvent was evaporated, and the $^1$H nmr spectrum of the crude product could not be used to detect signals for two or more adducts due to line broadening. Flash column chromatography (10% ethyl acetate / hexane) afforded a light pink oil 57 (0.125 g, 48%). About 23 mg of the starting material was also obtained. During column chromatography some gases were released probably due to some decomposition of the adduct: $\nu_{\text{max}}$: 1709, 1519, 1415, 1360, 1245, 1062 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 6.00 - 4.35 (br, 2H), 4.38 (d, $J = 3.3$ Hz, 1H), 4.19 - 4.11 (m, 2H), 1.24 (dd, $J = 7.2$, 14.7 Hz, 3H); $^{13}$C nmr (CDCl$_3$) $\delta$: 155.4 (9), 125.3 (1), 102.3 (1) 63.8 (1), 62.3 (2), 61.4 (2), 14.1 (3), 0.06 (3); ms: 356 (M$^+$ - C$_4$H$_7$O, 3), 284 (19), 244 (26), 229 (5), 211 (22), 196 (7), 176 (76), 176 (10), 153 (10), 147 (100), 138 (46), 126 (28), 109 (53), 98 (15), 83 (52), 73 (32), 66 (18), 61 (28), 55 (36), 45 (47). Exact Mass calcd. for C$_{13}$H$_{22}$N$_2$O$_5$ (M$^+$ - C$_9$H$_4$OSi$_2$): 284.1012; found: 284.1023.
Diels-Alder reaction of 40a with DEAD: Diethyl (3α,4β,7α,7β)-3α,4,5,5a-tetrahydro-2,2-dimethyl-4,7-etheno-1,3-dioxolo[4,5-d]pyridazine-5,6-dicarboxylate (58).

To the acetonide 40a (0.108 g, 0.711 mmol) in benzene (4.0 mL) was added DEAD (0.112 mL, 0.711 mmol), and the solution was stirred at room temperature for 24 hours, and the 1H nmr spectrum of the crude reaction mixture revealed only one product. The solvent was evaporated and flash column chromatography of the residue (30% ethyl acetate / hexane) gave 58 (0.222 g, 96%) as colorless oil: \( \nu_{\text{max}} \): 2952, 2924, 1736, 1725, 1452, 1356, 1300, 1240, 1093 cm\(^{-1}\); 1H nmr (CDCl\(_3\)) \( \delta \): 6.51 (br t, \( J = 6.3 \) Hz, 1H), 6.36 (br t, \( J = 7.0 \) Hz, 1H), 5.15 (br m, 2H), 5.04 (br m, 1H), 4.47 (br m, 2H), 4.40 - 4.10 (m, 4H), 1.33 - 1.25 (m, 6H); \( ^{13} \text{C nmr (CDCl}_3 \) \( \delta \): 133.4 (0), 128.7 (1), 111.0 (0), 73.6 (1), 73.0 (1), 62.9 (1), 62.6 (1), 53.4 (2), 51.3 (2), 25.5 (3), 25.4 (3), 14.4 (3), 14.3 (3); nOe data: 6.50 (5.15, 10%; 5.03, 11%; 1.29, 0.1%), 5.15 (6.50, 11%; 6.36, 11%; 4.46, 8%), 4.47 (5.15, 14%; 5.03, 14%; 1.29, 0.4%), 4.18 (5.15, 3%; 5.03, 2%; 1.29, 1.2%), 1.29 (6.50, 3.5%; 6.36, 3%; 4.46, 5%; 4.18, 5%); 1.29 (6.50, 20%; 6.36, 2%; 4.46, 9%; 4.18, 5%); ms: 326 (M\(^+\), 1.5), 311 (7), 268 (2), 226 (6), 196 (6), 195(5), 166 (14), 153 (20), 123 (16), 95 (29), 81 (100), 80 (13) (8), 43 (22). Exact Mass calcd. for C\(_{14}\)H\(_{15}\)O\(_6\)N\(_2\) (M\(^+\) - CH\(_3\)): 311.1241; found: 311.1253.

Diels-Alder reaction of 41a with DEAD: Diethyl (2β,3αβ,4α,7α,7β)-3α,4,5,5a-tetrahydro-2-phenyl-4,7-etheno-1,3-dioxolo[4,5-d]pyridazine-5,6-dicarboxylate
(60) and \((2\alpha,3\alpha\beta,5\alpha\epsilon,6\alpha\alpha,6\alpha,8\beta,9\alpha,10\alpha,10\alpha\alpha,10\alpha\beta)-3a,5a,6a,9a,10,10a,10b\-octahydro-2,8-diphenyl-3a,5a,6,10-ethenenaphthol-1,3,7,9-tetraoxole (61)

To a solution of the diene 41a (0.153 g, 0.764 mmol) in benzene (8.0 mL) was added the DEAD (0.24 mL, 1.5 mmol), and the solution was stirred at room temperature for 24 hours. The \(^1\)H nmr spectrum of the crude product showed signals for the dimer, which completely masked those for adduct 60 in the methine region of the spectrum. Chromatographic separation on silica gel (30% ethyl acetate / hexane) afforded the adduct 60 as yellow oil (0.142 g, 50%) and the dimer 61 (0.033 g, 12%). For 60: ir \(\nu_{\max} \): 3064, 2982, 2934, 1720, 1619, 1478, 1451, 1311, 1239, 1116, 1073, 872 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \(\delta\): 7.35 (br m, 5H), 6.67 (t, \(J = 5.3\) Hz, 1H), 6.56 (t, \(J = 6.7\) Hz), 6.02 (s, 1H), 5.27 (br m, 1H), 5.17 (br m, 1H), 4.69 (br m, 1H), 4.33 - 4.10 (m, 4H), 1.35 - 1.23 (m, 6H); nOe data: 6.67 (6.02, 8%; 5.27, 10%; 5.17, 11%), 6.56 (6.02, 8%; 5.27, 10%; 5.17, 10%), 6.02 (7.35, 1%), 5.27 (6.67, 11%; 6.56, 11%; 4.69, 9%; 4.56, 9%), 5.17 (6.67, 12%; 6.56, 11%; 4.69, 9%; 4.56, 9%), 4.69 (7.35, 0.5%; 6.02, 3%; 5.27, 12%; 5.17, 12%), 4.56 (7.35, 0.5%; 6.02, 3%; 5.27, 12%; 5.17, 12%), 4.20 (1.27, 2%), 1.27 (4.20, 0.1%); \(^{13}\)C nmr (CDCl\(_3\)) \(\delta\): 138.1 (0), 134.3 (1), 130 (1), 129.0 (0), 128.3 (1), 125.7 (1), 106.0 (1), 74.6 (1), 73.8 (1), 62.9 (2), 62.6 (2), 53.3 (1), 51.3 (1), 14.3 (3), 14.2; ms: 374 (M\(^+\), 0.5), 302 (3), 268 (3), 239 (5), 196 (10), 195 (8), 167 (19), 153 (22), 123 (18), 105 (12), 95 (11), 91 (8), 81 (100), 80 (12), 78 (10), 77 (12). Exact Mass calcd. for C\(_{19}\)H\(_{1\alpha}\)N\(_{2}\)O\(_6\): 374.1476; found: 374.1472.
For 61: mp 176 - 179°C; ir νₐ₅: 3034, 2943, 1457, 1368, 1224, 1097, 1066 cm⁻¹;
¹H nmr (CDCl₃) δ: 7.45 - 7.30 (m, 10H), 6.18 (t, J = 3.6 Hz, 1H), 6.04 (s, 1H),
5.85 (d, J = 1.8 Hz, 1H), 5.83 (s, 1H), 5.81 (dd, J = 1.5, 4.2 Hz, 1H), 5.60 (d, J =
10.1 Hz, 1H), 4.50 (dd, J = 1.7, 4.5 Hz, 1H), 4.41 (s, 2H), 4.25 (d, J = 4.8 Hz,
1H), 3.04 (br s, 2H), 2.43 (ddd, J = 1.8, 3.6, 9.0 Hz, 1H), 2.35 (d, J = 9.0 Hz, 1H);
NOE data: 6.19 (6.04, 6%; 4.51, 5%; 3.06, 6%), 6.04 (7.36, 0.3%; 6.19, 0.8%;
4.43, 0.5%), 5.85 (7.43, 3%; 5.62, 10%; 3.06, 3%; 2.46, 4%), 5.83 (7.43, 0.9%;
5.62, 8%; 3.06, 3%; 2.46, 4%), 5.82 (5.85, 15%, 5.84, 2%; 5.83, 3%; 4.51, 4%),
4.51 (7.36, 0.05%; 6.19, 2%; 5.85, 1%; 5.62, 6%; 4.26, 5%; 2.46, 1%; 2.35, 1%),
4.43 (7.36, 1%; 6.04, 3%; 3.06, 6%; 2.46, 14%; 2.35, 16%); 4.26 (7.43, 2%; 5.84,
1%; 4.51, 10%; 3.06, 8%; 2.46, 0.6%; 2.35, 3%) 3.06 (6.19, 8%; 6.04, 1%; 5.84,
16%; 5.83, 18%; 4.43, 5%; 4.26, 15%; 2.46, 4%; 2.35, 2%), 2.46 (5.85, 8%; 5.83,
5%; 4.43, 5%; 3.06, 2%; 2.35, 10%), 2.35 (5.84, 1%; 4.43, 5%; 4.26, 3%; 3.06,
1%; 2.46, 11%); ¹³C nmr (CDCl₃) δ: 139.2, 138.7, 133.2, 132.5, 130.8, 129.7,
129.7, 128.7, 128.3, 126.2, 125.8, 124.2, 104.8, 101.0, 79.3, 79.1, 77.2, 71.7,
68.0, 41.3, 40.9, 38.6, 34.4, 33.1, 30.2, 23.6, 22.9; ms: 399 (M⁺ - H, 2) 294 (7),
188 (14), 172 (11), 159 (12), 148 (5), 144 (8), 141 (8), 129 (11), 119 (12), 105
(100), 94 (32), 91 (34), 78 (42), 66 (11).

