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

SUNNY M. OGBOMO

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by

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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 acethylenedicarboxylate (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 $LiClO_4$ in ether. However, selectivity was with $LiClO_4$ in water. Solubility and concentration phenomena are used to rationalize these selectivities.

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Glossary of Abbreviations

Ac	acetyl
APT	attached proton test
COSY	correlation spectrum
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DEAD	diethyl azodicarboxylate
DMAD	dimethyl acetylenedicarboxylate
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
EDG	electron-donating group
EP	ethyl propiolate
Et	ethyl
EWG	electron-withdrawing group
GC/MS	gas chromatography-mass spectrometry
HOMO	highest occupied molecular orbital
IR	infrared [spectroscopy]
LUMO	lowest unoccupied molecular orbital
MA	maleic anhydride
MP	melting point
MS	mass spectrometry
mCPBA	*meta*-chloroperoxybenzoic acid

NMR	nuclear magnetic resonance [spectroscopy]
n.O.e.	nuclear Overhauser effect
NPM	*N*-phenylmaleimide
PTAD	4-phenyl-1,2,4-triazoline-3,5-dione
*p*TsOH	*para*-toluenesulfonic acid
TCNE	tetracyanoethylene
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
UV	ultraviolet [spectroscopy]

Dedication

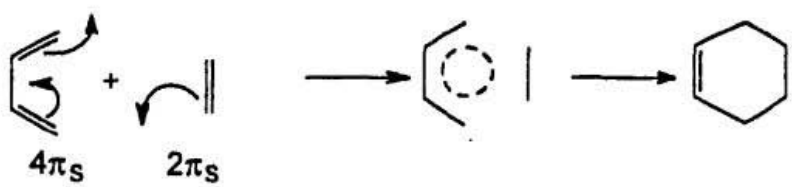
To my wife, Joan, and my children, Efosa and Iziegbe.

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.[1,2,3] Cycloadditions provide useful routes for the creation of a wide variety of rings. Important classes of cycloadditions include [2+2] photochemical reactions of alkenes and alkynes, the 1,3-dipolar addition and the [4+2] thermal addition.[1,3,4]

The latter class of cycloadditions, known originally as the "diene synthesis",[5] has become universally recognized as the Diels-Alder reaction (Scheme 1), although this reaction may have been known for quite a long time



Scheme 1. Diels-Alder reaction of 1,3-butadiene with ethylene

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[5] in 1875. A

1

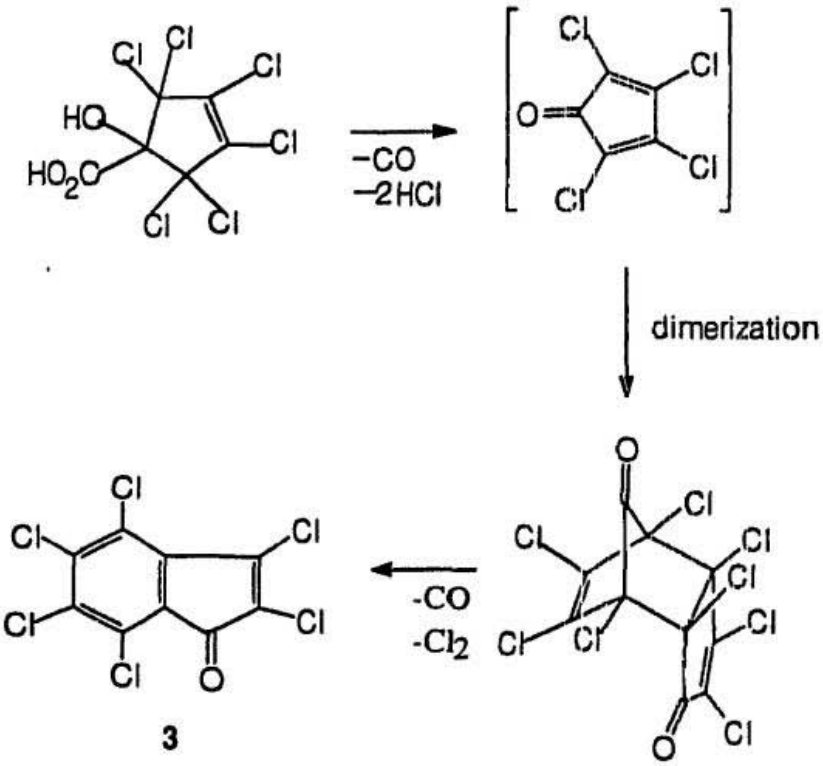
Limonene

Scheme 2: Dimerization of 2-methyl-1,3-butadiene (isoprene)

couple of years later, Ipatieff[5] 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[1] 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[5] 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.[5] It was not until 1928 that Otto Diels and Kurt Alder[5] clearly

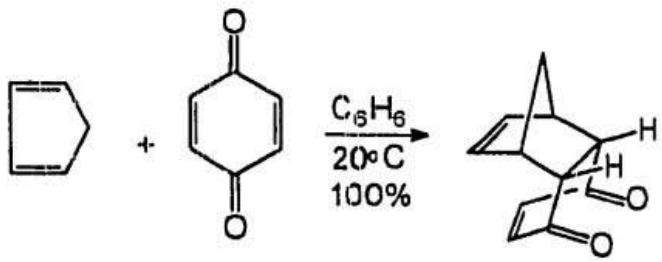


Scheme 3: Dimerization of tetrachlorocyclopentadienone

established the correct structure **4**. They also presented structure **7** for the reaction of cyclopentadiene and diethyl azodicarboxylate[1,5] (Scheme 5). The work of Diels and Alder opened a new, very promising page in the annals of organic chemistry,[5] and they jointly received a Nobel Prize in 1950 for their work.[7,8]

The Diels-Alder reaction has become one of the most important tools for the construction of six-membered carbo- and heterocyclic ring systems. The Diels-Alder reaction is a $[4_{\pi s}+2_{\pi s}]$ cycloaddition (Scheme 1) in which a

conjugated diene (1,3-diene) undergoes an addition to another component,



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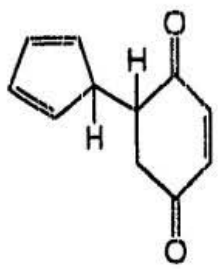

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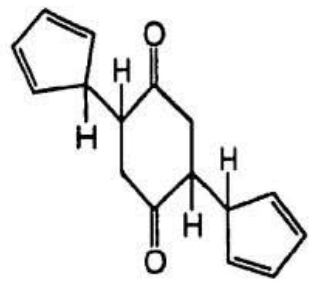

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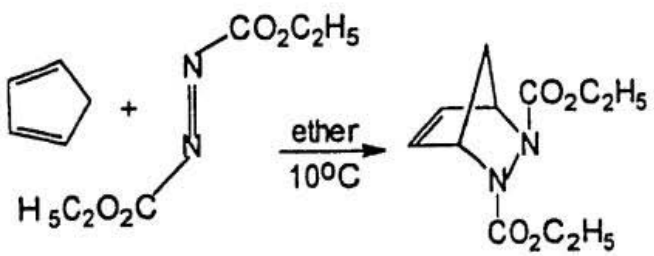
Scheme 4: Reaction of cyclopentadiene with *para*-benzoquinone to afford **4.**



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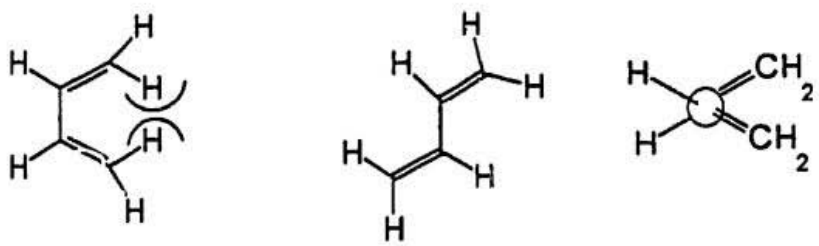
Scheme 5: Diels-Alder reaction of cyclopentadiene and diethyl azodicarboxylate

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.[8]

The Diels-Alder reaction is a thermally allowed, stereospecific, suprafacial process with a concerted, one-step synchronous or nearly synchronous mechanism.[9] This is consistent with the low solvent and polarity effects on the reaction rate, which rules out zwitterionic intermediates.[8,9,10] In support of the concerted mechanism[3,14,16] 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-



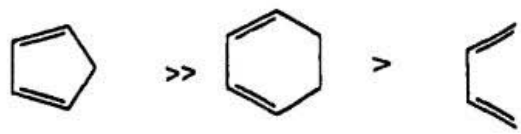
s-cis *s-trans* *skewed*

Scheme 6: 1,3-butadiene conformations

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.[11] The skewed conformation is more stable than the planar s-*cis*, but the energy difference is very small.[12]

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.[8] 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



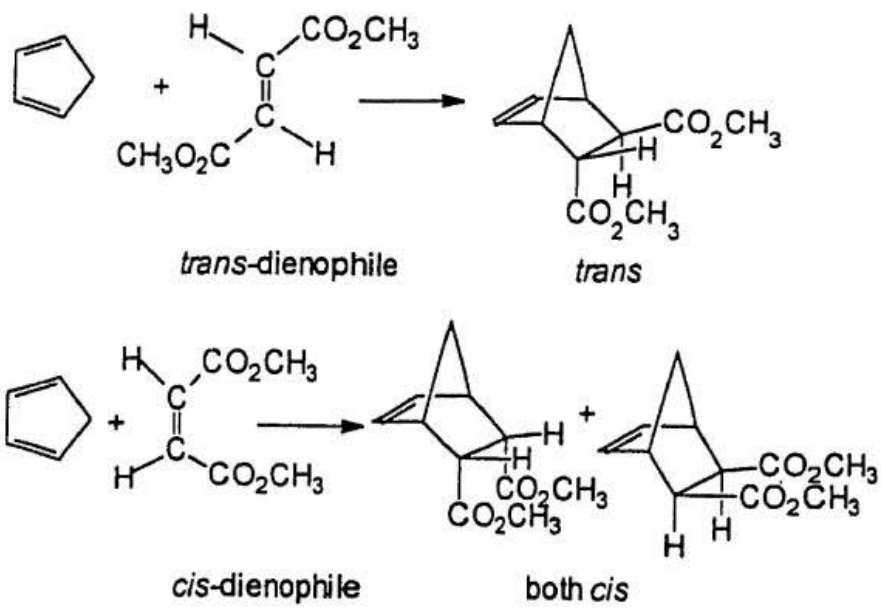
Scheme 7: Sequence of reactivity of dienes

flat whereas the latter is puckered.

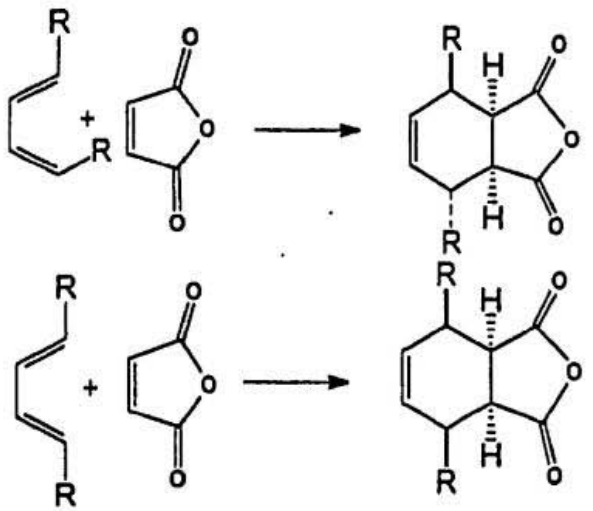
Stereospecificity of the Diels-Alder reaction

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.[1,3,5,13] For examples, *trans* and *cis* dienophiles gives *trans* and *cis* adduct (scheme 8). Furthermore, a *cis*-



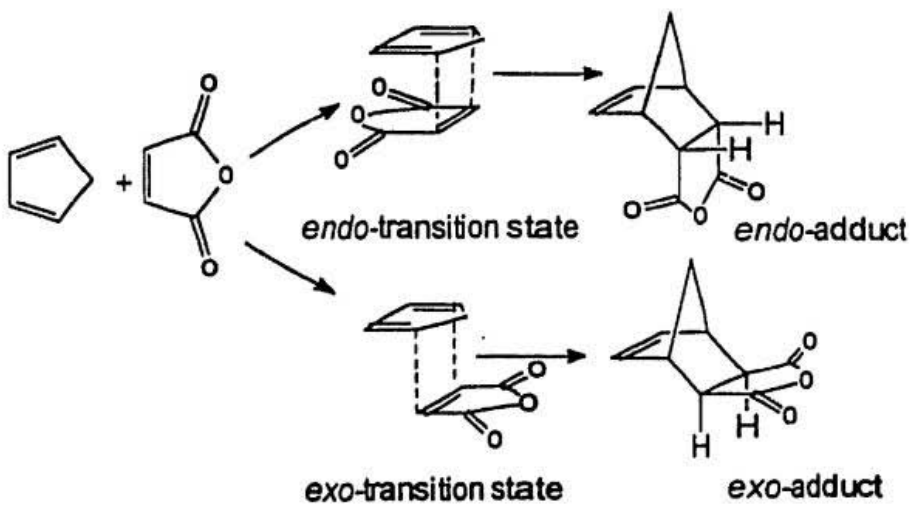
Scheme 8: *Cis* principle



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".[14] Woodward and Hoffman[15] and subsequently Houk,[16] Salem[17] and Alston[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.[19] Consider the reaction of cyclopentadiene and maleic anhydride in Scheme 10. In Figure 1, the primary



Scheme 10: *Endo-exo* stereoselectivity

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.[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

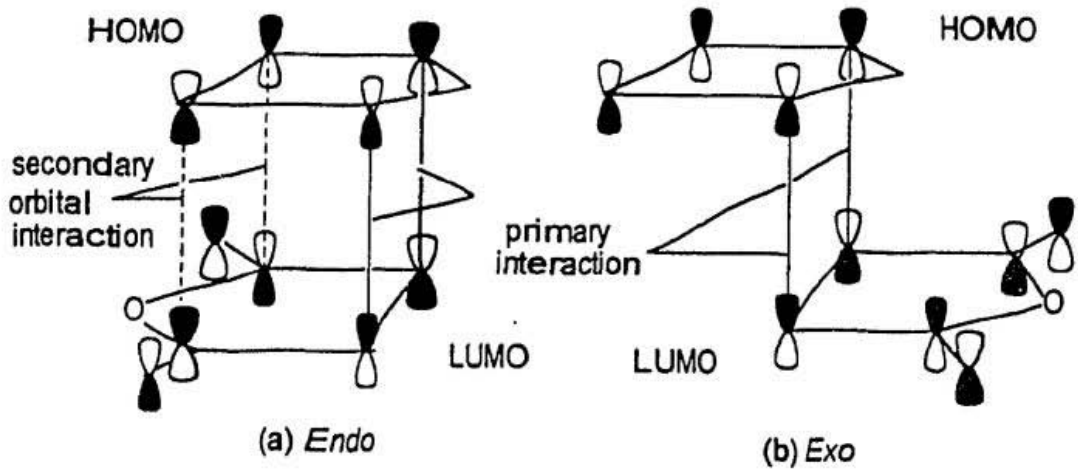
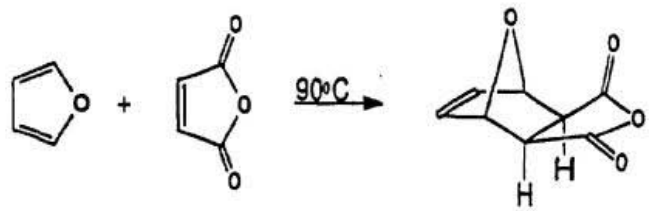


Figure1: Frontier molecular orbital diagrams of both *endo* and *exo* transition states of the Diels-Alder reaction of cyclopentadiene with maleic anhydride

because the polar group is directed away from the diene's π-system. Dipole dipole,[21] charge transfer interactions between polar groups in the dienophile and an easily polarized diene,[21] electrostatic,[23] inductive,[22] steric,[9] and geometrical considerations[24] 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.[1] The *endo* rule is violated by the reaction of furan with maleic anhydride (Scheme 11).[3,9] 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 *exo* isomer.[1,5,13] Indeed, in some other



Scheme 11: Diels-Alder reaction of furan with maleic anhydride

Diels-Alder reactions, prolonged reaction times may lead to the formation of some *exo* isomer at the expense of the *endo*.[5,13]

Substituent effects

The success of the Diels-Alder reaction depends largely on structural features of the reacting components.[13] The Diels-Alder reaction is more rapid if the diene bears one or more electron-donating groups such as C_6H_5, OCH_3, CH_3, OAc, $N(CH_3)_2$, etc., and the dienophile bears electron-withdrawing substituents such as COR, CN, NO_2, CO_2CH_3, CHO.[1,3,5] 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

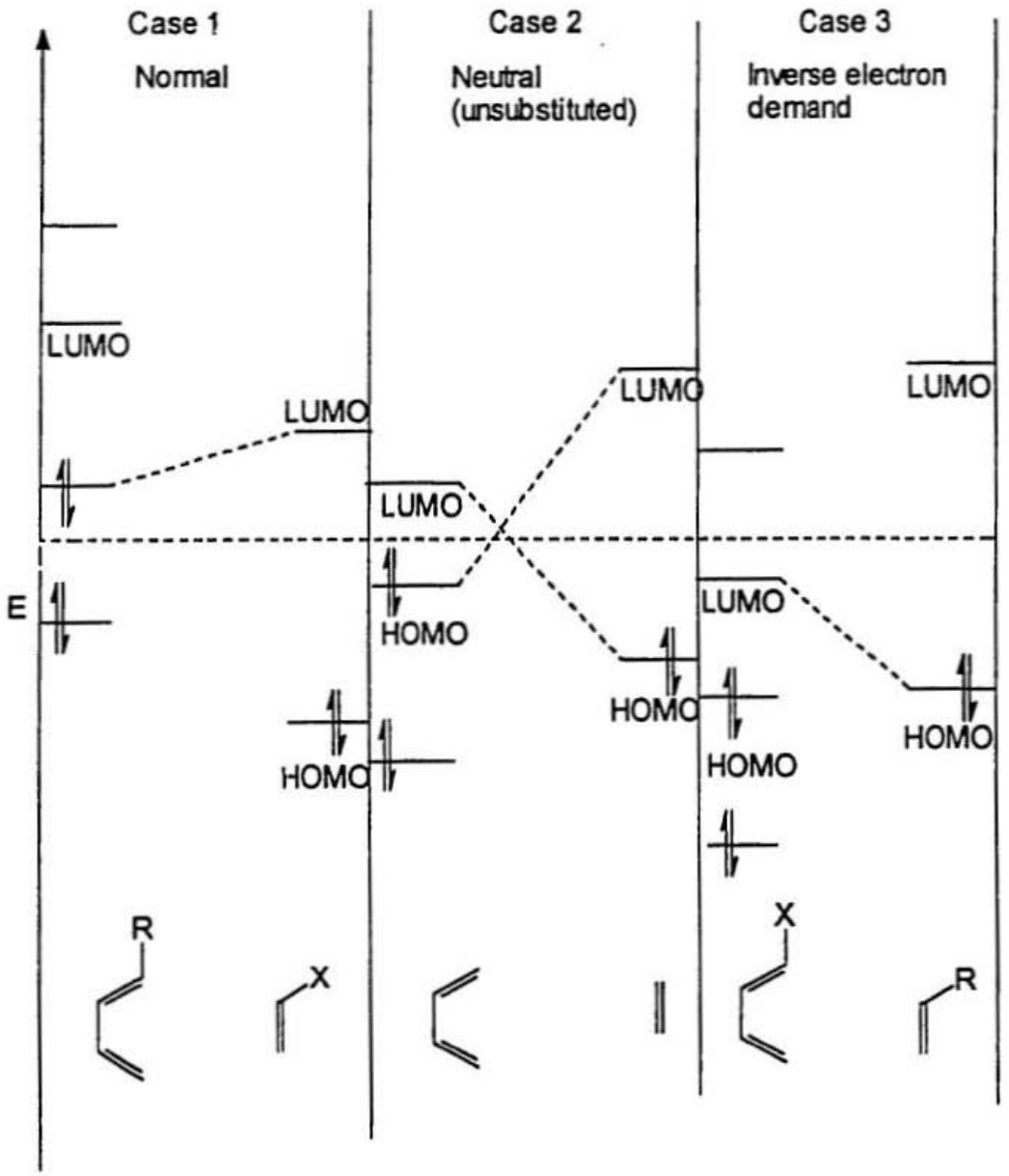
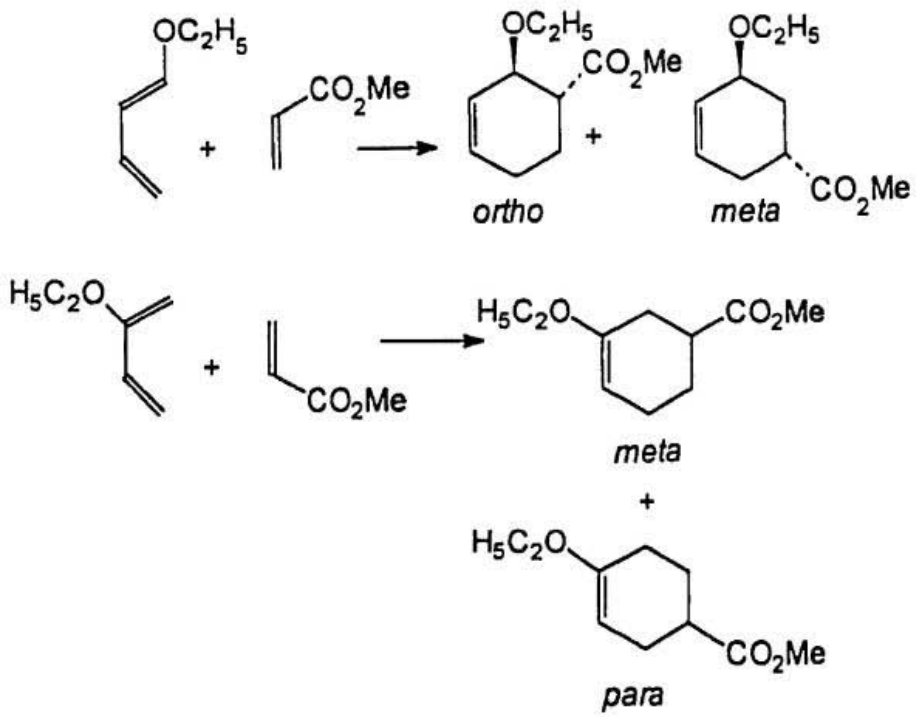


Figure 2: Frontier orbital energy diagram for normal, neutral and inverse-electron-demand Diels-Alder reactions
R = electron-donating group and X = electron-withdrawing group

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.[9] 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[5,9] in Scheme 12, can be rationalized in terms of resonance



Scheme 12: The regioselectivity of unsymmetrically substituted dienes and dienophiles

contributors and perturbation molecular orbital theory[10] (see Figures 3 and 4). Secondary molecular orbital interactions have been considered as additional

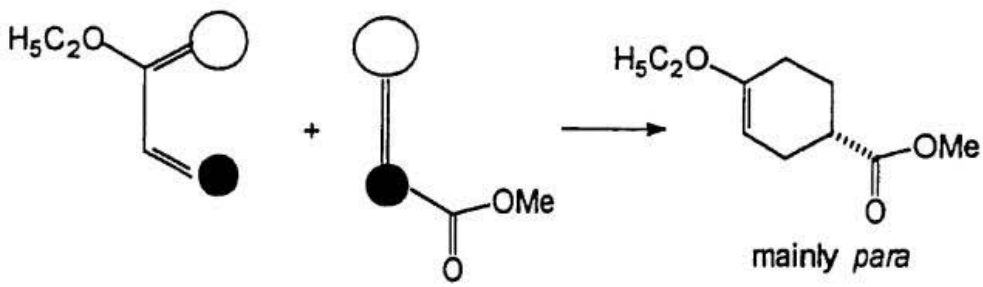


Figure 3: Orbital interactions in a 2-substituted diene case

modifying factors favoring the *ortho* and *para* isomers[9] (Figure 5). This regioselectivity phenomenon is also referred to as the *ortho/para* rule.

Pertubation 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[23] 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

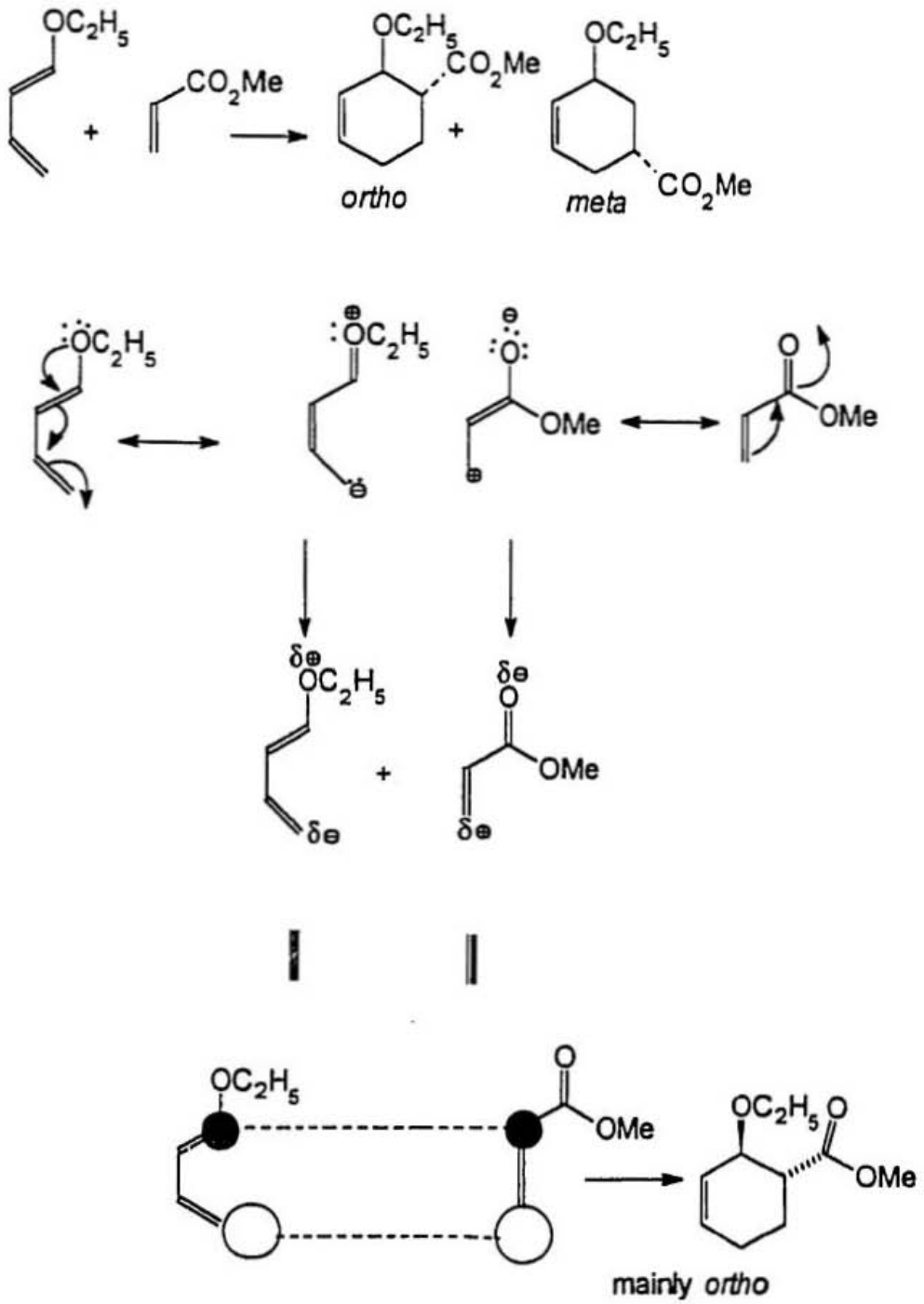


Figure 4: Frontier molecular orbital control in regiochemistry

accelerated by high or ultrahigh pressure conditions. An enormously high

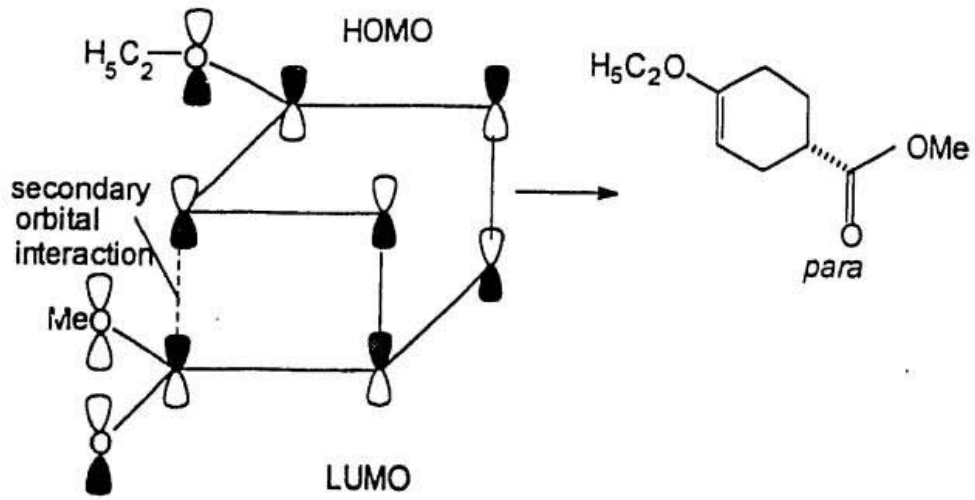


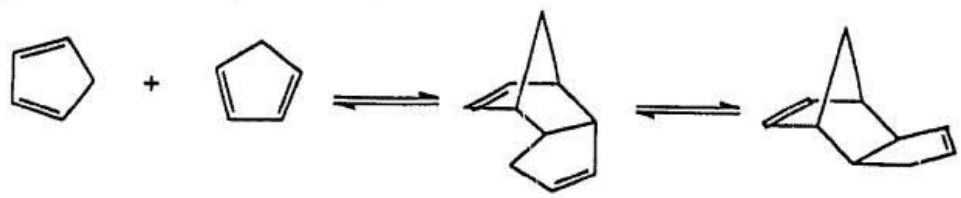
Figure 5: Secondary orbital interaction as a stabilising factor in regiocontrol of a Diels-Alder reaction

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 ΔH = 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.[5,29] 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,



endo *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.[11] Therefore, the s-*trans* conformation requires this energy in order to be isomerized into the s-*cis* conformation suitable for Diels-Alder reaction.[5,11] Finally, prolonged exposure of adducts to heat or high temperatures usually leads to dissociation or decomposition (retro-Diels-Alder reaction).[2,9]

Catalysis: Until Yates and Eaton[30] in 1960 recognized that some Diels-Alder reactions proceed much more rapidly in the presence of $AlCl_3$ it was thought that the Diels-Alder reaction could be influenced only slightly by catalysis.[31] It was

subsequently discovered that the reaction is also catalyzed by other Lewis acids such as (BF_3, $SnCl_4$, $TiCl_4$).[3] Lewis acids not only accelerate the rate but also alter the isomer distribution (regiochemistry) when both addends are unsymmetrical.[3] 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.[10]

The explanation for these phenomena is contained in frontier molecular orbital changes.[10] The Lewis acid catalyst lowers the dienophile LUMO energy. This then allows for a stronger interaction between the addends and lowers the activation energy.[10] 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.[3,13] An earlier transition state for the catalyzed reaction is known to increase diastereoselectivity as well as *endo-exo* ratios.[32]

π-Facial Selectivity

The stereochemistry of the Diels-Alder reaction has three controlling factors. They are the *cis*-principle, the *endo*-principle and the π-facial stereoselectivity. It is this last facet that decides the *syn-anti* isomerism.[3]

The issue of facial stereoselectivity has attracted considerable attention in

recent years especially in the area of asymmetric organic synthesis.[33] It is fascinating that a single allylic heteroatom substituent on the dienophile,[34] or the diene,[35] can control diastereofacial selectivity in Diels-Alder reactions. Studies of facial selectivity in dienes may be grouped into two main classes.[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 π-facial selectivity is demonstrated in the reaction of 1,2,3,4,5-pentamethylcyclopentadiene with substituted ethylenic dienophiles (Figure 6).[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.[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

