STERIC VERSUS STEREOELECTRONIC CONTROL OF THE FACIAL SELECTIVITY IN THE DIELS-ALDER REACTION

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Steric Versus Stereoelectronic Control of the Facial Selectivity in the Diels-Alder Reaction

by

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Abstract

The Diels-Alder reactions of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene and a number of its derivatives, 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, 5-methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, 5-chloro-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, 5-bromo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene and 5-iodo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene were studied. Additions to these dienes with a number of dienophiles, such as *N*-phenylmaleimide, 1,4-naphthoquinone, 1,1,2,2- tetracyanoethene, dimethyl acetylenedicarboxylate and 4-phenyl-1,2,4-triazoline-3,5-dione were studied. The results suggest that the facial selectivity of 5-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes is controlled primarily by steric interactions between the diene and dienophile rather than some stereoelectronic factor. The facial selectivity of 5-alkyl-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes demonstrated only a slight dependence upon the dienophile used. Differences in facial selectivity for the 5-halo-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes when different dienophiles were employed have been attributed to electrostatic repulsions between the lone pair electrons of the C-5 substituent and lone pairs on the attacking dienophile. It was observed that dienes such as 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene and 5-methoxymethyl-1,2,3,4,5- pentamethyl-1,3-cyclopentadiene showed selectivity that demonstrated a large dependence upon the conformation of the substituents on the diene.

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Glossary of abbreviations

FMO	frontier molecular orbital (theory)
FT	Fourier transform
HET-CORR	^{1}H-^{13}C heteronuclear correlation (spectroscopy)
HOMO	highest occupied molecular orbital
ir	infrared (spectroscopy)
LUMO	lowest unoccupied molecular orbital
MO	molecular orbital
MNDO	moderate neglect of differential overlap
mp	melting point
ms	mass spectrometry
N-HOMO	next-highest occupied molecular orbital
nmr	nuclear magnetic resonance (spectroscopy)
nOe	nuclear Overhauser effect
TLC	thin layer chromatography
RES	reactivity enhanced selectivity (theory)
rt	room temperature
UV	ultraviolet

Introduction

Since the discovery of the Diels-Alder reaction[1] much effort has gone into its investigation. An early emphasis in the study of the reaction concentrated upon the debate as to whether the cycloaddition reaction proceeds in a concerted or in a stepwise fashion. The experimental and computational evidence for a concerted $4\pi + 2\pi$ cycloaddition mechanism now seems unequivocal.[2] In the past few decades, however, the emphasis of mechanistic research in this field has shifted more toward studies into the π-facial selectivity of various substituted diene and dienophile systems and the closely related area of chiral induction. Although many research groups have studied the Diels-Alder reaction and have attempted to explain the forces governing the facial selectivity, a consensus regarding this aspect of the mechanism has not been forthcoming. In fact, after almost 70 years, the chemical community is still unable to agree on what is causing the facial selectivity in Diels-Alder reactions. In some cases the major adduct of the reaction is opposite to that which might be reasonably predicted by a perfunctory examination of the starting materials.

To understand the dilemma with which researchers in this field are dealing, a more in-depth look at the Diels-Alder reaction and the various theories concerning facial selectivity in the reaction are necessary.

The simplest Diels-Alder reaction would be between an unsubstituted diene, 1,3-butadiene, and the simplest dienophile, ethene, to form cyclohexene (Scheme 1). The

Scheme 1. Diels-Alder reaction between 1,3-butadiene and ethene to form cyclohexene

synthetic utility of the reaction would lie in the fact that two carbon-carbon bonds are formed in one step, but the total synthesis of complex organic molecules would require the use of substituted dienes and dienophiles. Their combination could lead to many possible outcomes. However, several factors are now fairly well understood, and this allows reasonably accurate predictions to be made.

The reaction of an unsymmetrical diene such as 1-methoxy-1,3-pentadiene, an electron-rich diene, and propenal could lead to two different regioisomers, **1** and **2**.[3] It is generally held that regioselectivity in Diels-Alder reactions is not directed significantly by steric factors, but it is influenced primarily by interactions between valence orbitals on the diene and the dienophile. Steric arguments would suggest that the dominant product of the reaction would be **1** rather than **2**. In truth, **2** is by far the dominant reaction product. The most frequently used explanation for this involves the use of frontier molecular orbital (FMO) theory. The magnitude and sign of orbital components for each of the reacting centres on both the diene and dienophile are determined, and regioselectivity is then predicted based upon optimal matching of these components (See Figure 1, in which the light lobes represent positive orbital components, shaded lobes represent negative orbital components, and the sizes of the lobes are proportional to the magnitudes of the orbital

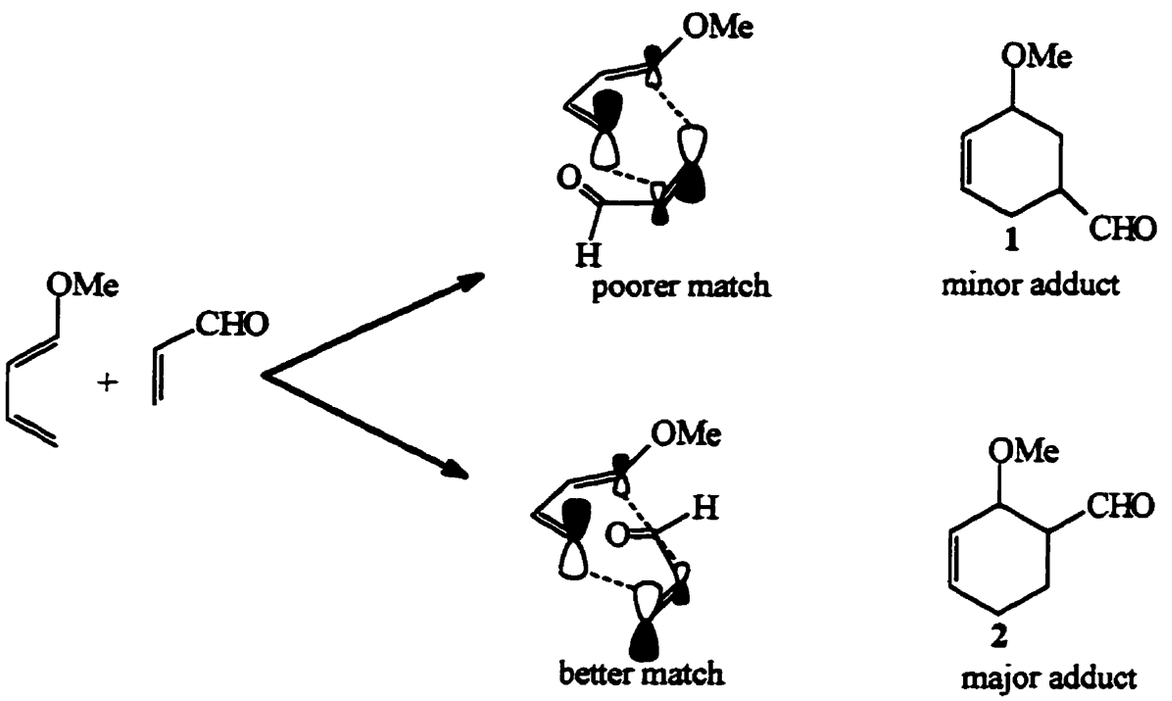


Figure 1. Frontier orbital control of the regiochemistry for the reaction of 1-methoxy-1,3-butadiene and propenal

components.) The FMO approach appears to be effective only for simpler cases, and it is increasingly inaccurate as the complexity of the substitution pattern increases.

Kahn and Hehre[4] proposed an alternative method for predicting regioselectivity by "mapping" the diene and dienophile surfaces by computational methods, to determine the nucleophilicity and electrophilicity of the various reacting centres. They contended that this was more effective in predicting the selectivity for many more cases than was the FMO approach, but acceptance of their theory does not appear to be widespread.