Diels-Alder reaction of 42a with DEAD: (2α,3αα,4β,7αα,7β)-3α,4,5,5a-
tetrahydro-2-phenyl-4,7-etheno-1,3-dioxolopyridazine-5,6-dicarboxylate
(62) and (2β,3αβ,5αα,6α,6αα,8α,9αα,10α,10αα,10βα)-
To a solution of the diene 42a (0.222 g, 1.10 mmol) in benzene (8.0 mL) was added DEAD (0.44 mL, 2.8 mmol), and the solution was stirred at room temperature for 24 hours. The sample was evaporated and chromatographed (30% ethyl acetate / hexane) to afford two products 62 (0.224 g, 54%), as light pink oil, and dimer 63 (0.014 g, 3.5%). For 62: $\text{IR } \nu_{\text{max}}$: 2981, 2915, 1736, 1703, 1591, 1462, 1402, 1373, 1310, 1238, 1067 cm$^{-1}$; $^1\text{H NMR (CDCl}_3\text{)}$ $\delta$: 7.37 (m, 5H), 6.69 (br t, $J = 8.1$ Hz, 1H), 6.55 (br t, $J = 8.6$ Hz, 1H), 5.69 (s, 1H), 5.30 (m, 1H), 5.17 (br m, 1H), 4.69 (m, 1H), 4.56 (br m, 1H), 4.31 - 4.12 (m, 4H), 1.27 (br t, $J = 7.0$ Hz, 6H); $^{13}\text{C NMR (CDCl}_3\text{)}$ $\delta$: 135.1 (0), 133.8 (2), 129.8 (1), 128.9 (0), 128 (1), 127.1 (1), 104.7 (1), 73.9 (1), 73.4 (1), 62.9 (2), 62.6 (2), 14.4 (3), 14.2 (3); nOe data: 6.61 (7.37, 0.6%; 5.30, 4%; 5.20, 4%), 6.47 (7.37, 0.6%; 5.30, 4%), 5.20 (5.30, 5%); 5.69 (7.37, 2%; 4.53, 3%), 5.30 (6.61, 5%; 6.47, 5%; 4.53, 4%), 5.20 (6.61, 7%; 6.47, 6%; 4.53, 5%); 4.53 (5.69, 6%; 5.30, 6%; 5.20, 5%); ms: 374 (M$^+$, 0.7), 302 (2), 268 (2), 239 (4), 196 (9), 167 (16), 153 (21), 123 (16), 105 (18), 95 (11), 91 (9), 80 (100), 78 (11), 77 (15). Exact Mass calcd. for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_4$ (M$^+$ - $\text{C}_3\text{H}_4\text{O}_2$): 302.1265; found: 302.1268. For 63: mp 152 - 154°C; $\text{IR } \nu_{\text{max}}$: 3066, 1601, 1521 cm$^{-1}$; $^1\text{H NMR (CDCl}_3\text{)}$ $\delta$: 7.49 - 7.40 (m, 10H), 6.17 (t, $J = 3.9$, 2H), 5.84 (br s, 1H), 5.72 - 5.63 (dd, $J = 0.6$, 25.5 Hz, 1H), 5.67 (t, $J = 2.2$ Hz, 1H), 5.61 (s, 1H), 4.37 (dd, $J = 2.7$, 3.0, 11.1 Hz, 2H), 4.31 (t, $J = 5.1$ Hz, 1H), 3.13 (d, $J = 2.7$ Hz, 1H), 3.07 (d, $J = 2.7$ Hz, 1H), 2.44 (dd, $J = 9.3$, 13.8 Hz,
2H); nOe data: 6.17 (7.44, 0.9%; 4.37, 1%; 4.30, 1%; 3.14, 4%; 3.07, 4%), 5.84 (7.44, 2%; 4.37, 0.6%; 4.30, 7%), 5.68 (7.44, 0.7%; 4.37, 1.4%; 3.07, 4%; 2.45, 1%), 5.68 (7.44, 2%; 4.37, 3%), 4.37 (6.17, 2%; 5.84, 4%; 5.68, 2%; 5.61, 9%; 3.14, 6%; 3.07, 3%; 2.45, 10%), 4.30 (6.17, 1.3%; 5.84, 12%; 5.61, 3%; 3.14, 13%; 2.45, 4%), 3.14 (6.17, 4%; 5.68, 2%; 4.37, 2%; 4.30, 13%; 2.45, 2%), 3.07 (6.17, 4%; 5.68, 5%; 4.37, 2%; 4.30, 2%; 2.45, 2%), 2.45 (5.68, 3%; 4.37, 9%; 3.14, 4%; 3.07, 5%); $^{13}$C nmr (CDCl$_3$) δ: 137.8, 136.0, 132.8, 129.7, 129.0, 128.2, 127.3, 127.1, 126.4, 103.1, 79.6, 78.9, 70.5, 40.8, 34.5, 33.5; ms: 400 (M$^+$, 1), 399 (4), 294 (5), 188 (61), 170 (27), 159 (36), 145 (27), 131 (24), 129 (22), 119 (31), 105 (100), 94 (39), 91 (72), 77 (54), 66 (29), 50 (13). Exact Mass calcd. for C$_{12}$H$_{12}$O$_2$ (M$^+$ - C$_{14}$H$_2$O$_2$): 188.0836; found: 188.0834.

**Diels-Alder reaction of 49 with 4-phenyl-1,2,4-triazoline-3,5-dione (59):**

(5α,8α,10S',11R')- (64) and (5α,8α,10R',11S')-5,8-Dihydro-10,11-dihydroxy-2-phenyl-5,8-etheno-1H-[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (65)

To a solution of diol 49 (0.109 g, 0.89 mmol) was added slowly 4-phenyl-1,2,4-triazoline-3,5-dione (0.171 g, 0.98 mmol) dissolved in acetone (1.0 mL), and the mixture was stirred at room temperature for 18 hours. TLC indicated two spots, and flash column chromatography gave 64 (0.193 g, 68%) as a white solid and 65 (0.019 g, 7%), also as a white solid. For 64: mp 226 - 228°C; ir $\nu_{max}$: 3354, 2927, 1779, 1737, 1502, 1434, 1288 cm$^{-1}$; $^1$H nmr (CDCl$_3$/CD$_2$OD) δ: 7.46-7.44 (m, 5H), 6.50 (dd, $J = 3.2$, 4.0 Hz, 1H), 5.00 (m, 2H), 3.95 (m, 2H), 3.20 (m,
nOe data: 6.50 (7.45, 0.2%; 5.00, 2%), 5.00 (7.45, 0.1%; 6.50, 4%; 3.95, 3%), 3.95 (7.45, 0.3%; 6.50, 2%; 5.00, 7%; 3.20, 1%), 3.20 (7.45, 0.5%; 6.50, 0.4%; 5.00, 3%; 3.95, 2%);\(^{13}\)C nmr (CDCl\(_3\)) δ: 130.0, 129.1, 125.5, 62.1, 56.0; ms: 287 (M\(^+\), 2.5), 258 (7), 228 (15), 119 (41), 91 (12), 79 (100), 38 (12). Exact Mass calcd. for C\(_{14}H_{13}N_3O_4\): 287.0905; found: 287.0893. For 65: \(^1\)H nmr (CDCl\(_3\)) δ: 7.43-7.42 (m, 5H), 6.55 (t, \(J = 3.6\) Hz, 2H), 5.04 (m, 2H), 4.43 (br m, 2H), 2.76 (2 x OH, 2H).