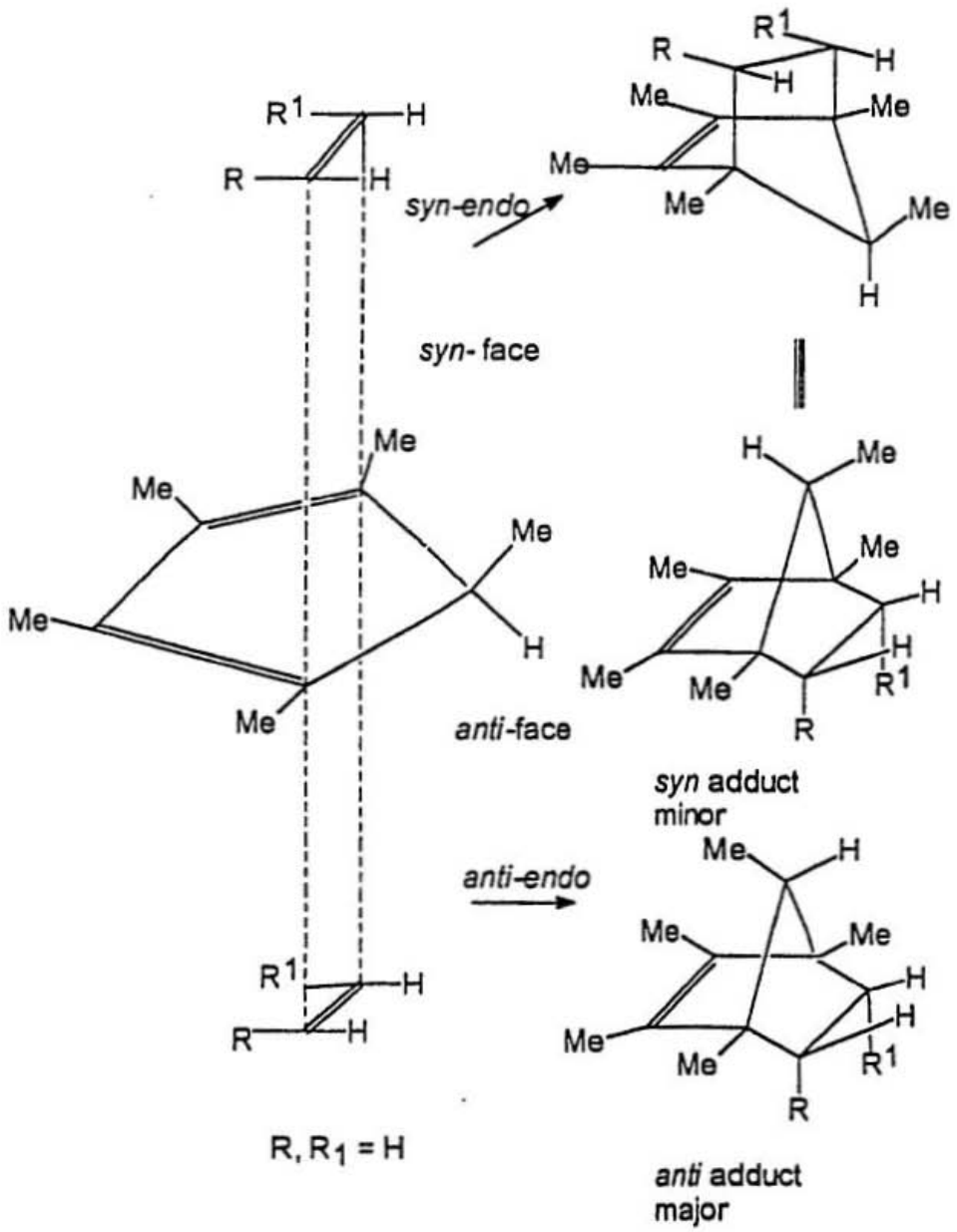
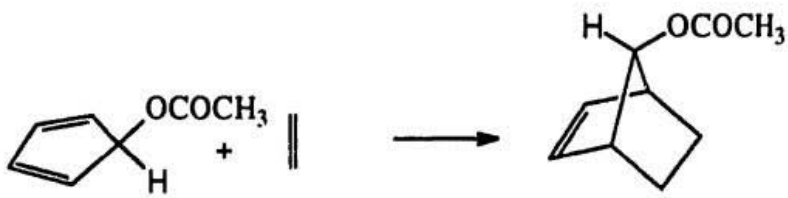


Figure 6: *Syn -anti* stereoselectivity in the Diels-Alder reaction of 1,2,3,4,5-pentamethylcyclopentadiene with ethylenic dienophiles

facial selectivity.[35] 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.[39]

Carbocyclic Five-Membered Ring Systems

In 1955 Woodward and coworkers[40] reported an exclusive *syn*-addition product **9** from the reaction of 5-acetoxycyclopentadiene **8** with ethylene (Scheme 14). However, no reason whatsoever was advanced for this



8 **9**
syn-adduct

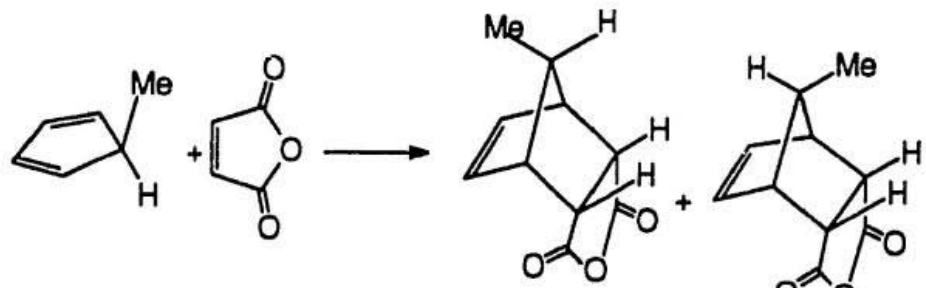
Scheme 14: Diels-Alder reaction of 5-acetoxycyclopentadiene with ethylene

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[41] 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**

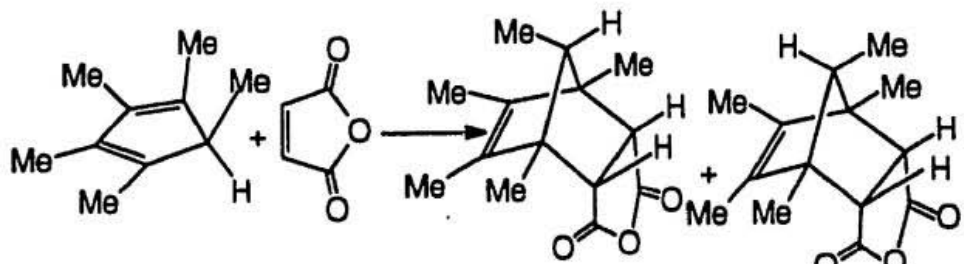


10 **11**

anti-endo

major

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



12 **13**

anti-endo

major

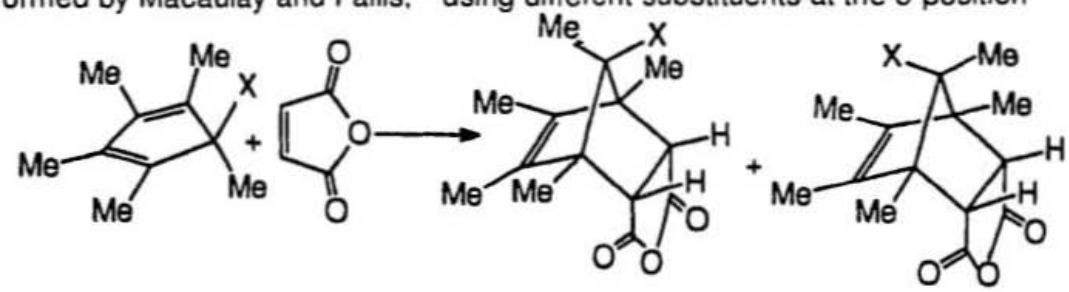
Scheme 16: Diels-Alder reaction of 1,2,3,4,5-pentamethylcyclopentadiene **10** with maleic anhydride

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,[42] using different substituents at the 5-position



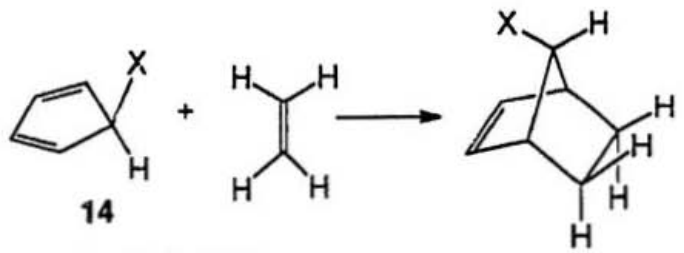
syn *anti*

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

entry.	X	*% endo-syn* adduct	*% endo-anti* adduct
1	Cl	100	0
2	OH	100	0
3	OCH_3	100	0
4	NH_2	100	0
5	NHAc	100	0
6	SH	55	45
7	SMe	10	90
8	SCH_2Ph	3	97
9	SOMe	0	100
10	SO_2Me	0	100

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.

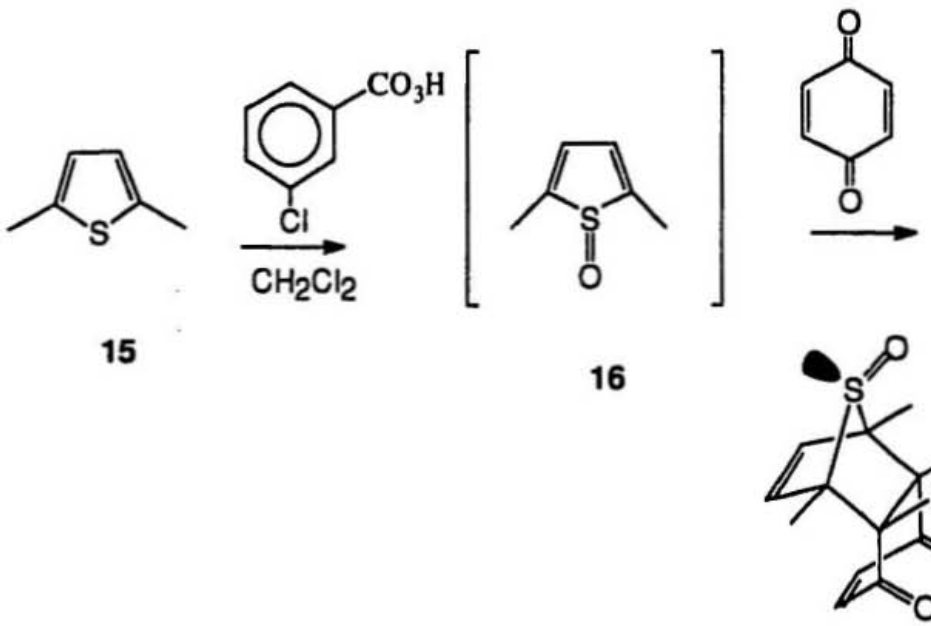


14

X = SeR, TeR

anti

Scheme 18: Diels-Alder reaction of **14** with dienophiles



15

16

Scheme 19: Diels-Alder reaction of 2,5-dimethylthiophene s-oxide **16** with benzoquinone

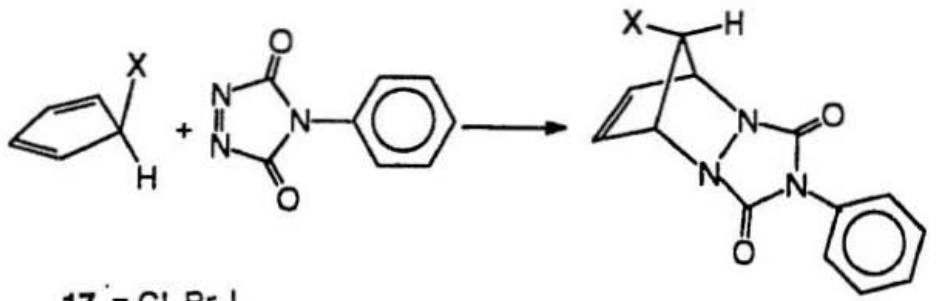
Orbital mixing rule arguments have been extended to the heteroatom directed π-facial stereoselectivity experienced with 5-substituted-1,3-cyclopentadienes **14** shown in Scheme 18 by invoking the mixing of σ orbitals of the carbon framework with that of the 5-substituents.[43]

Naperstkow and coworkers[44] established that the 2,5-dimethylthiophene oxide **16** obtained *in situ* by peracid oxidation of 2,5-dimethylthiophene **15** reacted with a number of dienophiles *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.[44] Products of the reactions of the (halo)dienes[45] **17** with various dienophiles (Scheme 20) were exclusively *anti*. The bromo derivative **18** reacted 100% *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.[47] The adduct obtained was 100% *syn* as shown in Scheme 21. Williamson and others[3,48] have observed that 1,2,3,4,5-pentachlorocyclopentadiene **21** reacted with some dienophiles to give mainly the *syn-endo* adducts (Scheme 22 and Table 2).

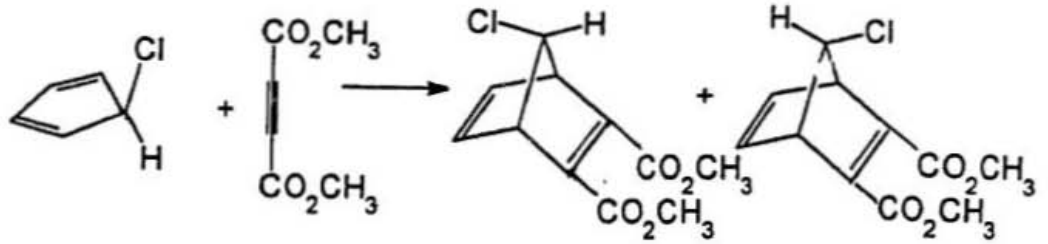
Substituted 1,3-Cyclohexadiene Systems

Gillard and Burnell[49] studied the cycloadditions of the plane-nonsymmetric six-membered diene system **22**. They found that *N*-phenylmaleimide added to the diene and many of its derivatives preferentially to the face *syn* to the *cis*-



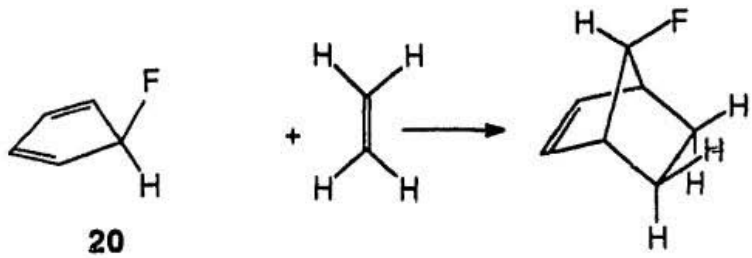
17 = Cl, Br, I

18



19 major minor

Scheme 20: Diels-Alder reaction of 5-halocyclopentadienes with some dienophiles

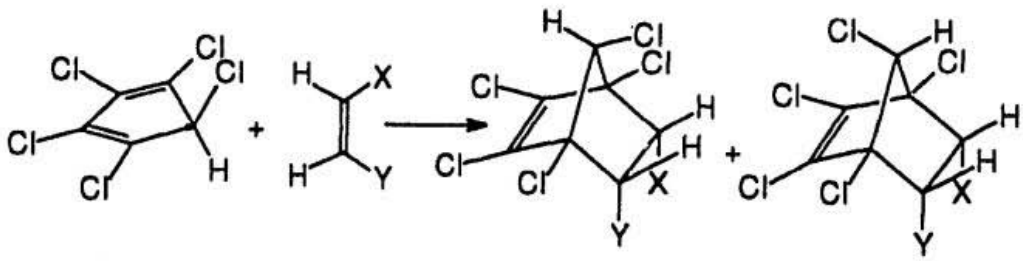


20 *syn*

Scheme 21: Diels-Alder reaction of 5-fluorocyclopentadiene **20** with ethylene

oxygen substituents (Scheme 23 and Table 3). Their 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-acetoxycyclopentadiene by Woodward and coworkers,[40] and they are among the cases in which electronic factors overide steric hindrance. In a related reaction, Werbitzky and coworkers[50] 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.

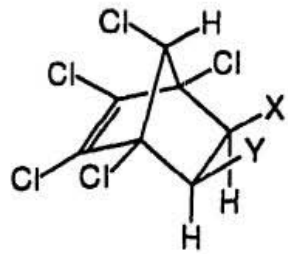
Bio-oxidation of benzene derivatives such as toluene, chlorobenzene etc., with *Pseudomonas putida* have produced dienes of synthetic importance.[51] For example, compounds **26** and **27** in Scheme 25 are optically active, and Hudlicky and Price[52] utilized these for the preparation of enantiomerically pure



21

syn-endo

anti-endo

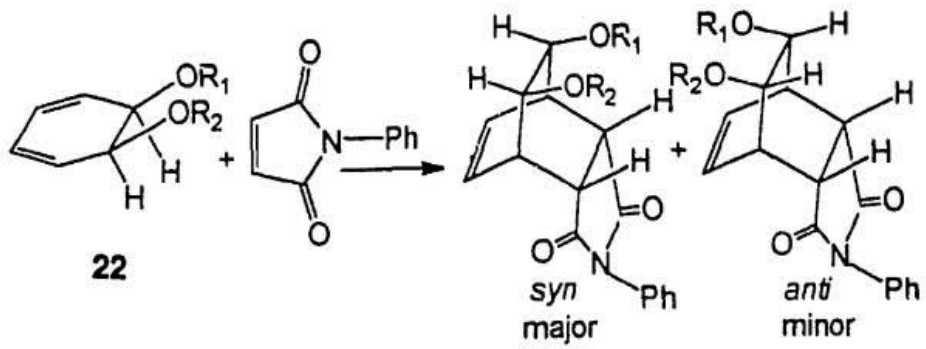


anti-exo

Scheme 22: Diels-Alder reaction of 1,2,3,4,5-pentachlorocyclopentadiene **21** with some dienophiles

entry	dienophile	*endo-syn %*	*endo-anti %*	*exo-anti %*
1	maleic anhydride	91	9	-
2	acrylonitrile	72	15	13
3	methyl acrylate	53	37	10
4	vinyl acrylate	47	45	7
5	vinylchloride	46	40	14
6	styrene	38	62	-
7	propene	31	12	57

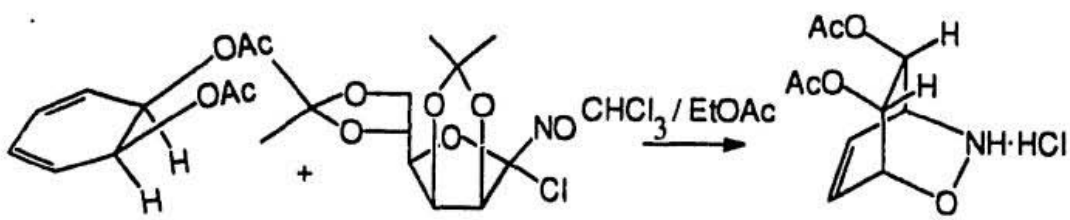
Table 2: Summary of the reactions of **21** with dienophiles



Scheme 23: Diels-Alder reaction of diol derivatives **22** with NPM

entry	R_1	R_2	*syn*	*anti*
1	H	H	94	6
2	Ac	Ac	88	12
3	$Si(CH_3)_3$	$Si(CH_3)_3$	100	0
4	$-Si(CH_3)_2-$		65	35
5	$-C(CH_3)_2-$		60	40

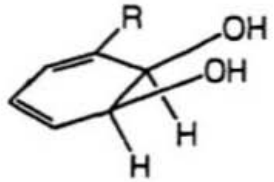
Table 3: Relative amounts of adducts in % involved in reaction above



Scheme 24: Diels-Alder reaction of diene diacetate **23** with chiral heterodienophile **24**

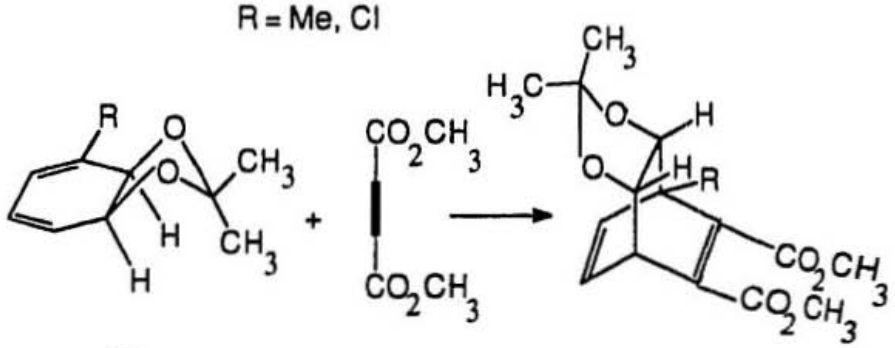
prostaglandins and sugar derivatives.

Pittol *et al.*[53] and Mahon *et al.*[54] treated the four dienes **27** in Scheme 25



26

R = Me, Cl



27

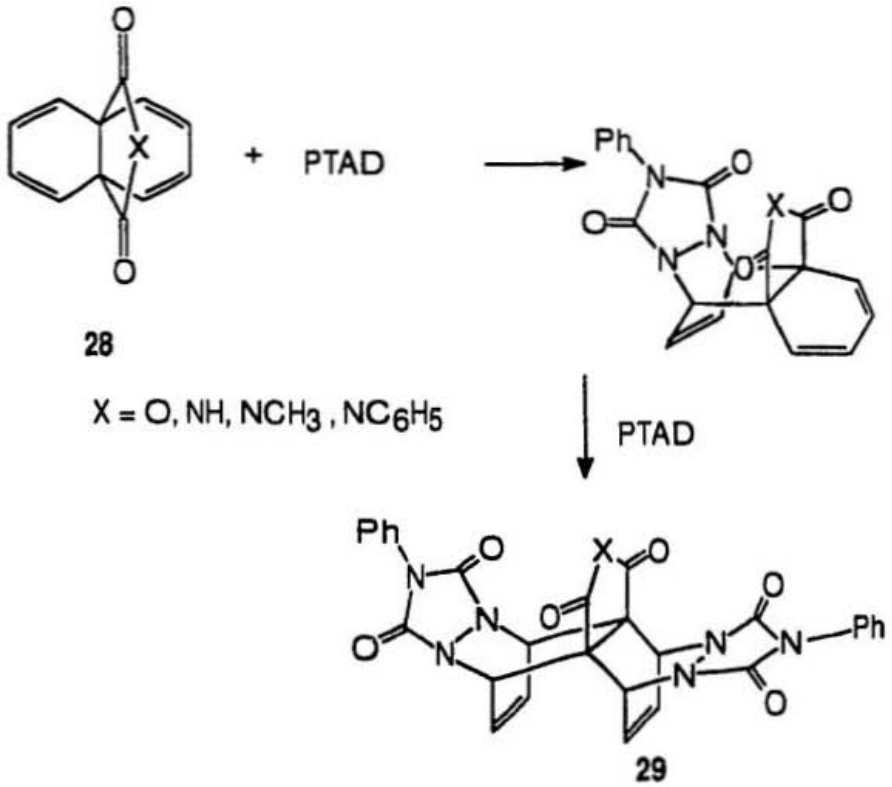
R = H, F, CF_3, 7-norbornadienyl *anti*

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 *anti* adducts observed in all cases.

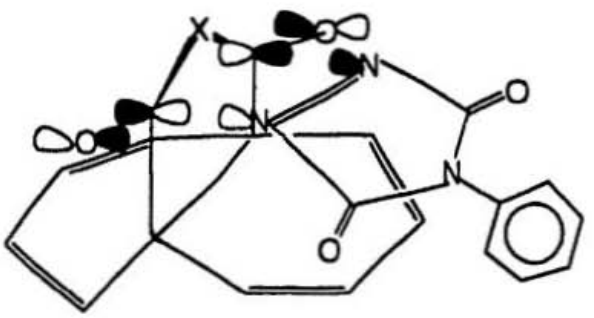
Multicyclic Systems

Ginsburg and Gleiter[55] demonstated 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 *N*-phenyltriazolinedione, selectivity was in favor of the *syn-syn*-bis adduct **29.** An explanation for this was advanced by Gleiter[55] who

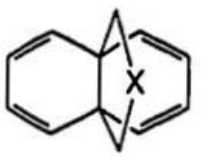


Scheme 26: Diels-Alder reactions of propellanes

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



syn-transition state

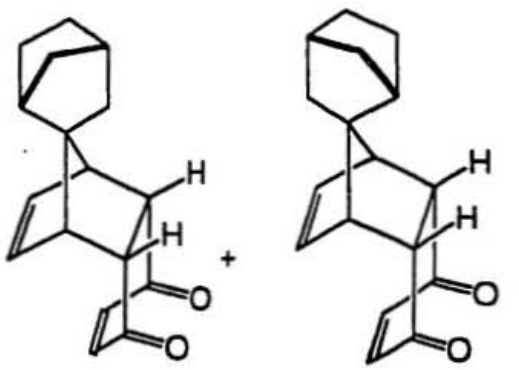


30

X = S, SO, SO_2

Figure 7: Transition state and propellane structures

31



major minor

Scheme 27: Diels-Alder reaction of **31** with benzoquinone

of high electron density around the oxygen centers of the SO_2 group and the charge deficient region on either side of the π-plane of the dienophile. However, Macaulay and Fallis[57] stated that the results obtained were cases of how neighbouring double-bonds could influence selectivity.

Burnell *et al*[58] 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.[60]

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 σ-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

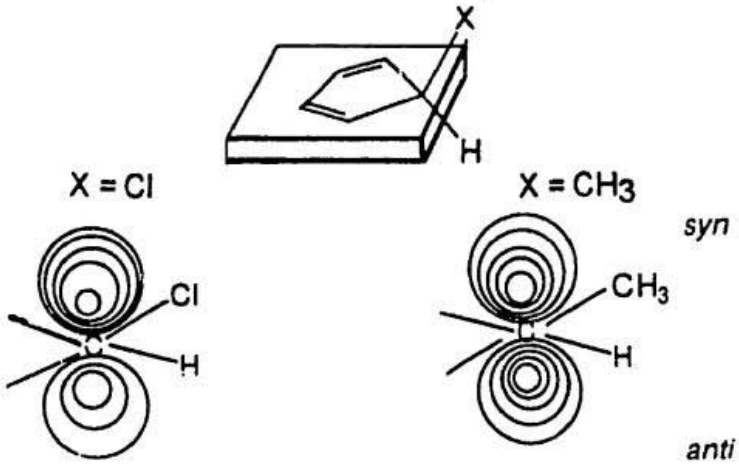


Figure 8: Fukui's postulate of HOMO electron density distributions of 5-chloro- and 5-methylcyclopentadiene

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[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[63] model was based on the assumption that there might be an

attractive interaction between the lone pair orbitals of the allylic heteroatom and

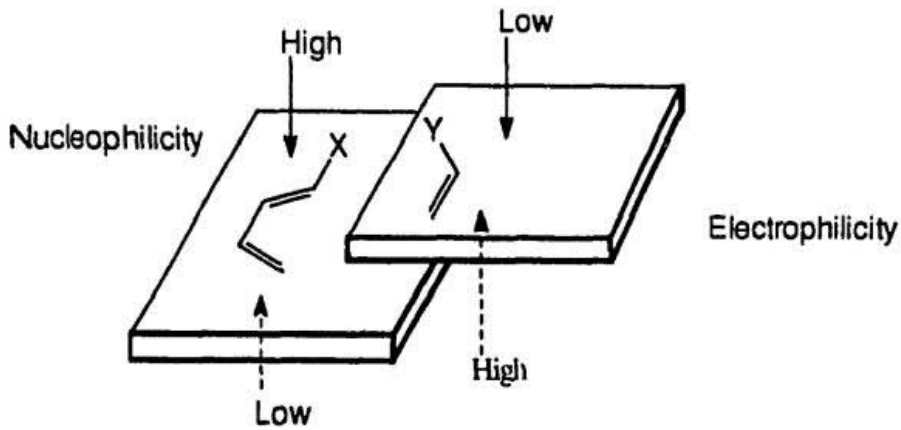


Figure 9: Kahn and Hehre's postulate of electrostatic interaction

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

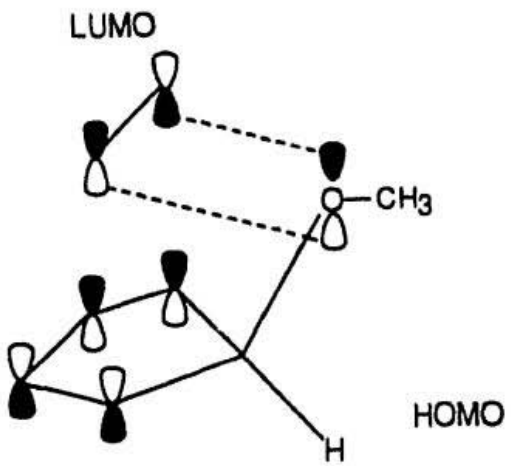
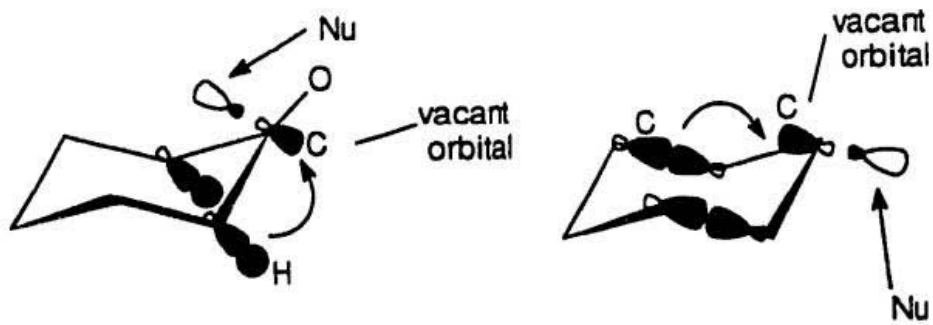


Figure 10: Anh's postulate

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-facially selective reactions which invokes the interaction of the incipient bond with the two nonequivalent faces was put forward by Cieplak[39] (Figure 11). He stated that the hyperconjugation of the antiperiplanar



favored σCH > σCC

Figure 11: Cieplak's postulate of the favored axial attack of a nucleophile

σ-bond gives rise to transition state stabilization by σ-electron donation into the vacant σ*orbital associated with the incipient bond. Macaulay[57] gave Epiotis list of order of increasing σ-donor ability as σCS > σCH > σCC > σCCl > σCN > σCO. The Cieplak model could be used to rationalize *syn* attack to chlorine in the reaction of 1,2,3,4,5-pentachlorocyclopentadiene (Figure 12). This was because σCH is a better donor than σCCl.

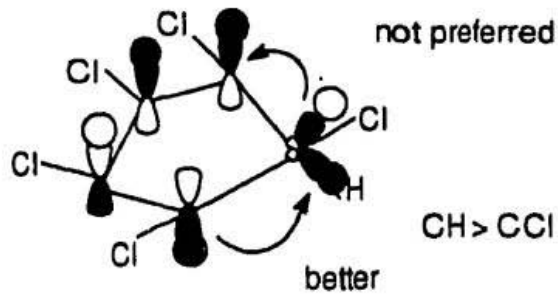


Figure 12: Rationalization of the *syn*-adduct obtained in the reaction of 1,2,3,4,5-pentachlorocyclopentadiene

Macaulay and Fallis[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 σ-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 σ-donor than the CC bond, therefore addition should occur *anti* to the CS bond, hence the *anti* adduct was formed.

Le Noble and coworkers[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 σ-bond.