For facial selectivity studies, however, the problem of different regiochemical outcomes of reactions can be circumvented by the use of symmetrical dienophiles, such as

N-phenylmaleimide, maleic anhydride, and dimethyl acetylenedicarboxylate. Nevertheless, even though regioisomeric products are not possible from the reaction of 1,3-cyclopentadiene and maleic anhydride, two stereoisomeric products can arise from what is known as *endo/exo* selectivity. As the dienophile approaches the diene it may do so in two different ways, which lead to stereochemically distinct products. In one type of approach, the bulk of the dienophile is situated over the diene's π-system. This type of attack is known as *endo* addition, and it leads to the product that has the carbonyl groups pointing away from the methylene bridge, as in **3**. In the other mode of attack the bulk of the dienophile is pointing away from the approaching diene. This type of addition is known as *exo* addition, and it leads to the product that has the carbonyls close to the methylene bridge, as in **4** (Figure 2).

The more common symmetrical dienophiles including *N*-phenylmaleimide, maleic anhydride and 1,4-naphthoquinone, show very high *endo* selectivity in their Diels-Alder reactions due to favourable secondary orbital overlap between the carbonyl carbons of the dienophile and the innermost carbons of the diene.[5,6] As illustrated in Figure 3, this secondary orbital overlap can stabilize the *endo* transition state, but no such stabilizing interaction can be present in the *exo* transition state. The explanation also accounts for the poorer *endo/exo* selectivity observed for unactivated or singly activated dienophiles such as methyl propenoate, chloroacrylonitrile, and propenal.[7]

Facial selectivity manifests itself in the Diels-Alder reaction when one face of the diene or dienophile is different from the other, i.e., the diene and/or the dienophile is

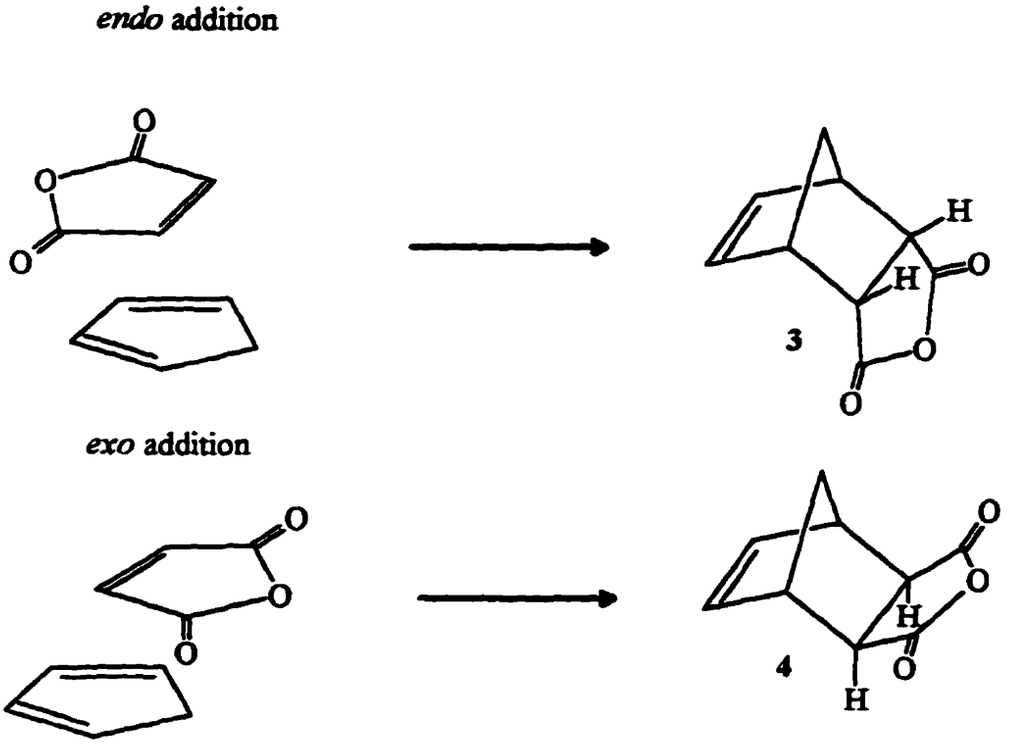


Figure 2. *Endo* and *exo* attack modes for the reaction of 1,3-cyclopentadiene and maleic anhydride

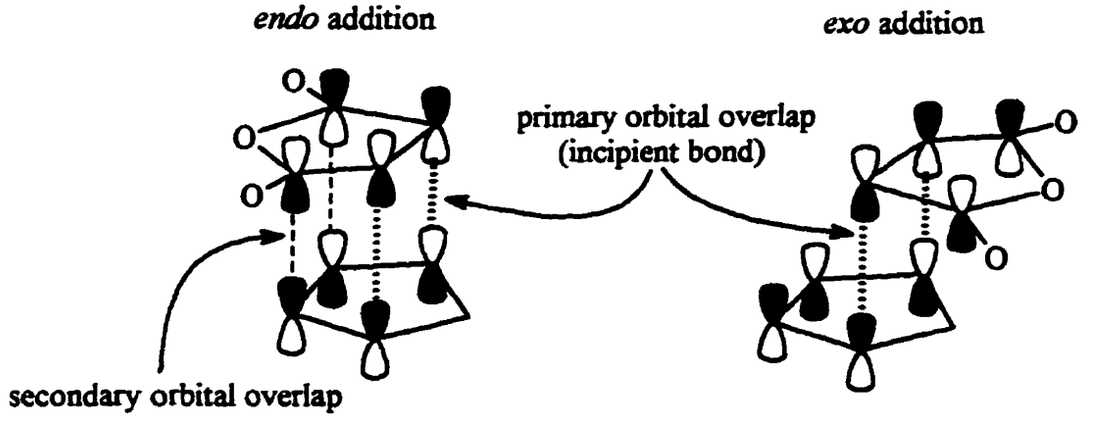
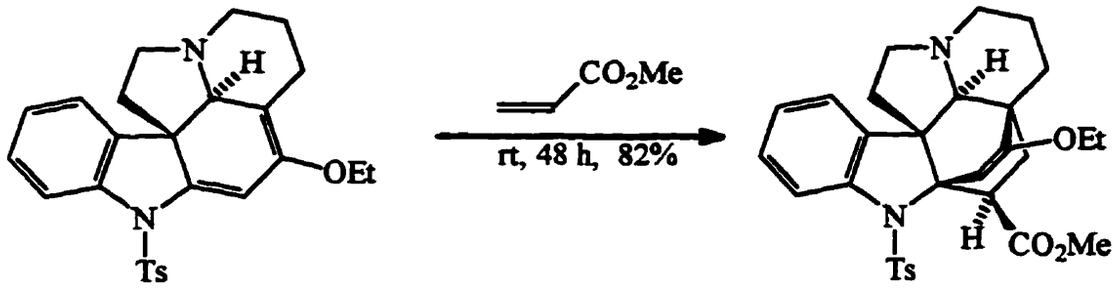


Figure 3. Representation of secondary orbital overlap for *endo* and *exo* addition of maleic anhydride to 1,3-cyclopentadiene

plane-nonsymmetric. It must be stressed that the ability to predict the facial outcome of a Diels-Alder addition is essential if the reaction is to be used for the synthesis of complex organic molecules. This fact becomes quite evident in examples such as the synthesis of 17-oxoaspidofractinine by Le Ménez *et al.*[8] where controlling the facial selectivity in the reaction was pivotal for the addition of methyl propenoate to **5**, which gave **6** in 82% yield (Scheme 2).