Diels-Alder reaction of 50 with 59: (5α,8α,11R\(^{\prime}\),10S\(^{\prime}\))- (66) and
(5α,8α,11S\(^{\prime}\),10R\(^{\prime}\))-10,11-Bis(acetyloxy)-8,5-dihydro-2-phenyl-5,8-etheno-1H-[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (67)

To diene 60 (0.163 g, 0.830 mmol) was pipetted slowly 4-phenyl-1,2,4-triazoline-3,5-dione (0.145 g, 0.830 mmol) dissolved in acetone (5.0 mL), and the mixture was stirred at room temperature for 16 hours. The carmine red colour of the dienophile was discharged. TLC analysis of the reaction mixture revealed two spots. The solvent was evaporated under vacuum, and the \(^1\)H nmr spectrum of the crude sample showed an adduct ratio of 9:1. Flash column chromatography of the residue on silica gel (20% ethyl acetate / hexane) afforded a white solid 66, which was recrystallized from hexane to give 0.238 g of product (77%), and minor adduct 67, which was also recrystallized from hexane to give 0.039 g of adduct (13%). For 66: mp 219-220°C; \(\nu_{\text{max}}\): 3071, 2978, 1749, 1718, 1501, 1421, 1374, 1240, 1144, 1067 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) δ:
7.44 (m, 5H), 6.58 (apparent dd, J = 3.2, 4.1 Hz, 2H), 5.46 (m, 2H), 5.12 - 5.08 (m, 2H), 2.05 (s, 6H); nOe data: 6.58 (5.11, 11%; 2.05, 0.2%), 5.47 (5.11, 16%; 2.05, 0.5%), 5.05 (6.58, 8%; 5.46, 8%; 2.05, 0.2%), 2.05 (7.42, 0.4%; 6.58, 1.6%; 5.46, 1.6%; 5.11, 1.2%); ^13C nmr (CDCl$_3$) δ: 169.1 (0), 130.9 (2), 129.4 (2), 129.0 (0), 128.4 (0), 125.3 (2), 67.0 (2), 51.4 (2), 20.2 (6); ms: 371 (M$^+$, 1.3), 329 (1), 269 (12), 228 (15), 227 (76), 118 (27), 81 (12), 80 (62), 43 (100). Anal. calcd. for C$_{18}$H$_{17}$O$_6$N$_3$: C, 58.23; H, 4.58; N, 11.32; found: C, 58.35; H, 4.63; N, 11.38. For 67: mp 224 - 225°C; ir v$_{max}$: 2922, 1743, 1706, 1599, 1504, 1417, 1370 cm$^{-1}$; ^1H nmr (CDCl$_3$) δ: 7.45 (m, 5H), 6.59 (apparent dd, J = 3.1, 4.2 Hz, 2H), 5.12 - 5.08 (m, 2H), 5.03 (m, 2H), 2.15 (s, 6H); nOe data: 6.59 (5.10, 10%; 5.03, 1%; 2.14, 0.1%), 5.10 (6.59, 9%; 5.03, 7%; 2.14, 1%), 5.03 (6.59, 2%; 5.10, 13%; 2.14, 0.2%), 2.14 (7.42, 0.6%; 6.59, 0.1%; 5.10, 0.9%; 5.03, 1%); ^13C nmr (CDCl$_3$) δ: 169.8 (0), 155.3 (0), 130.0 (2), 129.2 (2), 128.5 (0), 125.5 (2), 63.3 (2), 53.1 (2), 20.5 (6); ms: 371 (M$^+$, 2.7), 228 (22), 227 (100), 119 (25), 109 (13), 80 (55), 43 (70). Anal. calcd. for C$_{18}$H$_{17}$N$_2$O$_6$: C, 58.27; H, 4.58; N, 11.32; found: C, 58.27; H, 4.61; N, 11.34.

**Diels-Alder reaction of 51 with 59: (5α,8α,10R',11S')-5,8-Dihydro-2-phenyl-10,11-bis[(trimethylsilyl)oxy]-5,8-etheno-1H-[1,2,4]triazolo[1,2-a]pyridazine-1,2(2H)-dione (68)**

To a solution of diene 51 (85 mg, 0.33 mmol) was pipetted slowly 4-phenyl-1,2,4-triazoline-3,5-dione (60 mg, 0.33 mmol) dissolved in acetone (1.0
mL), and the mixture was stirred at room temperature for 16 hours. $^1$H nmr analysis of the crude sample revealed signals for only one adduct. The solvent was evaporated, and the residue was chromatographed on silica gel (30% ethyl acetate/hexane) to afford 68 (0.103 g, 72%) as a white solid: mp 62-63°C; $\text{IR } v_{\text{max}}$: 2955, 1774, 1718, 1509, 1503, 1404, 1252, 1120 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 7.42 - 7.36 (m, 5H), 6.54 (apparent dd, $J = 3.2, 4.0$ Hz, 2H), 4.82 - 4.79 (m, 2H), 4.33 (narrow, 2H), 0.21 (s, 18H); NOe data: 6.53 (4.80, 10%), 4.80 (6.53, 10%; 4.33, 8%; 0.20, 0.3%), 4.33 (4.80, 16%; 0.20, 0.7%), 0.20 (6.53, 2%; 4.80, 5%; 4.33, 5%), 0.21 (6.54, 1.5%; 4.80, 5%; 4.33, 5%); $^{13}$C nmr (CDCl$_3$) $\delta$: 155.6 (0) 130.1 (0), 129.5 (2), 129.2 (1), 128.4 (1), 125 (1), 68.4 (1), 54.5 (1), 0.23 (3); ms: 416 ($M^+$ - CH$_3$, 2), 227 (100), 204 (15), 147 (15), 118 (16), 90 (4), 79 (43), 75 (12), 73 (60), 45 (8). Anal. calcd. for C$_{29}$H$_{29}$N$_3$O$_4$Si$_2$: C, 55.66; H, 6.71; N, 9.74; found: C, 55.70; H, 6.66; N, 9.79.

**Diels-Alder reaction of 41a with 59:** (2α,3αβ,4α,10α,10αβ)-3a,4,10,10a-Tetrahydro-2,7-diphenyl-4,10-etheno-6H-1,3-dioxolo[4,5-d][1,2,4]triazolo[1,2-a]pyridazine-6,8(7H)-dione (70)

To a solution of the diene 41a (0.126 g, 0.63 mmol) in acetone (4.0 mL) was pipetted slowly 4-phenyl-1,2,4-triazoline-3,5-dione (0.110 g, 0.63 mmol) dissolved in acetone (1.0 mL), and the solution was stirred at room temperature for 16 hours after which time the mixture turned orange in colour. The solvent was evaporated under vacuum. $^1$H nmr analysis of the residue led to an
inaccurate determination of the adduct ratio because of contamination by signals of the dimer. Flash column chromatography of the residue on silica gel (30% ethyl acetate / hexane) gave white solid, which was recrystallized from hexane to give 0.129 g of 70 (55%) and the dimer 61 (0.056 g, 21%). For 70: mp 238 - 239°C; ir νmax: 2922, 1782, 1718, 1596, 1501, 1407, 1112 cm⁻¹; ¹H nmr (CDCl₃) δ: 7.45 - 7.36 (m, 10H), 6.61 (apparent ddt, J = 3.2, 4.0¹z, 2H), 6.09 (s, 1H), 5.27 (m, 2H), 4.82 (nar m, 2H); nOe data: 6.61 (6.09, 7%; 5.27, 8%), 6.09 (7.37, 1%; 6.61, 3%; 4.82, 0.5%), 5.27 (6.61, 5%; 6.09, 0.7%; 4.82, 6%), 4.82 (7.37, 1%; 6.09, 2%; 5.27, 11%); ¹³C nmr (CDCl₃) δ: 155.5 (0), 134.6 (0), 131.0 (0), 131.1 (0), 129.1 (2), 128.4 (1), 127.2 (1), 125.4 (1), 105.6 (2), 74.1 (2), 52.3 (1); ms: 375 (M⁺, 11), 269 (83), 240 (64), 227 (96), 121 (45), 119 (75), 105 (18), 94 (10), 91 (30), 79 (100), 78 (59), 65 (18), 50 (13). Exact Mass calcd. for C₁₂H₁₇N₃O₄: 375.1218; found: 375.1200. Anal. calcd. for C₁₂H₁₇N₃O₄: C, 64.28; H, 4.28; N, 20.00. found: C, 64.08; H, 4.29; N, 20.04.