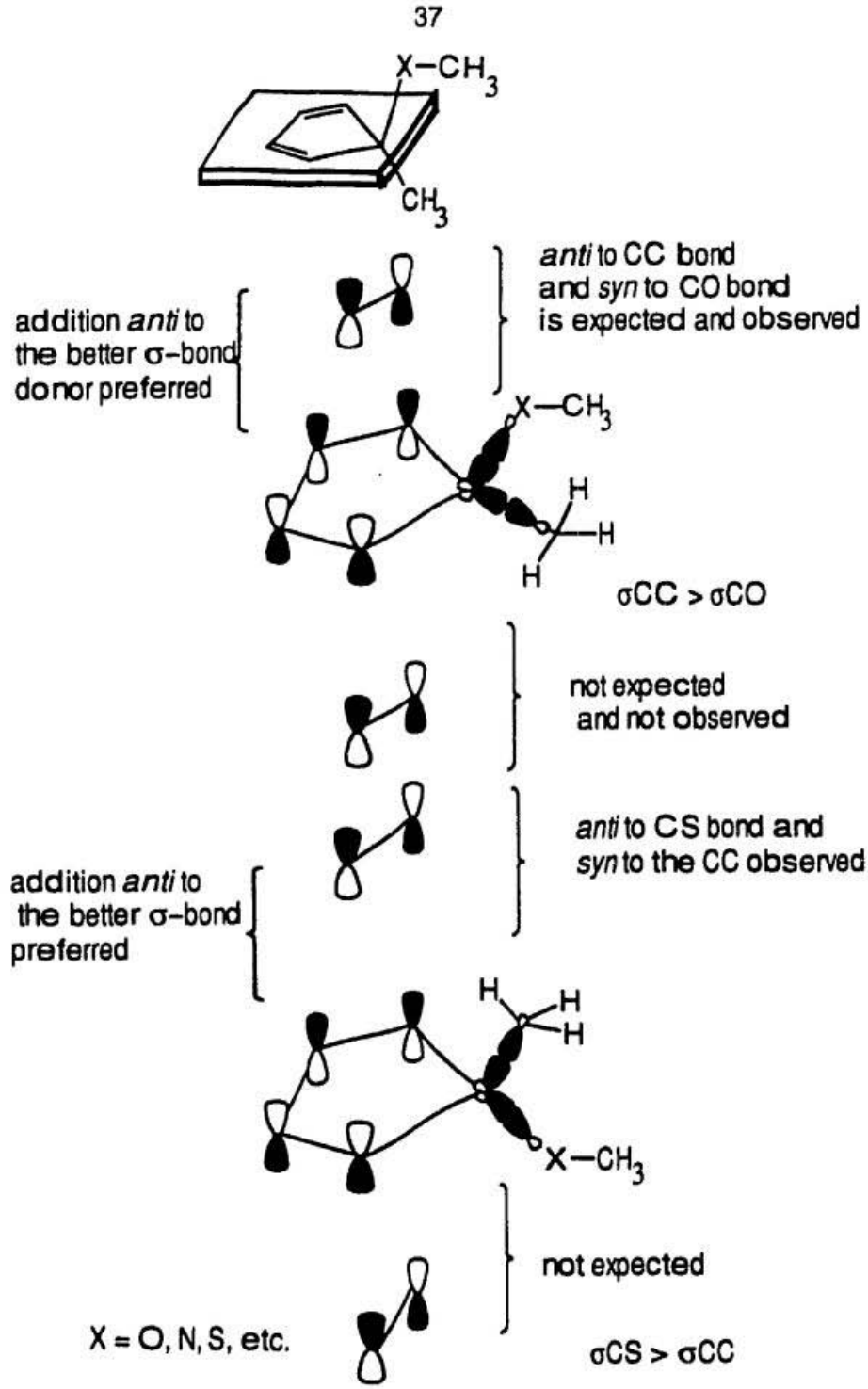
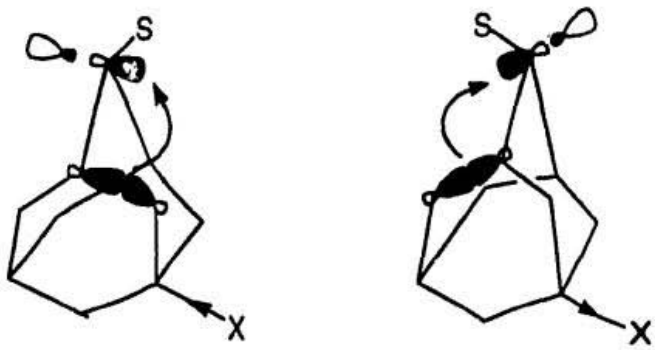


Figure 13: An extension of Cieplak's hyperconjugative σ-bond assistance by Macaulay and Fallis



X = electron-donating group X = electron-withdrawing group

Figure 14: An extension of Cieplak's hyperconjugative σ –bond or assistance by le Noble

Water and Selectivity

Hopff and Rautenstrauch[65] in 1942 reported the first Diels-Alder reaction conducted in water. Sauer[66] 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,[65] 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.[67]

However, in 1980 Breslow and his coworker[68] 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 isooctane to water as solvent

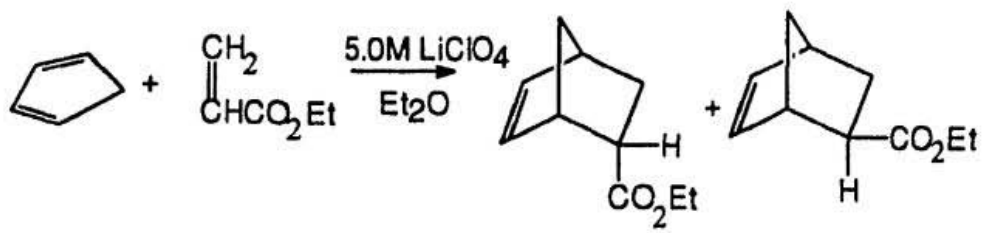
entry	solvent	additional component	rate
		cyclopentadiene + butenone, 20°C	(k_2 X 10^5, $m^{-1}s^{-1}$)
1	isooctane	-	5.94±0.3
2	MeoH	-	75.5
3	H_2O	-	4000±70
4	H_2O	LiCl	10800
5	H_2O	$C(NH_2)_3{}^+Cl^-$	4300
6	H_2O	β–cyclodextrin	10900
7	H_2O	α–cyclodextrin	2610

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).



endo : *exo*

8 : 1

Scheme 28: *Endo/exo* stereoselectivity

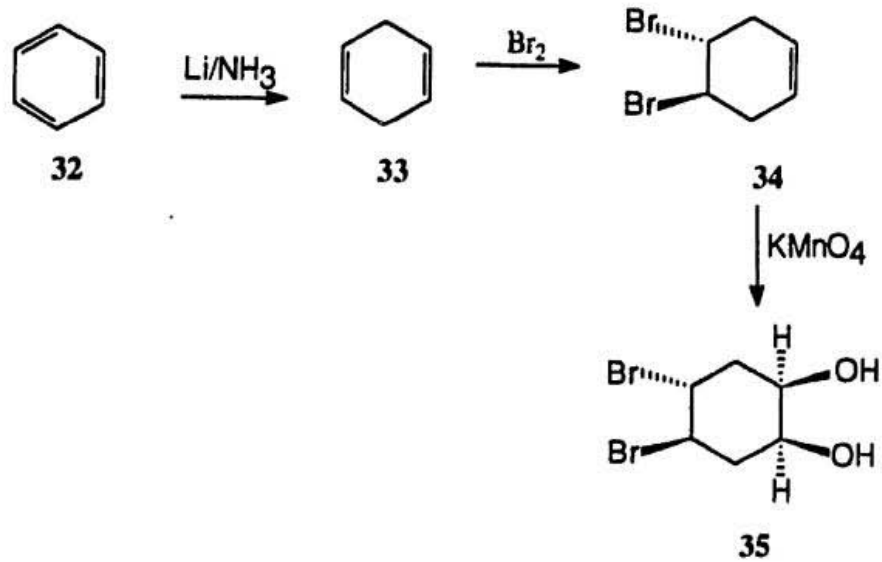
As an alternative explanation, Forman and his coworkers[74] claimed that the rate enhancement by LPDE was not due to internal pressure but to Lewis acid catalysis with the lithium ion functioning as the Lewis acid. It is important to note that LPDE should be handled with care because a recent report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

From the work of Gillard and Burnell[49] two things were remarkable: (a) that the Diels-Alder reaction of *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, *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 *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

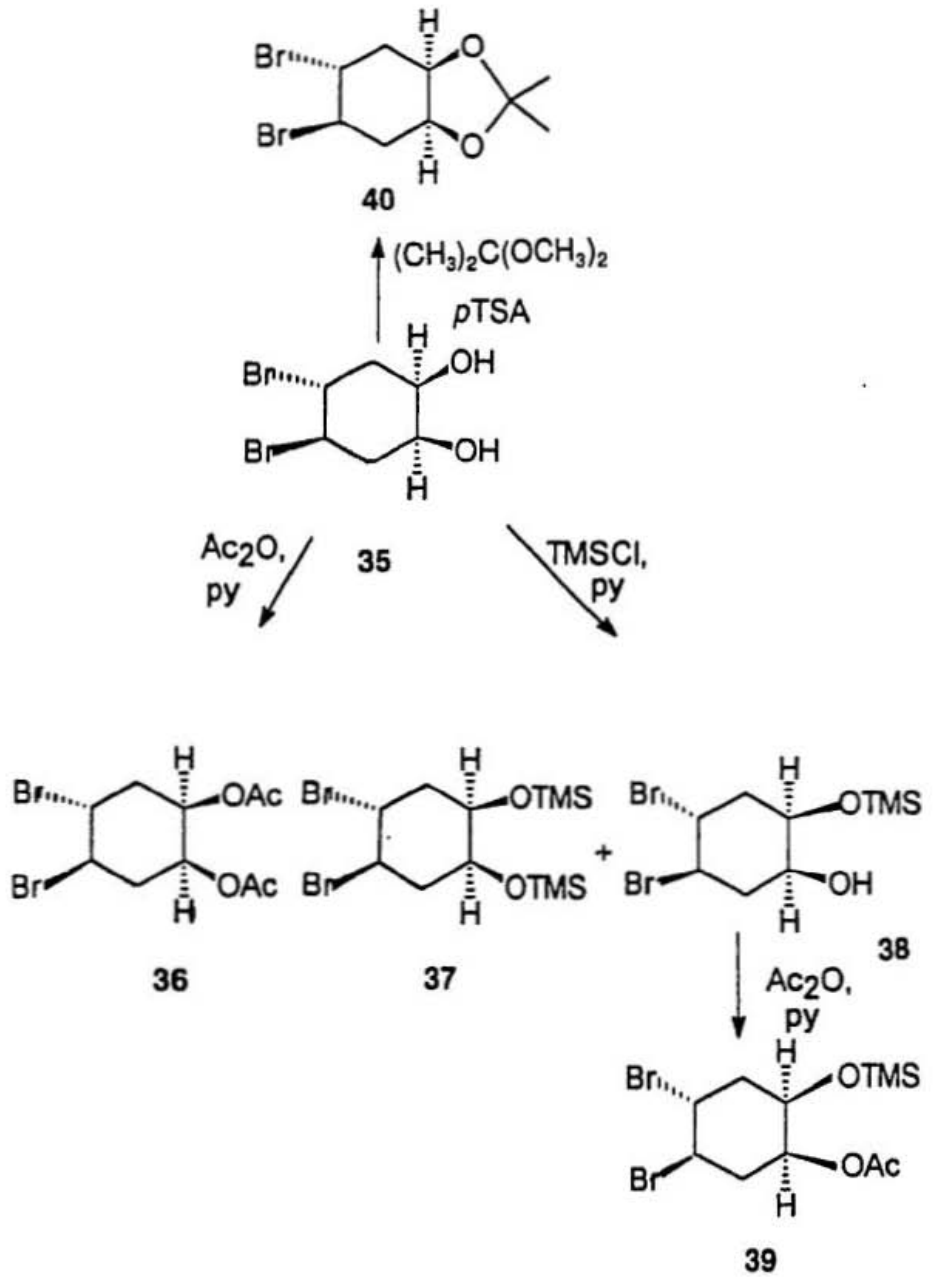


32 33 34 35

Scheme 29: Dibromodiol **35** from benzene

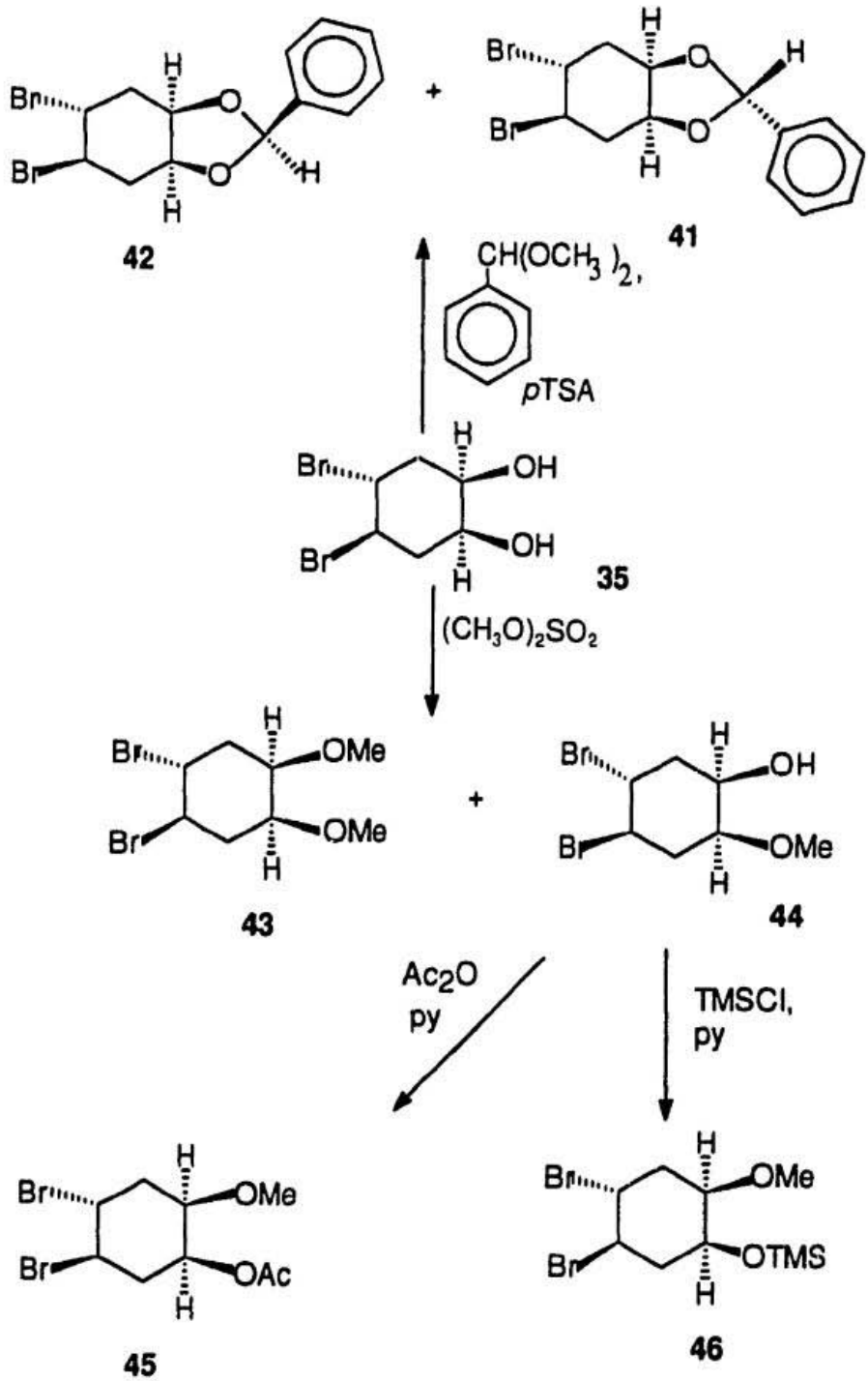
anhydride in pyridine provided compound **36** (90%). When compound **35** was treated with chlorotrimethylsilane in pyridine, **37** was obtained in 72% yield along with a small amount of **38** (Scheme 30). A phase-transfer reaction utilizing a

procedure by Merz[80] with dimethylsulfate as the methylating agent resulted in



Scheme 30: Derivatization of dibromodiol **35**

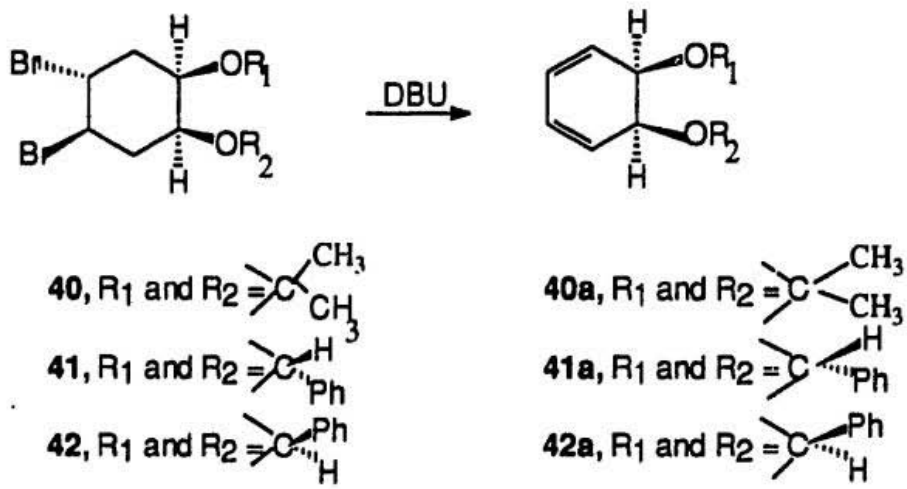
dibromo derivatives **43** (60%) and **44** (10%) in Scheme 31. Compound **40** was



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 *p*TsOH (Scheme 30).[78] The benzylidine derivatives[78] **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).

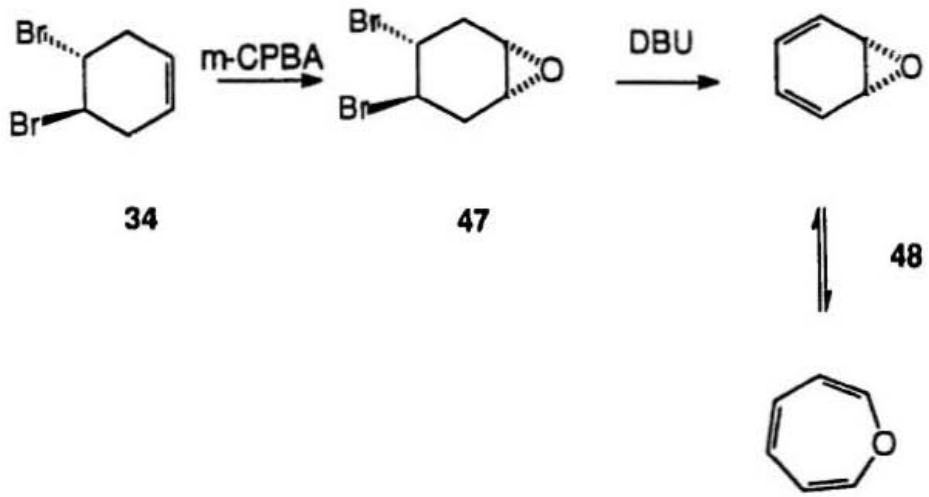
Double dehydrobromination[78] of **40, 41,** and **42** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in boiling benzene yielded dienes **40a**, **41a**, and **42a** (Scheme 32). These dienes were chromatographed on silica gel



Scheme 32: Dienes from different derivatives of dibromodiol

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

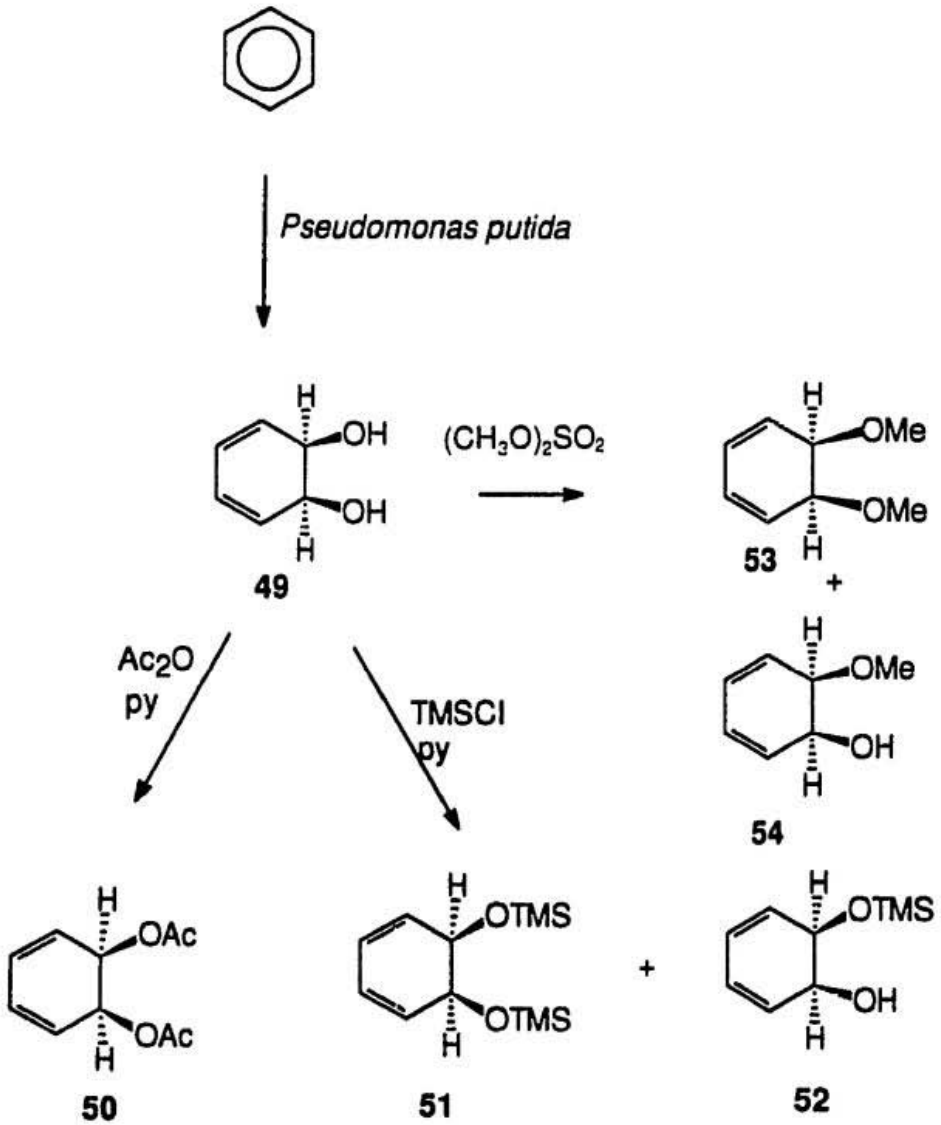


Scheme 33. Method for the preparation of benzene oxide - oxepin

oxide and oxepin, its valence tautomer.[81] The ^{1}H nmr spectrum of this product displayed a single set of signals, which according to Vogel and coworkers,[81] 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 dimethylsulfate) as shown in Scheme 34. Diol **49** has been produced by stereospecific microbial oxidation of benzene by mutants of

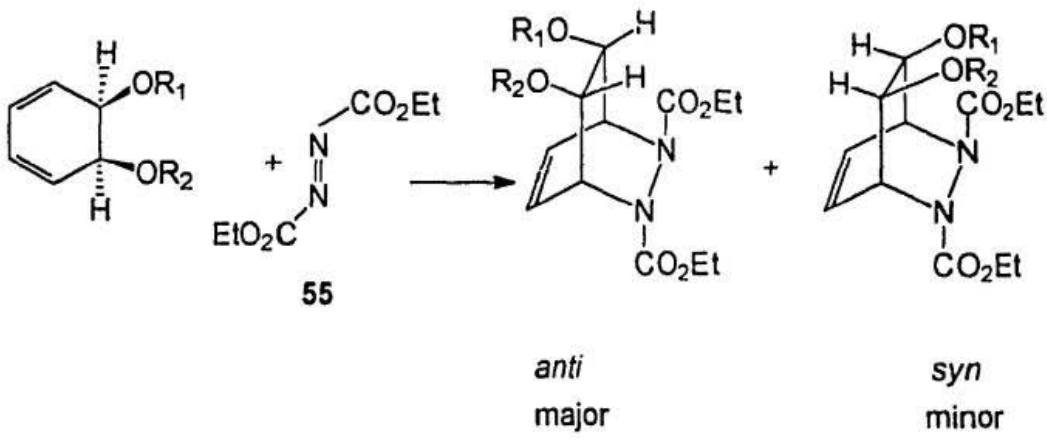
Pseudomonas putida, a soil bacterium.[82]



Scheme 34: Derivatization of *cis*-cyclohexa-3,5-diene-1,2-diol

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

entry	diene	adduct ratio exclusively *anti* .	% yield
1	50	*a*	73
2	51	100	43
3	40a	100	96
4	41a	100	54
5	42a	100	50

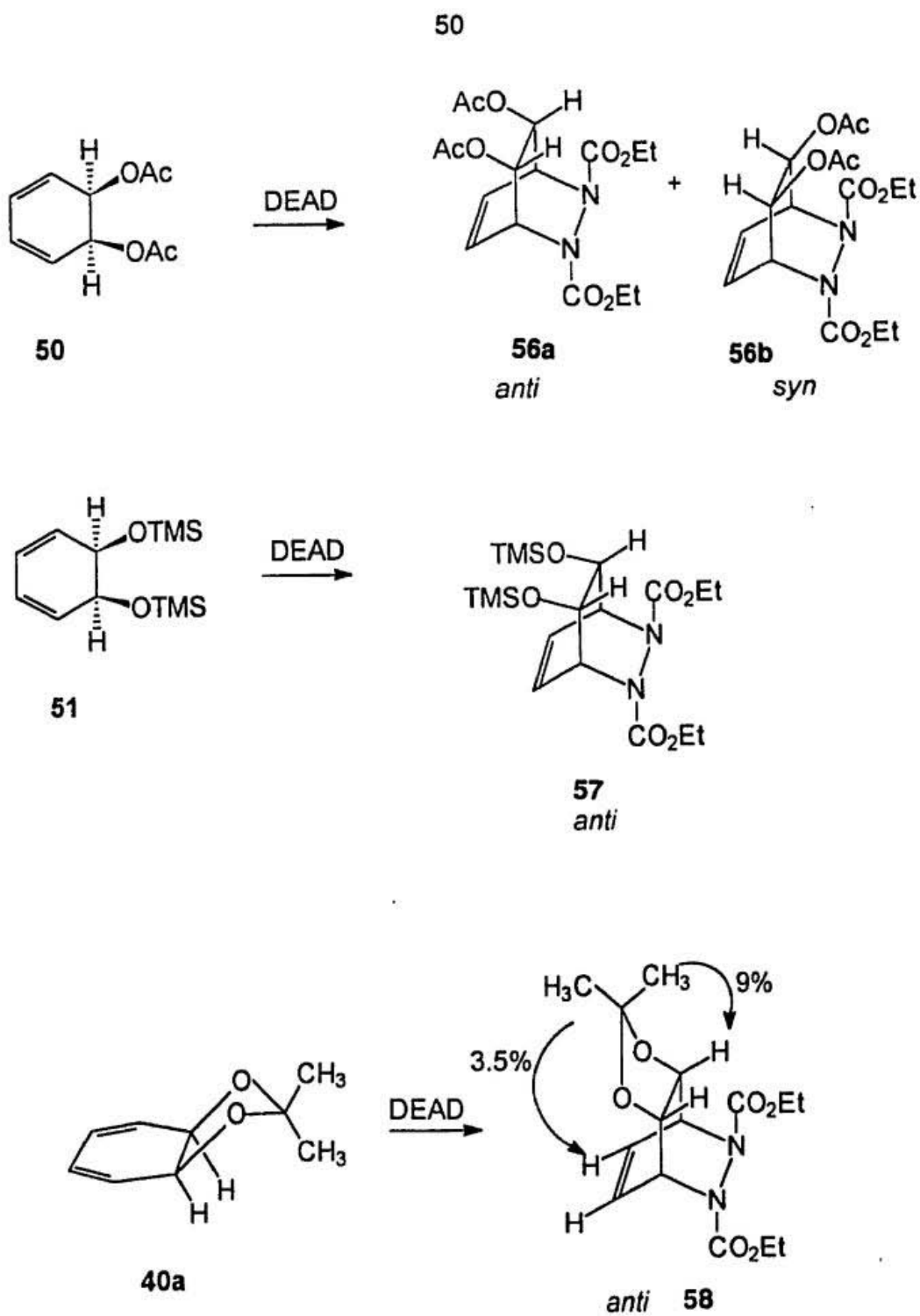
[a]adduct ratio could not be obtained

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 σ 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)

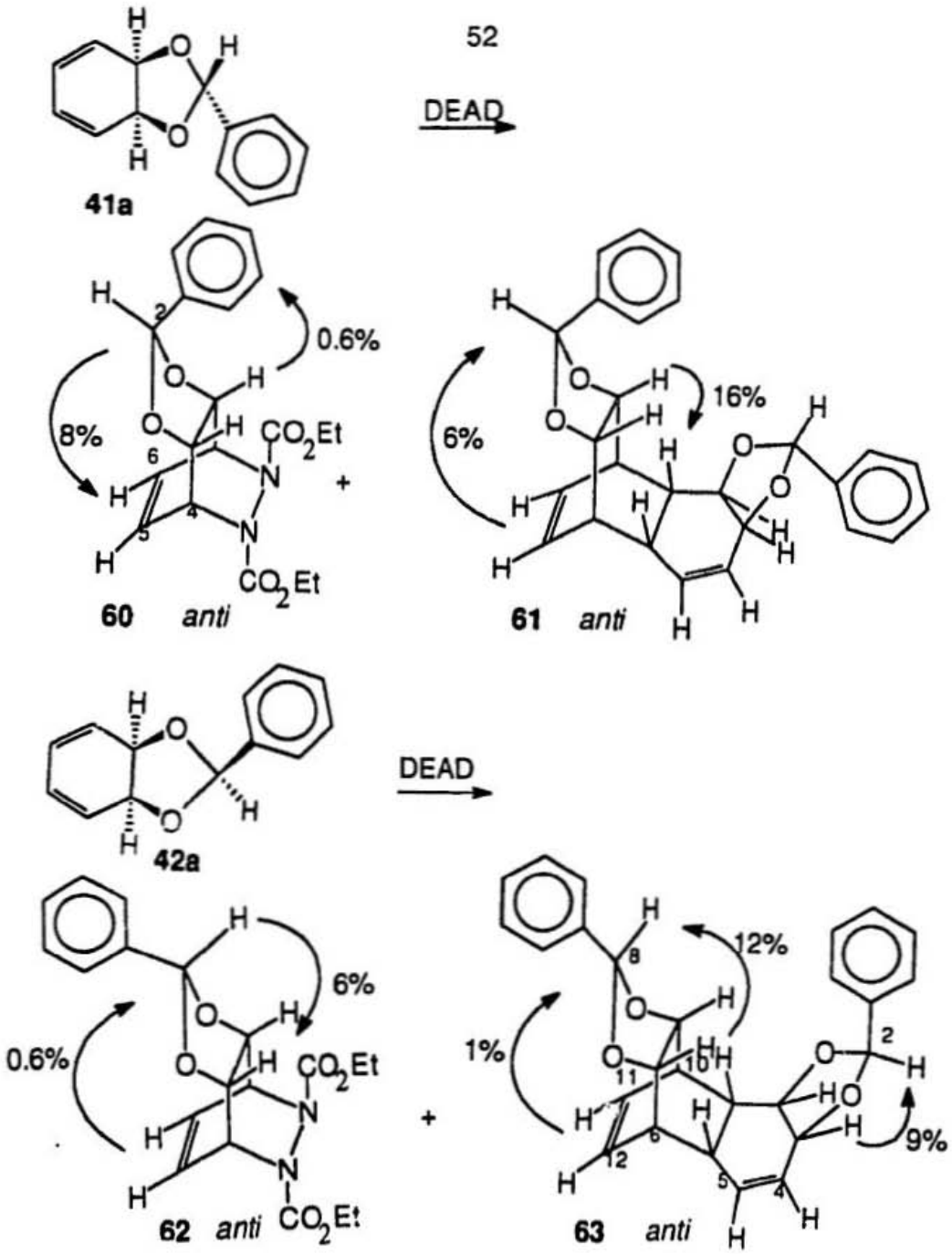


Scheme 36. Diels-Alder reaction **40a**, **50** and **51** with DEAD

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 ^{1}H 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 ^{1}H 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