5 **6**

Scheme 2. Diels-Alder reaction in the total synthesis of 17-oxoaspidofractinine[8]

A simpler example of facial selectivity in the Diels-Alder reaction can be seen with 5-trimethylsilyl-1,3-cyclopentadiene and maleic anhydride, for which there are two possible *endo* adducts. The dienophile could add either to the face of the diene *syn* to, i.e., same side as, the trimethylsilyl substituent or to the face of the diene which is *anti* to, i.e., the face opposite to, the trimethylsilyl substituent. This would lead to the diastereomeric adducts **8** and **9**, respectively (Figure 4).[9] In fact, *anti* addition is by far the

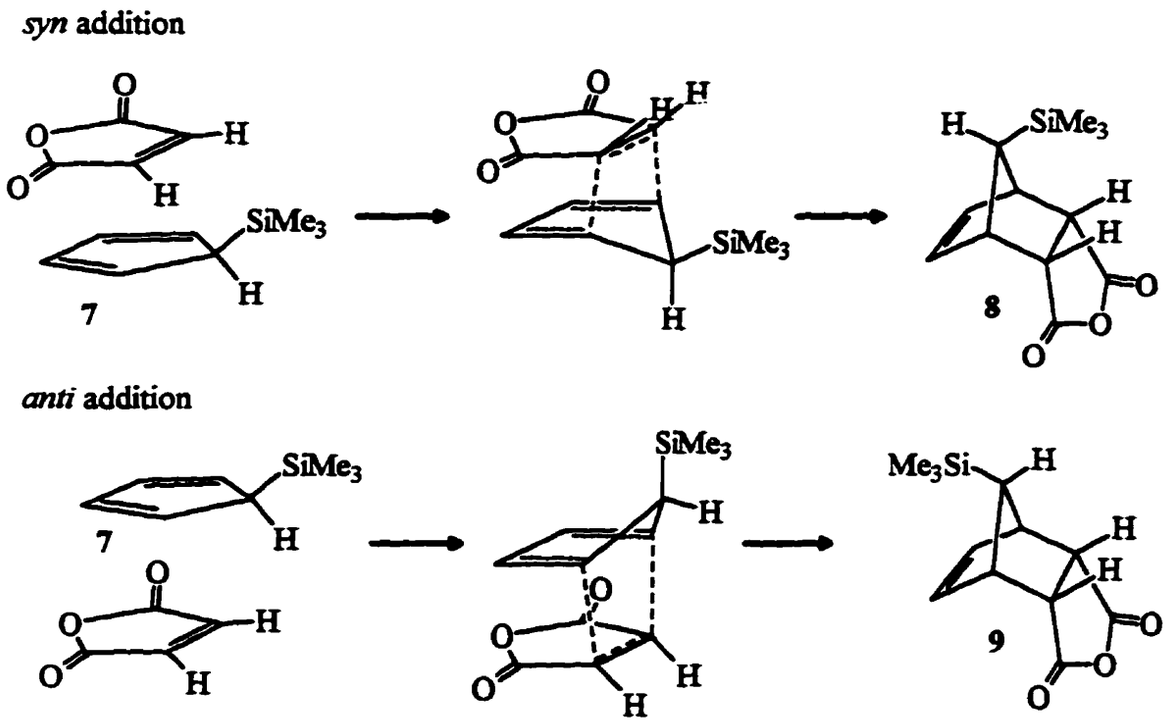


Figure 4. *Syn* and *anti* attack modes for the reaction of 5-trimethylsilyl-1,3-cyclopentadiene and maleic anhydride[9]

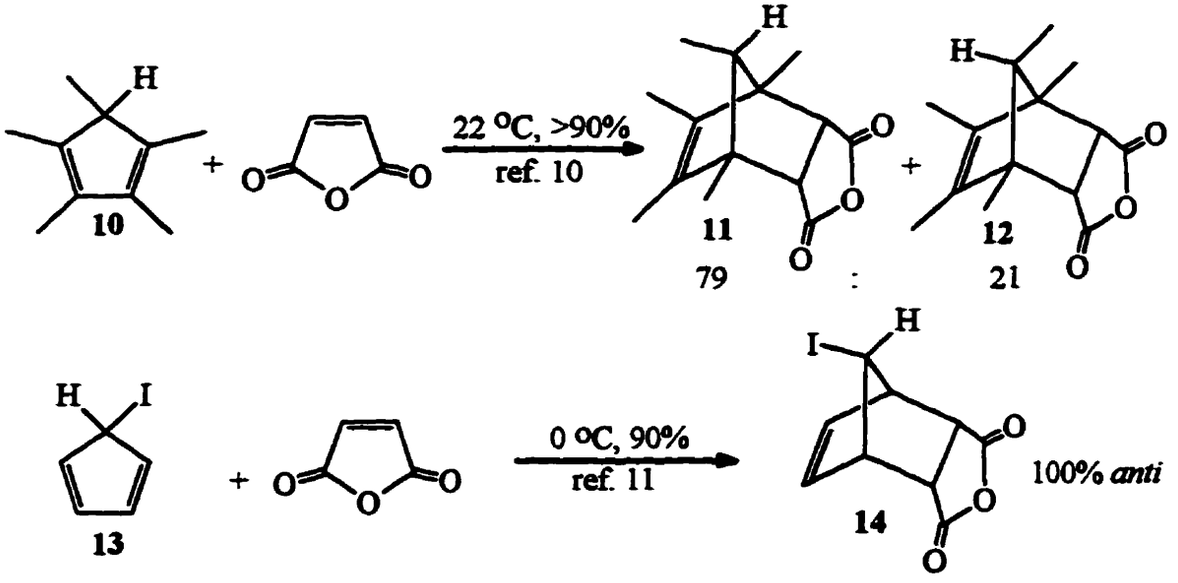
preferred mode of addition, and **9** was the only product observed in this reaction. The result can be rationalized in terms of steric hindrance.

Simple steric arguments can also be used to predict the major products of Diels-Alder reactions involving a number of other 1,3-cyclopentadienes. For instance, the two faces of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **10** are not identical.[10] At the 5-position of one face there is a methyl group but on the other face there is a hydrogen atom. A methyl should be more sterically demanding than a hydrogen, and, therefore, additions to this diene would be expected to prefer to proceed by attack to the face *anti* to the methyl to give **11**. Indeed, when the reaction was carried out with maleic anhydride as

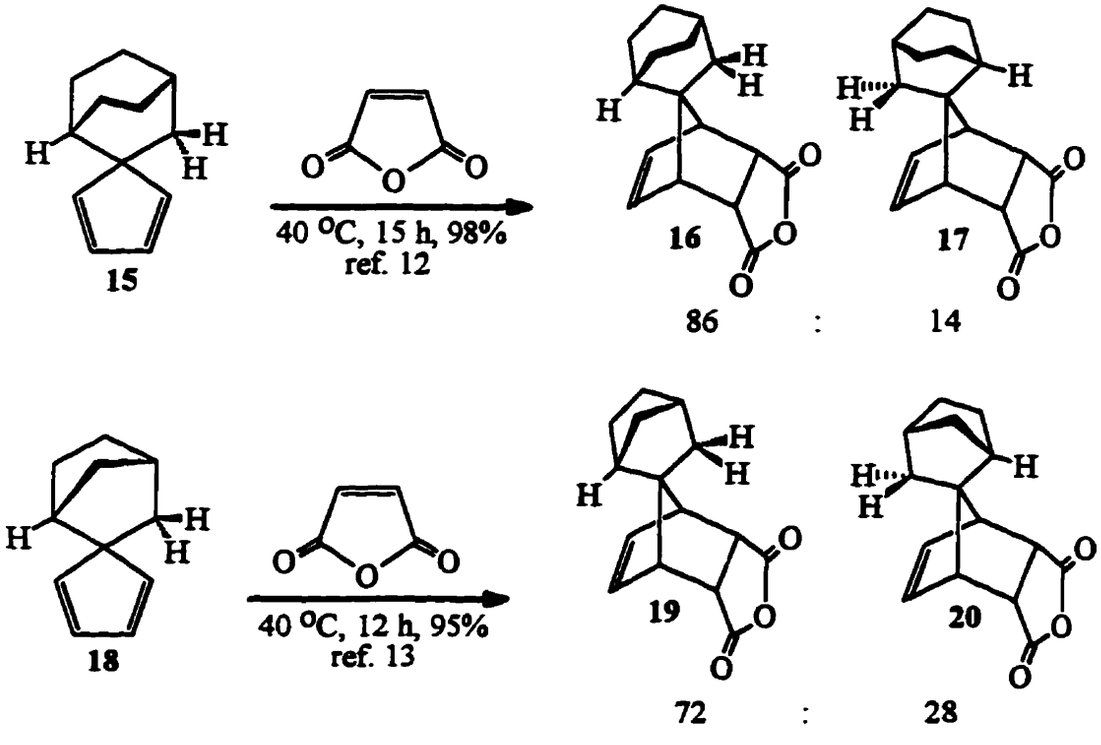
the dienophile it was found that there was a 79 : 21 ratio of adducts favouring addition to the face *anti* to the methyl (Scheme 3).

Another example of facial selectivity that could be predicted by consideration of steric hindrance is the reaction between 5-iodo-1,3-cyclopentadiene **13** and maleic anhydride, which proceeded by addition exclusively *anti* to the iodo substituent, to give **14**.[11] Although these and many other examples seem to follow simple steric guidelines in their facial selectivities, there are many others that do not.