**Diels-Alder reaction of 42a with 59: (2α,3αα,4β,10β,10αα)-3a,4,10,10a-Tetrahydro-2,7-diphenyl-4,10-etheno-6H-1,3-dioxolo[4,5-d][1,2,4]triazolo[1,2-a]pyridazine-6,8(7H)-dione (71)**

To a solution of diene 42a (0.167 g, 0.83 mmol) was pipetted slowly a solution of 4-phenyl-1,2,4-triazoline-3,5-dione (0.146 g, 0.83 mmol) dissolved in acetone (4.0 mL) at room temperature, and the mixture was stirred at room temperature for 16 hours. The solvent was evaporated to leave a yellow orange
residue, which was chromatographed on silica gel (30% ethyl acetate / hexane) to afford 71 (0.195 g, 62%) and dimer 63 (0.036 g, 12%). For 71: mp 193 - 195°C; \( \text{ir } v_{\text{max}}: 2921, 1783, 1719, 1596, 1501, 1406 \text{ cm}^{-1} \); \( ^1\text{H nmr (CDCl}_3\text{)} \delta: 7.46 - 7.41 \text{ (m, 10H), 6.52 (apparent dd, } J = 3.1, 4.0 \text{ Hz, 2H), 5.79 (s, 1H), 5.31 - 5.21 \text{ (m, 2H), 4.73 (m, 2H); nOe data: 6.53 (7.38, 1%, 5.29, 11%), 5.79 (7.38, 3%, 4.73, 7%), 5.29 (6.53, 7%, 4.73, 7%), 4.73 (5.79, 17%; 5.29, 15%); }^{13}\text{C nmr (CDCl}_3\text{)} \delta: 155.5 \text{ (0), 130.1 (0), 129.1 (2), 129.1 (2), 128.4 (2), 127.2 (2), 125.4 (2), 105.5 (1), 74.0 (1), 52.1 (1); ms: 375 (M\,^+\text{, 8), 269 (58), 240 (58), 227 (65), 167 (15), 153 (18), 123 (16), 121 (37), 119 (60), 105 (33), 95 (14), 91 (32), 80 (100), 78 (56), 65 (20), 50 (16), 38 (24). Exact Mass calcd. for C\text{\textsubscript{21}}H\text{\textsubscript{17}}N\text{\textsubscript{2}}O\textsubscript{4}: 375.1217; found: 375.1225.}

**Diels-Alder reaction of 40a with 59: (3aβ,4β,10β,10αα)-3a,4,10,10a-Tetrahydro-2,2-dimethyl-7-phenyl-4,10-etheno-6H-1,3-dioxolo[4,5-d][1,2,4]triazolo[1,2-a]pyridazine-6,8(7H)-dione (69)**

To acetonide 40a (0.104 g, 0.689 mmol) in acetone (4.0 mL) was pipetted slowly 4-phenyl-1,2,4-triazoline-3,5-dione (0.120 g, 0.689 mmol) dissolved in acetone (4.0 mL). The mixture was stirred at room temperature for about 16 hours and after which time the solution was evaporated, and flash column chromatography on silica gel (30% ethyl acetate / hexane) afforded light grey compound 69 (0.256 g, 97%): mp 248 - 250°C; \( \text{ir } v_{\text{max}}: 2923, 1777, 1712, 1596, 1500, 1401, 1253 \text{ cm}^{-1} \); \( ^1\text{H nmr (CDCl}_3\text{)} \delta: 7.45 - 7.43 \text{ (m, 5H), 6.41 (dd, } J = 3.5, 2.3 \text{ Hz, 2H), 5.37 (apparent dd, } J = 3.5, 4.0 \text{ Hz, 2H}, 4.71 \text{ (dd, } J = 3.5, 2.3 \text{ Hz, 2H); nOe data: 6.41 (7.38, 1%, 5.37, 11%), 5.37 (7.38, 3%, 4.71, 7%), 4.71 (5.37, 17%; 4.71, 15%); }^{13}\text{C nmr (CDCl}_3\text{)} \delta: 155.5 \text{ (0), 130.1 (0), 129.1 (2), 129.1 (2), 128.4 (2), 127.2 (2), 125.4 (2), 105.5 (1), 74.0 (1), 52.1 (1); ms: 375 (M\,^+\text{, 8), 269 (58), 240 (58), 227 (65), 167 (15), 153 (18), 123 (16), 121 (37), 119 (60), 105 (33), 95 (14), 91 (32), 80 (100), 78 (56), 65 (20), 50 (16), 38 (24). Exact Mass calcd. for C\text{\textsubscript{21}}H\text{\textsubscript{17}}N\text{\textsubscript{2}}O\textsubscript{4}: 375.1217; found: 375.1225.**
3.8 Hz, 2H), 5.16 - 5.12 (m, 2H), 4.66 (m, 2H), 1.35 (s, 6H); nOe data: 6.42 (5.14, 10%; 1.35, 0.1%), 5.14 (6.42, 9%; 4.66, 6%); 4.66 (5.14, 14%; 1.35, 1%), 1.35 (6.42, 3%; 4.66, 11%); $^{13}$C nmr (CDCl$_3$) δ: 155.5 (0), 130.7 (0), 129.1 (1), 128.8 (1), 128.4 (0), 125.4 (1), 112.1 (1), 73.8 (1), 52.3 (1), 25.4 (3), 25.3 (3); ms: 327 (M$^+$, 2), 312 (11), 269 (23), 240 (41), 227 (100), 121 (29), 119 (59), 95 (73), 91 (18), 80 (67), 78 (42), 43 (83). Exact Mass calcd. for C$_{17}$H$_{17}$N$_2$O$_4$: 327.1217, found: 327.1210.

trans-4,5-Dibromocyclohexane oxide (47)

To a solution of 47 (1.40 g, 5.85 mmol) in CHCl$_3$ (2.0 mL) was added MCPBA (1.30 g) dissolved in CHCl$_3$ (4.0 mL), and the solution was heated at reflux for 17 hours. The white precipitate was filtered, washed with NaHSO$_3$ (2 x 50 mL), NaHCO$_3$ (2 x 50 mL), H$_2$O (2 x 50 mL), saturated NaCl (2 x 50 mL), and dried over MgSO$_4$. The solution was filtered and evaporated to afford white crystals 47 (0.582 g, 39%): mp 68 - 69°C; ir ν$_{max}$: 1415, 1009, 889 cm$^{-1}$; $^1$H nmr (CDCl$_3$) δ: 4.30 (ddd, $J = 4.6, 6.7, 7.7$ Hz, 1H), 4.19 (ddd, $J = 6.3, 6.3, 7.7$ Hz, 1H), 3.23 (m, 2H), 2.99 (dd, $J = 4.5, 16.0$ Hz), 2.89 (ddd, $J = 3.5, 6.3, 16.5$ Hz, 1H), 2.65 (dd, $J = 6.3, 16.5$ Hz, 1H), 2.46 (ddd, $J = 3.2, 6.5, 16.0$ Hz, 1H); $^{13}$C nmr (CDCl$_3$) δ: 50.7 (1), 50.2 (1), 48.7 (1), 47.3 (1), 33.3 (2), 32.3 (2); ms: 256 (M$^+$, 0.1), 177 (3), 176 (2), 175 (3), 174 (2), 95 (21), 67 (100).

1,3,5-cyclohexatriene 1,2-oxide / oxepin 48
To a solution of 47 (1.50 g, 5.89 mmol) in benzene (8 mL) was added DBU (3.52 mL, 23.5 mmol) as a solution in benzene (1.0 mL), and the mixture was heated at reflux for about 6 hours, and after which time the solution was washed with NaHCO₃ (3 x 25 mL) and saturated NaCl (3 x 25 mL), and dried over K₂CO₃. The solution was filtered and concentrated, and the sample was chromatographed on silica gel (30% ethyl acetate / hexane) to afford a light yellow oil 48 (0.385 g, 70%): ¹H nmr (CDCl₃) δ: 6.26 (m, 2H), 5.88 (m, 2H), 5.12 (d, J = 4.5 Hz, 2H); ¹³C nmr (CDCl₃) δ: 130.7, 128.6, 122.3, 120.2, 110.0, 107.5; ms: 94 (M⁺, 61), 78 (7), 68 (35), 66 (100), 65 (82).

**Diels-Alder reaction of 48 with 59: (5α,8α,10R',11R')-10,11-Epoxy-5,8-dihydro-2-phenyl-5,8-etheno-1H-[1,2,4]triazolo[1,2-a]pyridazine-1,3(2H)-dione (72)**

To the diene 48 (0.11 g, 0.125 mmol) was added a solution of 4-phenyl-1,2,4-triazoline-3,5-dione (21.9 mg, 0.12 mmol) in benzene (1.0 mL), and the mixture was stirred for about 16 hours. The solvent was evaporated, and flash column chromatography of the residue on silica gel (30% ethyl acetate / hexane) afforded white solid 72 (0.324 g, 97%): mp 177 - 178°C; ir νmax: 3064, 2987, 1773, 1717, 1501, 1404, 1265, 1060 cm⁻¹; ¹H nmr (CDCl₃) δ: 7.45 - 7.40 (m, 5H), 6.17 (t, J = 3.8 Hz, 2H), 5.31 - 5.30 (m, 2H), 3.72 (m, 2H); nOe data: 6.17 (5.30, 7%), 5.30 (6.17, 7%; 3.72, 9%), 3.72 (5.30, 9%); ¹³C nmr (CDCl₃) δ: 156.2 (0), 130.9 (0), 129.1 (1), 128.4 (1), 125.4 (1), 125.0 (1), 54.5 (1), 41.8 (1); ms: 271 (M⁺ + 1, 0.5), 269 (M⁺, 5), 268 (32), 239 (23), 121 (21), 118 (75), 94 (100), 91.
Anal. calcd. for C$_{14}$H$_{11}$N$_3$O$_3$: C, 62.43; H, 4.12; N, 15.61; found: C, 62.56; H, 4.15; N, 15.72.