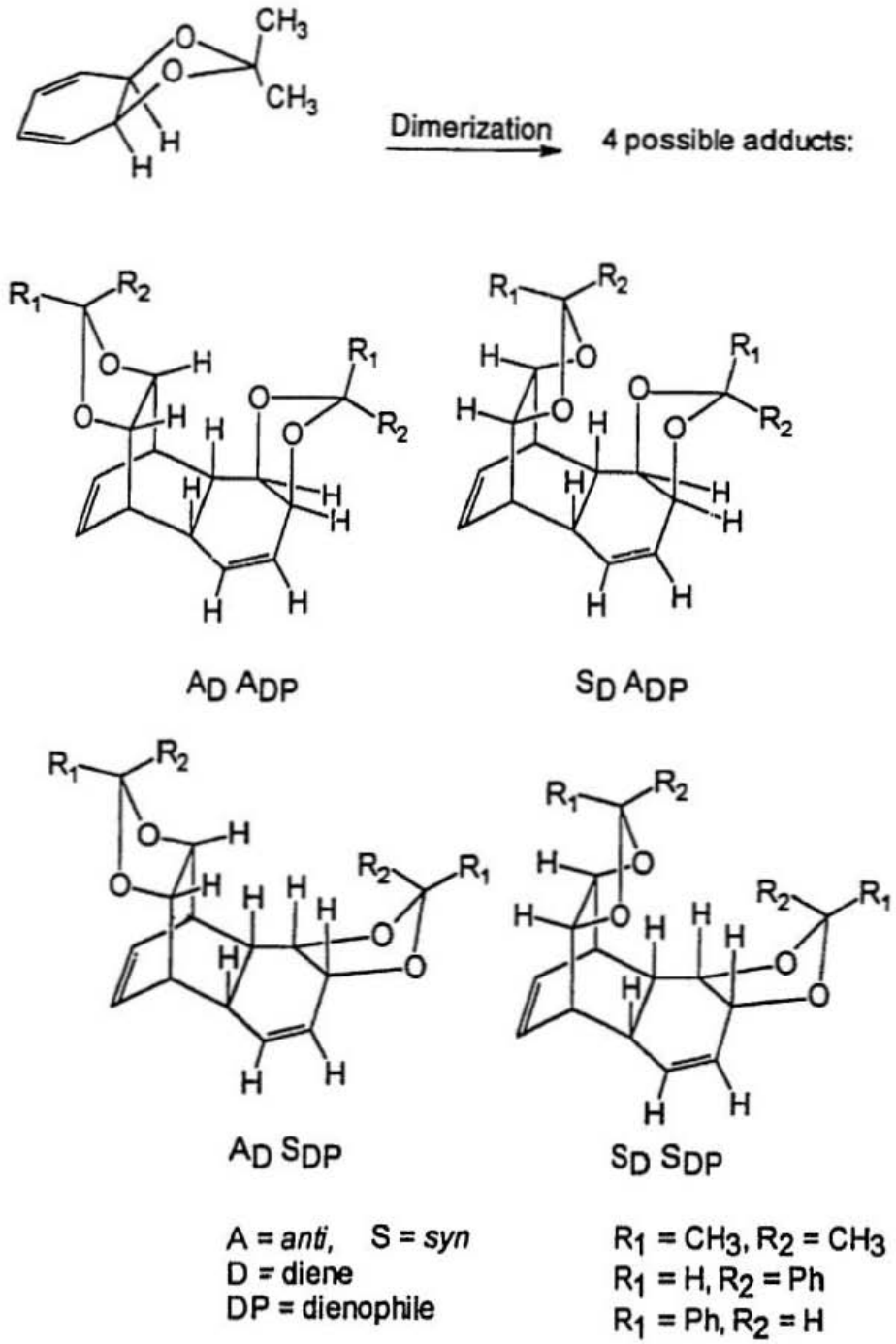
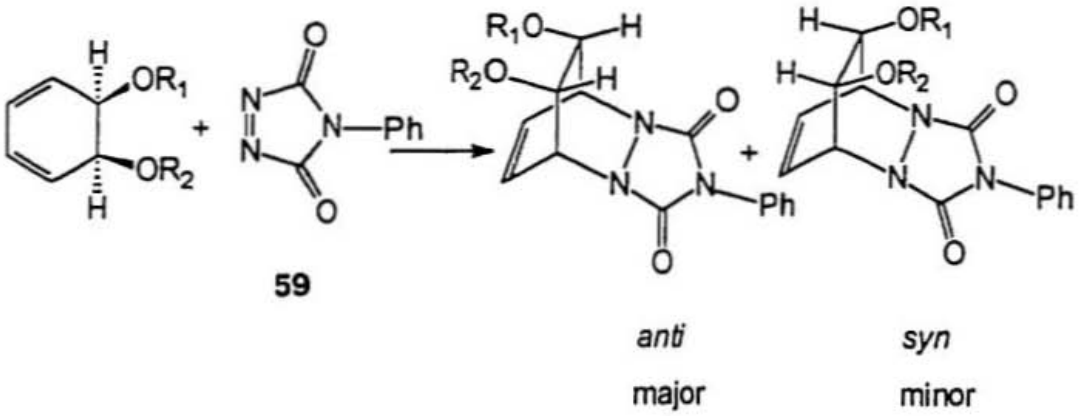


Figure 15: Four possible adducts in dimerization of the acetonide and benzylidene dienes

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-phenylurazole by the action of *t*-butylhypochlorite[83] 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}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}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**

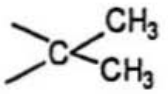
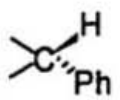
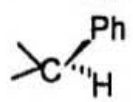
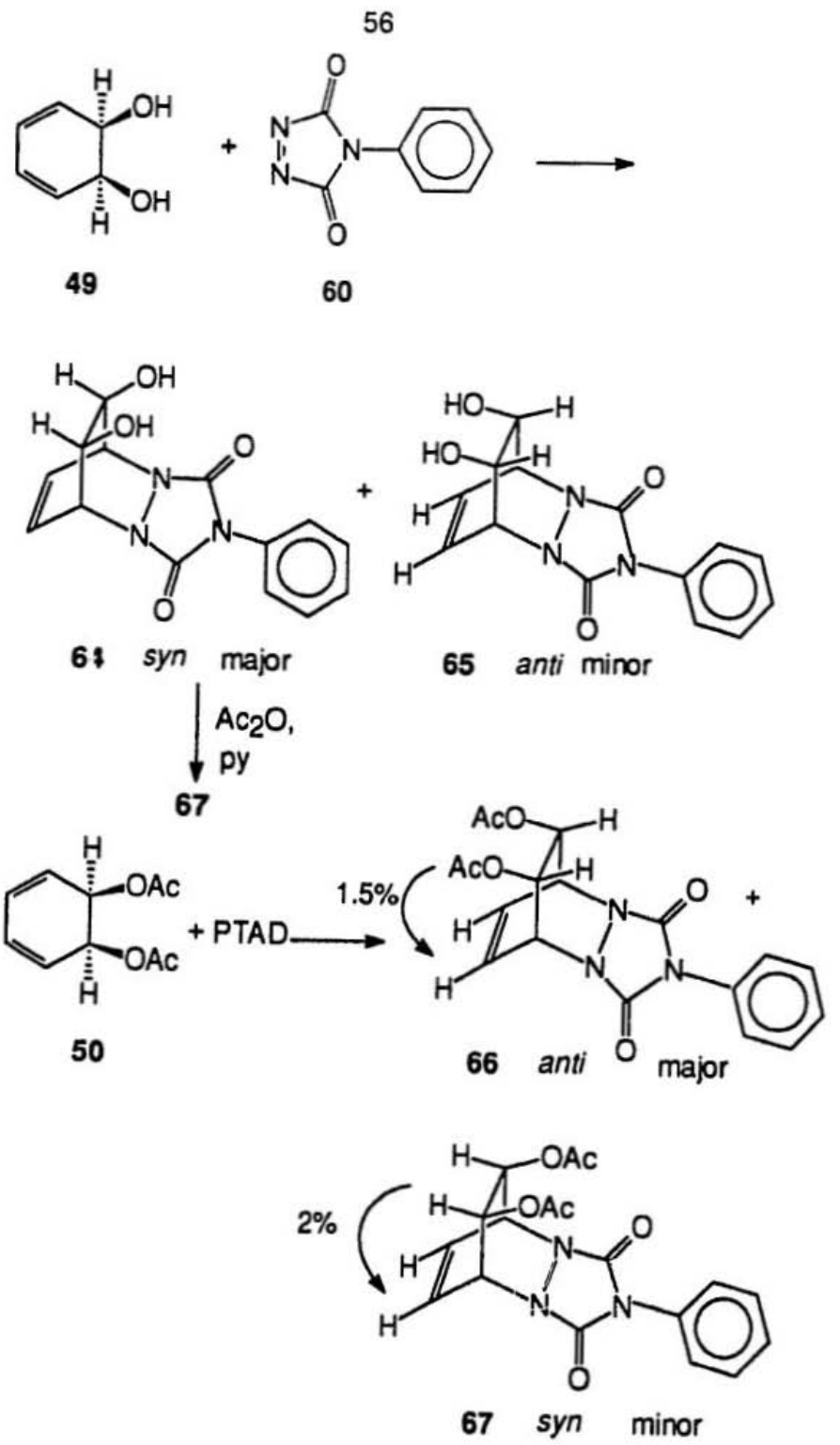
entry	R_1	R_2	relative amount of adduct *anti* : *syn*	% yield
1	H	H	77 : 23	75
2	Ac	Ac	90 : 10	90
3	TMS	TMS	100 : 0	72
4			100 : 0	97
5			100 : 0	62
6			100 : 0	55

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)

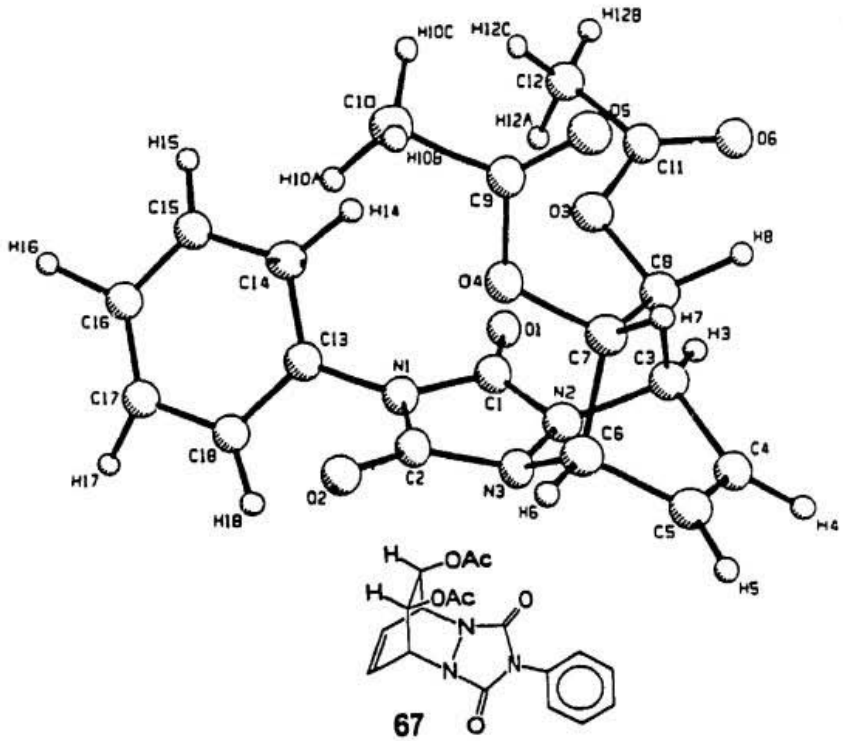
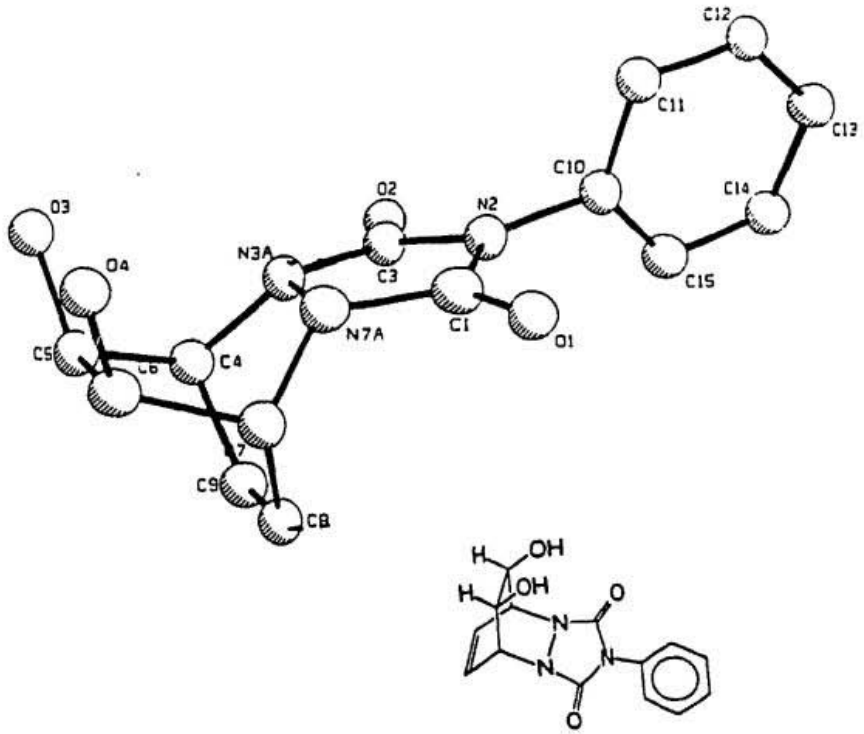


Figure 16: Perspective view of **67**

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

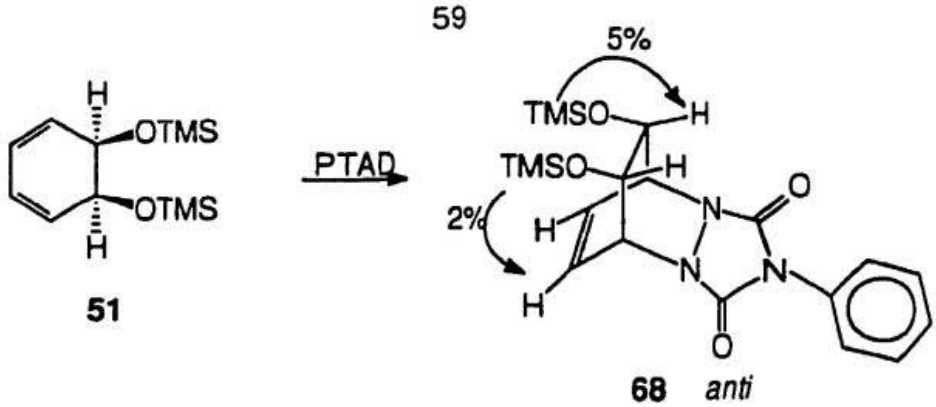


64

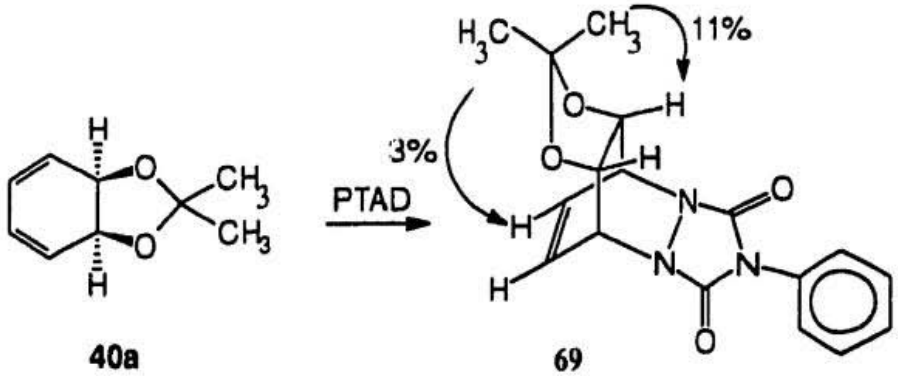
Figure 17: Perspective view of **64**

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 unambiguosly 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

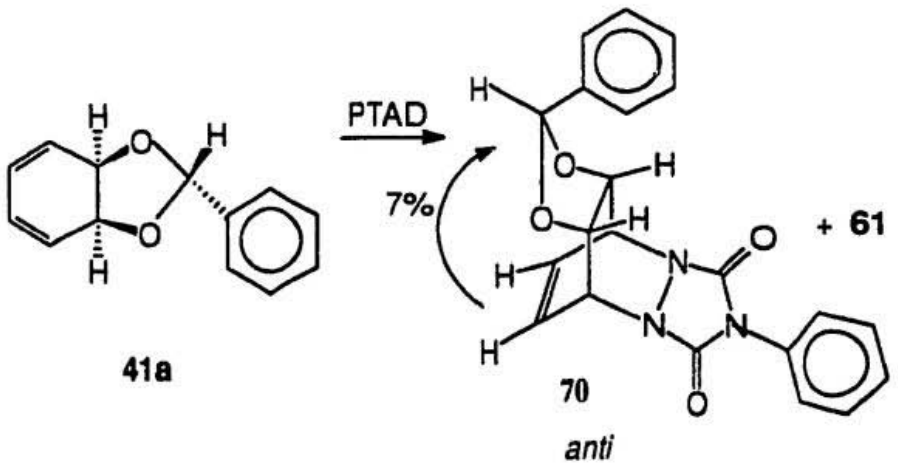


51 **68** *anti*



40a **69**

anti



41a **70**

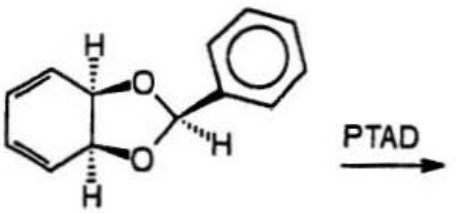
anti

Scheme 40: Diels-Alder reactions of **40a**, **41a** and **51** with PTAD

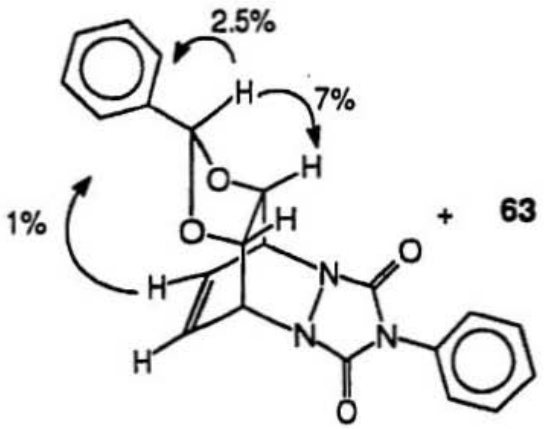
the reaction mixture revealed a component with a molecular ion at *m/z* 416, corresponding to the mass of the new adduct. The ^{1}H nmr spectrum of the resultant crude sample showed signals for a single adduct. Flash column chromatography afforded the product **68** as a colorless solid. There was evidence from nOe experiments that the stereochemistry of **68** resulted from addition to the *anti* face of the diene.

The Diels-Alder reactions of the benzylidene 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 benzylidene 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

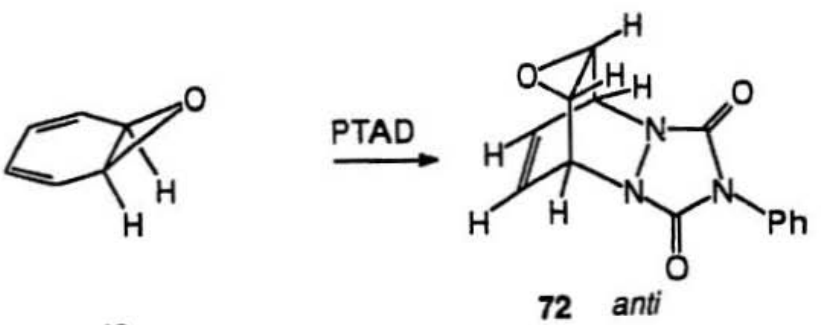
the olefinic hydrogen on C-10 than was the phenyl group on C-2 (Scheme 41).



42a



71 *anti*



48

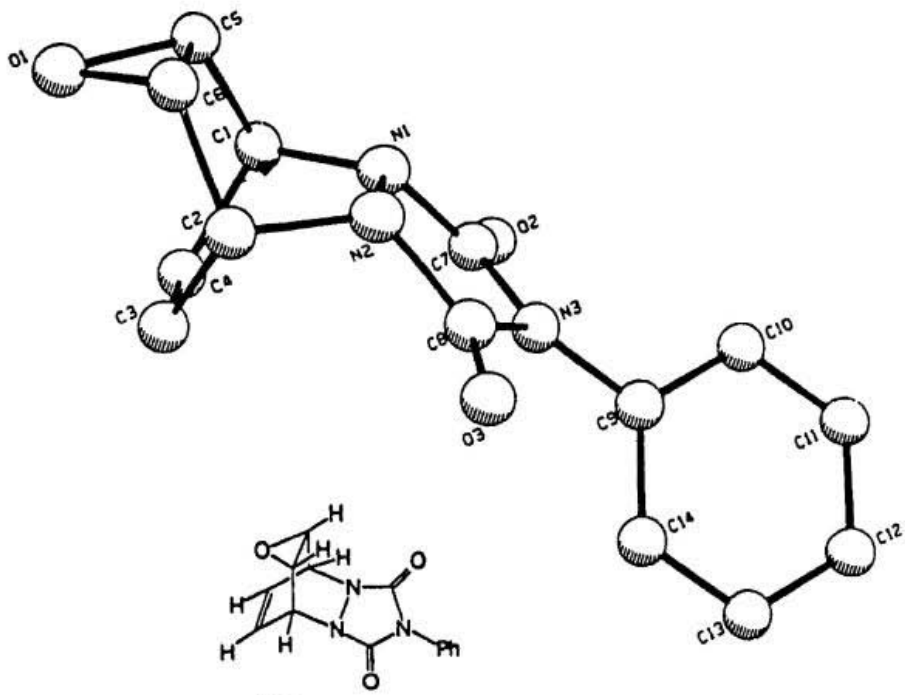
72 *anti*

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 *anti* 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



72

Figure 18: Perspective view of **72**

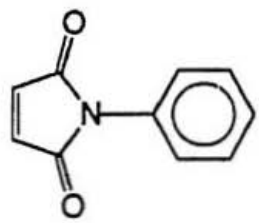
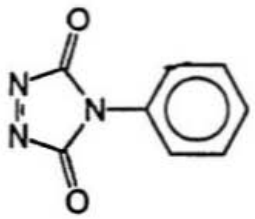
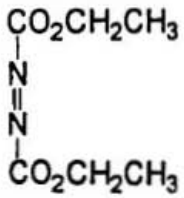
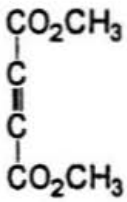
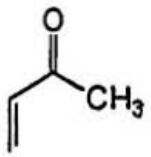
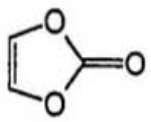
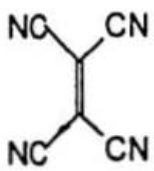
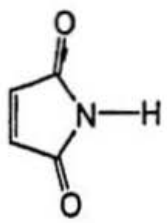
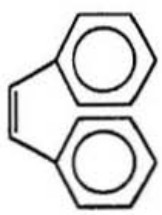
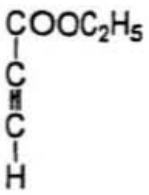
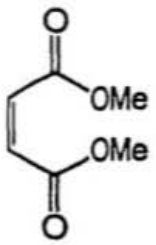
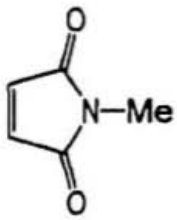
entry	dienophiles	*anti-endo*	*syn-endo*	% yield
1		40	60	80
2		100	0	97
3		100	0	96
4		100	0	86
5		82	18[a]	74

Table 7: Results of cycloaddition of the acetonide **40a** with different dienophiles

entry	dienophiles	*anti-endo*	*syn-endo*	% yield
6		69	31	65
7		16	84	47
8		100	0	63
9		b		
10		59	41	83
11		b		

entry	dienophiles	*anti-endo*	*syn-endo*	% yield
12		100	0	61
13		50	50	46
14		53	47	77

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

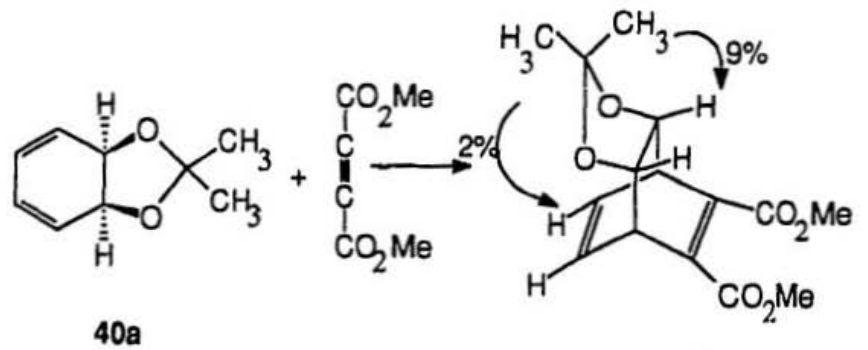
Table 7: Results of cycloaddition of the acetonide **40a** with different dienophiles

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).

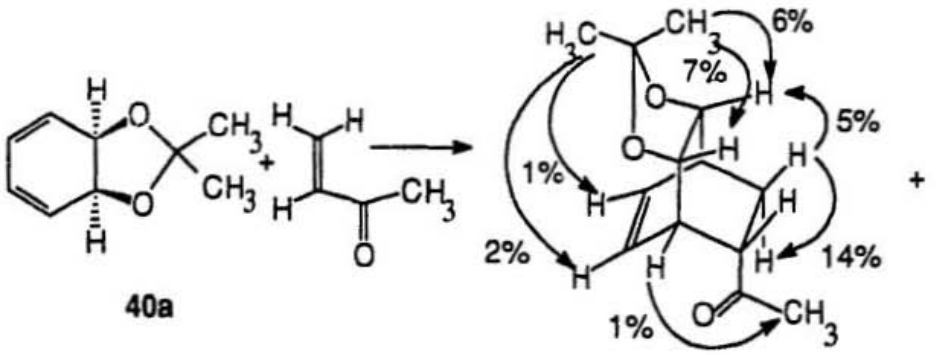
Following the same method of reaction of the acetonide with the nitrogen dienophiles, the Diels-Alder reactions of acetonide **40a** with a wide variety of dienophiles were conducted (Table 7). An *anti*-addition product was observed exclusively in the cases involving the acetylenic dienophiles. Tetracyanoethylene 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 ^{1}H 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).

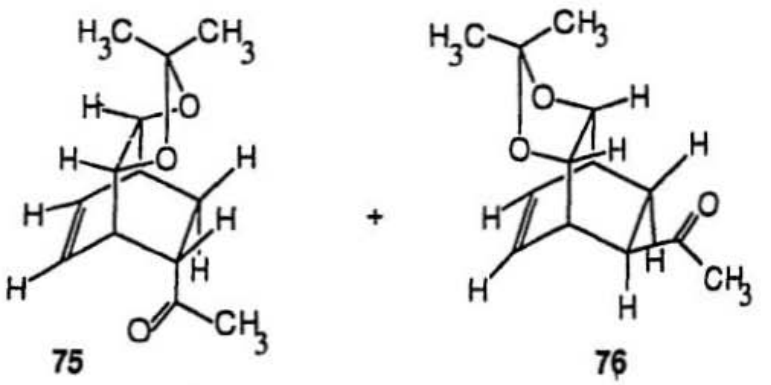
The Diels-Alder reactions of the acetonide diene **40a** with maleimide in various solvents were perfomed (Scheme 47). Results revealed a steady



40a *anti* **73**

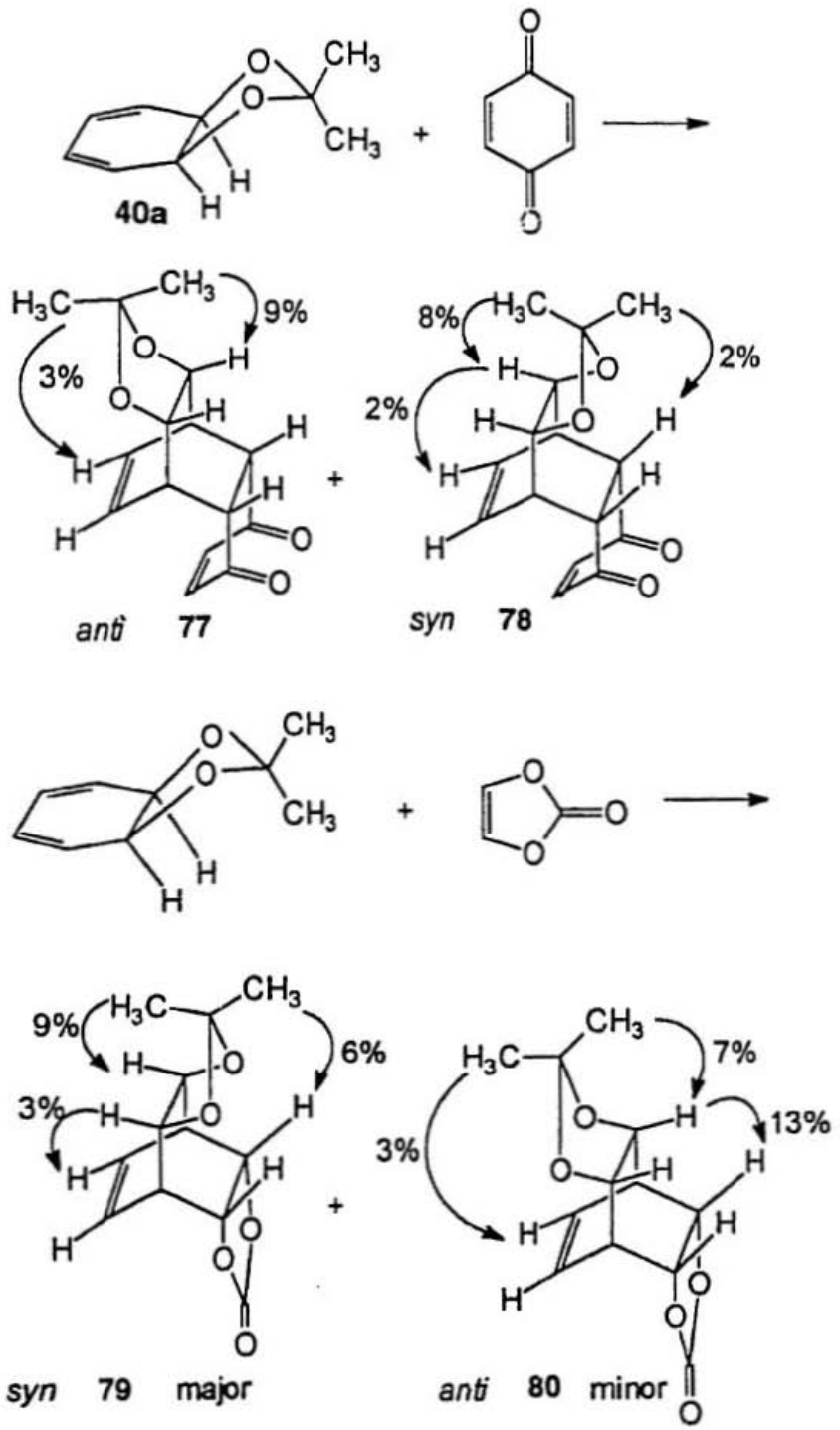


40a *anti-endo* **74** major

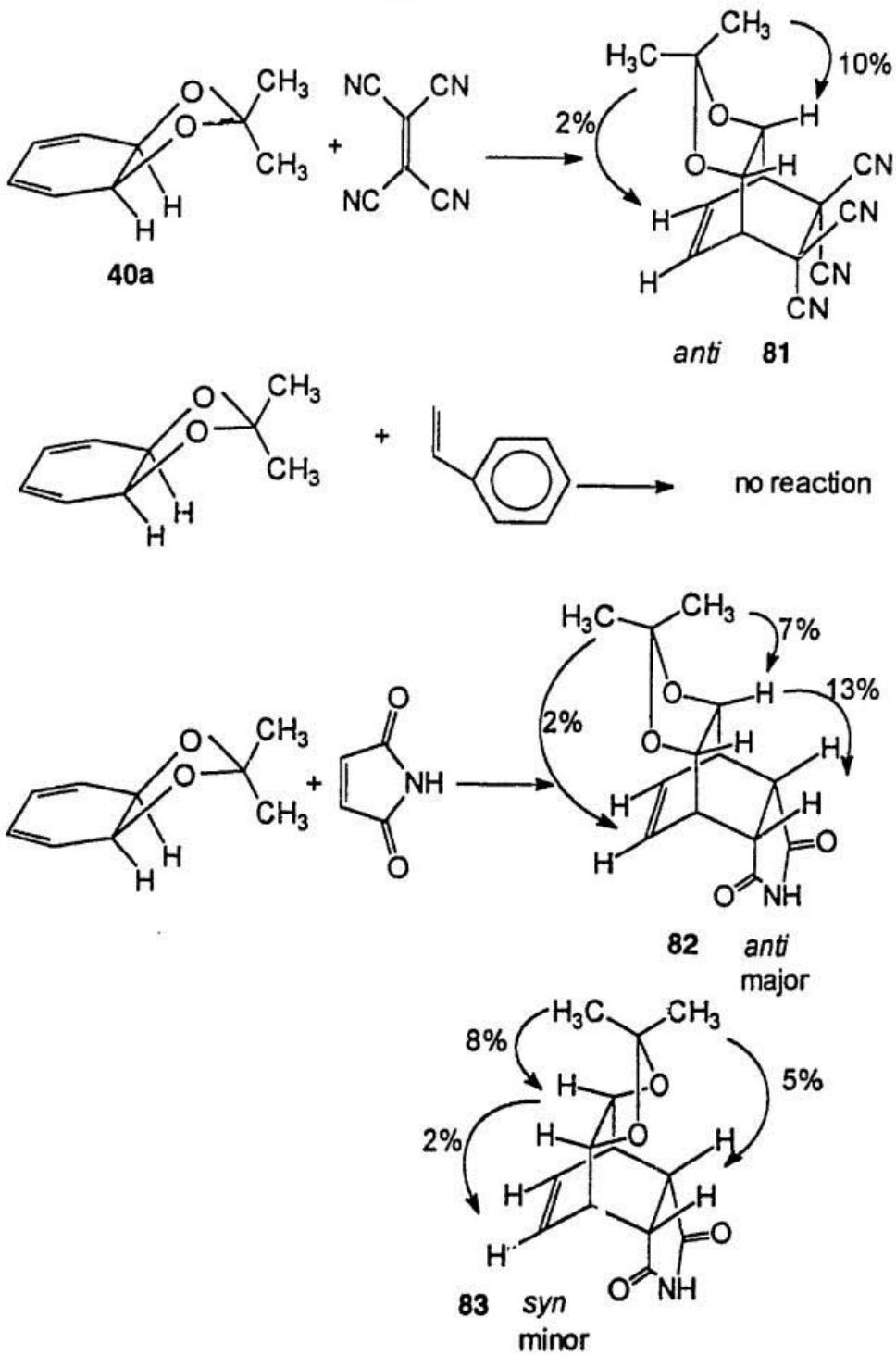


75 *syn-endo* **76** *anti-exo*

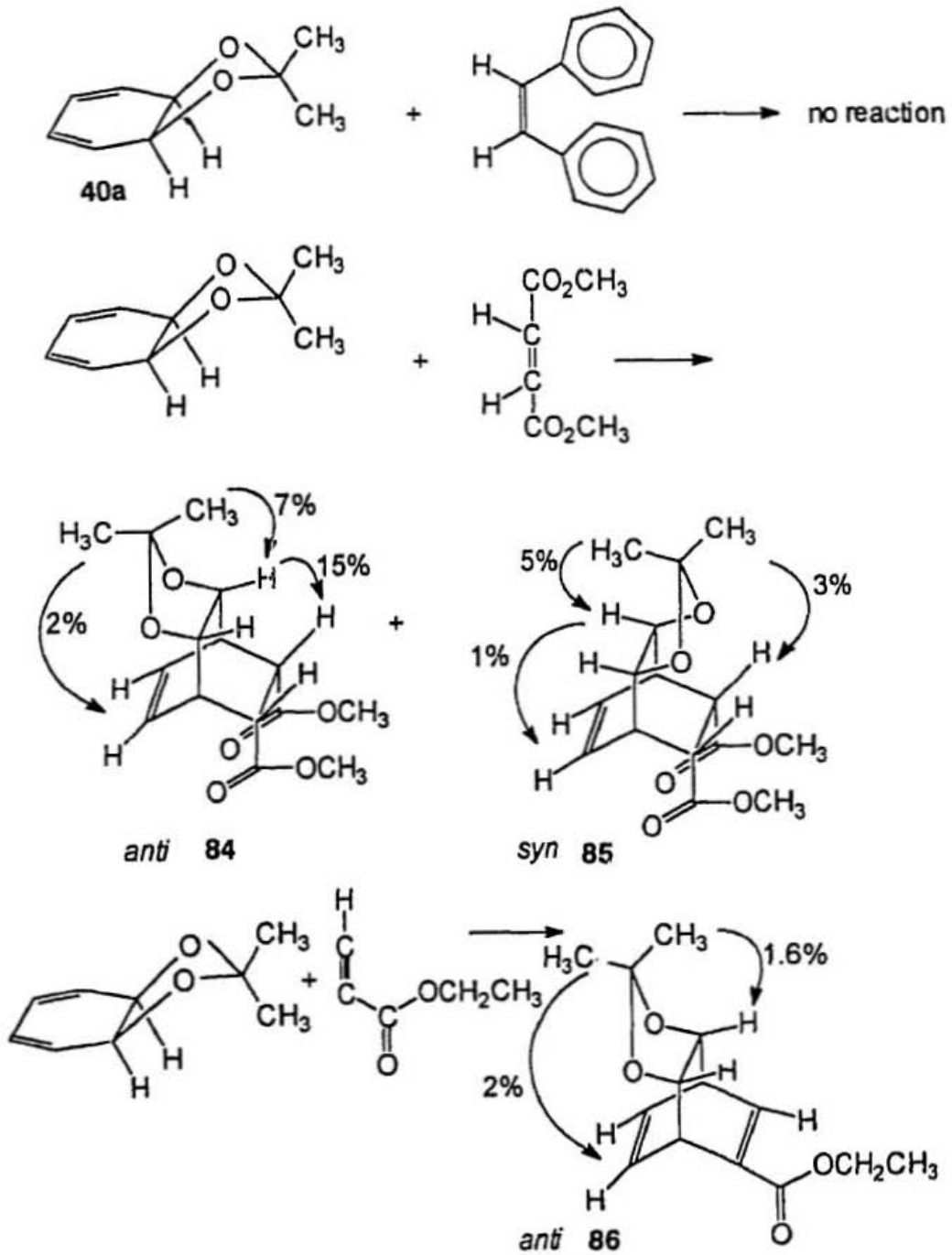
Scheme 42: Diels-Alder reactions of **40a** with DMAD and butenone