Valenta[12,13] examined 1,3-cyclopentadienes that are spiro-fused at the 5-position to bicyclo[2.2.2]octane **15** and bicyclo[2.2.1]heptane **18**. These dienes demonstrated facial selectivities in their additions to maleic anhydride that were quite surprising, considering the similarity between the two faces of each diene. These dienes have one face that bears a methylene and the other face has a methine attached to the 5-position of the diene. In the case of the methylene, there are two hydrogens pointing out toward the incoming dienophile and in the case of the methine there is only one hydrogen pointing out toward the incoming dienophile. When the reaction was carried out the results showed there to be a significant facial selectivity with **16** being the major adduct from the bicyclo[2.2.2]octane-diene. A similar facial bias was observed for the bicyclo[2.2.1]heptane-diene, for which **19** was the preferred adduct (Scheme 4). Although the prediction of the facial selectivities of these dienes is not simple, Valenta and co-workers were able to come up with an explanation of the selectivities based on a



Scheme 3. Diels-Alder additions of various 5-substituted-1,3-cyclopentadienes

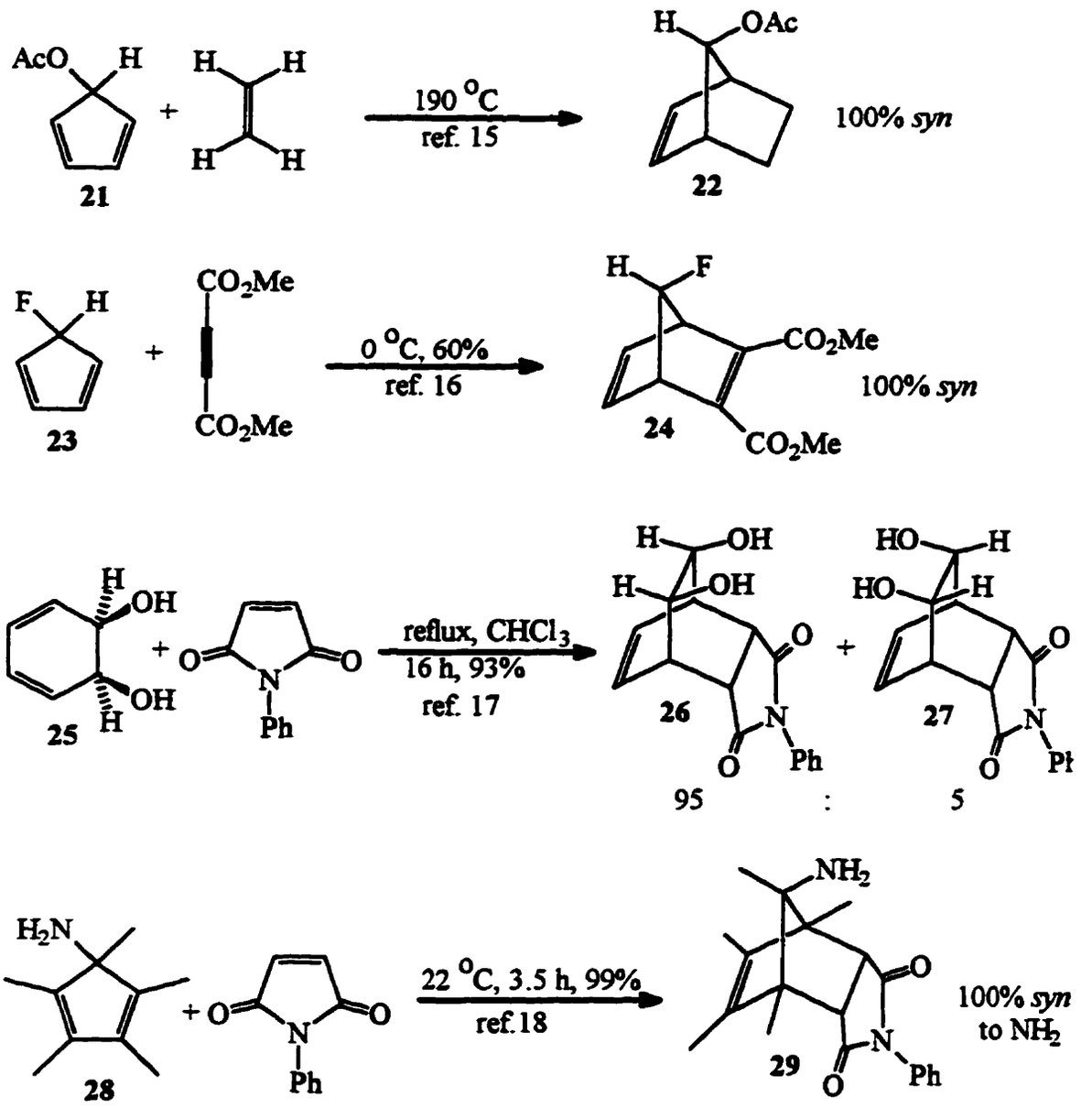


Scheme 4. Diels-Alder additions of bridged-ring 1,3-cyclopentadienes with maleic anhydride

slightly more complex steric argument that was corroborated by computational modelling.[14]

Several theories have been proposed in the past two decades that attempt to explain the facial selectivities of the various dienes that do not follow simple steric control, but the debate continues as to the nature of the forces controlling the product distributions. Many of the "contrasteric" cases involve 1,3-cyclopentadiene derivatives substituted at the 5-position with a heteroatom. The reaction of 5-acetoxy-1,3-cyclopentadiene **21** is probably one of the more famous examples of a Diels-Alder reaction that does not seem to follow steric guidelines for the facial selectivity. The addition of ethene was reported to proceed exclusively onto the face of the diene **21** *syn* to the larger acetoxy substituent to form **22**.[15]

How could steric arguments explain the selectivity observed for **21**, or the exclusively *syn* selectivity in the reactions of 5-fluoro-1,3-cyclopentadiene **23**, in which the size difference between the C-5 substituents is small?[16] Also, how is it possible that dienophiles prefer to attack the *syn* face of cyclohexa-3,5-diene-1,2-diol **25** to give **26** as the major product when it is clear that hydroxyl groups are larger than hydrogens and that sterically the selectivity should be the reverse?[17] Other dienes such as 5-amino-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene[18] **28**, show selectivity that is difficult to explain by steric reasoning. As a result of these anomalies, many of the theories concentrate upon properties of the heteroatom and use these to describe what controls the facial selectivity.



Scheme 5. Contrasteric examples of Diels-Alder additions

In the early 1970's, Anh[19] proposed that the facial selectivity of 1,3-cyclopentadienes, substituted with an oxygen at the C-5 position such as **21**, are controlled by an orbital-mixing interaction. He suggested that lone pair electrons situated

on the oxygen had the ability to mix favourably with the π^* antibonding orbital, the lowest unoccupied molecular orbital (LUMO) of the incoming dienophile. This interaction would result in a net stabilisation, and, therefore, a preference for addition *syn* to the oxygen to give **22** would be expected. Anh presented the diagram reproduced in Figure 5 as an illustration of this theory. His representation, however, seems to show both filled sp^3 orbitals on oxygen simultaneously mixing with the LUMO of the dienophile. A more reasonable representation might be the one depicted in Figure 6, which shows a component on the oxygen in the N-HOMO of the heteroatom-substituted diene mixing with the LUMO of the incoming dienophile.

Anh also used his argument to rationalize the facial selectivity in the additions of 1,2,3,4,5-pentachloro-1,3-cyclopentadiene **33** (Scheme 6).[6,20,21] He suggested that the slight decrease in selectivity in these additions was due to a combination of an increase in substituent size, which would result in an increase in steric repulsions and a decrease in the energy level of the lone pairs because of a decrease in electronegativity.

Unfortunately, Anh's theory is not successful in explaining the selectivity observed in Diels-Alder additions of dienes such as **36**[22] and **38**[23] in Scheme 6, that should have the ability to undergo the required orbital mixing even though the heteroatom is not attached to the C-5 position of the 1,3-cyclopentadiene ring. As well, it seems unlikely that his decision to use molecular orbitals (MO) calculated from only a small portion of the diene could be an accurate representation of the orbital landscape for this molecule.