**Diels-Alder reaction of 40a with dimethyl acetylenedicarboxylate:** Dimethyl (3α,4β,7β,7αα,8S',9S')3α,4,7α,7-dihydro-2,2-dimethyl-4,7-etheno-1,3-benzodioxole-8,9-dicarboxylate (73)

To a solution of the acetonide 40a (0.118 g, 0.182 mmol) in benzene (2.0 mL) was added dimethyl acetylenedicarboxylate (0.111 g, 0.782 mmol), and the mixture was stirred at room temperature for 17 hours. TLC showed a spot for the adduct at R$_f$ = 0.48 (30% ethyl acetate / hexane). The solution was concentrated, and the residue was chromatographed on silica gel (30% ethyl acetate / hexane) to afford white solid 73, which was recrystallized from hexane to give 0.198 g (86%): mp 93 - 94°C; ir v$_{max}$: 2995, 2946, 1731, 1713, 1644, 1615, 1433, 1383, 1340, 1270, 1245, 1164, 1057 cm$^{-1}$; $^1$H nmr (CDCl$_3$) δ: 6.39 (dd, J = 3.1, 4.3 Hz, 2H), 4.39 (m, 2H), 4.25 - 4.20 (m, 2H), 3.79 (s, 6H), 1.34 (s, 3H), 1.26 (s, 3H); nOe data: 6.39 (4.23, 11%; 1.34, 0.2%), 4.39 (4.23, 7%; 1.26, 2%), 4.23 (6.39, 9%; 4.39, 5%), 1.34 (6.39, 2%; 4.39, 2%), 1.26 (4.39, 9%); $^{13}$C nmr (CDCl$_3$) δ: 165.7 (0), 141.2 (0), 131.2 (1), 113.5 (0), 78.0 (0), 52.3 (1), 44.2 (3), 25.7 (3), 25.5 (3); ms: 279 (M$^+$ - CH$_3$, 3), 163 (19), 100 (85), 85 (100), 77 (10), 43 (22).
Diels-Alder reaction 40a with butene: (3α,4α,7α,7αα) - (74) and (3β,4α,7α,7αβ) - 3α, 4, 7, 7α-tetrahydro-2,2-dimethyl-1,3-dioxole-6H-4,7-ethenotricyclo[5.2,2.0 α,7α]undec-8-ene (75)

To the acetonide 40a (0.126 g, 0.833 mmol) in toluene (5.0 mL) was added butene in large excess (1.0 mL) and hydroquinone (about 0.01 g). The mixture was heated at reflux for about 72 hours after which time the solvent was evaporated, and the residue was chromatographed on silica gel (20% ethyl acetate / hexane) to afford solid 74, which was recrystallized from hexane to give (0.119 g, 64.4%), and colorless oil (0.017 g, 9%), which contained two inseparable adducts 75 and 76. For 74: mp 61 - 62°C; ir νmax: 2995, 2963, 2915, 2886, 1709, 1459, 1368, 1279, 1160, 1060 cm⁻¹; ¹H nmr (CDCl₃) δ: 6.17 (t, J = 7.3 Hz, 1H), 5.97 (t, J = 7.2 Hz, 1H), 4.28 (dd, J = 3.1, 7.2 Hz, 1H), 4.22 (dd, J = 3.2, 7.2 Hz, 1H), 3.24 - 3.21 (m, 1H), 2.92 (m, 1H), 2.48 (dd, J = 2.0, 5.1, 9.7 Hz, 1H), 2.16 (s, 3H), 1.81 (ddd, J = 4.2, 4.3, 13.4 Hz, 1H), 1.46 (ddd, J = 2.3, 9.8, 13.4 Hz, 1H), 1.34 (s, 3H), 1.34 (s, 3H), 1.29 (s, 3H); nOe data: 6.17 (5.96, 3%; 2.92, 3%), 5.97 (6.17, 3%; 3.23, 3%), 4.28 (3.23, 4%; 2.92, 1%; 2.48, 8%; 1.46, 1%; 1.29, 1%), 4.22 (2.92, 3%; 2.48, 2%; 1.46, 4%), 3.23 (5.97, 5%; 4.28, 3%; 4.22, 0.2%; 2.48, 2%; 2.16, 1%), 2.92 (6.17, 5%; 4.28, 0.2%; 4.22, 3%; 1.81, 3%; 1.46, 2%), 2.48 (4.28, 7%; 4.22, 1%; 3.23, 3%; 1.46, 4%), 1.81 (2.92, 5%; 1.46, 9%), 1.46 (4.28, 0.04%; 4.22, 5%; 2.92, 2%; 2.48, 5%; 1.81, 14%), 1.34 (6.17, 1%; 5.97, 2%), 1.29 (4.28, 7%; 4.22, 7%); ¹³C nmr (CDCl₃) δ: 207.5 (0), 132.3 (1), 127.7 (1), 108.6 (0), 127.7 (1), 108.6 (0), 78.2 (1), 78.2 (1), 48.8 (1),
Diels-Alder reaction of 40a with para-benzoquinone: (4α,5α,5αα,8αα,9α,9αα)-
(77) and (4α,5α,5αβ,8αβ,9α,9αα)-4α,5α,8α,9α-4a,5,8a,9a-hexahydro-7,7-dimethyl-
1,4,5,9-dietheno-6,8-dioxolo-5a,8a-naphthyl-1,4-dione (78)

To diene 40a (0.358 g, 2.35 mmol) in benzene (2.0 mL) was added para-
benzoquinone (0.385 g, 3.53 mmol), and the mixture was stirred at room
temperature for 72 hours. The solvent was evaporated, and the residue was
chromatographed on silica gel (20% ethyl acetate / hexane) to afford a brown
solid 77, which was recrystallized first from ethyl acetate / hexane and then three
times from hexane to give a colourless solid (0.084 g, 9%), and 78 as a light
brown solid, which was recrystallized from ethyl acetate / hexane once and then twice from hexane to afford a white solid (0.511 g, 56%). For 77: mp 151-152°C; \textit{ir} \nu_{\text{max}}: 2987, 2914, 1693, 1619, 1598, 1377, 1319, 1294, 1060 cm$^{-1}$; \textit{^1H nmr}
(CDCl$_3$) $\delta$: 6.68 (s, 2H), 6.40 (dd, $J = 3.0, 4.3$ Hz, 2H), 4.58 - 4.54 (m, 2H), 4.27 (t, $J = 1.7$ Hz, 4H), 1.36 (s, 3H), 1.25 (s, 3H); nOe data: 6.40 (4.56, 7%; 1.36, 0.2%), 4.56 (6.40, 6%; 4.27, 4%), 4.27 (4.56, 10%; 1.25, 2%), 1.36 (6.40, 3%; 4.56, 1%; 4.27, 1%), 1.25 (4.27, 9%); \textit{^13C nmr} (CDCl$_3$) 5: 183.3 (0), 135.9 (1), 131.4 (1), 113.6 (0), 78.3 (1), 39.4 (1), 25.6 (3), 25.4 (3); ms: 260 (M$^+$, 10), 245 (27), 231 (18), 202 (29), 185 (23), 173 (36), 157 (11), 145 (18), 129 (15), 119 (46), 99 (89), 91 (57), 85 (21), 81 (87), 77 (16), 65 (21), 54 (50), 50 (12), 43 (100). Exact Mass calcd. for C$_{15}$H$_{16}$O$_4$: 260.1047; found: 260.1031. For 78: mp 122 - 123°C; \textit{ir} \nu_{\text{max}}: 2987, 2953, 1745, 1745, 1621, 1446, 1408, 1293, 1222, 1016 cm$^{-1}$; \textit{^1H nmr} (CDCl$_3$) $\delta$: 6.69 (s, 2H), 6.17 (dd, $J = 2.8, 4.4$ Hz, 2H), 4.09 (t, $J = 1.9$ Hz, 2H), 3.50 (s, 4H), 1.50 (s, 3H), 1.36 (s, 3H); nOe data: 6.17 (4.09, 1%; 3.50, 2%), 4.09 (6.17, 2%; 3.50, 4%; 1.36, 2%), 3.50 (6.69, 2%; 6.17, 9%; 4.09, 7%; 1.50, 1%), 1.50 (3.50, 3%; 1.36, 1%), 1.36 (4.09, 9%; 1.50, 1%); \textit{^13C nmr} (CDCl$_3$) 5: 199.3 (0), 141.8 (1), 132.7 (1), 112.1 (0), 73.8 (1), 42.0 (1), 39.2 (1), 26.4 (3), 24.3 (3); ms: 260 (M$^+$, 10), 245 (50), 202 (13), 185 (17), 173 (23), 157 (13), 145 (15), 129 (16), 119 (28), 117 (15), 115 (10), 99 (46), 91 (43), 85 (15), 81 (53), 77 (13), 65 (17), 54 (32), 50 (10), 43 (100). Exact Mass calcd. for C$_{15}$H$_{16}$O$_4$: 260.1047; found: 260.1070. Exact Mass calcd. for C$_{14}$H$_{13}$O$_4$ (M$^+$ - CH$_3$): 245.0812; found: 245.0815.
Diels-Alder reaction of 40a with vinylene carbonate: (3αα,4β,4αβ,7αβ,8β,8αα)-(79) and (3αα,4β,4αα,7αα,8β,8αα)-3α,4,4α,7α,8,8α-hexahydro-6,6-dimethyl-2-oxo-4,8-ethenobenzof[1,2-d]:4,5-d]bis[1,3]dioxole (80).