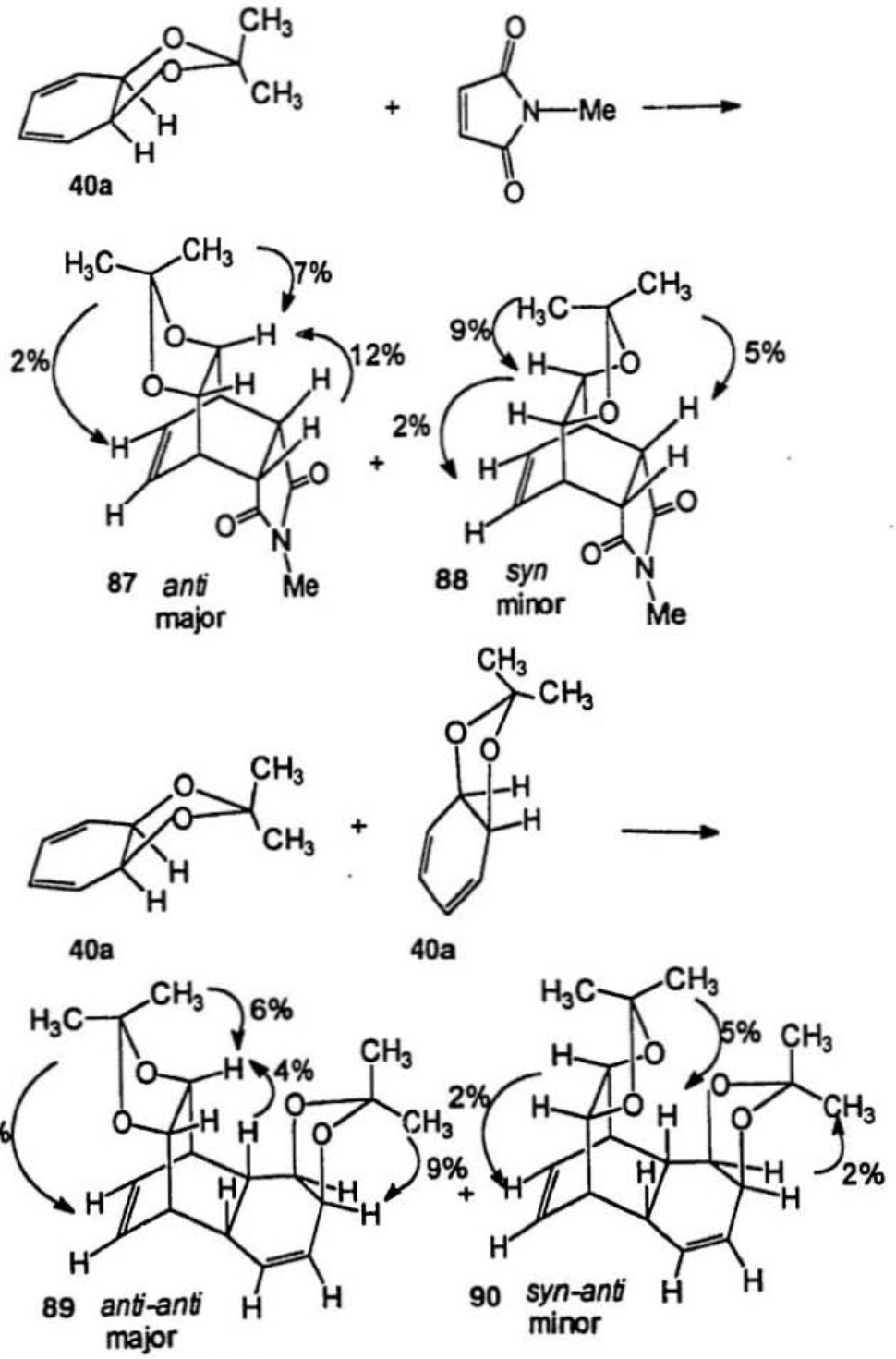
Scheme 43: Diels-Alder reaction of **40a** with benzoquinone and vinylene carbonate



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

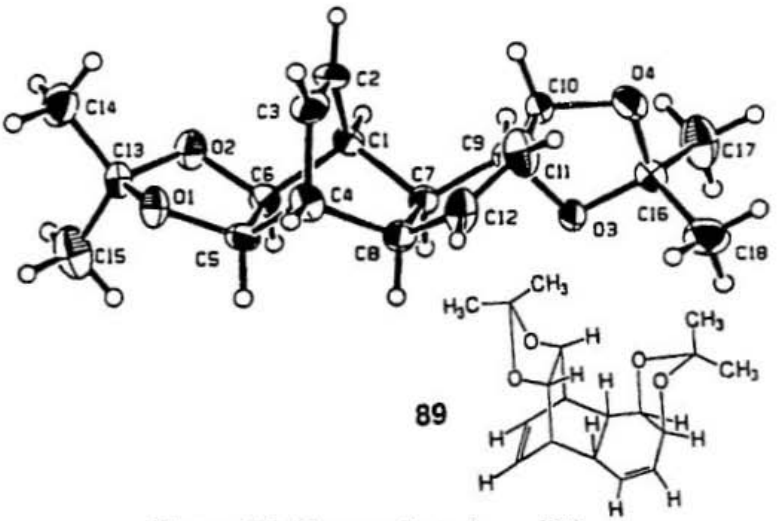


Figure 19: Perspective view of **89**

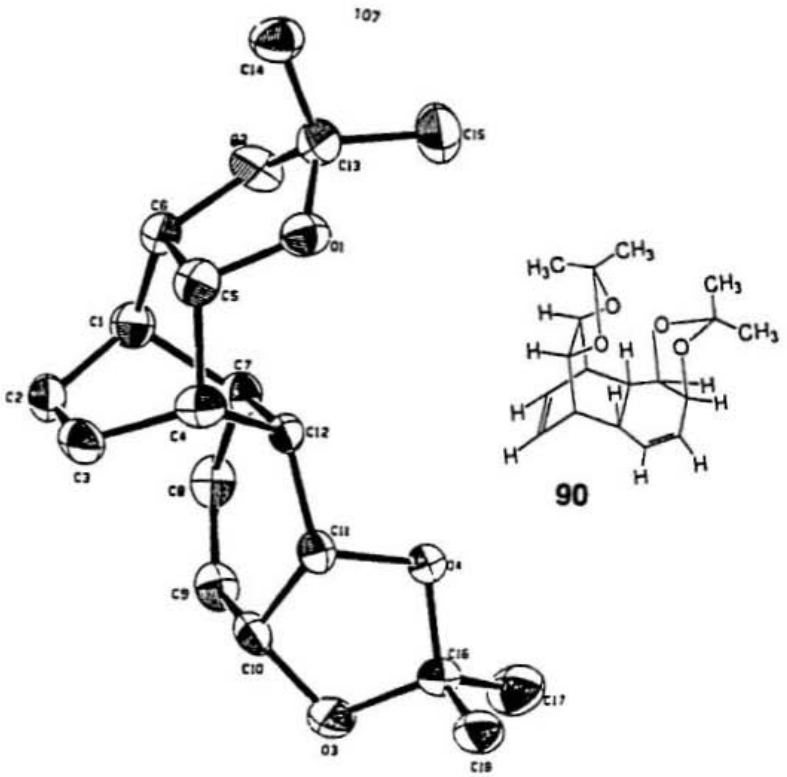
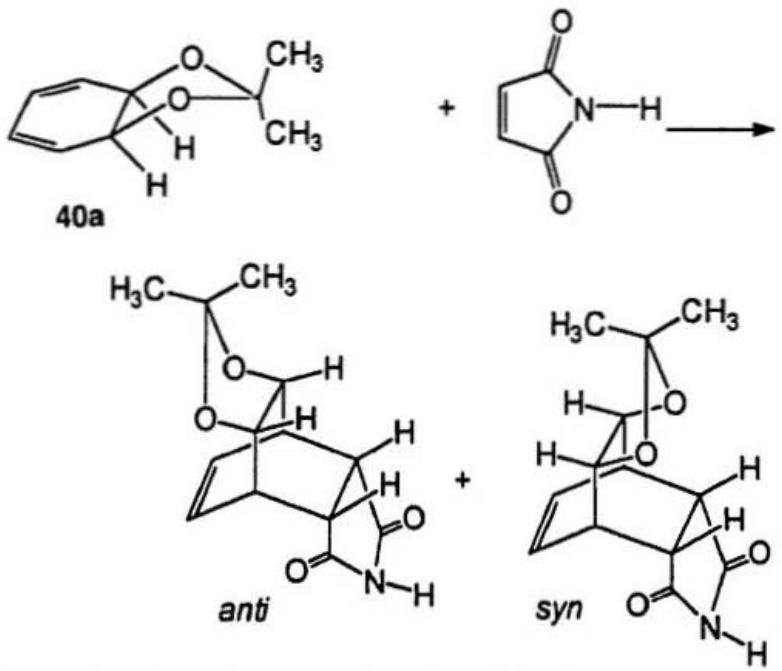


Figure 20: Perspective view of **90**



Scheme 47: Diels-Alder reaction of maleimide with acetonide **40a**

entry	solvent	ratio of adduct *anti* : *syn*	% yield
1	benzene	1.4 : 1	83
2	dichloromethane	1.6 : 1	99
3	pyridine	2.5 : 1	97
4	methanol	2.7 : 1	94
5	acetonitrile	3.7 : 1	99
6	dimethyl sulfoxide	6.1 : 1	97
7	neat	2.7 : 1	99
8	chloroform	1 : 1	99
9	ether	1.2 : 1	90
10	water (2.0 mL)	4.2 : 1	94
11	water (100 mL)	9.4 : 1	89
12	water (1000 mL)	4.5 : 1	86
13	1M LiCl (100 mL water)	6.4 : 1	81
14	1M $LiClO_4$ (100 mL water)	4.4 : 1	85
15	5M $LiClO_4$ (2.0 mL ether)	2.1 : 1	92

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 $LiClO_4$) 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.[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.[40] Other heteroatoms in a similar position direct addition mainly *anti* to the heteroatoms.[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.[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.[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.[39,42] Many of these are not consistent with our results. For example, an extension of the proposals of Anh[86] and of Kahn and Hehre[87] to our

results with our dienes **40a, 41a, 42a,** and **48 - 51** would indicate that the

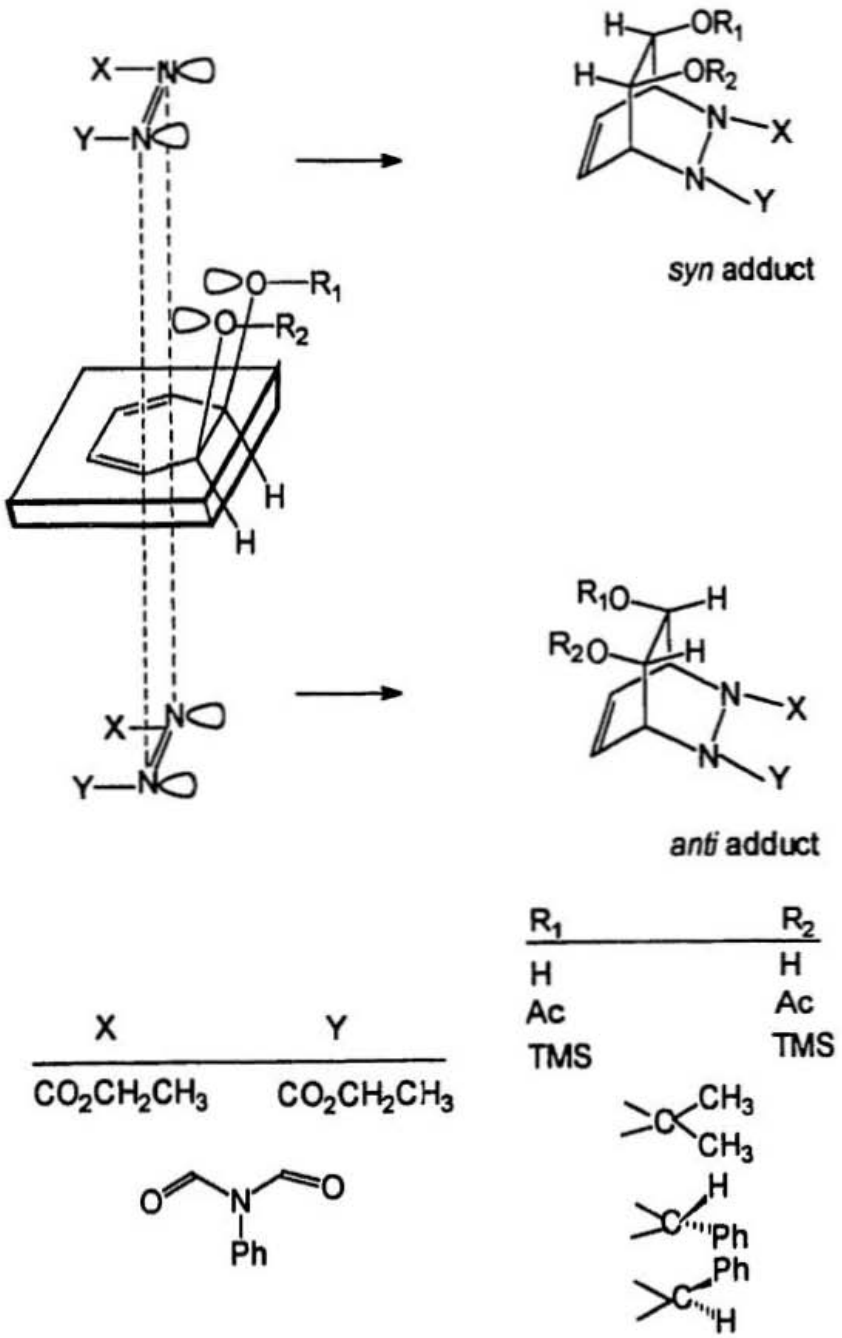


Figure 21: Possible orientation of nitrogen dienophiles with diol **49** and its derivatives

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[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.[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 *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*.[88]

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

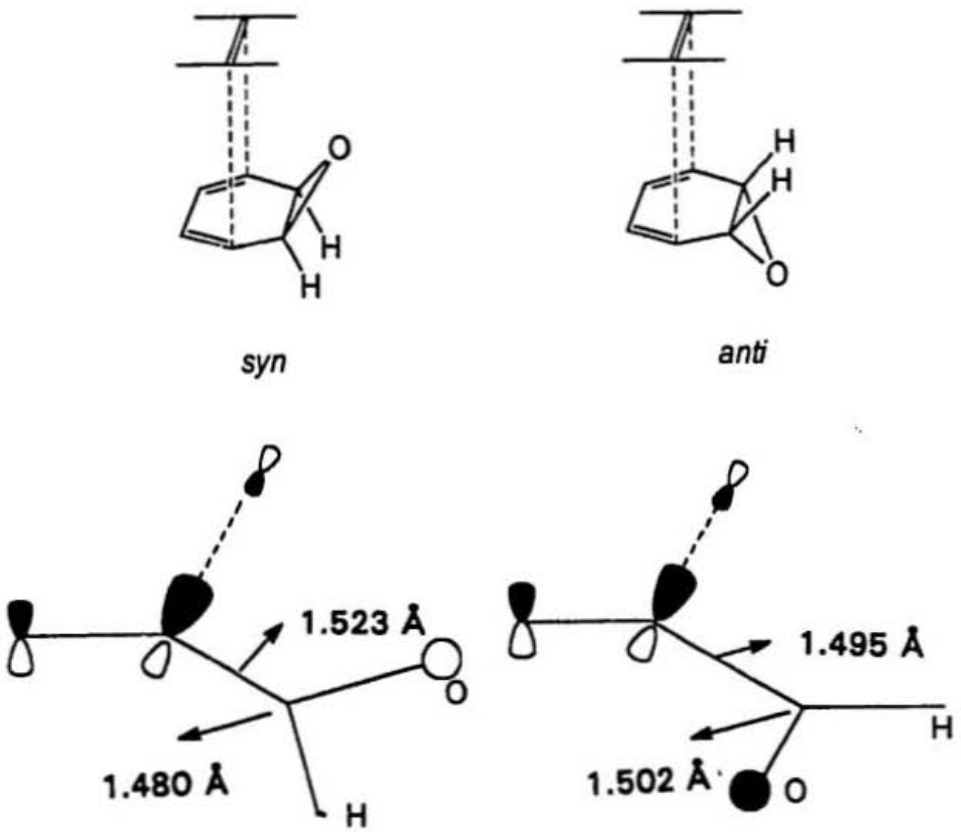
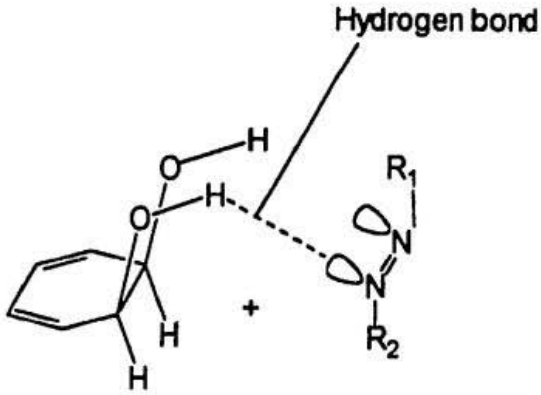


Figure 22: **Highest occupied asymmetric MO's for the *syn* and *anti* additions to the epoxide**

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[89] 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



R_1	R_2
$CO_2CH_2CH_3$	$CO_2CH_2CH_3$

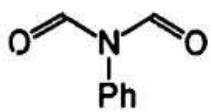
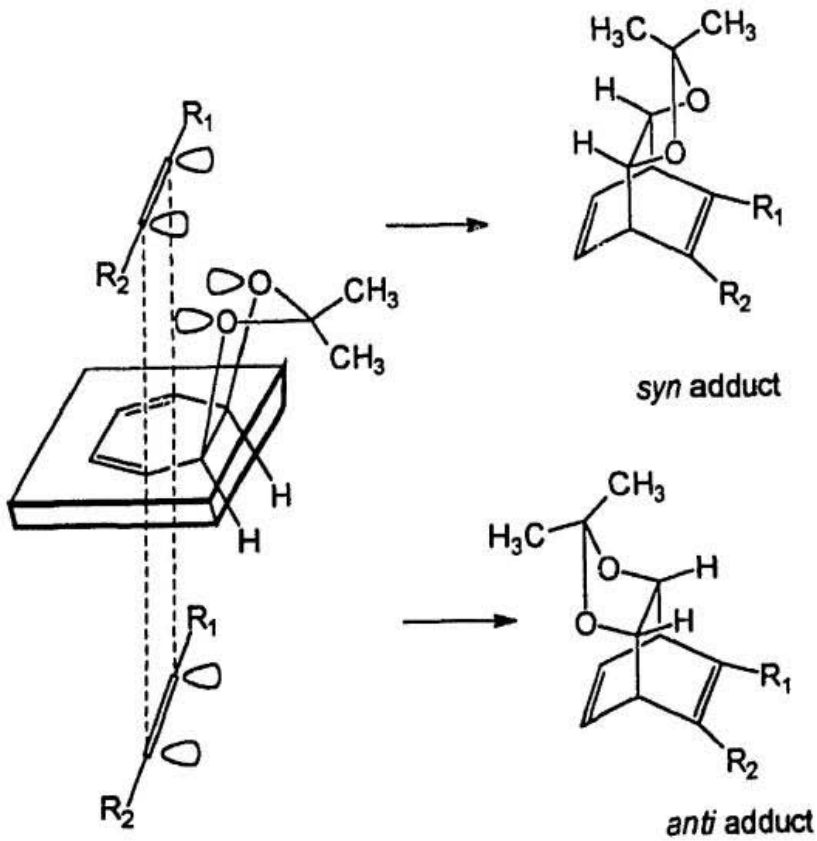


Figure 23: **Hydrogen bond phenomenon as a stabilising factor for *syn* addition of diol**

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



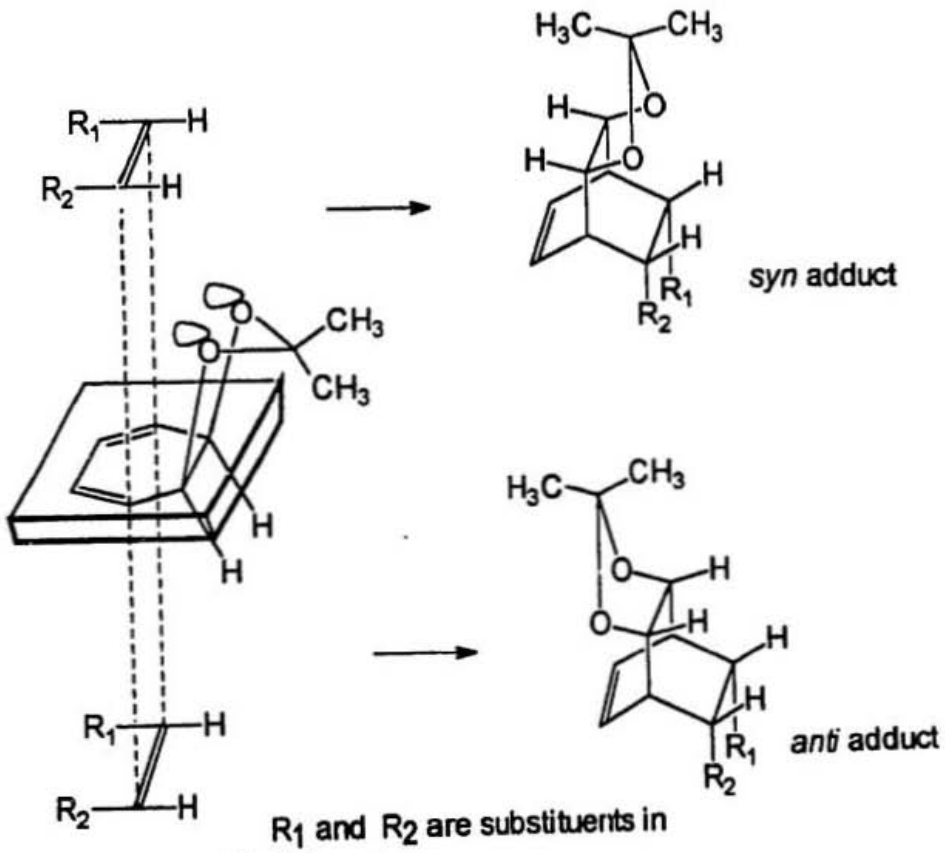
$R_1 = CO_2Me, R_2 = CO_2Me$

$R_1 = H, R_2 = CO_2CH_2CH_3$

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.

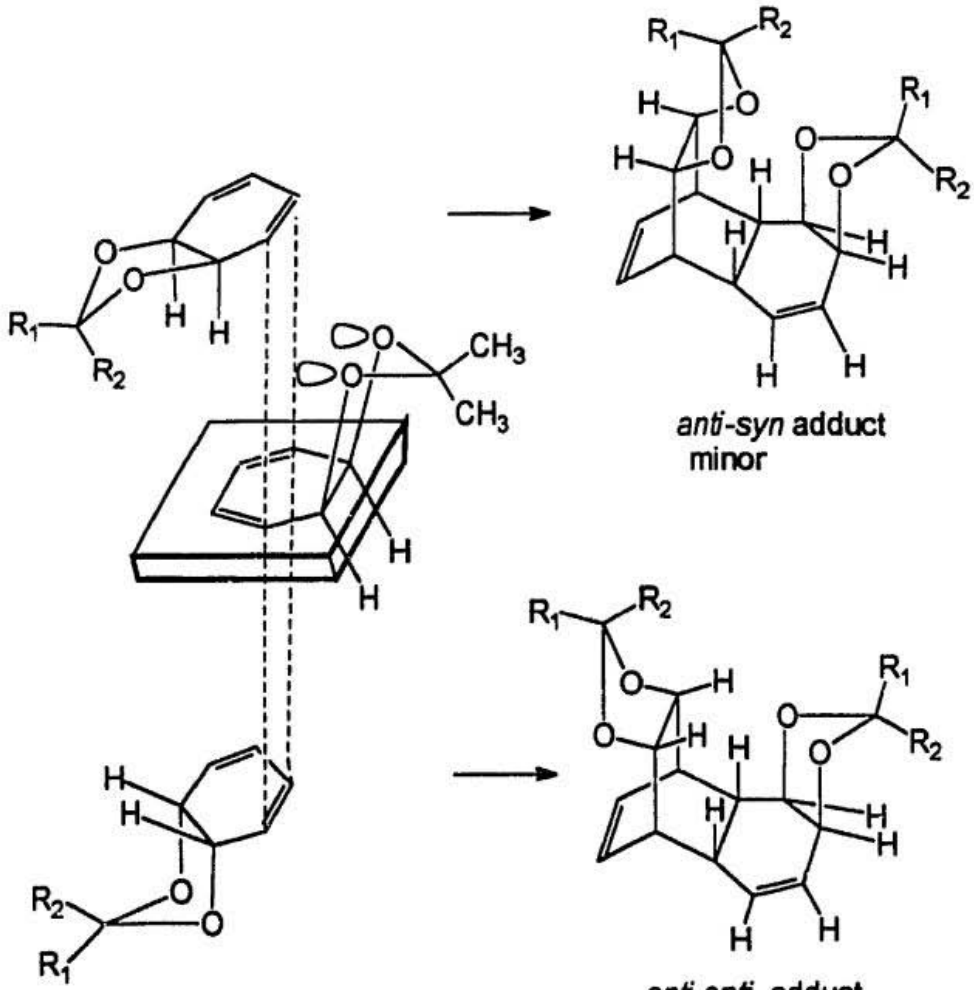
An alternative approach to rationalizing the facial selectivity of systems such as 5-heterosubstituted cyclopentadienes and 1,3-cyclohexadiene



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



R_1	R_2
CH_3	CH_3
H	Ph
Ph	H

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 σ-withdrawing group to carbon. In the *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 *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 *syn* addition as did addition to oxygen-substituted cyclopentadienes.

Opposing this *syn*-directing phenomenon is the sort of *anti*-directing interaction that was described with triazolinedione and acetylenic dienophiles. Even with alkene dienophiles, some unfavorable repulsive interation must be present between the π-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 *syn*-directing tendency, but, except with the nitrogen dienophiles and the acetylenic dienophiles, the two effects are nearly balanced and both *syn* and *anti* addition were observed.

It was noted that diene **41a** showed high facial selectivity both in its

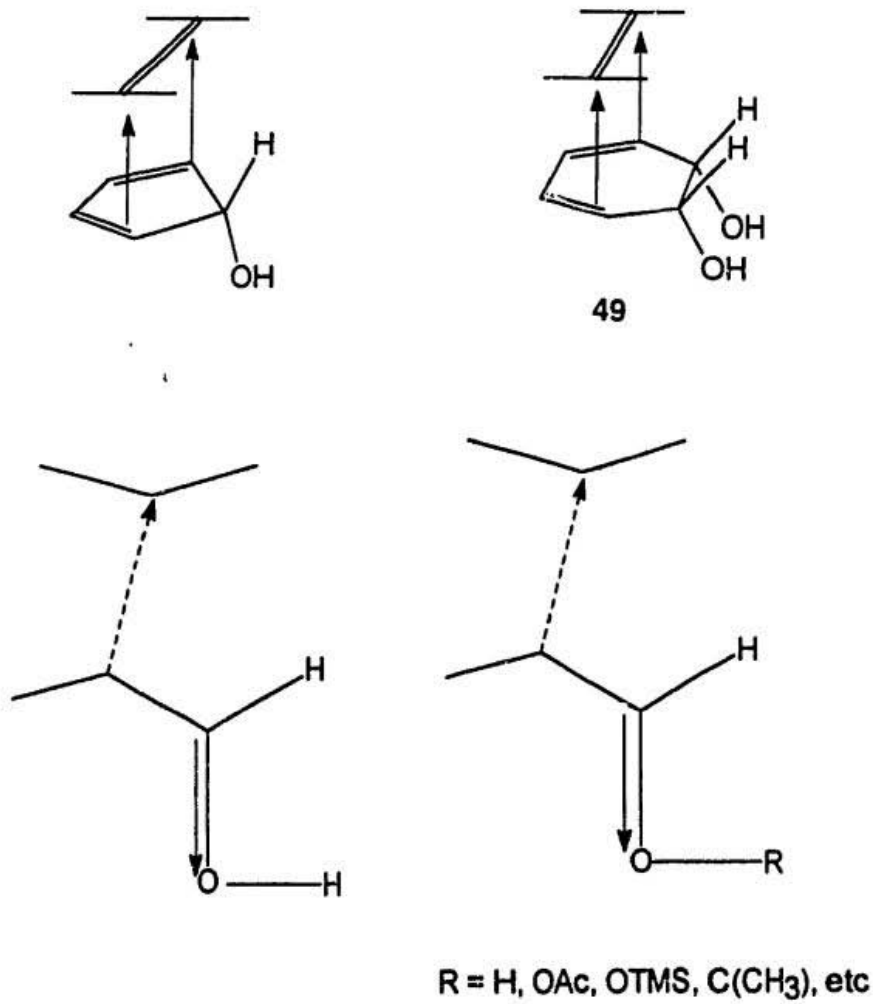
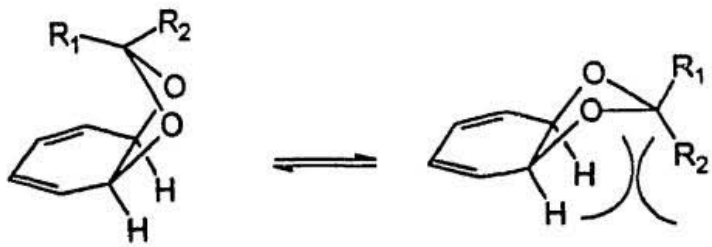


Figure 27: Electron-donating and electron-withdrawing phenomenon in 5-acetoxycyclopentadienes and diol **49** and its derivatives

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

moiety.[91] Therefore, diene **41a** prefers conformation A (R_1 = H, R_2 = C_6H_5), i.e.,



A **B**

R_1	R_2
CH_3	CH_3
Ph	H
H	Ph

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.[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.[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.[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, $LiClO_4$ in ether were used[70] (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 $LiClO_4$ in ether. The effect on our additions was that it decreased the proportion of the *anti* adduct. The reason for these selectivities with LiCl, $LiClO_4$ 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 uncorrrected. 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 ^{1}H shifts of $CDCl_3$ 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 ^{13}C 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 ^{1}H experiments (16k) of 8 transients cycled 12 to 16 times through the list of frequencies to be saturated. The decoupler was gated

on in 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).