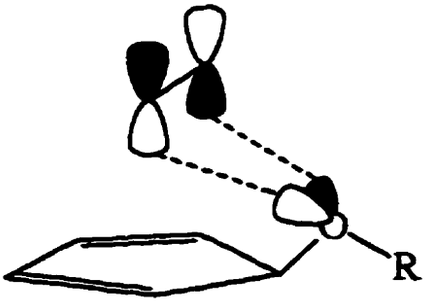


Figure 5. Anh's representation of his theory of substituent-dienophile interaction

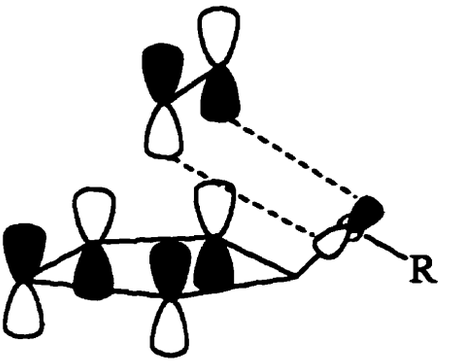
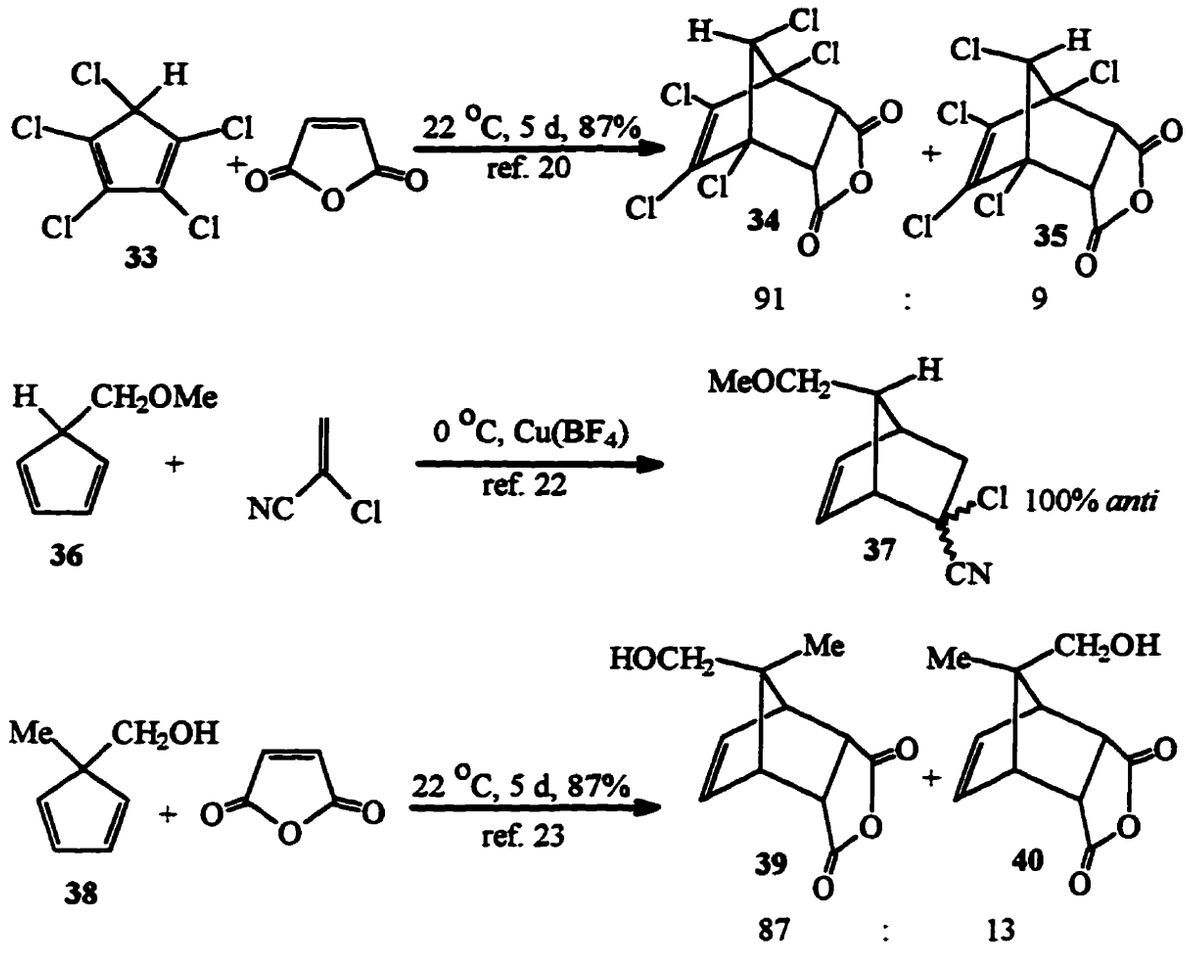


Figure 6. Alternative representation of Anh's theory of substituent-dienophile interaction

Kahn and Hehre[24] preferred to take a simpler approach to the issue of facial selectivity in the Diels-Alder reaction. They argued that for normal-electron-demand Diels-Alder reactions, being the reaction between an electron-rich diene and an electron-deficient dienophile, one can easily predict the diastereofacial selectivity of both the diene and dienophile. One can determine the more nucleophilic face of the diene and the more electrophilic face of the dienophile, in the same way that predictions of regiochemical