To a solution of acetonide 40a (0.152 g, 1.00 mmol) in benzene (8.0 mL) was added vinylene carbonate (0.12 mL, 2.0 mmol), and the mixture was heated at reflux for 7 days. The solution was concentrated, and the residue was chromatographed on silica gel (30% ethyl acetate / hexane) to afford a white solid, which was recrystallized from hexane to give 0.182 g (38%) of 79, and 80 which was also recrystallized from hexane to give 0.043 g (9%) of adduct. For 79: mp 167 - 169°C; lr νmax: 2985, 1795, 1594, 1371, 1267, 1166, 1050 cm⁻¹; ¹H nmr (CDCl₃) δ: 6.22 (dd, J = 3.0, 4.5 Hz, 2H), 5.16 (m, 2H), 4.21 (t, J = 2.1 Hz, 2H), 3.47 - 3.45 (m, 2H), 1.45 (s, 3H), 1.30 (s, 3H); nOe data: 6.22 (4.20, 1%; 3.46, 5%), 5.16 (4.20, 0.2%; 3.46, 5%; 1.45, 0.7%), 4.20 (6.22, 2%; 3.46, 8%; 1.29, 2%), 3.46 (6.22, 7%; 5.16, 5%; 4.20, 5%), 1.45 (6.22, 0.1%; 5.16, 6%; 4.20, 0.2%), 1.29 (5.22, 0.4%; 4.20, 9%); ¹³C nmr (CDCl₃) δ: 155.0 (0), 130.4 (1), 112.1 (0), 74.2 (1), 73.7 (1), 38.4 (1), 25.8 (3), 23.2 (3); ms: 239 (M⁺+1, 1), 223 (45), 179 (43), 118 (14), 107 (41), 94 (68), 91 (27), 79 (29), 66 (20), 43 (100).

Exact Mass calcd. for C₁₁H₁₁O₅ (M⁺ - CH₃): 223.0605; found: 223.0604. For 80: mp 205 - 207°C; lr νmax: 2987, 1771, 1594, 1536, 1462, 1375, 1207, 1172, 1053 cm⁻¹; ¹H nmr (CDCl₃) δ: 6.16 (dd, J = 3.2, 4.1 Hz, 2H), 4.67 (m, 2H), 4.20 (m, 2H), 3.48 - 3.46 (m, 2H), 1.34 (s, 3H), 1.27 (s, 3H); nOe data: 6.16 (3.47, 5%; 1.35, 0.2%), 4.66 (4.19, 10%; 3.47, 7%), 4.19 (4.66, 13%, 3.47, 7%; 1.35, 0.1%);
Diels-Alder reaction of 40a with tetracyanoethylene: (3α,4α,7α,7αα)-5,5,6,6-tetracyano-3α,4,7,7a-tetrahydro-2,2-dimethyl-1,3-dioxolo-4,7-ethenotricyclo[5.2.2.03,7]undec-8-ene (81)

To a solution of the acetonide 40a (0.122 g, 0.802 mmol) in benzene (0.802 mmol) was added tetracyanoethylene (0.102 g, 0.802 mmol), and the mixture was heated at reflux for 24 hours. TLC showed a spot (yellow in iodine Rf = 0.35; 30% ethyl acetate / hexane). The solvent was evaporated, and the residue was chromatographed on silica gel (30% ethyl acetate / hexane) to afford a light brown solid 81 (0.141 g, 63%): mp 218 - 220°C; ir νmax: 2984, 2959, 2233, 1632, 1469, 1379, 1271, 1238, 1089 cm⁻¹; ¹H nmr (CDCl₃/CD₃COCD₃) δ: 6.66 - 6.52 (dd, J = 2.9, 4.6 Hz, 2H) 4.78 (m, 2H), 3.93 - 3.89 (m, 2H), 1.34 - 1.40 (s, 3H), 1.34 - 1.33 (s, 3H); nOe data: 6.52 (3.64, 7%), 4.55 (3.85, 11%; 1.33, 0.2%; 1.13, 0.7%), 3.85 (6.52, 7%; 4.55, 4%; 1.33, 0.4%), 1.13 (6.52, 2%; 4.55, 9%); ¹³C nmr (CDCl₃/CD₃COCD₃) δ: 132.1/130 (1), 112.8/111.7, 111.7/110.7 (0), 109/111.6 (0), 73.4/72.3 (1), 43.3/42.8, 25.0/25.0 (3); ms: 280 (M⁺, 0.6), 265
123
(29), 192 (2), 140 (2), 114 (2), 99 (17), 95 (56), 85 (11), 77 (4), 66 (5), 58 (48),
43 (100). Exact Mass calcd. for C_{14}H_{39}N_{2}O_{2} \text{ (M}^+ - \text{CH}_3\text{)}: 265.0725; found:
265.0730. Anal. calcd. for C_{15}H_{12}N_{4}O_{2}: C, 64.26; H, 4.34; N, 20.00; found: C,
64.08; H, 4.29; N, 20.04.

Attempted Diels-Alder reaction of 40a with styrene

To a solution of diene 40a (0.241 g, 1.59 mmol) in benzene (1.0 mL) was
added styrene in large excess (1.0 mL), and the mixture was stirred at room
temperature for 7 days, after which TLC showed spots for the unreacted starting
materials and two products: the dimers. The reaction was repeated at reflux in
benzene and still there was no reaction.

Diels-Alder reaction of 40a with maleimide: (3α,4α,4aβ,7β,8α,8αα)- (82) and
(3α,4β,4αα,7αα,8β,8αα)-4a,7a,8,8a-Tetrahydro-2,2-dimethyl-4,8-etheno-4H-
1,3-dioxolo[4,5-f]isoindole-5,7-(3αH,6H)-dione (63)

To a solution of the acetonide 40a (0.124 g, 0.817 mmol) in benzene (4.0
mL) was added maleimide (0.158 g, 1.63 mmol), and the mixture was stirred at
room temperature for 16 hours. The solvent was evaporated, and the
concentrated sample was chromatographed on silica gel (30% ethyl acetate /
hexane) to afford a white solid 82, which was recrystallized from benzene (0.152
g, 38%), and 63, which was also recrystallized from benzene (0.182 g, 45%).
For 82: mp 172 - 174°C; ir \nu_{max}: 3102, 2978, 2948, 1754, 1468, 1369, 1200, 1060
124
cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) data \(\delta\): 8.56 (br s, NH), 6.20 (m, 2H), 4.14 (dd, \(J = 1.5, 2.1\) Hz, 2H), 3.42 - 3.37 (m, 2H), 3.35 (m, 1H), 1.49 (s, 3H), 1.34 (s, 3H); nOe data:
6.20 (4.14, 1%; 3.39, 9%; 3.35, 0.1%; 3.35, 0.1%), 4.14 (6.20, 2%; 3.39, 14%);
3.35, 1%; 1.34, 2%), 3.39 (3.39, 8%; 4.14, 7%; 1.48; 0.3%), 3.36 (6.20, 4%);
4.14, 4%; 1.48, 1%), 1.48 (3.36, 5%; 1.34, 1%), 1.34 (4.14, 8%; 1.48, 1%);
\(^{13}\)C nmr (CDCl\(_3\)) \(\delta\): 179.7 (0), 131.5 (1), 112.4 (0), 73.7 (1), 38.9 (1), 36.4 (1), 26.2
(3), 24.2 (3); ms: 250 (M\(^+\) + 1, 5), 234 (64), 190 (62), 163 (40), 146 (35), 135
(47), 119 (63), 103 (24), 99 (73), 91 (81), 85 (52), 78 (48), 85 (54), 59 (25), 50
(29), 43 (100). Exact Mass calcd. for C\(_{12}\)H\(_{12}\)NO\(_4\) (M\(^+\) - CH\(_3\)): 234.0765; found:
234.0775. For 63: mp 233 - 234°C; ir \(\nu_{\text{max}}\): 3257, 2960, 1748, 1701, 1464, 1377,
1358, 1198, 1066 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \(\delta\): 8.26 (br s, NH), 6.12 (m, 2H), 4.28 (m,
2H), 3.45 - 3.42 (m, 2H), 2.81 (t, \(J = 1.3\) Hz, 2H), 1.33 (s, 3H), 1.29 (s, 3H); nOe
data: 6.12 (3.44, 7%; 1.33, 0.2%), 4.28 (3.43, 9%; 2.81, 13%; 1.29, 2%), 3.43
(6.12, 8%; 4.28, 5%), 2.81 (4.28, 11%; 3.43, 8%), 1.34 (6.12, 2%; 4.28, 1%),
1.29 (4.28, 7%); \(^{13}\)C nmr (CDCl\(_3\)) \(\delta\): 177.3 (0), 129.7 (1), 109.8 (0), 77.1 (1), 41.7
(1), 36.3 (1), 25.2 (3), 24.8 (3); ms: 250 (M\(^+\)+1, 0.7), 234 (30), 192 (17), 191 (23),
163 (14), 162 (12), 146 (12), 135 (14), 119 (23), 99 (31), 92 (54), 85 (19), 65
(15), 58 (11), 43 (100). Exact Mass calcd. for C\(_{12}\)H\(_{12}\)NO\(_4\) (M\(^+\) - CH\(_3\)): 234.0765;
found: 234.0773.