Solvents such as chloroform, dichloromethane, and carbon tetrachloride were purified by distillation from calcium hydride (CaH_2). 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 $CHCl_3$ (130 mL, i.e.; about 5 g of Br_2 to 10 mL of $CHCl_3$) dropwise while stirring slowly so that the temperature did not rise above -60°C. $CHCl_3$ (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 ($CDCl_3$) 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); ^{13}C nmr ($CDCl_3$) 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 $MgSO_4$ 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. $KMnO_4$ (20.0 g,

0.125 mol) was dissolved in H_2O(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 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 CH_2Cl_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°C; ir ν_{max}: 3380, 2910, 1445, 1295, 1060, 990 cm^{-1}; ^1H nmr (C_5D_5N) δ: 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_5D_5N) δ: 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 calcd. for $C_6H_8{}^{81}BrO$ (M^+ - ^{79}Br - H_2O): 176.9734; found: 176.9728.

(1R*,2S*,4R*,5R*)-4,5-Dibromo-1,2-bis(trimethylsilyloxy)cyclohexane (37) and (1R*,2S*,4R*,5R*)-4,5-Dibromo-2-hydroxy-1-trimethylsilyloxycyclohexane (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 O°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_{max}: 2956, 1251, 840 cm^{-1}; ^1H nmr ($CDCl_3$) 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); ^{13}C nmr ($CDCl_3$) 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 $M^+ - CH_3$), 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 $C_{11}H_{23}{}^{81}Br^{79}BrSi_2O_2$ ($M^+ - CH_3$): 402.9582; found: 402.9585. For **38**: mp 92 - 92.5°C; ir ν_{max}: 3498, 2933, 1469, 1251, 1111, 862 cm^{-1}; ^1H nmr ($CDCl_3$) 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, 4.8, 21.7 Hz, 1H), 0.01 (s, 9H); ^{13}C nmr ($CDCl_3$) 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 $M^+ - CH_3$), 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 $C_8H_{14}O_2Si^{81}Br^{79}Br$ ($M^+ - CH_3$): 330.9187; found: 330.9185.

(1R,2S*,4R*,5R*)-2-Acetoxy-4,5-dibromo-1-trimethylsilyloxycyclohexane (**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_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 ν_{max}: 2959, 1738, 1438, 1376, 1239, 1188, 1078 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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, Hz, 1H), 0.01 (s, 9H); ^{13}C nmr ($CDCl_3$) δ: 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^+ - $C_5H_{15}O_2Si$), 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 ν_{max}: 1741, 1596, 1365, 1224 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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,

1H), 2.69 (ddd, J = 4.9, 4.9, 14.8 Hz, 1H), 2.56 (ddd, = 4.2, 4.3, 13.6 Hz, 1H), 2.44 (ddd, J = 10.2, 10.2, 13.6 Hz, 1H), 2.12 (dd, J = 2.8, 25.3 Hz, 1H), 2.12 (s, 3H), 2.11 (s, 3H); ^{13}C nmr ($CDCl_3$) at room temperature δ: 169.8 (0), 169.6 (0), 68.9 (1), 68.2 (1), 50.6 (1), 37.1 (2), 20.9 (3), 20.8 (3); ^{13}C nmr at -60°C δ: 170.7 (0), 68.8 (1), 68.3 (1), 67.0 (1), 66.9 (1), 51.4 (1), 51.1 (1), 50.4 (1), 44.6 (1), 38.3 (2), 36.0 (2), 29.6 (2), 27.9 (2), 21.5 (3), 21.1 (3), 20.9 (3); ^{13}C nmr at 60°C δ: 169.5 (0), 169.3 (0), 68.9 (1), 68.3 (1), 50.6 (1), 50.1 (1), 36.9 (2), 35.6 (2), 20.7 (3), 20.6 (3); ms: 258 (6), 256 (13), 254 (7) (all $M^+ - C_4H_6O_3$), 219 (25), 217 (23), 175 (7), 137 (15), 95 (21), 78 (9), 67 (13), 43 (100).

(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 CH_2Cl_2 (75 mL) was added 50% NaOH/H_2O (50 mL), followed by dimethylsulfate (1 mL), and tetra-*n*-butylammonium iodide (1.0 g), which had already been dissolved in CH_2Cl_2 (1 mL). The mixture was stirred for 24 hours, and CH_2Cl_2 (50 mL) was added, and the organic layer was separated. This was washed with H_2O (50 mL) and dried over $MgSO_4$. 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 ν_{max}: 3427, 2985, 2944, 2897, 1636, 1439, 1196, 1104, 1030, 932 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 4.66 (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 =

6.5, 13.6 Hz, 1H), 1.71 (dt, *J* = 2.7, 6.8 Hz, 1H); gc / ms: 177 (2), 175 (2) (all M^+ - Br - CH_4O), 141 (34), 109 (62), 97 (38), 88 (25), 79 (39), 45 (100). For **43**: ir ν_{max}: 2930, 2892, 2829, 1460, 1364, 1308, 1195, 1112, 1001, 946 and 828 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 4.27 (ddd, *J* = 4.3, 4.5, 17.2 Hz, 1H), 4.03 (ddd, *J* = 4.5, 4.8, 16.8 Hz, 1H), 3.66 (d, *J* = 8 Hz, 1H), 3.44 (s, 3H), 3.38 (s, 3H), 3.27 (ddd, *J* = 3.2, 3.3, 11.1 Hz, 1H), 2.77 (ddd, *J* = 4.4, 4.5, 15.5 Hz, 1H), 2.55 - 2.48 (m, 1H), 2.40 (t, *J* = 11.4 Hz, 1H), 1.83 (ddd, *J* = 2.1, 2.4, 24.1 Hz, 1H); ^{13}C nmr ($CDCl_3$) δ: 78.9 (1), 75.6 (1), 57.3 (1), 56.5 (1), 52.6 (2), 52.0 (2), 36.1 (3); gc / ms: 223 (58), 222 (6), 221 (all M^+ - $C_4H_8O_2$), 191 (24), 189 (24), 165 (16), 97 (43), 88 (28), 45 (100).

(1R,2S*,4R*,5R*)-4,5-Dibromo-1-methoxy-2-trimethylsilyloxycyclohexane (**46**)*

To a solution of **44** (2.06 g, 7.17 mmol) and pyridine (5.0 mL) was added TMSCl (2.0 mL, 14.3 mmol) at O°C, and the solution was stirred at room temperature for 2 hours. The solution was extracted with CCl_4 (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 ν_{max}: 3434, 2987, 1652, 1445, 1380, 1265 cm^{-1}; ^1H nmr ($CDCl_3$) 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^+-CH_3), 280 (22), 278 (22), 264 (12), 242 (11), 246 (4), 176 (7), 150 (6), 108 (7), 95 (24), 88 (100), 82 (14), 75 (16), 73 (87), 67 (52), 58 (27), 45 (32),

40 (13). Exact Mass calcd. for $C_9H_{17}Si^{81}Br^{79}BrO_2$ (M^+ - CH_3): 344.9343; found: 344.9352.

(1R,2S*,4R*,5R*)-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}; ^1H 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, 4.5, 14.7Hz, 1H), 2.55 (ddd, = 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^+ - $C_3H_4O_2$), 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 ($C_7H_{10}{}^{81}Br^{79}BrO$): 269.9078; found: 269.9065.

*(3aα,5α,6β,7aα)-5,6-Dibromo-3a,7a-hexahydro-2,2-dimethyl-1,3-benzodioxole (**40**)*

To the dibromodiol **35** (4.28 g, 0.015 mol) in CH_2Cl_2 (50 mL) was added *para*-toluenesulfonic acid (*p*TsOH) (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 R_f = 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 $MgSO_4$. 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 ν_{max}: 2940, 2906, 1439, 1364, 1289, 1182, 1117, 1062 and 1062 cm^{-1}; ^1H nmr ($CDCl_3$) 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); ^{13}C nmr ($CDCl_3$) 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 R_f = 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 $NaHCO_3$ (50 mL x 2) and dried

over $MgSO_4$. 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%): ir ν_{max}: 2987, 1379, 1209, 1032 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 6:00 (m, 2H), 5.93 - 5.87 (m, 2H), 4.66 (t, J = 1.7 Hz, 2H), 1.43 (s, 3H), 1.40 (s, 3H); ^{13}C nmr ($CDCl_3$) δ: 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 calcd. for $C_8H_9O_2$ (M^+ - CH_3): 137.0680; found: 137.0599.

(2a,3aα,5a,6β,7aα)- ***(41)*** *and (2a,3aβ,5β,6a,7aβ)-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_2Cl_2 (15 mL) was added *p*TsOH (1.05 g) and benzaldehyde dimethyl acetal (17.7 g, 116 mmol) as a solution in dry CH_2Cl_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 ν_{max}: 2903, 1459, 1362, 1219, 1107, 1069, 976 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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 ($CDCl_3$) δ: 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 $C_{13}H_{13}{}^{81}Br_2O_2$($M^+$ - H): 362.9241; found: 362.9231. For **42:** mp 63 - 65°C; ir ν_{max}: 1412, 1173, 1069, 1011 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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), 2.84 (ddd, *J* = 4.8, 5.4, 15.5 Hz, 1H), 2.79 (ddd, *J* = 3.8, 5.7, 15.0 Hz, 1H), 2.49 (ddd, *J* = 6.0, 6.7, 15.5 Hz, 1H), 2.28 (ddd, *J* = 5.2, 8.0, 15.0 Hz, 1H); ^{13}C nmr ($CDCl_3$) δ: 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 $C_{13}H_{13}{}^{79}Br_2O_2$ (M^+ - H): 358.9283; found: 358.9293.

*(2α,3aα,7aα)-3a,7a-Dihydro-2-phenyl-1,3-benzodioxole (**41a**)*

To the dibromoacetal **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 $NaHCO_3$ (100 mL x 2), H_2O (100 mL x 2), and saturated NaCl (100 mL x 2) followed by drying over $MgSO_4$. The solvent was carefully removed to give **41a** (0.679 g, 64%) as a light yellow cloudy oil: ir ν_{max}: 3043, 2927, 1641, 1217, 1068 cm^{-1}; ^1H nmr ($CDCl_3$) 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 ($CDCl_3$) 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 calcd. for $C_{13}H_{12}O_2$: 200.0837; found: 200.0828.

(2α,3aβ,7aβ)-3a,7a-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 $NaHCO_3$ (100 mL x 2), H_2O (100 mL x 2), and saturated NaCl (100 mL x 2) followed by drying over $MgSO_4$. The solvent was evaporated to give **42a** as a light yellow oil (0.549 g, 60%): ir ν_{max}: 3044, 2883, 1459, 1401, 1217, 1061 cm^{-1};

^{1}H nmr ($CDCl_3$) δ: 7.50 - 7.46 (m, 2H), 7.36 - 7.32 (m, 3H), 6.08 - 6.01 (m, 2H), 6.00 - 5.94 (m, 2H), 5.64 (s, 1H), 4.66 (t, J = 1.6 Hz); nOe data δ: 5.64 (7.50 - 7.46, 4%; 4.66, 4%), 4.66 (6.00 - 5.94, 4%; 5.64, 9%); ^{13}C nmr ($CDCl_3$) δ: 136.5 (0), 129.4 (1), 128.2 (2), 126.8 (2), 124.1 (2), 123.8 (2), 98.2 (1), 71.0 (2); ms: 200 (M^+, 4), 199 (3), 172 (6), 154 (39), 106 (35), 105 (90), 94 (100), 78 (64), 77 (86), 66 (100), 51 (50). Exact Mass calcd. for $C_{13}H_{12}O_2$: 200.0837; found: 200.0836.

*cis-1,2-Diacetoxy-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: ir ν_{max}: 3054, 1740, 1371, 1241 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 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 ($CDCl_3$) δ: 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 $C_{10}H_{12}O_4$: 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

TMSCl (2.8 mL) at 0°C. The solution was allowed to warm up to room temperature for 1 hour before CCl_4 (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:** ir ν_{max}: 2958, 1412, 1252, 1119, 840 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 5.99 - 5.94 (m, 2H), 5.89 - 5.84 (m, 2H), 4.14 (t, J = 1.1 Hz, 2H), 0.15 (s, 18 H); ^{13}C nmr ($CDCl_3$) δ: 130.4 (1) 124.0 (1), 68.9 (1), 0.2 (3); ms: 256 (M^+, 21), 191 (10), 167 (2), 147 (17), 73 (100), 45 (17). Exact Mass calcd. for $C_{12}H_{24}O_2Si_2$: 256.1314; found: 256.1314. For **52**: ^1H nmr ($CDCl_3$) δ: 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); ^{13}C nmr ($CDCl_3$) δ: 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/H_2O (50 mL) solution was added CH_2Cl_2 (75 mL), the diol **49** (0.344 mL, 2.77 mmol), dimethylsulfate (1.59 mL, 16.6 mmol), and tetra-*n*-butylammonium iodide 40% w/w (0.6 g), which had been dissolved in CH_2Cl_2 (1.0 mL). This was stirred at room temperature for 16 hours. More CH_2Cl_2 (50 mL) was added to the mixture, and the organic extract was washed with H_2O (50 mL), saturated $NaHCO_3$ solution (50 mL), H_2O (50 mL), and saturated NaCl (50 mL), and dried over $MgSO_4$. 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 ν_{max}: 2929, 1464, 1122 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 6.04 - 6.03 (m, 4H), 4.00 - 3.99 (m, 1H), 3.81 (s, 1H), 3.44 (s, 6H); ^{13}C nmr ($CDCl_3$) δ: 126.9 (1), 124.8 (1), 73.9 (1), 56.2 (3). For **54:** ^1H nmr ($CDCl_3$) δ: 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 ($CDCl_3$) δ: 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(3α,6α,7α,8α,7R*,8S*)- **(56a)** and (3α,6α,7β,8β,7S*,8R*)-3a,6,7,8a-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 ^1H 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 ν_{max}: 2984, 1736, 1607, 1480, 1406, 1405, 1300, 1233, 1060 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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**: ir ν_{max}: 2984, 1727, 1606, 1489, 1373, 1324, 1236, 1203 and 1061 cm^{-1}; ^1H nmr ($CDCl_3$) δ : 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: (3α,6α,7α,8α,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 ^1H 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: ir ν_{max}: 1709, 1519, 1415, 1360, 1245, 1062 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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 ($CDCl_3$) δ: 155.4 (0), 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_4H_7O, 3), 284 (19), 244 (26), 229 (5), 211 (22), 196 (7), 176 (76), 176 (10), 153 (10), 147 (100), 138 (46), 126 (26), 109 (53), 98 (15), 83 (52), 73 (32), 66 (18), 61 (28), 55 (36), 45 (47). Exact Mass calcd. for $C_{13}H_{20}N_2O_5$ (M^+ - $C_5H_{14}OSi_2$): 284.1012; found: 284.1023.

*Diels-Alder reaction of **40a** with DEAD: Diethyl (3aα,4β,7aα,7β)-3a,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 ^{1}H 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: ir ν_{max}: 2952, 2924, 1736, 1725, 1452, 1356, 1300, 1240, 1093 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 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}C nmr ($CDCl_3$) δ: 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 $C_{14}H_{19}O_6N_2$ (M^+ - CH_3): 311.1241; found: 311.1253.

*Diels-Alder reaction of **41a** with DEAD: Diethyl (2β,3aβ,4α,7α,7aβ)-3a,4,5,5a-tetrahydro-2-phenyl-4,7-etheno-1,3-dioxolo[4,5-d]pyridazine-5,6-dicarboxylate*

*(**60**) and (2α,3aβ,5aα,6aα,6α,8β,9aα,10α,10aα,10bβ)-3a,5a,6,6a,9a,10,10a,10b-octahydro-2,8-diphenyl-3a,5a,6,10-ethenonaphthol-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 ν_{max}: 3064, 2982, 2934, 1720, 1619, 1478, 1451, 1311, 1239, 1116, 1073, 872 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 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 ($CDCl_3$) δ: 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 $C_{19}H_{22}N_2O_6$: 374.1476; found: 374.1472.

For **61**: mp 176 - 179°C; ir ν_{max}: 3034, 2943, 1457, 1368, 1224, 1097, 1066 cm^{-1}; ^1H nmr ($CDCl_3$) 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%), 5.62 (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%); ^{13}C nmr ($CDCl_3$) 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,3aα,4β,7aα,7β)-3a,4,5,5a-tetrahydro-2-phenyl-4,7-etheno-1,3-dioxolo[4,5-d]pyridazine-5,6-dicarboxylate (**62**) and (2β,3aβ,5aα,6α,6aα,8α,9aα,10α,10aα,10bβ)-*

*3a,5a,6,6a,9a,10,10a,10b-octahydro-2,8-diphenyl-3a,5a,6,10-ethenonaphthol-1,3,7,9-tetraoxole (**63**)*

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:** ir ν_{max}: 2981, 2915, 1736, 1703, 1591, 1462, 1402, 1373, 1310, 1238, 1067 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.37 (m, 5H), 6.69(br t, *J* = 6.1 Hz, 1H), 6.55 (br t, *J* = 6.6 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}C nmr ($CDCl_3$) δ: 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%), 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 $C_{16}H_{18}N_2O_4$ ($M^+ - C_3H_4O_2$): 302.1265; found: 302.1268. For **63:** mp 152 - 154°C; ir ν_{max}: 3066, 1601, 1521 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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 (ddd, *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. 129.2, 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^+ - $C_{14}H_{12}O_2$): 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 ν_{max}: 3354, 2927, 1779, 1737, 1502, 1434, 1288 cm^{-1}; ^1H nmr ($CDCl_3/CD_3OD$) 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,

2H); 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:** ^1H 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*,10S*)- (**66**) and (5α,8α,11S*,10R*)-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 ^1H 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; ir ν_{max}: 3071, 2978, 1749, 1718, 1501, 1421, 1374, 1240, 1144, 1067 cm^{-1}; ^1H 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%); ^{13}C 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 $C_{18}H_{17}O_6N_3$: 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 ν_{max}: 2922, 1743, 1706, 1599, 1504, 1417, 1370 cm^{-1}; ^{1}H 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%); ^{13}C 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 $C_{18}H_{17}N_3O_6$: 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; ir ν_{max}: 2955, 1774, 1718, 1509, 1503, 1404, 1252, 1120 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 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 (nar m, 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 ($CDCl_3$) δ: 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 $C_{20}H_{29}N_3O_4Si_2$: 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,3aβ,4α,10α,10aβ)-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 ν_{max}: 2922, 1782, 1718, 1596, 1501, 1407, 1112 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.45 - 7.36 (m, 10H), 6.61 (apparent ddt, J = 3.2, 4.0 Hz, 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%); ^{13}C nmr ($CDCl_3$) 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 (84), 227 (96), 121 (45), 119 (75), 105 (18), 94 (10), 91 (30), 79 (100), 78 (59), 65 (18), 50 (13). Exact Mass calcd. for $C_{21}H_{17}N_3O_4$: 375.1218; found: 375.1200. Anal. calcd. for $C_{12}H_{17}N_3O_4$: 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,3aα,4β,10β,10aα)-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; ir ν_{max}: 2921, 1783, 1719, 1596, 1501, 1406 cm^{-1}; 1H nmr ($CDCl_3$) δ: 7.46 - 7.41 (m, 10H), 6.52 (apparent dd, J = 3.1, 4.0 Hz, 2H), 5.79 (s, 1H), 5.31 - 5.21 (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}C nmr ($CDCl_3$) δ: 155.5 (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^+, 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 $C_{21}H_{17}N_3O_4$: 375.1217; found: 375.1225.

*Diels-Alder reaction of **40a** with **59**: (3aβ,4β,10β,10aα)-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; ir ν_{max}: 2923, 1777, 1712, 1596, 1500, 1401, 1253 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.45 - 7.43 (m, 5H), 6.41 (dd, J = 3.5,

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 $C_{17}H_{17}N_3O_4$: 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_2O (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}; ^1H 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 $NaHCO_3$ (3 x 25 mL) and saturated NaCl (3 x 25 mL), and dried over K_2CO_3. 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%): ^{1}H nmr ($CDCl_3$) δ: 6.26 (m, 2H), 5.88 (m, 2H), 5.12 (d, J = 4.5 Hz, 2H); ^{13}C nmr ($CDCl_3$) δ: 130.7, 128.6, 122.3, 120.2, 110.0, 107.5; ms: 94 (M^+, 61), 78 (7), 68 (35), 66 (100), 65 (68).

*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 ν_{max}: 3064, 2987, 1773, 1717, 1501, 1404, 1265, 1060 cm^{-1}; ^{1}H nmr ($CDCl_3$) 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%); ^{13}C nmr ($CDCl_3$) 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

(31), 80 (14), 78 (35), 68 (20), 66 (68), 64 (20), 50 (15), 43 (14), 39 (24), 28 (12). Anal. calcd. for $C_{14}H_{11}N_3O_3$: 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 (3aα,4β,7β,7aα,8S*,9S*)3a,4,7a,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, 0.782 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 ν_{max}: 2995, 2946, 1731, 1713, 1644, 1615, 1433, 1383, 1340, 1270, 1245, 1164, 1057 cm^{-1}; ^1H 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 butenone: (3aα,4α,7α,7aα)- (**74**) and (3aβ,4α,7α,7aβ)-3a,4,7,7a-tetrahydro-2,2-dimethyl-1,3-dioxole-6H-4,7-ethenotricyclo[5.2.2.0^{3a,7a}]undec-8-ene (**75**)*

To the acetonide **40a** (0.126 g, 0.833 mmol) in toluene (5.0 mL) was added butenone 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 ν_{max}: 2995, 2963, 2915, 2886, 1709, 1459, 1368, 1279, 1160, 1060 cm^{-1}; ^{1}H nmr ($CDCl_3$) 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 (ddd, *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, 2%), 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%); ^{13}C nmr ($CDCl_3$) 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), 46.8 (1),

37.1 (1), 34.4 (1), 28.3 (3), 25.3 (3), 24.9 (3), 22.9 (2); ms: 221 (M^+, 0.9), 206 (12), 164 (19), 147 (6), 120 (62), 105 (11), 103 (36), 99 (25), 93 (15), 90 (22), 85 (19), 77 (23), 58 (16), 43 (100), 40 (12), 38 (16). Exact Mass calcd. for $C_{13}H_{17}O_3$ (M^+ - H): 221.1176; found: 221.1186. For **75:** ^{1}H nmr ($CDCl_3$) δ: 6.25 - 6.13 (m, 2H), 6.06 (t, *J* = 7.0 Hz, 1H), 5.99 (t, *J* = 3.0 Hz, 1H), 4.17 (dd, *J* = 3.1, 7.3 Hz, 1H), 4.10 - 4.06 (m, 2H), 4.02 (ddd, *J* = 1.0, 3.6, 3.7 Hz, 2H), 3.21 - 3.15 (m, 4H), 2.96 - 2.90 (m, 1H), 2.87 - 2.81 (m, 2H), 2.56 - 2.49 (m, 1H), 2.23 (s, 3H), 2.13 (s, 3H), 1.86 (ddd, *J* = 1.9, 5.5, 13.5 Hz, 1H), 1.53 (s, 3H), 1.35 (s, 3H), 1.31 (s, 3H), 1.22 (s, 3H); ^{13}C nmr ($CDCl_3$) δ: 209.9 (0), 208.9 (0), 134.0 (1), 132.2 (2), 130.5 (1), 130.2 (1), 111.6 (0), 107.7 (0), 77.7 (1), 74.7 (1), 74.2 (1), 48.7 (1), 36.7 (3), 36.5 (1), 34.9 (1), 34.5 (3), 29.0 (1), 28.2 (1), 26.3 (2), 25.3 (2), 24.8 (3), 24.3 (3), 21.9 (3), 21.9 (3), 20.6 (3).

*Diels-Alder reaction of **40a** with para-benzoquinone: (4aα,5α,5aα,8aα,9α,9aα)-(**77**) and (4aα,5α,5aβ,8aβ,9α,9aα)-4a,5,5a,8a,9,9a-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; ir ν_{max}: 2987, 2914, 1693, 1619, 1598, 1377, 1319, 1294, 1060 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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%); ^{13}C nmr ($CDCl_3$) δ: 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; ir ν_{max}: 2987, 2953, 1745, 1745, 1621, 1446, 1408, 1293, 1222, 1016 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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%); ^{13}C nmr ($CDCl_3$) δ: 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: (3aα,4β,4aβ,7aβ,8β,8aα)-(**79**) and (3aα,4β,4aα,7aα,8β,8aα)-3a,4,4a,7a,8,8a-hexahydro-6,6-dimethyl-2-oxo-4,8-ethenobenzo[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; ir ν_{max}: 2985, 1795, 1594, 1371, 1267, 1166, 1050 cm^{-1}; ^1H nmr ($CDCl_3$) 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%); ^{13}C nmr ($CDCl_3$) 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 $C_{11}H_{11}O_5$ (M^+ - CH_3): 223.0605; found: 223.0604. For **80:** mp 205 - 207°C; ir ν_{max}: 2987, 1771, 1594, 1536, 1462, 1375, 1207, 1172, 1053 cm^{-1}; ^1H nmr ($CDCl_3$) 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%;

1.27, 2%), 3.47 (6.16, 6%; 4.66, 3%; 4.19, 3%), 1.35 (6.16, 2%; 4.19, 1%), 1.27 (6.16, 0.7%; 4.19, 7%); ^{13}C nmr ($CDCl_3$) δ: 154.5 (0), 128.3 (1), 74.4 (1), 74.0 (1), 38.8 (1), 25.0 (3), 24.6 (3); ms: 239 (M^++1, 0.5), 223 (53), 179 (8), 136 (5), 118 (14), 107 (47), 99 (12), 94 (43), 91 (26), 85 (7), 78 (35), 77 (23), 67 (12), 58 (39), 45 (11), 43 (100). Exact Mass calcd. for $C_{11}H_{11}O_5$ (M^+ - CH_3): 223.0605; found: 223.0606.

*Diels-Alder reaction of **40a** with tetracyanoethylene: (3aα,4α,7α,7aα)-5,5,6,6-tetracyano-3a,4,7,7a-tetrahydro-2,2-dimethyl-1,3-dioxolo-4,7-ethenotri-cyclo[5.2.2.0^{3a,7a}]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 R_f = 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 ν_{max}: 2984, 2959, 2233, 1632, 1469, 1379, 1271, 1238, 1089 cm^{-1}; ^{1}H nmr ($CDCl_3$/CD_3COCD_3) 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%); ^{13}C nmr ($CDCl_3$/CD_3COCD_3) 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

(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 $C_{14}H_9N_2O_2$ (M^+ - CH_3): 265.0725; found: 265.0730. Anal. calcd. for $C_{15}H_{12}N_4O_2$: 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: (3aα,4α,4aβ,7aβ,8α,8aα)- (**82**) and (3aα,4β,4aα,7aα,8β,8aα)-4a,7a,8,8a-Tetrahydro-2,2-dimethyl-4,8-etheno-4H-1,3-dioxolo[4,5-f]isoindole-5,7-(3aH,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 ν_{max}: 3102, 2978, 2948, 1754, 1468, 1369, 1200, 1060

cm^{-1}; ^1H nmr ($CDCl_3$) data δ: 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 ($CDCl_3$) δ: 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), 65 (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 ν_{max}: 3257, 2960, 1748, 1701, 1464, 1377, 1358, 1198, 1066 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 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 ($CDCl_3$) δ: 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: (3aα,4β,5α,7β,7aα,8S*,9R*)-(**84**) and (3aα,4α,7α,7aα,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 ν_{max}: 2982, 2951, 2905, 1737, 1449, 1382, 1310, 1205, 1162, 1057 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 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 ($CDCl_3$) δ: 173.5 (0), 131.5 (1), 112.0 (0), 73.9 (1), 51.7 (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), (20), 77 (13), 65 (12), 58 (37), 45 (14), 43 (57). Exact Mass calcd. for $C_{15}H_{20}O_6$: 296.1258; found: 296.1258. For **85:** mp 196 - 197°C; ir ν_{max}: 2988, 2971, 1741, 1741, 1432, 1369, 1311, 1185 cm^{-1}; ^1H nmr ($CDCl_3$) 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%); ^{13}C nmr ($CDCl_3$) 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 $C_{15}H_{20}O_6$: 296.1258; found: 296.1249.

*Diels-Alder reaction of **40a** with ethyl propiolate: (3aα,4β,7β,7aα)-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 ν_{max}: 2962, 2907, 2935, 1712,

1633, 1597, 1458, 1379, 1260, 1221, 1159, 1056, 885 cm^{-1}; ^1H nmr ($CDCl_3$) 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 $C_{13}H_{15}O_4$ (M^+ - CH_3); 235.0969; found: 235.0957.

*Diels-Alder reaction of **40a** with N-methylmaleimide: (3aα,4α,4aβ,7aβ,8α,8aα)-(**87**) and (3aα,4β,4aα,7aα,8β,8aα)-4a,7a,8,8a-Tetrahydro-2,2,6-trimethyl--4,8-etheno-4H-1,3-dioxolo[4,5-f]isoindole-5,7-(3aH,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 ν_{max}: 2986, 2913, 1757, 1747, 1410, 1354, 1298, 1083 cm^{-1}; ^1H nmr ($CDCl_3$) 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 $C_{13}H_{14}NO_4$ (M^+ - CH_3): 248.0921; found 248.0913. For **88:** mp 188 - 190°C; ir ν_{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 $C_{13}H_{14}NO_4$ (M^+ - CH_3): 248.0922; found: 248.0922.

Diels-Alder dimerization of acetonide ***40a****: (3aβ,5aα,6α,6aα,9aα,10α,10aα, 10bβ)-* ***(89)*** *and (3aβ,5aα,6aβ,6α,9aβ,10α,10aα,10bβ)-3a.5a,6,6a,9a,10,10a,10b-octahydro-2,2,8,8-tetramethyl-3a,5a,6,10-*

*diethenonaphthol-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 ^{1}H 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 ν_{max}: 2986, 2929, 2911, 2884, 1456, 1364, 1278, 1236, 1161, 1046, 886 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 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, 2 H), 2.36 (br d, 2H), 2.23 (d, *J* = 9.0 Hz, 1H), 1.36 (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%); ^{13}C nmr ($CDCl_3$) δ: 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

$C_{18}H_{24}O_4$: 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%; 2.96, 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%); ^{13}C 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.

REFERENCE

1. R. Huisgen, R. Grashey, and J. Sauer in: The Chemistry of Alkenes, S. Patai, Ed., Interscience, London, 1964. p.739
2. W. Carruthers, Cycloaddition Reactions in Organic Synthesis, Tetrahedron Organic Chemistry Series, Pergamon, **8**, 1990.
3. J. Sauer. Angew. Chem. Int. Ed. Engl. **6**, 13 (1967), and references cited therein.
4. R. Huisgen. Angew. Chem. Int. Ed. Engl. **7**, 321 (1968).
5. A. S. Onishchenko. Diene Synthesis, translated from the Russian by the Israel Program for Scientific Translations, Jerusalem, 1964.
6. (a) M. Berthelot. Liebigs Ann. Chem. **142,** 251 (1867); (b) R.A. Firestone and J.S. Amato. Tetrahedron **26**, 5196 (1970).
7. S.N. Ege. Organic Chemistry, D.C. Heath, Lexington, MA, 1984. p.530.
8. F. Fringuelli and A. Taticchi. Dienes in the Diels-Alder Reaction, John Wiley and Sons, Inc., New York, 1991. p.1.
9. J. Sauer and R. Sustmann. Angew. Chem. Int. Ed. Engl. **19**, 779 (1980), and references cited therein.
10. K.N. Houk. Acc. Chem. Res. **8**, 361 (1975).
11. F.A. Carey and R.J. Sundberg. Advanced Organic Chemistry, Part A, Structure and Mechanism, Plenum, New York, 1990. p.117.