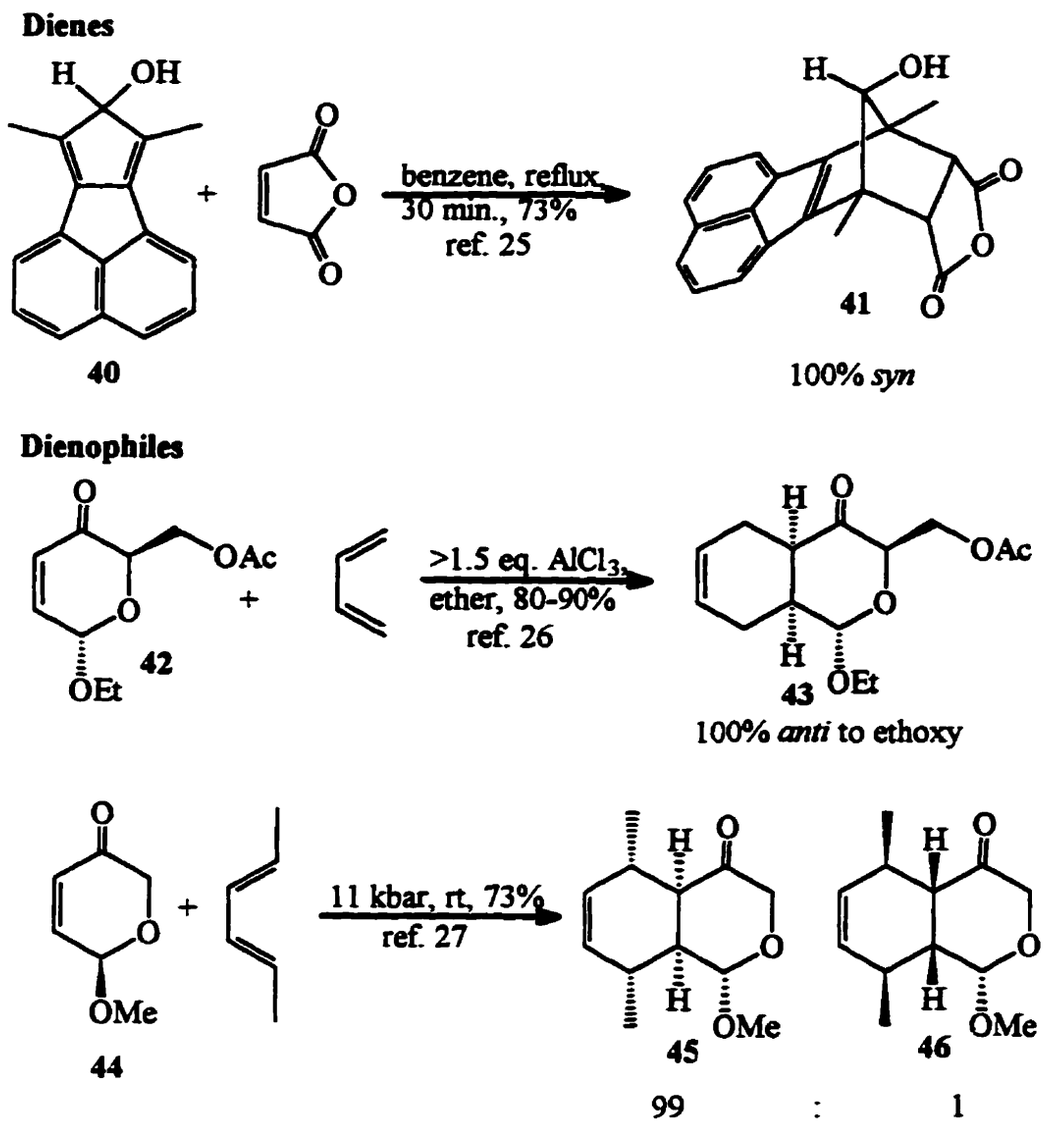


Scheme 6. Additions of some heteroatom-containing 1,3-cyclopentadienes

selectivity are done, and these would be expected to associate preferentially. Their theory also accounted for the facial selectivity of inverse-electron-demand cycloadditions, being the reactions between electron-poor dienes and electron-rich dienophiles. Their theory was said to be predictive for not only plane-nonsymmetric dienes but also for plane-nonsymmetric dienophiles.

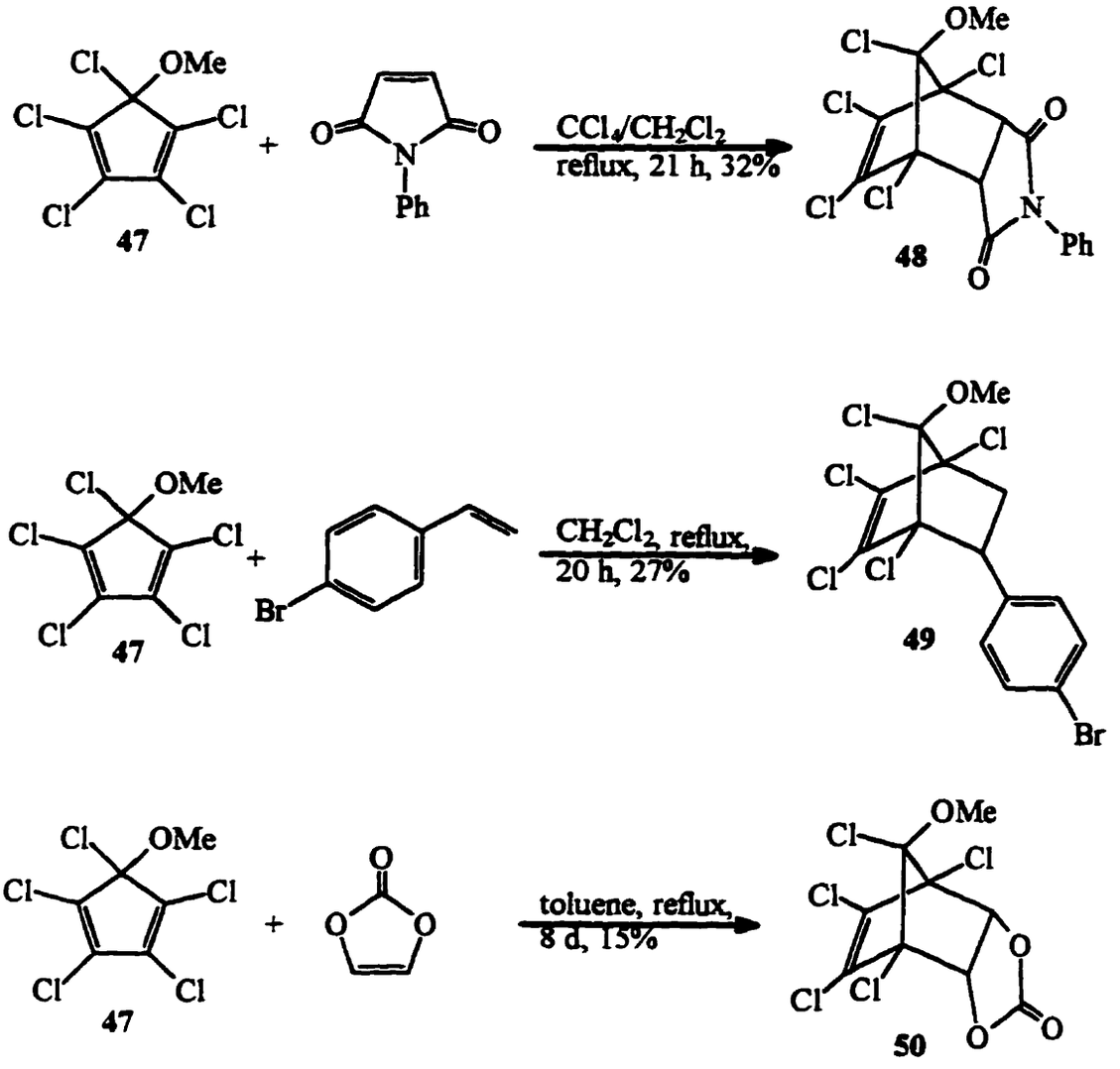
Kahn and Hehre used numerous examples from the literature, some of which are given in Scheme 7,[25,26,27] to support their theory. With the exception of the 5-hydroxy-1,3-cyclopentadiene derivative **40**, it is unclear whether it is a demonstration of the nucleophilic and electrophilic properties of the dienes and dienophiles at work or simply a matter of steric repulsions governing the reaction outcomes. Dienophile **42**, by the anomeric effect, should adopt a conformation in which the ethoxy group is pseudo-axial, thus causing the potentially more sterically hindering methylene to be in the pseudo-equatorial position. In this conformation, the face *syn* to the ethoxy group would be more sterically hindering, and it would be expected that the dienophile would add preferentially to the face *anti* to the ethoxy group to give **43**. However, Kahn and Hehre attributed the facial selectivity of these examples to their theory, with no mention of the conformation of the dienes and dienophiles. As well, work done by Burry *et al.*[28] appears to discredit Kahn and Hehre's theory. For inverse-electron-demand dienes reacting with electron-rich dienophiles, the selectivity should be reversed from normal-electron-demand cases. Burry *et al.* synthesized 1,2,3,4,5-pentachloro-5- methoxy-1,3-cyclopentadiene **47** and reacted it with a number of Diels-Alder dienophiles ranging from electron-poor, such as *N*-phenyl-maleimide, to electron-rich, such as vinylene carbonate (Scheme 8). What was observed was addition *syn* to methoxy in all cases, regardless of whether the reaction was normal-electron-demand or inverse-electron- demand.

Cieplak[29,30] related a theory to explain nucleophilic additions to carbonyl groups in cyclic six-membered-ring ketones, and this was adopted by Fallis[31,32] to explain π-facial



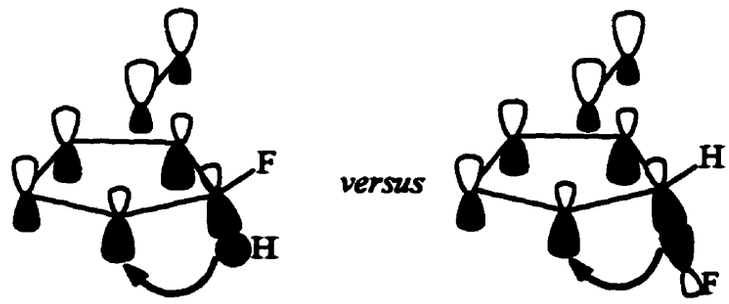
Scheme 7. π-Facial selectivities of dienes and dienophiles with α-chiral centres containing heteroatom functionalities

selectivity in the Diels-Alder reaction. The theory is based upon the proposition that, during the attack of a nucleophile upon a carbonyl, there is electron donation from hyperconjugation of the antiperiplanar σ-bond into the vacant σ^*-orbital that develop



Scheme 8. Additions of 1,2,3,4,5-pentachloro-5-methoxy-1,3-cyclopentadiene[28]

along with the formation of the incipient σ-bond. As a result, it was generalised that in Diels-Alder reactions with 5-substituted-1,3-cyclopentadienes, dienophiles should add to the face opposite to the better σ-donor (Figure 7). To add support for this theory Fallis and co-workers[32] synthesized a number of adducts of 2,5-dimethylthiophene-S-oxide **51**