**Attempted Diels-Alder reaction of 40a with cis-stilbene**

To the acetonide 40a (0.250 g, 1.51 mmol) in benzene (1.0 mL) was
added cis-stilbene (0.272 g, 0.26 mL), and the mixture was stirred at room temperature for 17 hours after which TLC showed that there was no reaction. The mixture was stirred for another two weeks, and subsequent TLC analysis showed unreacted cis-stilbene and two dimers. The $^1$H nmr spectrum of the concentrated solution showed no signals for for stilbene adduct. Repeating the process at reflux led to the same result.

**Diels-Alder reaction of 40a with dimethyl maleate: (3α,4β,5α,7β,7α,8S',9R')-**

(84) and (3α,4α,7α,7α,8R',9S')-4,7-dihydro-2,2-dimethyl-etheno-1,3-benzodioxole-8,9-dicarboxylate (85)

To the acetonide 40a (0.120 g, 0.794 mmol) in benzene (1.0 mL) was added dimethyl maleate (0.229 g, 1.58 mmol), and the mixture was stirred at room temperature for 5 days. TLC showed some unreacted starting materials and two new adducts. The solvent was evaporated, and the residue was chromatographed on silica gel (20% ethyl acetate / hexane) to afford 84 (0.025 g, 11%) and 85 (0.083 g, 35%) as white solids. For 84: mp 134 - 135°C; ir $\nu_{max}$: 2982, 2951, 2905, 1737, 1449, 1382, 1205, 1162, 1057 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 6.29 (dd, $J = 3.0$, 4.8 Hz, 2H), 4.05 (t, $J = 2.1$ Hz, 2H), 3.61 (s, 6H), 3.54 (s, 2H), 3.16 - 3.12 (m, 2H), 1.53 (s, 3H), 1.34 (s, 3H); nOe data: 6.29 (4.09, 1%; 3.14, 4%), 4.09 (6.29, 1%; 3.14, 6%; 1.34, 2%), 3.54 (3.14, 3%; 1.53, 1%), 3.14 (6.29, 4%; 4.09, 4%; 3.54, 3%), 1.53 (3.54, 3%), 1.34 (4.09, 5%); $^{13}$C nmr (CDCl$_3$) $\delta$: 173.5 (0), 131.0 (1), 112.0 (0), 73.9 (1), 51.0 (1), 39.2 (1), 37.4 (3),
26.3 (3), 24.2 (3); ms: 296 (M⁺, 0.3), 281 (2), 264 (22), 237 (51), 205 (22), 178 (27), 160 (9), 146 (100), 125 (8), 118 (37), 105 (8), 103 (14), 99 (58), 90 (55), 85 (20), 77 (13), 65 (12), 58 (37), 45 (14), 43 (57). Exact Mass calcd. for C₁₅H₂₀O₆: 296.1258; found: 296.1258. For 85: mp 196 - 197°C; ir νmax: 2988, 2971, 1741, 1741, 1432, 1369, 1311, 1185 cm⁻¹; ¹H nmr (CDCl₃) δ: 6.20 (dd, J = 3.1, 4.5 Hz, 2H), 4.21 (m, 2H), 3.62 (s, 6H), 3.21 - 3.20 (m, 2H), 2.83 (s, 2H), 1.33 (s, 3H), 1.27 (s, 3H); NOE data: 6.20 (3.62, 0.2%; 3.20, 8%; 1.33, 0.3%), 4.21 (3.20, 10%; 2.83, 15%; 1.27, 2%), 3.62 (6.20, 0.6%; 2.83, 0.6%), 3.20 (6.20, 10%; 4.21, 5%; 2.83, 4%), 2.83 (4.21, 15%; 3.20, 9%), 1.33 (6.20, 2%; 4.21, 2%), 1.27 (6.20, 0.4%; 4.21, 7%); ¹³C nmr (CDCl₃) δ: 172.2 (0), 129.3 (1), 109.2 (0), 51.9 (1), 42.9 (1), 39.5 (1), 25.3 (3), 25.0 (3); ms: 296 (M⁺, 0.9), 281 (4), 264 (19), 237 (15), 206 (20), 178 (26), 149 (7), 146 (100), 118 (32), 112 (11), 103 (11), 99 (31), 90 (56), 85 (28), 77 (16), 65 (12), 58 (42), 43 (62). Exact Mass calcd. for C₁₅H₂₀O₆: 296.1258; found: 296.1249.

Diels-Alder reaction of 40a with ethyl propiolate: (3α,4β,7β,7αα)-4,7-dihydro-2,2-dimethyl-4,7-etheno-1,3-benzodioxole-5-carboxylate (86)

To a solution of the acetonide 40a (618 mg, 0.455 mmol) in benzene (0.5 mL) was added ethyl propiolate (0.043 g, 0.40 mmol), and the mixture was stirred at room temperature for 3 days. The solvent was evaporated, and the residue was chromatographed on silica gel (20% ethyl acetate / hexane) to give sweet-smelling colorless oil 86 (0.063 g, 61%): ir νmax: 2962, 2907, 2935, 1712,
1633, 1597, 1458, 1379, 1260, 1221, 1159, 1056, 885 cm⁻¹; ¹H nmr (CDCl₃) δ:
7.21 (dd, J = 1.8, 6.3 Hz, 1H), 6.40 (ddd, J = 1.6, 5.9, 6.7 Hz, 1H), 6.30 (ddd, J =
1.7, 6.0, 6.7 Hz, 1H), 4.39 (m, 1H), 4.26 (m, 2H), 4.19 (dq, J = 0.8, 7.1, Hz, 2H),
4.01 - 3.97 (m, 1H), 1.35 (s, 3H), 1.29 (t, J = 7.1, 3H), 1.26 (s, 3H); nOe data:
7.21 (4.26, 0.6%; 3.99, 5%), 6.40 (4.39, 4%), 6.30 (3.99, 3%), 4.39 (7.21, 0.7%;
6.40, 4%; 3.99, 1%), 4.26 (7.21, 3%; 4.39, 5%; 1.29, 2%; 1.26, 2%), 4.19 (7.21,
0.9%; 1.29, 8%), 3.99 (7.21, 8%; 6.30, 5%; 4.26, 1%), 1.39 (6.40, 2%; 6.30, 2%;
4.26, 0.6%; 4.19, 1%), 1.29 (4.26, 2%), 1.26 (4.26, 4.26, 8%); ms: no M⁺, 235
(3), 163 (10), 135 (7), 121 (3), 117 (3), 105 (25), 103 (4), 99 (95), 90 (10), 85
(100), 77 (16), 59 (13), 43 (29). Exact Mass calcd. for C₁₃H₁₅O₄ (M⁺ - CH₃);
235.0969; found: 235.0957.

**Diels-Alder reaction of 40a with N-methylmaleimide: (3αα,4αα,4αβ,7αβ,8αβ,8αα)-**(87) and (3αα,4β,4αα,7αβ,8αβ,8αα)-4α,7αα,8αα-Tetrahydro-2,2,6-trimethyl-4,8-
etheno-4H-1,3-dioxolo[4,5-f]isoindole-5,7-(3αH,6H)-dione (88)**

To a solution of the acetonide 40a (0.108 g, 0.712 mmol) in benzene (1.0
mL) was added N-methylmaleimide (0.079 g, 0.712 mmol), and the mixture was
stirred at room temperature for 17 hours. The solvent was evaporated, and flash
column chromatography of the residue on silica gel (20% ethyl acetate / hexane)
gave 87 (0.071 g, 38%), and also a white solid 88 (0.074 g, 40%). For 87: mp
218 - 220°C; ir νmax: 2986, 2913, 1757, 1747, 1410, 1354, 1298, 1083 cm⁻¹; ¹H
nmr (CDCl₃) δ: 6.11 (dd, J = 2.9, 4.5 Hz, 1H), 4.14 (dd, J = 1.7, 2.2 Hz, 2H), 3.43
- 3.38 (m, 2H), 3.31 (m, 2H), 2.90 (s, 3H), 1.48 (s, 3H), 1.35 (s, 3H); nOe data: 6.11 (4.14, 1%; 3.40, 7%), 4.14 (6.11, 2%; 3.40, 10%; 1.34, 2%), 3.40 (6.11, 8%; 4.14, 7%), 3.31 (6.11, 1%; 4.14, 1%; 1.48, 1%), 2.90 (6.11, 0.7%), 1.48 (3.31, 5%), 1.34 (4.14, 9%); $^{13}$C nmr (CDCl$_3$) δ: 179.4 (0), 131.5 (1), 112.4 (0), 73.9 (1), 37.7 (1), 36.5 (1), 26.2 (3), 24.6 (3), 24.2 (3); ms: 264 (M$^+$+1, 2), 248 (34), 206 (51), 205 (47), 204 (16), 177 (31), 176 (25), 160 (21), 146 (37), 130 (7), 119 (21), 118 (22), 100 (73), 92 (100), 91 (100), 85 (39), 78 (28), 77 (22), 65 (33), 43 (100). Exact Mass calcd. for $C_{13}H_{16}NO_4$ (M$^+$ - CH$_3$): 248.0921; found 248.0913.