12. J. Breulet, T.J. Lee, and H.F. Schaefer. J. Am. Chem. Soc. **106**, 6250 (1984).

13. (a) W. Carruthers. Some Modern Methods of Organic Synthesis, Cambridge Univ. Press, 1971. p.115; (b) Y. Kobuke, T. Fueno, and J. Furukawa. J. Am. Chem. Soc. **92**, 6548 (1970).

14. K. Alder and G. Stein. Angew. Chem. **50**, 537 (1961).

15. R.B. Woodward and R. Hoffman. The Conservation of Orbital Symmetry, Verlag Chemie, Weinheim, and Academic Press, New York, 1970.

16. K.N. Houk. Tetrahedron Lett., 2621 (1970).

17. L. Salem. J. Am. Chem. Soc. **90**, 553 (1968).

18. P.V. Alston, R.M. Ottenbrite, and T. Cohen. J. Org. Chem. **43**, 1864 (1978).

19. K. Fukui. Acc. Chem. Res. **4**, 57 (1971).

20. T.H. Lowry and K.S. Richardson. Mechanism and Theory in Organic Chemistry, 3rd Ed., Harper and Row, New York, 1987.

21. A.J. Berson, Z. Hamlet, and W.A. Mueller. J. Am. Chem. Soc. **84**, 297 (1962).

22. A. Wassermann. J. Chem. Soc. 432 (1936).

23. S.D. Kahn, C.F. Pau, L.E. Overmann, and W.J. Hehre. J. Am. Chem. Soc. **108**, 7381 (1986).

24. W.C. Herndon and L.H. Hall. Tetrahedron Lett., 3095 (1967).

25. J. Feuer, W.C. Herndon and L.H. Hall. Tetrahedron **24**, 2576 (1968).

26. R. Sustmann. Tetrahedron Lett., 2721 (1971).

27. K.N. Houk. J. Am. Chem. Soc. **95**, 4092 (1973).

28. O. Eisenstein, J.M. Lefour, and N.T. Anh. Tetrahedron Lett., 969 (1971).

29. J.E. Baldwin. J. Am. Chem. Soc. **31**, 2441 (1966).

30. P. Yates and P. Eaton. J. Am. Chem. Soc. **82**, 4436 (1960).

31. A. Wassermann. J. Chem. Soc. (London), 618 (1942).

32. D.M. Birney and K.N. Houk. J. Am. Chem. Soc. **112**, 4127 (1990).

33. T. Tsuji, M. Ohkita, and S. Nishida. J. Org. Chem. **56**, 997 (1991), and references cited therein.

34. W. Oppolzer. Angew. Chem. Int. Ed. Engl. **23**, 876 (1984).

35. R.W. Frank, S.J. Argade, C.S. Subramanian, and D.M. Frechet. Tetrahedron Lett. **26**, 3187 (1985).

36. M.J. Fisher, W.J. Hehre, S.D. Kahn, and L.E. Overman. J. Am. Chem. Soc. **110**, 4625 (1988), and references cited therein.

37. D.J. Burnell and Z. Valenta. J. Chem. Soc. Chem. Commun., 1247 (1985).

38. R. Tripathy, R.W. Frank, and K.D. Onan. J. Am. Chem. Soc. **110**, 3257 (1988).

39. (a) A.S. Cieplak. J. Am. Chem. Soc. **103**, 4540 (1981); (b) A.S. Cieplak, B.D. Tait and C.R. Johnson. J. Am. Chem. Soc. **111**, 8447 (1989), and references cited therein; (c) W.S. Chung, N.J. Turro, S. Srivastava, H. Li,

and W.J. le Noble. J. Am. Chem. Soc. **110**, 7882 (1988).

40. S. Winstein, M. Shavatsky, C. Norton, and R.B. Woodward. J. Am. Chem. Soc. **77**, 4183 (1955).

41. V.A. Mironov, T.M. Fadeeva, and A.A. Akhrem. Dokl. Acad. Nauk SSR **174**, 852 (1967).

42. J.B. Macaulay, and A.G. Fallis. J. Am. Chem. Soc. **110**, 4074 (1988).

43. M. Ishida, Y. Beniya, S. Inagaki and S. Kato. J. Am. Chem. Soc. **112**, 8980 (1990).

44. A.M. Naperstkow, J.B. Macaulay, M.J. Newlands, and A.G. Fallis. Tetrahedron Lett. **30**, 5077 (1989).

45. R. Breslow, J.M. Hoffmann Jr., and C. Perchonok. Tetrahedron Lett., 3723 (1973).

46. M. Franck-Newman and M. Sedrati. Tetrahedron Lett. **24**, 1391 (1983).

47. M.A. McLinton and V. Sik. J. Chem. Soc., Perkin Trans. 1, 1891 (1992).

48. P.V. Alston and R.W. Ottenbrite. J. Org. Chem. **40**, 1111 (1975).

49. J.R. Gillard and D.J.Burnell. J. Chem. Soc., Chem. Commun., 1439 (1989).

50. O. Werbitzky, K. Klier, and H. Felber. Liebigs Ann. Chem., 267 (1990).

51. (a) I.C. Cotterill, S.M. Roberts, and J.O. Williams. J. Chem. Soc., Chem. Commun., 1628 (1988).

52. T. Hudlicky, and J.D. Price. Synlett, 159 (1990).

53. C.A. Pittol, R.J. Pryce, S.M. Roberts, G. Ryback, V. Sik, and J.O. Williams. J. Chem. Soc., Perkin trans. 1, 1160 (1989).

54. M.F. Mahon, K. Molloy, C.A. Pittol, R.J. Pryce, S.M. Roberts, G. Ryback, V. Sik, J.O. Williams and J.A. Winders. J. Chem. Soc. Perkin Trans. 1, 1255 (1991).

55. R. Gleiter and D. Ginsburg. Pure Appl. Chem. **51**, 1301 (1979).

56. D. Ginsburg. Tetrahedron **39**, 2095 (1983), and references cited therein.

57. J.B. Macaulay and A.G. Fallis. J. Am. Chem. Soc. **112**, 1136 (1990).

58. D.J. Burnell, H.B. Goodbrand, S.M. Kaiser, and Z. Valenta. Can. J. Chem. **65**, 154 (1987), and references cited therein.

59. D.J. Burnell and Z. Valenta. Can. J. Chem. **69**, 179 (1991).

60. F.K. Brown, K.N. Houk, D.J. Burnell, and Z. Valenta. J. Org. Chem. **52**, 3050 (1987).

61. S. Inagaki, H. Fujimoto and K. Fukui. J. Am. Chem. Soc. **98**, 4054 (1976).

62. S.D. Kahn and W.J. Hehre. J. Am. Chem. Soc **109**, 663 (1987).

63. N.T. Anh. Tetrahedron **29**, 3227 (1973).

64. R. Gleiter and L.A. Paquette. Acc. Chem. Res. **16**, 328 (1983).

65. H. Hopff and C.W. Rautenstrauch. Chem. Abs. **36**, 1046 (1942).

66. J. Sauer. Angew. Chem. Int. Ed. Engl. **6**, 16 (1967).

67. A. Lubbineau and Y. Queneau. J. Org. Chem. **52**, 1001 (1987).

68. D.C. Rideout and R. Breslow. J. Am. Chem. Soc. **102**, 7816 (1980).

69, P.A. Grieco, P. Garner, and H. Zhen-min. Tetrahedron Lett. **24**, 1897 (1983).

70. R. Breslow and C.J. Rizzo. J. Am. Chem. Soc. **113**, 4340 (1991).

71. W. Blokzijl, M.J. Blandamer, and J.B.F.N. Engberts. J. Am. Chem. Soc. **113**, 4241 (1991).

72. D.A. Jaegar, H. Shinozaki, and P. Goodson. J. Org. Chem. **56**, 2482 (1991).

73. P.A. Grieco, J.J. Numes, and M.D. Gaul. J. Am. Chem. Soc. **112**, 4595 (1990).

74. M.A. Forman and W.P. Dailey. J. Am. Chem. Soc. **113**, 2761 (1991).

75. R.A. Silva. Chem. Eng. News, **21**, 2 (1992).

76. A.J. Birch, A.L. Hinde, and L. Random. J. Am. Chem. Soc. **102**, 2370 (1980).

77. J.P. Wibaut and F.A. Hauk. Recl. Trav. Chim. Pays-Bas **67**, 91 (1948).

78. N.C. Yang, M.-J. Chen and P. Chen. J. Am. Chem. Soc. **106**, 7310 (1984).

79. J.E. Taylor, D. Williams, K. Edwards, D. Otonnaa, and D. Samanich. Can. J. Chem. **62**, 11 (1984).

80. A. Merz. Angew. Chem. Int. Ed. Engl. **12**, 846 (1973).

81. E. Vogel and H. Gunther. Angew. Chem. Int. Ed. Engl. **6**, 385 (1967).

82. D.T. Gibson, B. Gschwendt, W.K. Yeh, and V.M. Kobal. Biochemistry **12**,

1520 (1978).

83. H.M. Teeter and E.W. Bell. Org. Syn. Coll. **4**, 125 (1988).

84. V.M. Kobal, D.T. Gibson, R.E. Davis, and A. Garza. J. Am. Chem. Soc. **95**, 4421 (1973).

85. J.R. Gillard, M.J. Newlands, J.N. Bridson, and D.J. Burnell. Can. J. Chem. **69**, 1337 (1991).

86. N.T. Anh. Tetrahedron **29**, 3227 (1973).

87. S.D. Kahn and W.J. Hehre. J. Am. Chem. Soc. **109**, 663 (1987).

88. D.J. Burnell, C.C. Pye, and R.A. Poirier. Unpublished results.

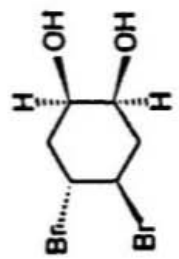
89. R.C. Cookson, S.S.H. Gilani, and I.D.R. Stevens. J. Am. Chem. Soc. 1905 (1967).

90. D.R. Boyd, M.R.J. Dorrity, M.V. Hand, J.F. Malone, N.D. Sharma, H. Dalton, D.J. Gray, and G.N. Sheldrake. J. Am. Chem. Soc. **113**, 666 (1991).

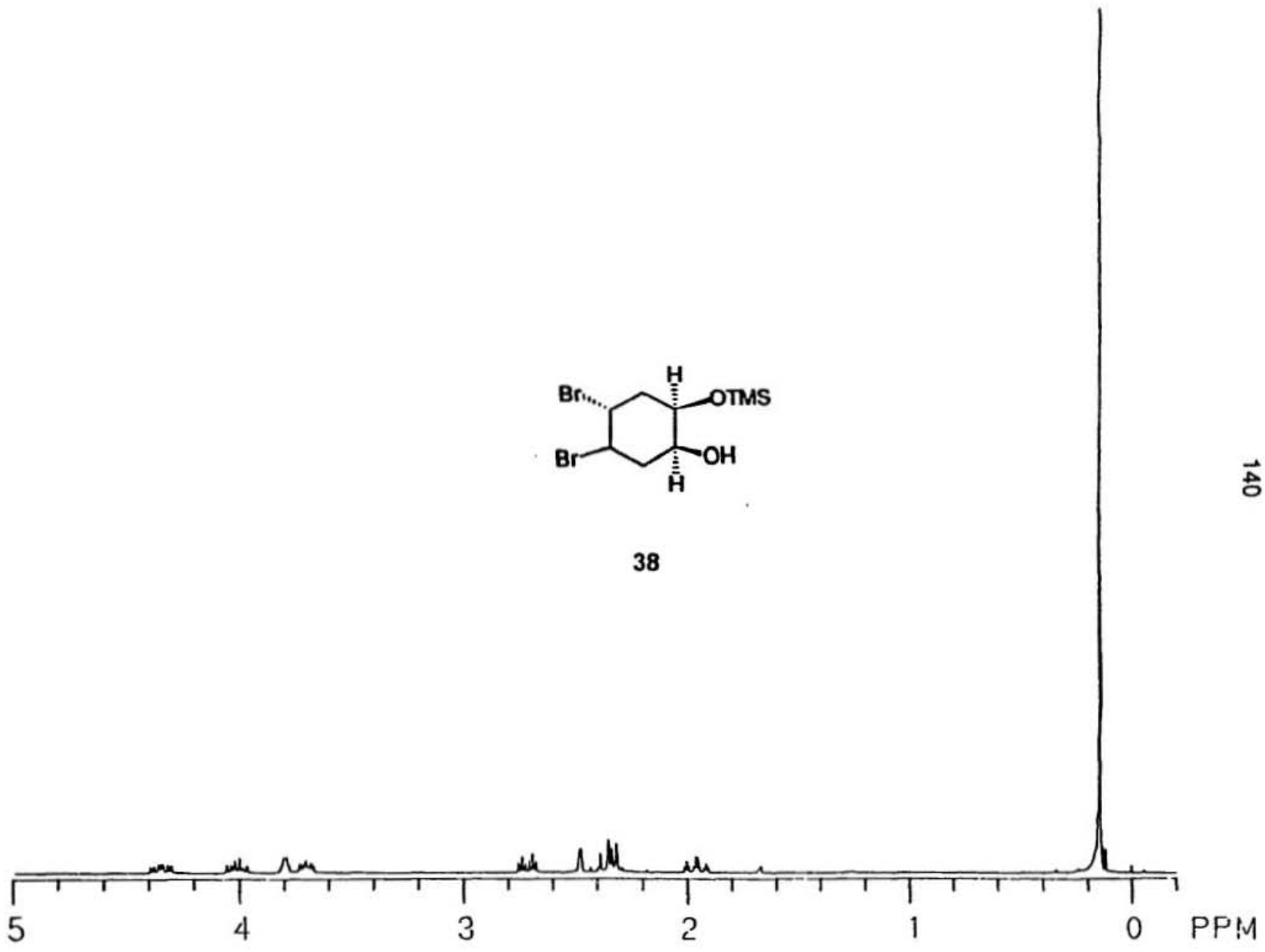
91 J.R. Gillard and D.J. Burnell. Can. J. Chem. **70**, 1296 (1992).

Appendix

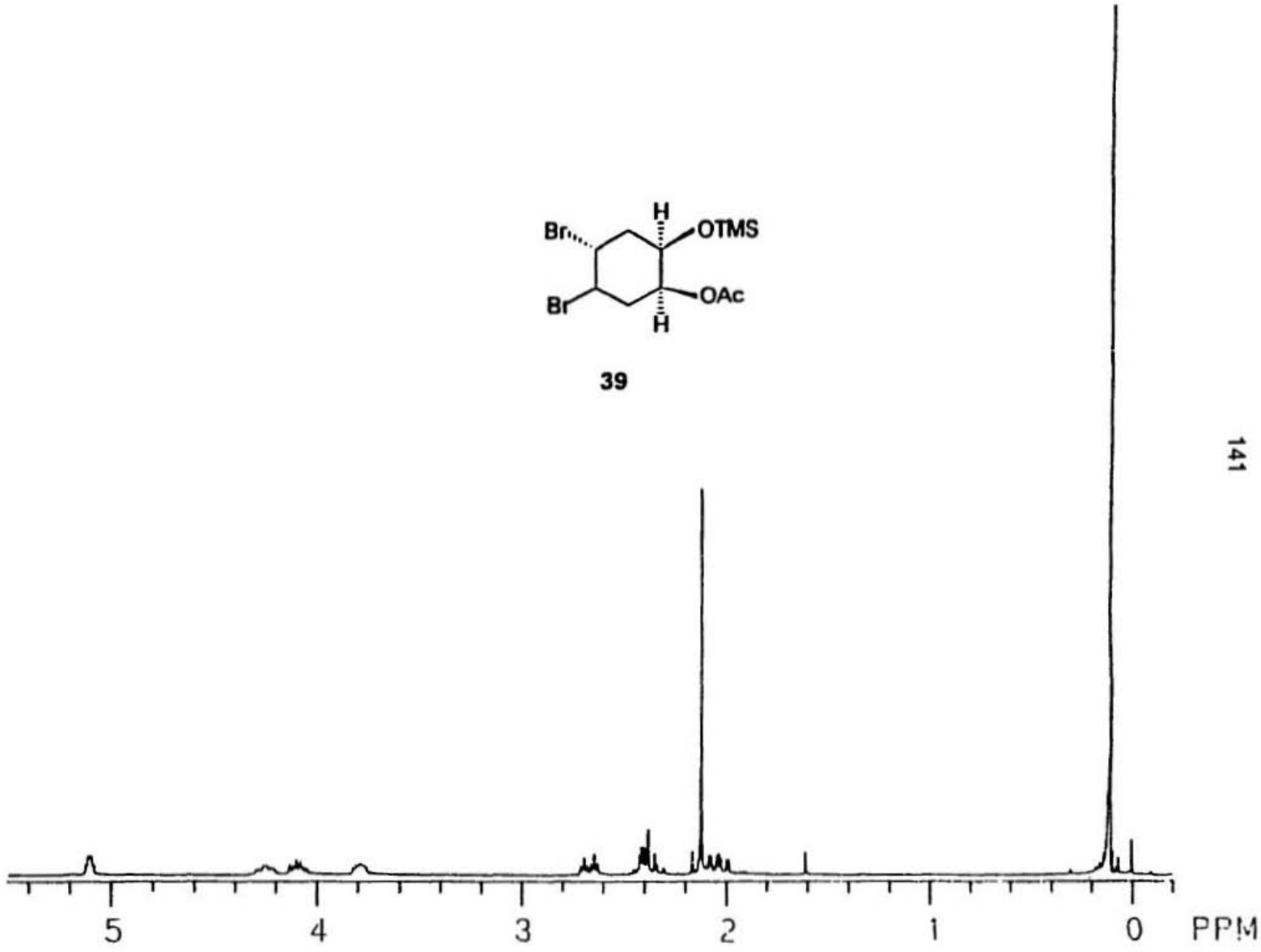
The selected ^1H nmr and the n.O.e.d spectra of dienes and adducts were arranged according to the order in which they appear in the text.



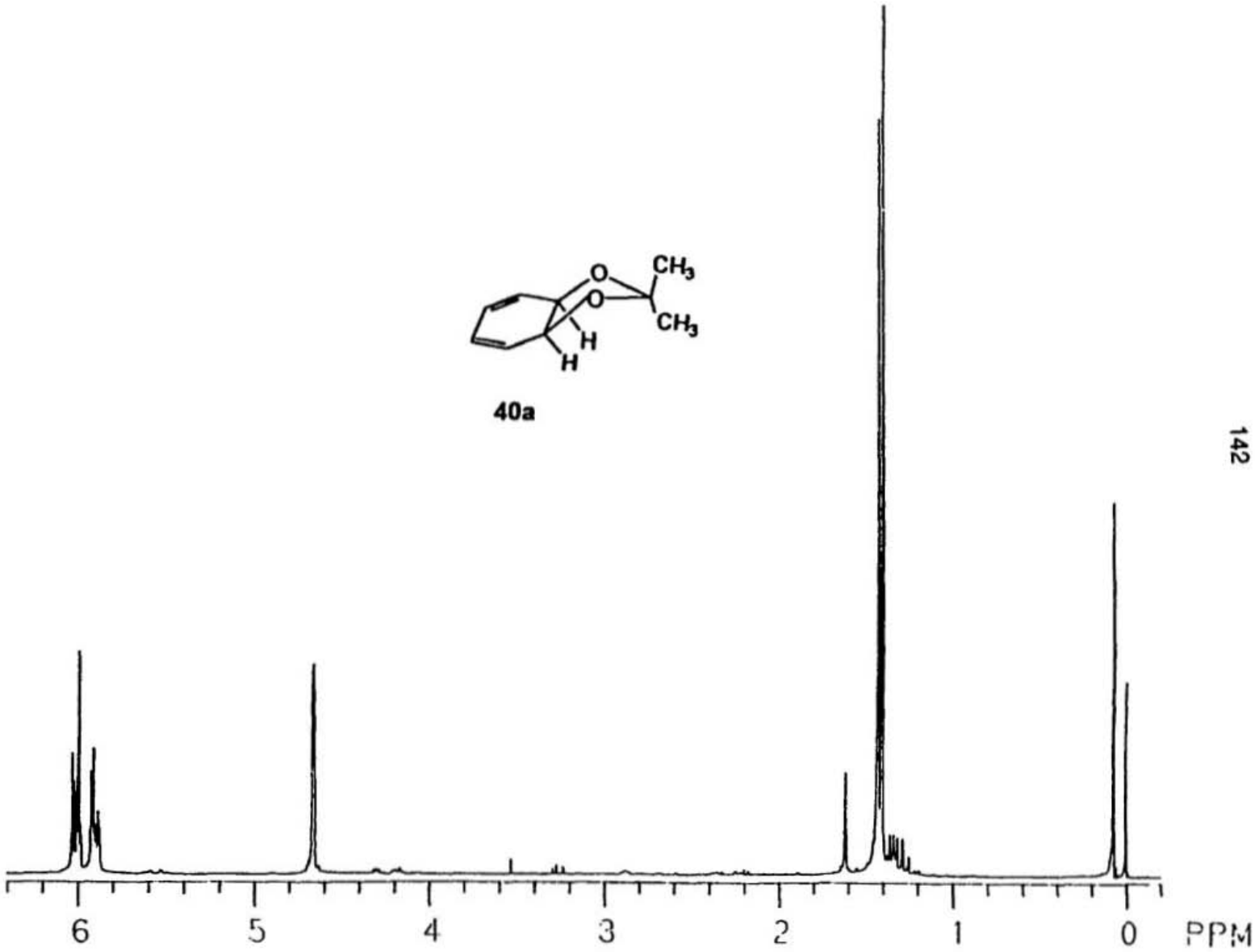
35



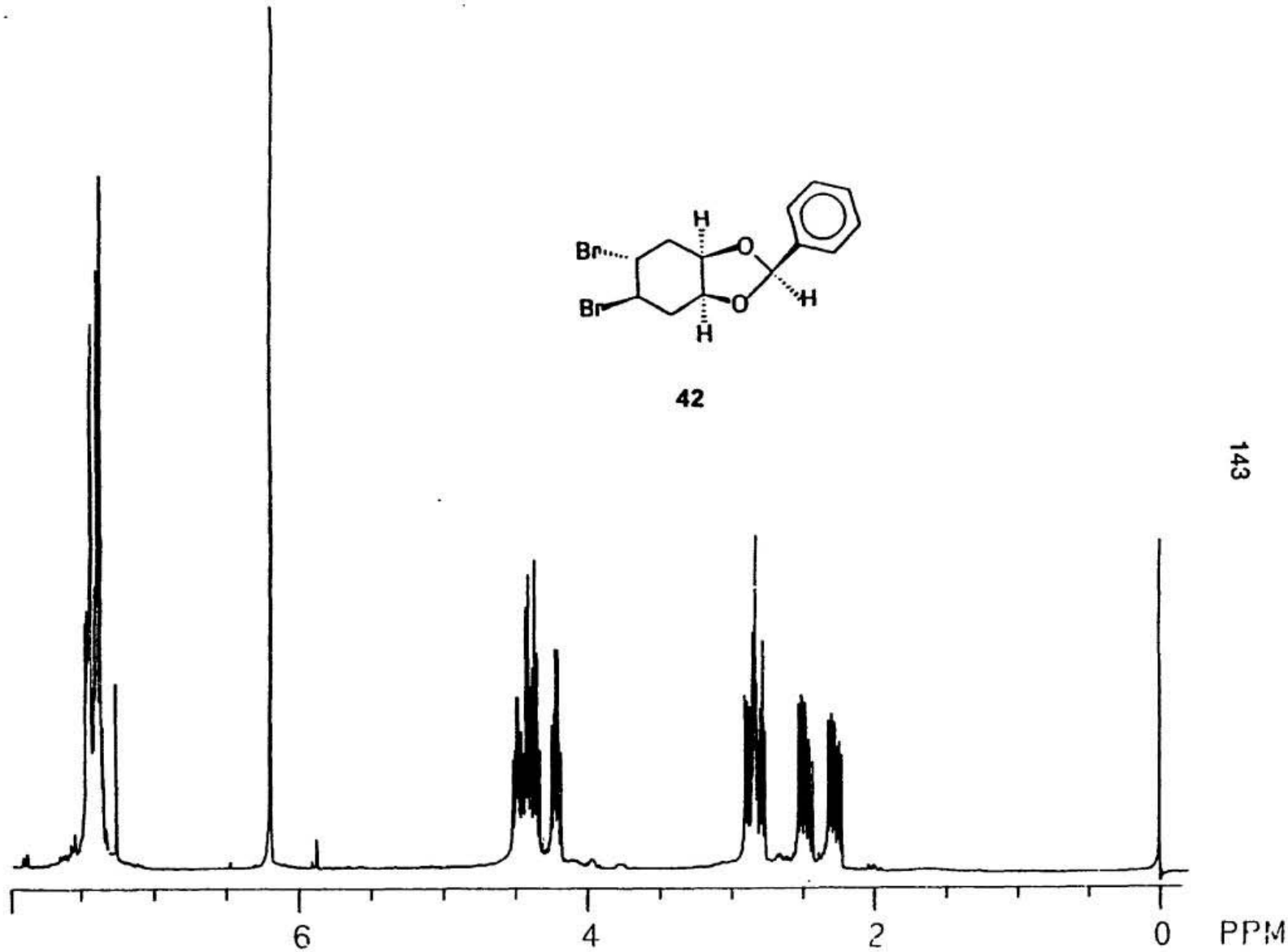
38



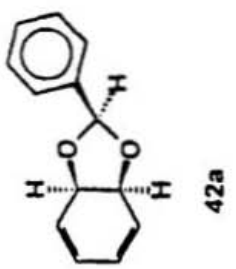
39



40a



42



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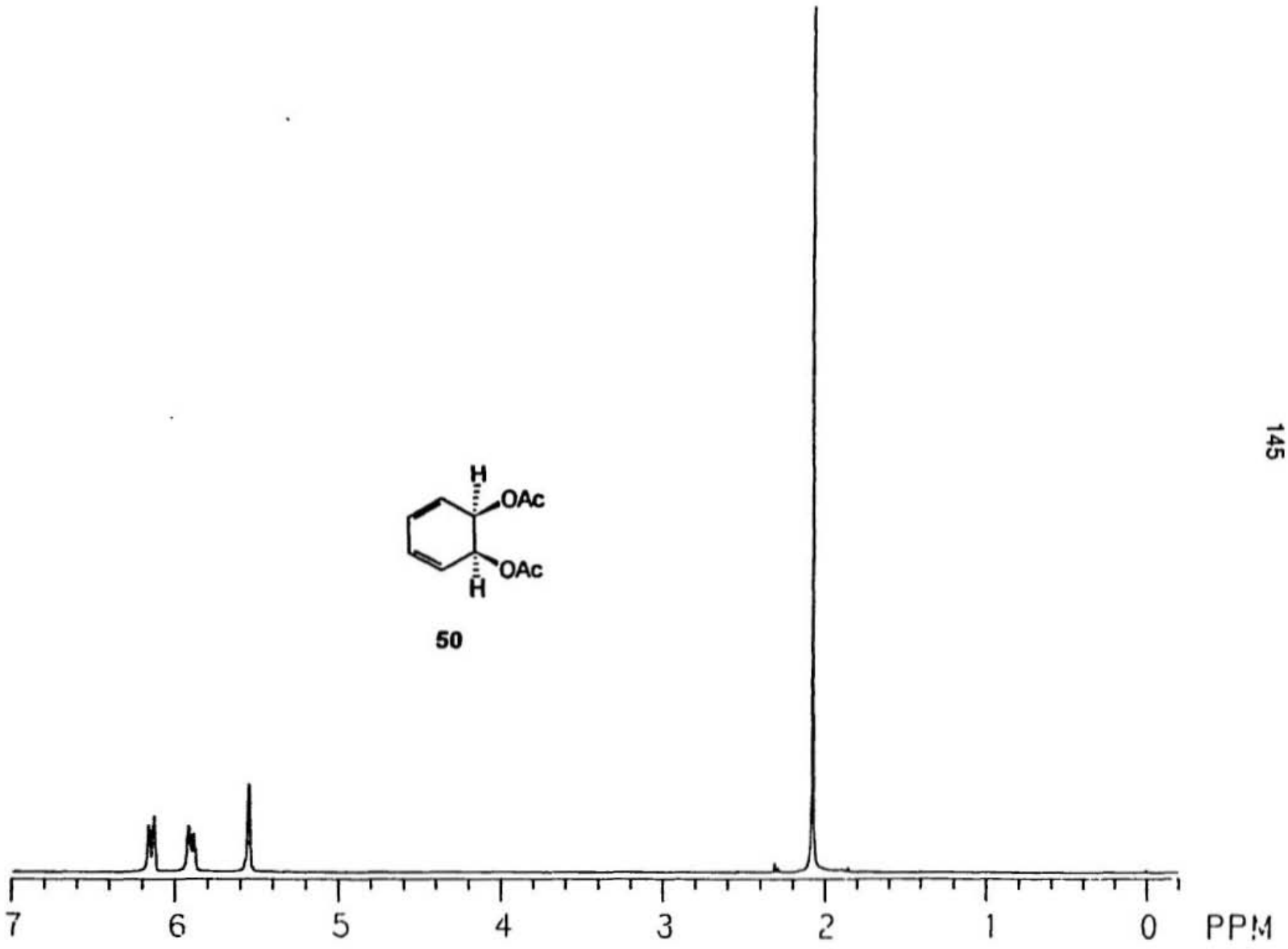

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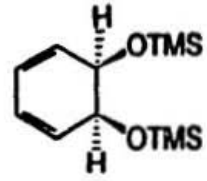

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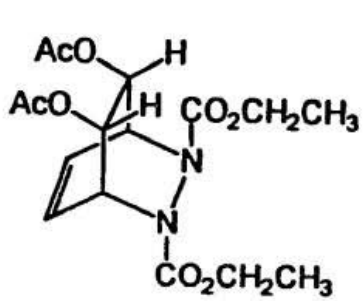

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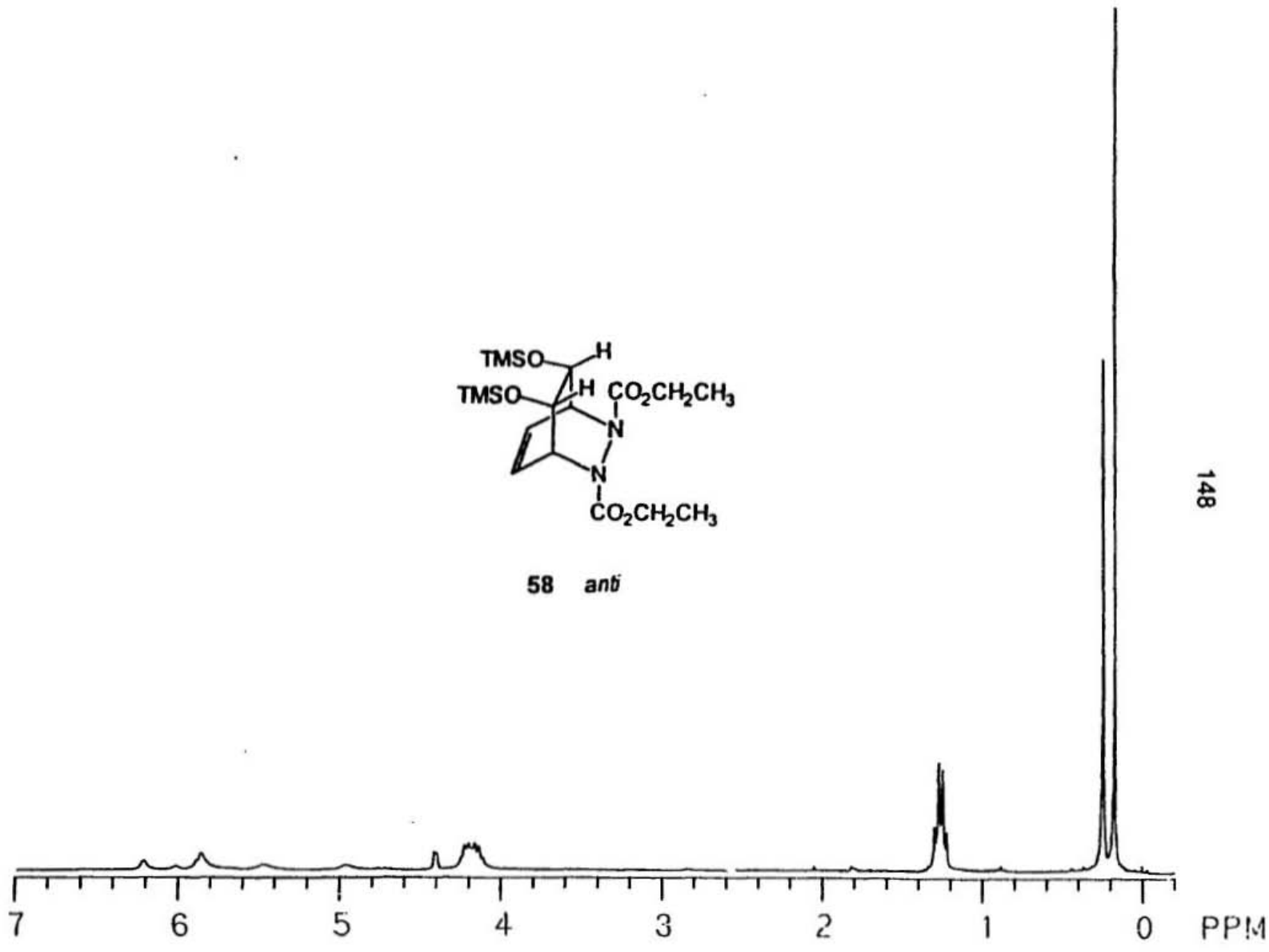
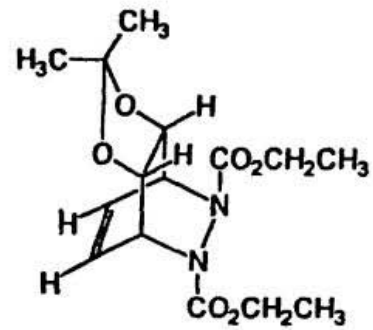