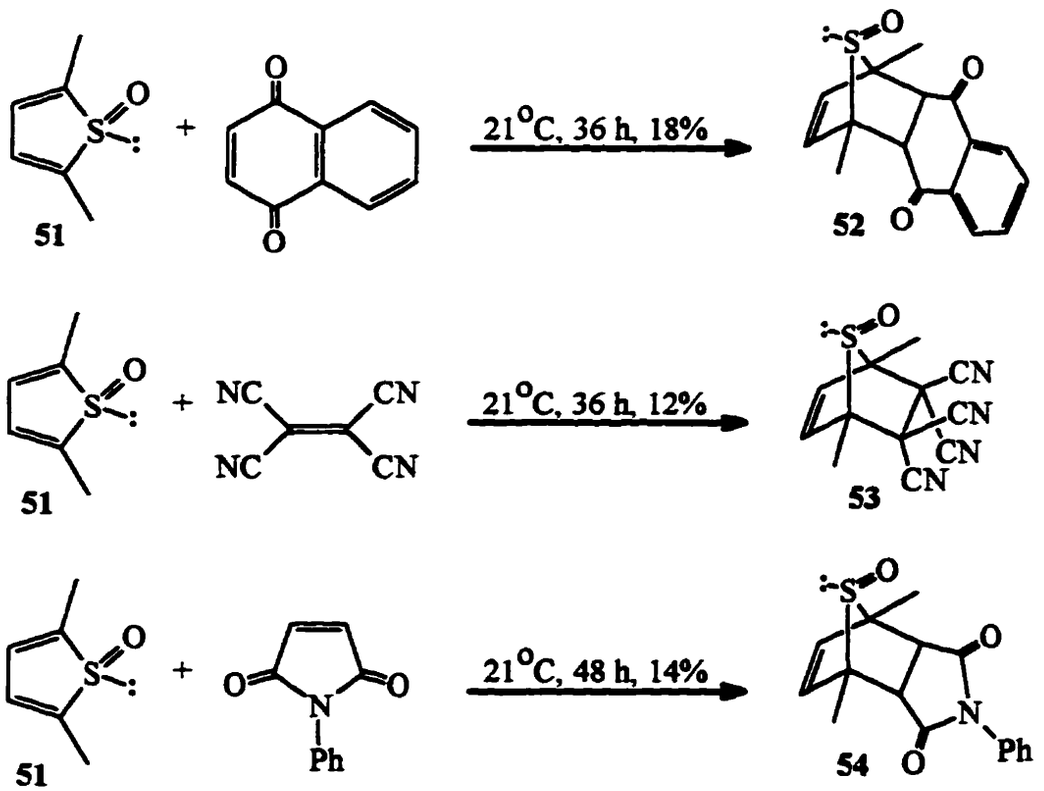


23

Figure 7. Representation of the Fallis model for hyperconjugation of the antiperiplanar σ^*-orbital in the Diels-Alder reaction of **23**

(Scheme 9). Fallis stated that the lone pair on the sulfur is a better σ-donor than is the oxygen, which resulted in the Diels-Alder additions to these dienes to proceed *syn* to the oxygen exclusively.

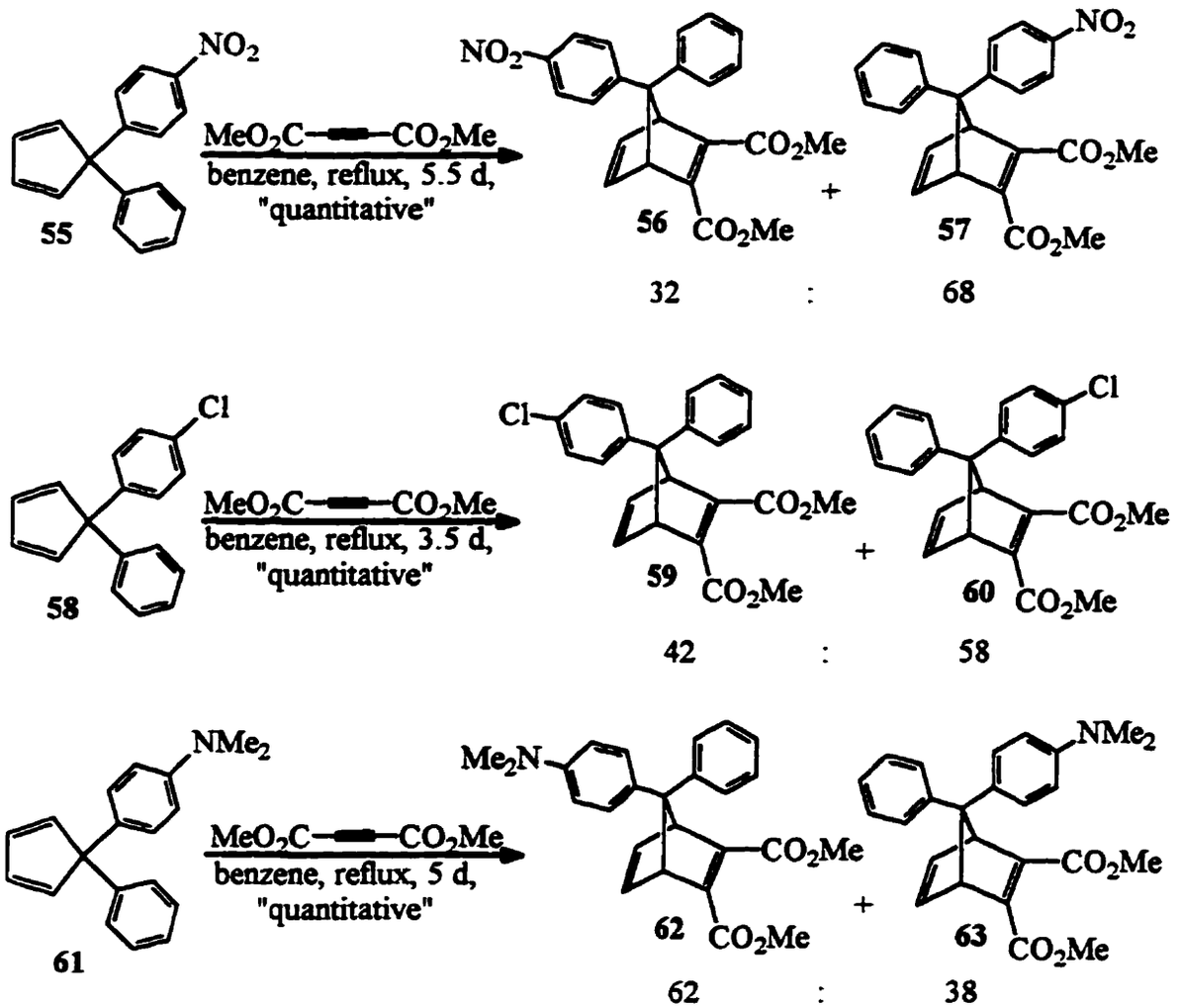
Halterman[33] suggested that the facial selectivity observed in the reactions of 5-(4-nitrophenyl)-, 5-(4-chlorophenyl)- and 5-(4-dimethylaminophenyl)-5-phenyl-1,3-cyclopentadiene **55**, **58** and **61**, respectively, with dimethyl acetylenedicarboxylate added credibility to the Fallis theory. He believed that since these dienes are sterically unbiased, yet electronically biased, the only plausible theory is the one proposed by Fallis (Scheme 10). It must be noted that of the work that has been done concerning the π-facial selectivity of 5-substituted 1,3-cyclopentadienes, these examples appear to be the ones which are most independent of steric influences. If this is the case then what their product ratios demonstrate is that the influence of electron-withdrawing and donating groups on



Scheme 9. Diels-Alder adducts of 2,5-dimethylthiophene-S-oxide substituted dienes[32]