For 88: mp 188 - 190°C; ir $\nu_{max}$: 2979, 2961, 2920, 1767, 1691, 1439, 1386, 1271, 1082, 1082 cm$^{-1}$; $^1$H nmr (CDCl$_3$) δ: 6.05 (dd, J = 3.0, 4.4 Hz, 2H), 4.30 (m, 2H), 3.47 - 3.44 (m, 2H), 2.92 (s, 3H), 2.76 (s, 2H), 1.33 (s, 3H), 1.29 (s, 3H); nOe data: 6.05 (3.46, 7%), 4.30 (3.46, 9%; 2.76, 14%; 1.29, 2%), 3.46 (4.30, 4%; 2.76, 5%), 2.76 (4.30, 12%; 3.46, 9%), 1.33 (6.05, 2%; 4.30, 1%), 1.29 (4.30, 7%); $^{13}$C nmr (CDCl$_3$) δ: 177.3 (0), 129.5 (1), 109.7 (0), 77.3 (1), 40.4 (1), 36.4 (1), 25.3 (3), 24.8 (3); ms: 264 (M$^+$+1, 1), 248 (41), 206 (45), 205 (41), 204 (16), 177 (32), 176 (22), 160 (20), 149 (10), 146 (33), 119 (40), 103 (10), 99 (54), 93 (14), 92 (100), 85 (37), 78 (28), 65 (24), 45 (19), 43 (93). Exact Mass calcd. for $C_{13}H_{16}NO_4$ (M$^+$ - CH$_3$): 248.0922; found: 248.0922.

*Diels-Alder dimerization of acetonide 40a: (3αβ,5αα,6αα,6αα,9αα,10αα,10αβ) - (89) and (3αβ,5αα,6αα,6αα,9αβ,10αα,10αα,10ββ) -
3a,5a,6a,9a,10,10a,10b-octahydro-2,2,8,8-tetramethyl-3a,5a,6,10-
diethanonaphthol-1,3,7,9-tetraoxole (90)

A neat liquid sample of acetonide 40a (0.214 g, 1.41 mmol) was kept in a sealed tube for 28 days. The \( ^1H \) nmr spectrum of the crude sample indicated a 6:1 ratio of dimers. Flash column chromatography of the sample on silica gel (10% ethyl acetate / hexane) afforded 89 (0.129 g, 60%) as the major dimer and 90 (0.412 g, 19%). For 89: mp 149 - 151°C; ir \( \nu_{max} \): 2986, 2929, 2886, 1456, 1364, 1278, 1236, 1161, 1046, 886 cm\(^{-1}\); \( ^1H \) nmr (CDCl\(_3\)) \( \delta \): 5.99 (m, 2H), 5.60 (dd, \( J = 3.8, 10.3 \) Hz, 1H), 5.51 (d, \( J = 10.2 \) Hz, 1H), 4.30 (m, 2H), 4.17 (m, 2H), 2.87 (m, 2H), 2.36 (br d, 2H), 2.23 (d, \( J = 9.0 \) Hz, 1H), 1.38 (s, 3H), 1.34 (s, 3H), 1.32 (s, 3H), 1.29 (s, 3H); nOe data: 5.99 (4.17, 4%; 2.87, 5%), 5.60 (2.87, 2%; 2.36, 2%), 5.51 (4.17, 2%; 2.36, 0.6%), 4.30 (2.87, 3%; 2.36, 5%; 2.23, 9%; 1.29, 1%), 4.30 (5.51, 1%; 2.87, 3%; 2.36, 8%; 2.23, 6%; 1.29, 1%), 4.17 (5.99, 2%; 5.51, 4%; 2.87, 2%; 2.23, 1%), 4.17 (2.87, 6%; 2.23, 3%), 2.87 (5.99, 7%; 5.60, 6%; 4.30, 4%; 2.36, 3%; 2.23, 3%), 2.36 (5.60, 4%; 4.30, 4%; 2.87, 2%; 2.23, 3%), 2.23 (4.30, 4%; 4.17, 2%; 2.36, 3%), 1.36 (5.51, 4%; 4.17, 0.5%; 2.87, 2%), 1.34 (5.51, 2%; 4.17, 2%; 4.30, 9%), 1.32 (5.99, 2%; 4.30, 2%; 4.17, 2%), 1.29 (5.99, 0.5%; 4.30, 7%); \( ^13C \) nmr (CDCl\(_3\)) \( \delta \): 132.3 (1), 129.2 (1), 128.7 (1), 126.6 (1), 108.5 (0), 107.6 (0), 78.5 (1), 78.3 (1), 77.6 (1), 70.8 (1), 40.9 (1), 40.6 (1), 34.2 (1), 33.1 (1), 28.3 (3), 26.8 (3), 25.3 (3), 24.9 (3); ms: no M\(^+\), 289 (12), 246 (7), 230 (7), 188 (49), 171 (19), 158 (25), 153 (14), 145 (18), 140 (15), 131 (18), 129 (21), 119 (22), 115 (13), 107 (6), 103 (6), 99 (30), 95 (72), 94 (22), 91 (35), 85 (17), 80 (14), 77 (20), 66 (16), 58 (13), 43 (100). Anal. calcd. for
C_{18}H_{22}O_{4}: C, 71.01; H, 7.95; found: C, 71.01; H, 7.76. Exact Mass calcd. for 
C_{17}H_{21}O_{4} (M^+ - CH_3); 289.1439; found: 289.1449. For 90: mp 92 - 93°C, ir ν_{max}:
3049, 3022, 2984, 2934, 1458, 1375, 1238, 1207, 1162, 1061, 887 cm^{-1}; ^1H nmr
(CDCl_3) δ: 6.07 (m, 2H), 5.55 (ddd, J = 1.3, 3.5, 11.5 Hz, 1H), 5.49 (br d, J = 10.3 Hz, 1H), 4.19 - 4.17 (m, 1H), 4.10 - 4.02 (m, 3H), 3.01 (br d, J = 9.0 Hz, 1H), 2.96 (br d, J = 9.0 Hz, 1H), 2.83 - 2.77 (m, 2H), 1.55 (s, 3H), 1.38 (s, 3H), 
1.35 (s, 3H), 1.33 (s, 3H); nOe data: 6.07 (4.19, 3%; 2.80, 5%), 5.56 (2.96, 3%; 
2.80, 1%), 5.49 (4.19, 2%; 2.80, 3%; 2.80, 1%), 5.49 (4.19, 2%; 3.01, 4%), 4.19 
(6.07, 2%; 5.49, 4%; 2.80, 0.8%) 4.06 (6.07, 2%; 5.49, 4%; 3.01, 0.6%; 2.80, 
0.8%), 4.06 (6.07, 2%; 4.19, 7%; 3.01, 2%; 5.49, 5%), 2.96 (5.56, 11%), 2.96 
(5.56, 11%; 4.06, 0.8%), 2.80 (6.07, 7%; 5.50, 4%; 5.49, 0.8%; 4.06, 8%; 3.01, 
4%; 2.96, 3%), 1.55 (3.01, 5%; 2.96, 5%; 1.35, 0.9%); ^13C nmr (CDCl_3) δ: 134.5 
(1), 131.1 (1), 130.3 (1), 126.8 (1), 111.8 (0), 107.4 (0), 77.9 (1), 75.2 (1), 74.7 
(1), 71.1 (1), 40.8 (1), 40.3 (1), 30.4 (1), 28.4 (3), 26.7 (3), 26.3 (3), 24.3 (3); ms:
no M^+, 289 (15), 275 (26), 231 (3), 188 (40), 171 (85), 169 (9), 159 (30), 153 
(19), 145 (20), 141 (17), 131 (14), 129 (26), 119 (15), 115 (16), 107 (11), 99 
(49), 95 (47), 91 (34), 85 (11), 77 (19), 66 (20), 58 (14), 45 (10), 43 (100). Exact 
Mass calcd. for C_{17}H_{21}O_{4} (M^+ - CH_3); 289.1439; found: 289.1445.
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The selected $^1$H nmr and the n.O.e.d spectra of dienes and adducts were arranged according to the order in which they appear in the text.