58 ***anti***



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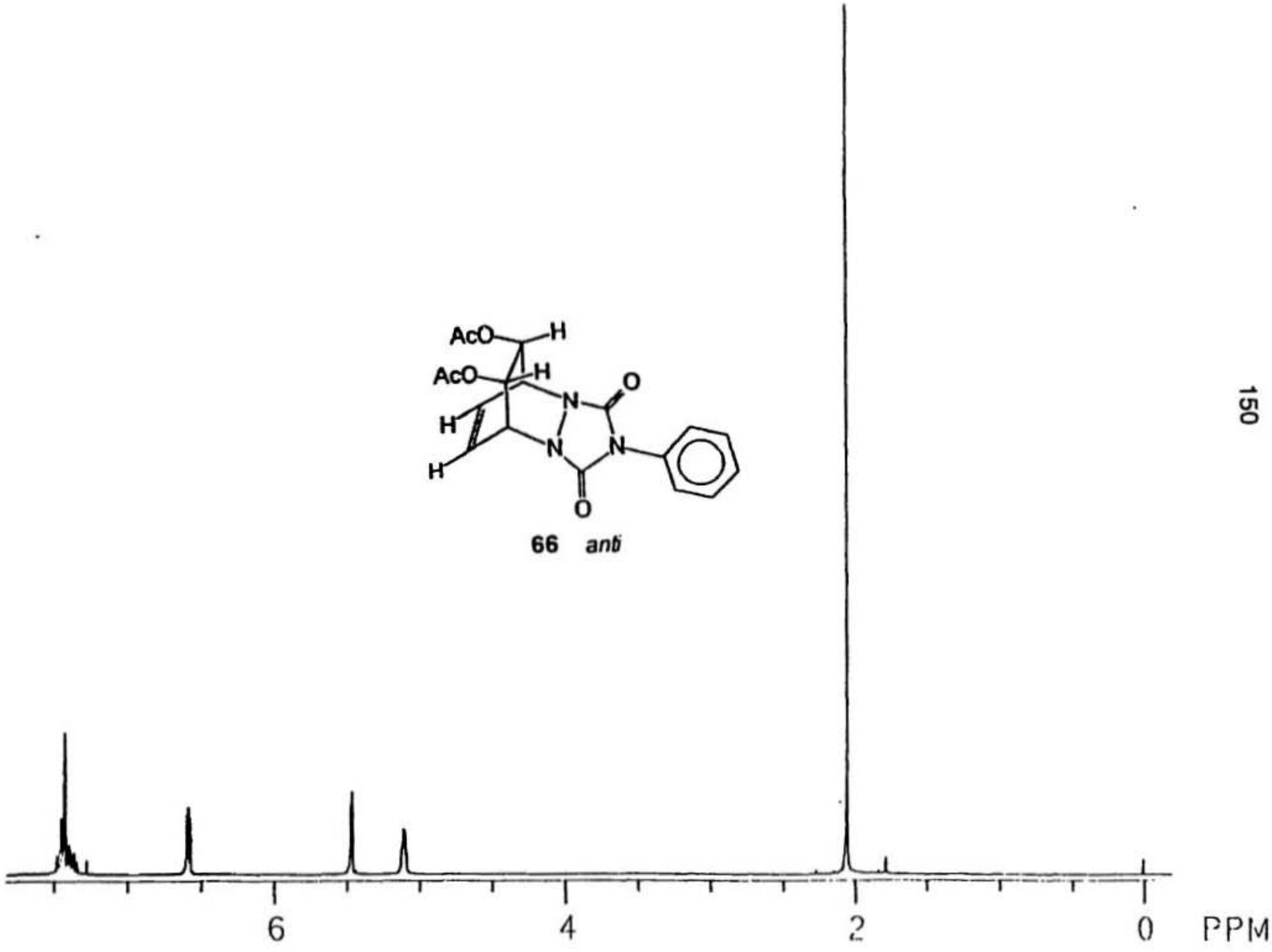
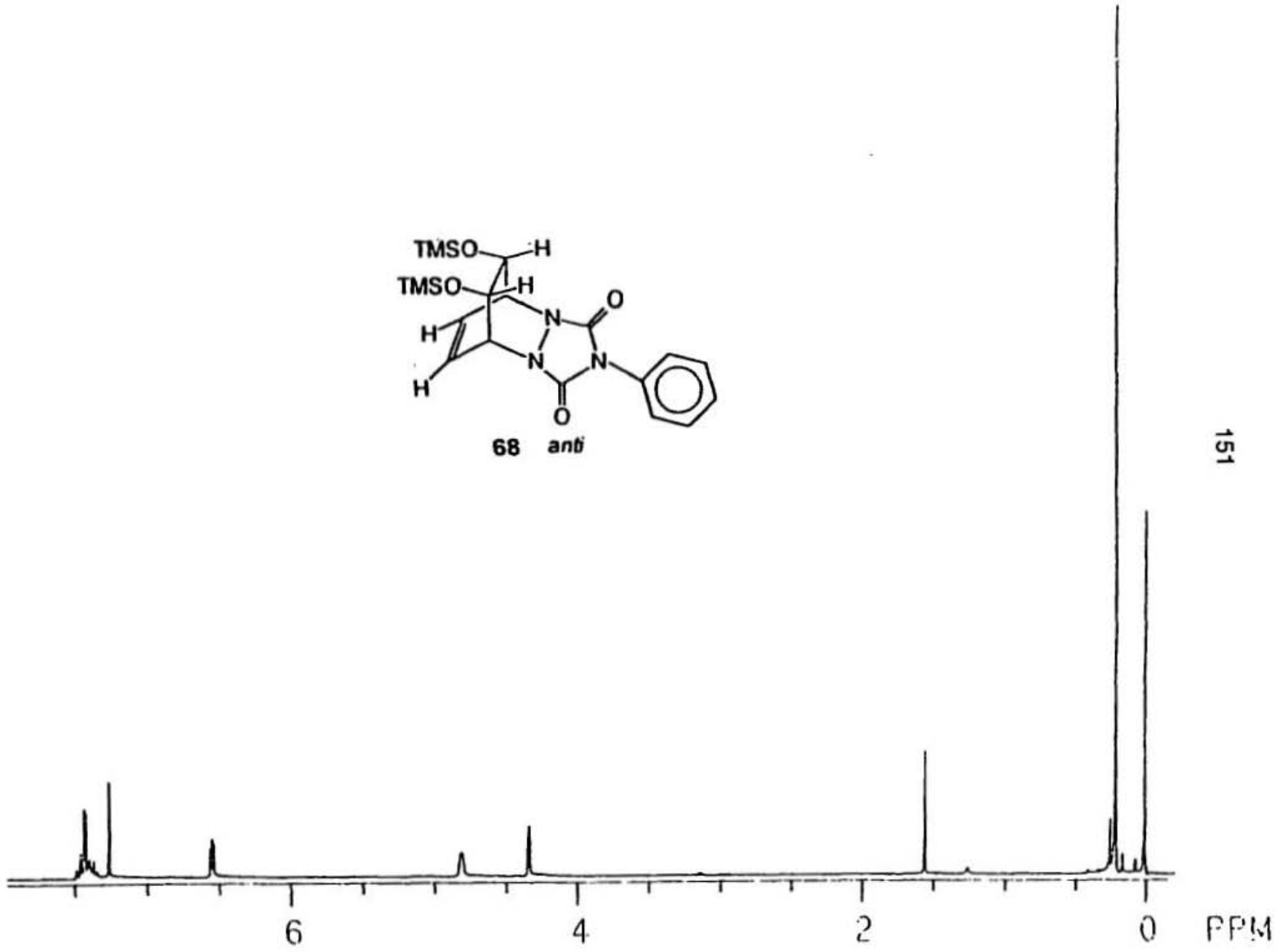


66 *anti*



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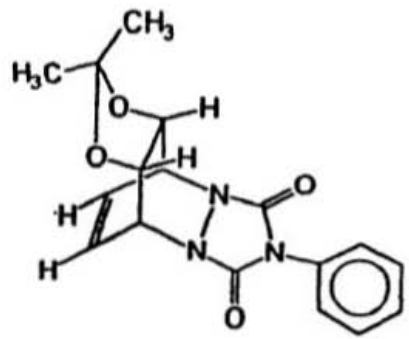

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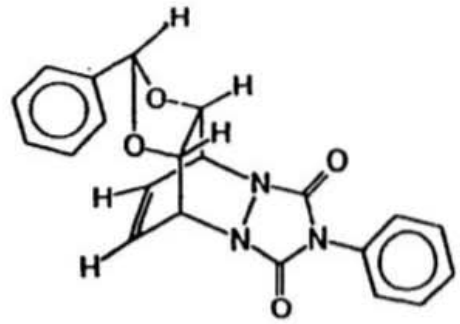

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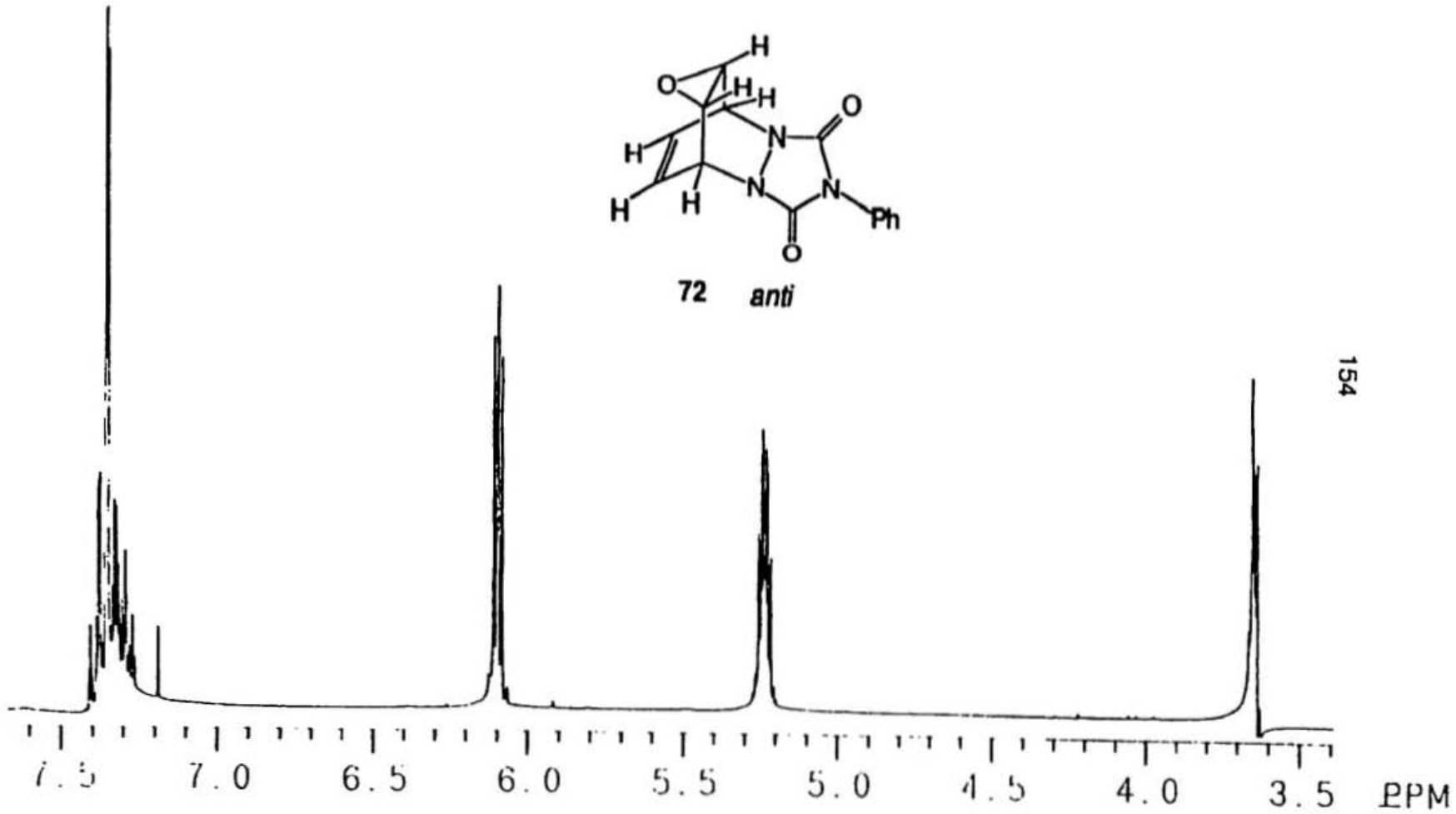

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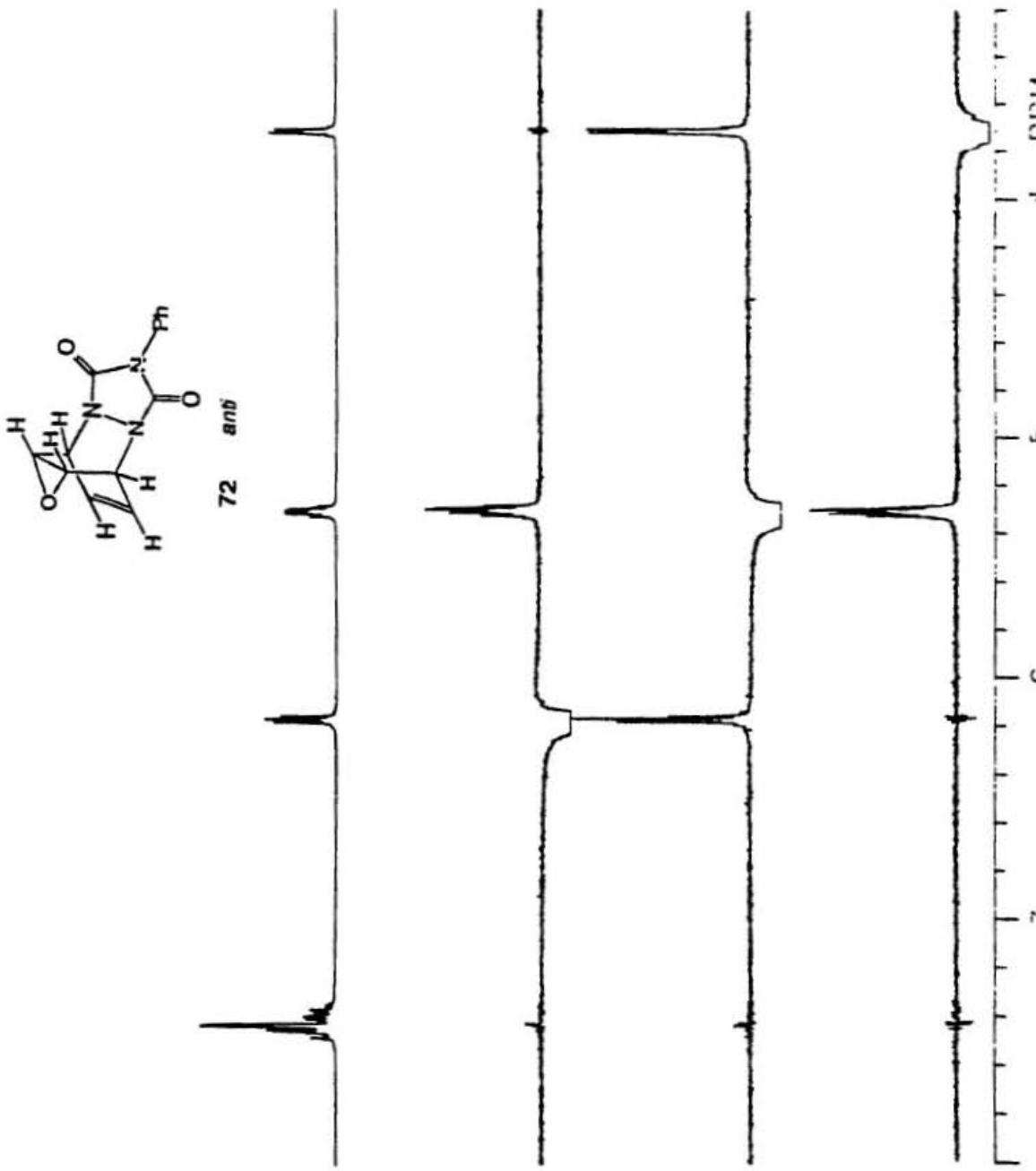
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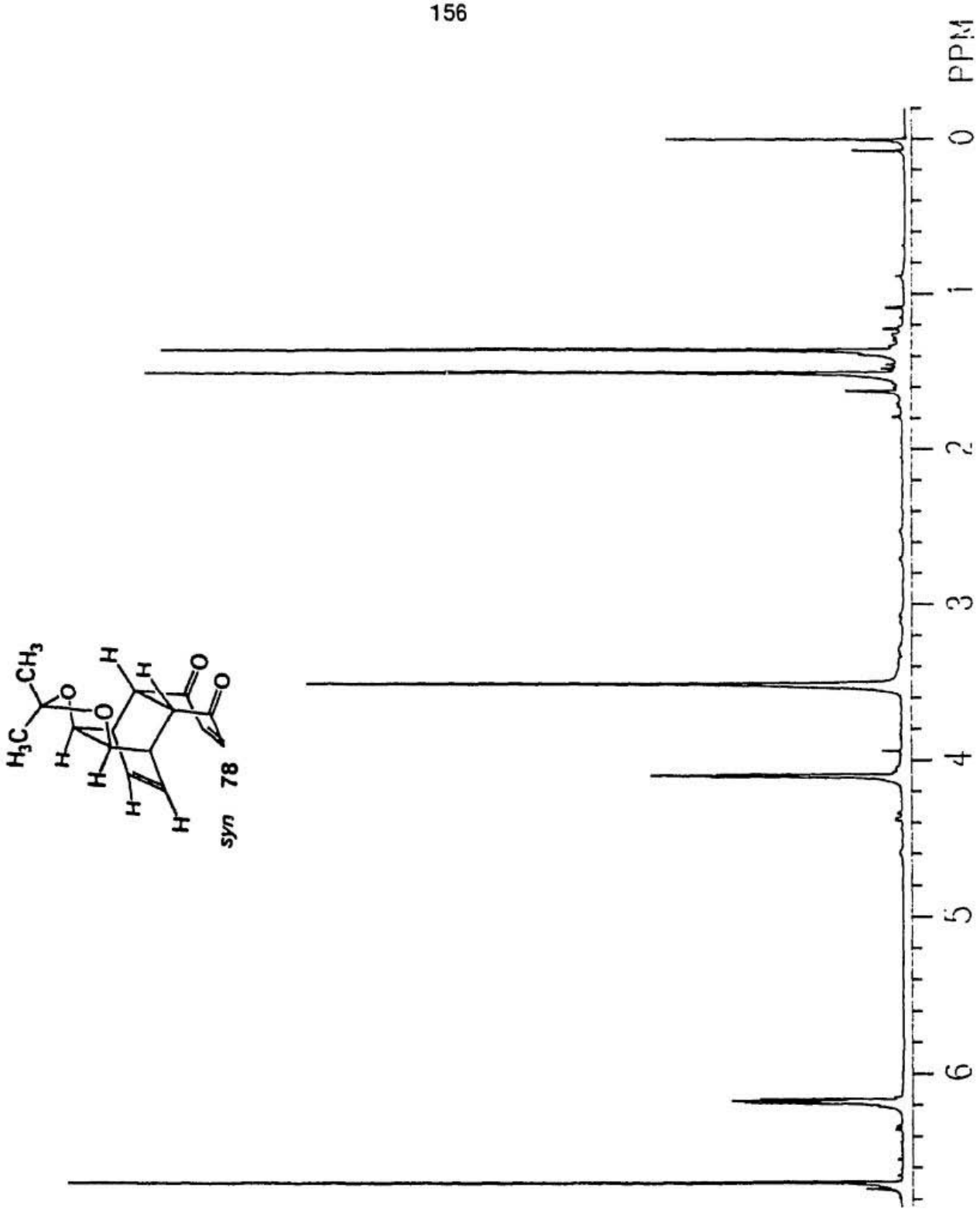
7
6
5
4


PPM
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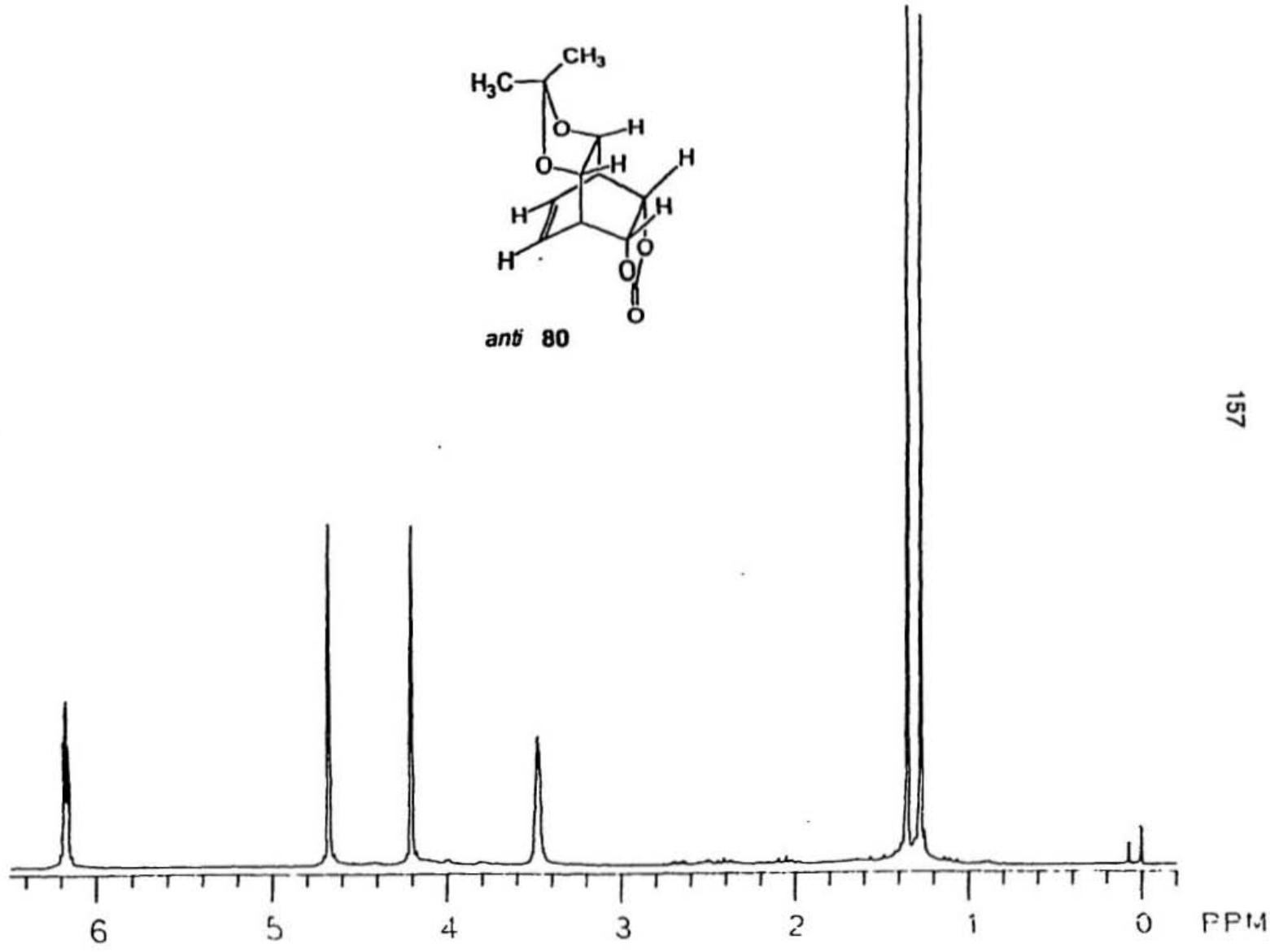
6
H3C
CH3
O
O
H
H
H
H
H
O
O
syn 78



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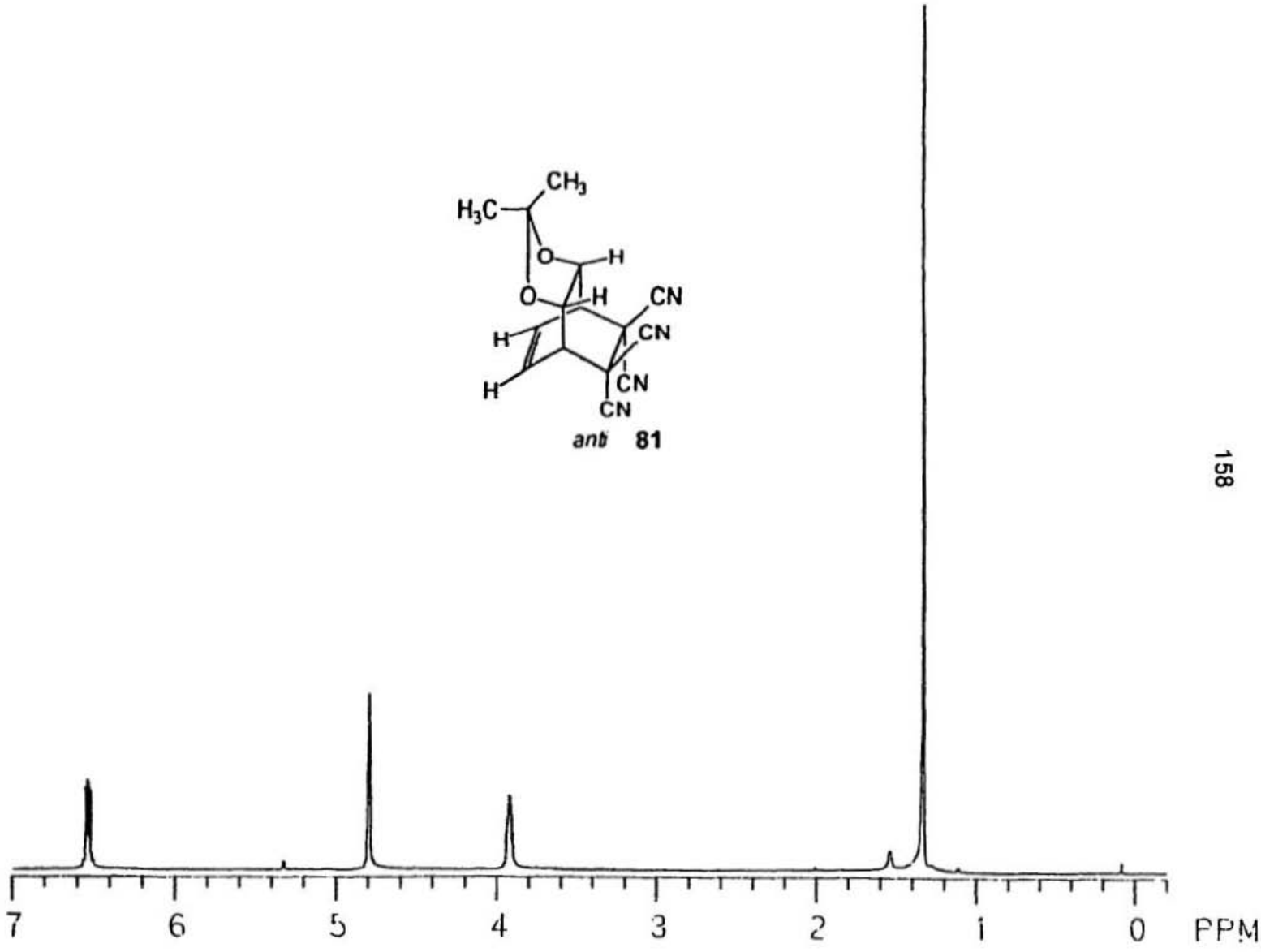
CH3
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CN
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CN
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5
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1
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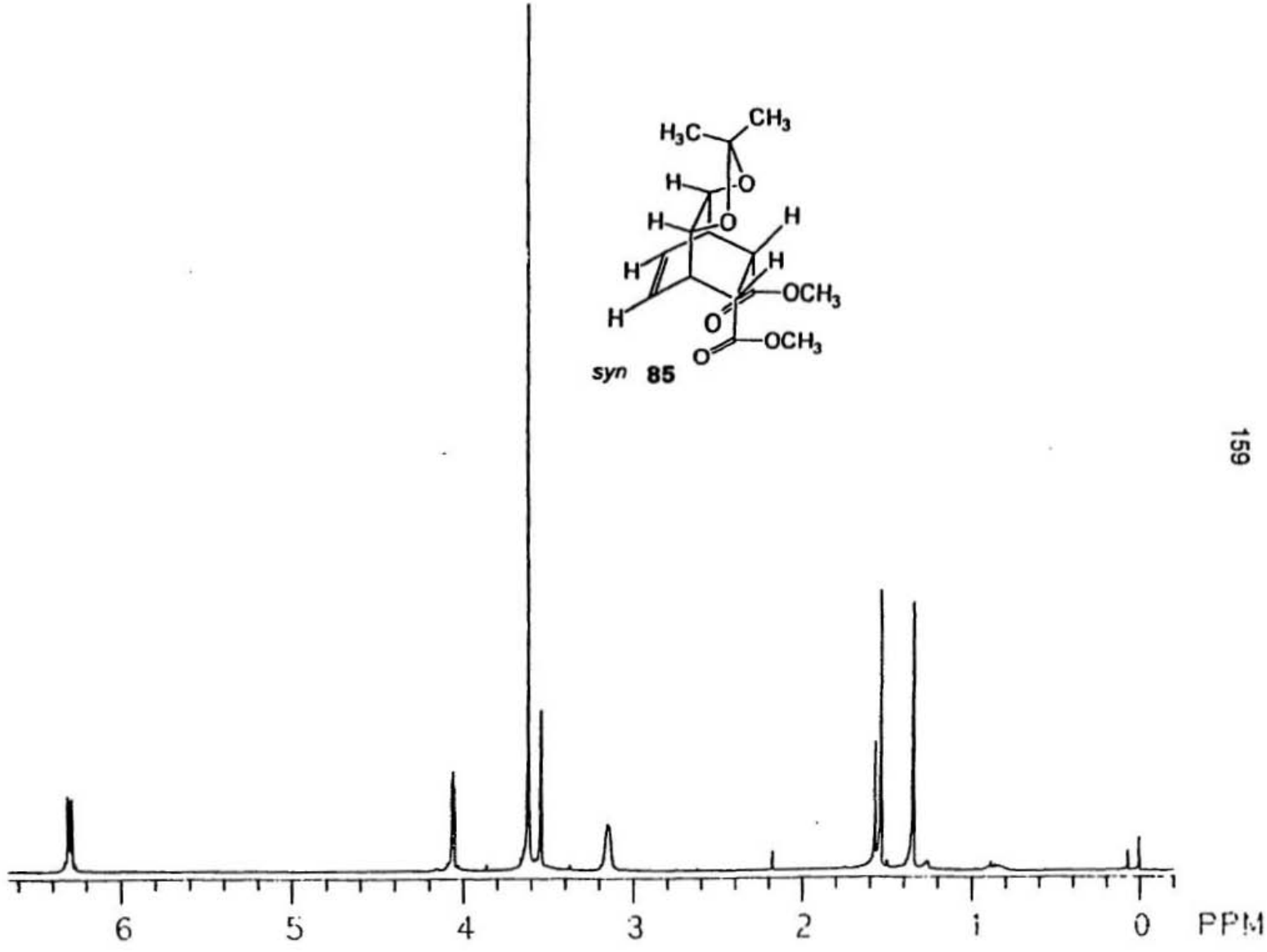
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syn 85
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2
1
0
PPM