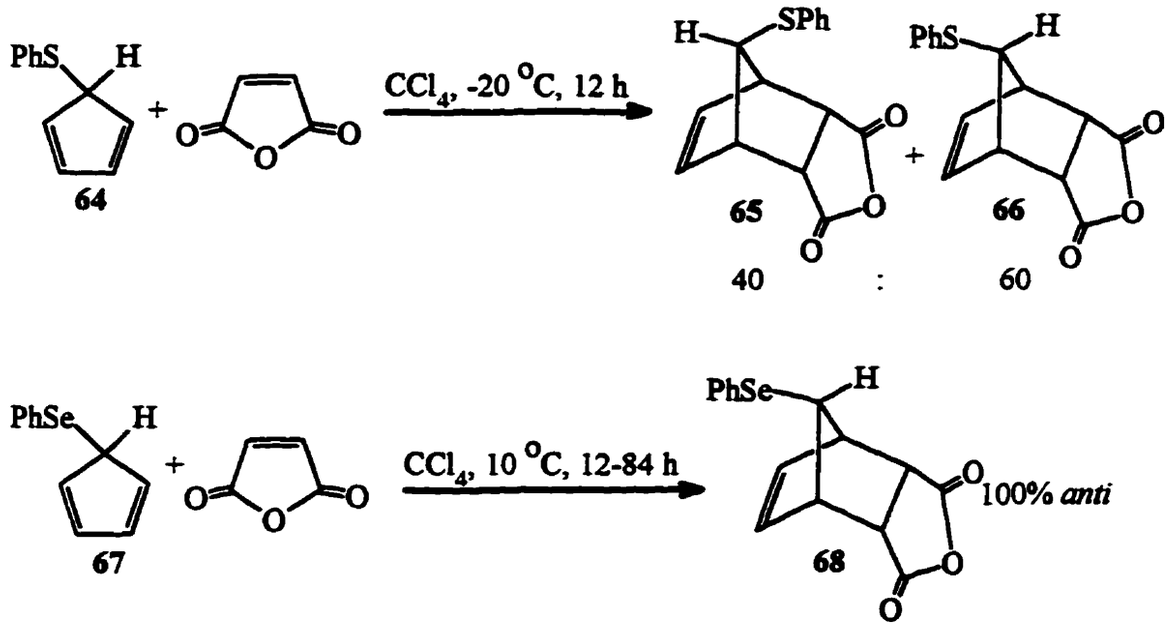
facial selectivity is very modest, and that perhaps other factors are dominating in systems where there are high facial selectivities.

Ishida, Aoyama and Kato[34] studied additions to 5-phenylthio- and 5-phenylseleno-1,3-cyclopentadiene, **64** and **67**. Diene **64** gave poor facial selectivity in its reaction with maleic anhydride (4 : 6, *syn : anti*). Diene **67** gave the exclusively the *anti* product **68** in its addition to maleic anhydride (Scheme 11). They explained that for 1,3-cyclopentadienes substituted with an oxygen substituent at the C-5 position, as in **21**,



Scheme 10. Diels-Alder additions of sterically unbiased yet electronically biased dienes[33]

that the *syn* transition state would be of lower energy due to a favourable interaction between the π-electrons of the forming norbornene double bond and the back of the polarized C-5 to oxygen bond (Figure 8). Comparing this to the sulfur and selenium substituents, it should be true that, due to the decrease in electronegativity of the larger



Scheme 11. Diels-Alder additions of 5-phenylthio- and 5-phenylseleno-1,3-cyclopentadiene and maleic anhydride [34]

substituents, less *syn* selectivity should be seen as one goes down the group from oxygen to sulfur and then to selenium.

Inagaki[35] suggested that, based upon the orbital mixing rule,[36] there is a non-equivalent extension of the π-HOMO (highest occupied molecular orbital) of the plane nonsymmetric dienes caused by mixing of the σ-orbitals of the carbon framework through the interaction with the low lying lone pair orbital of the C-5 substituent. In essence, the heteroatom causes the HOMO to be extended more on the face *syn* to the heteroatom and less on the face *anti* to the heteroatom (Figure 9).

Paquette has worked with a number of isodicyclopentadiene derivatives, some of which show high facial selectivity, although the two faces of the diene do not appear to

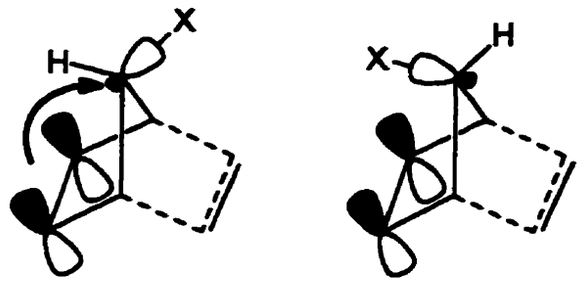


Figure 8. Representation of Kato's theory of the forming norbornene double bond donating electron density into the back of the polarized carbon-heteroatom σ-bond

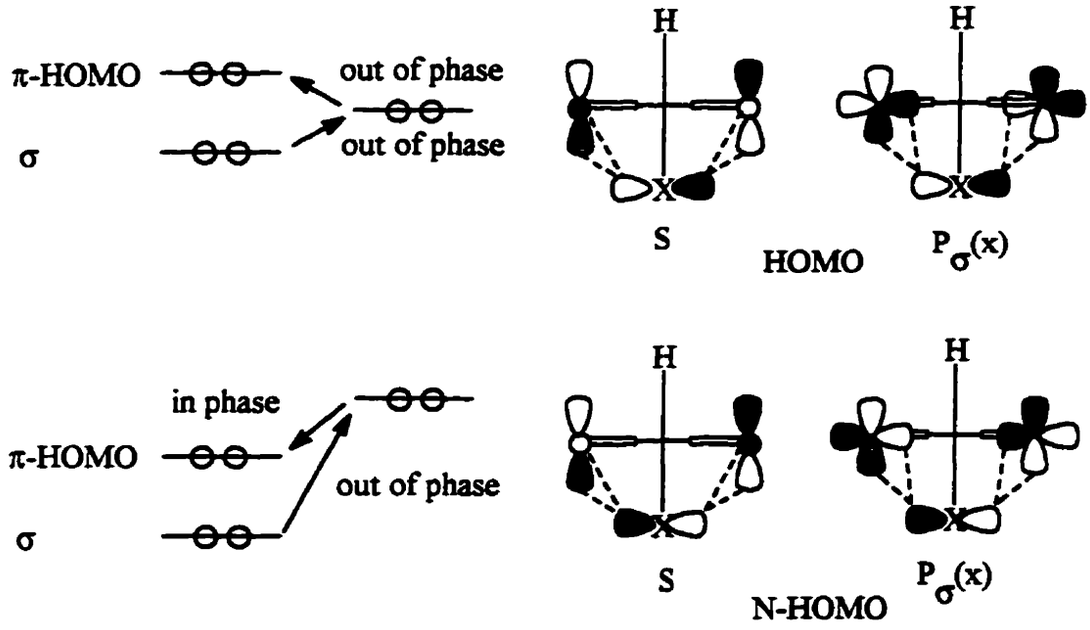


Figure 9. Orbital mixing rule applied to the non-equivalent extension of the HOMO and N-HOMO of 5-heteroatom-substituted 1,3-cyclopentadienes

have large differences either sterically or electronically. He believes that σ/π interactions were the cause of preferred endo attack in isodicyclopentadiene.[37] He postulated that there is considerable orbital tilting involved in the skeleton of norbornene caused by interactions between the π-system of the diene and the σ-orbitals of the carbon framework. Due to the inward rotation of the terminal diene lobes for attack *syn* to the methano bridge, a larger non-bonding interaction between the π_s of the diene and the HOMO of the dienophile was present. It was said that a decrease in the antibonding interaction would occur if attack proceeded from the underside (which was defined as *anti*) of the diene thus accounting for high *anti* preference (Figure 10).

Brown and Houk[38] modified Paquette's approach by postulating that, although there is considerable orbital tilting in the isodicyclopentadiene systems, it is the torsional strain of the molecule which determines the facial selectivity. They reasoned that less torsional strain and less atomic movement is involved in *anti*-attack, than in *syn*-attack accounting for the high *anti*-selectivity. It does, however, seem ironic that Brown and Houk based their theory on moderate neglect of differential overlap (MNDO) calculations, which they had previously criticised for not providing an accurate representation of the Diels-Alder reaction.[39] This particular type of calculation represents the Diels-Alder reaction as a two-step process proceeding via a radical pathway and not via the accepted one-step, concerted pathway.[2] If the method is so fundamentally wrong in its representation of the reaction mechanism, a certain amount of scepticism should be

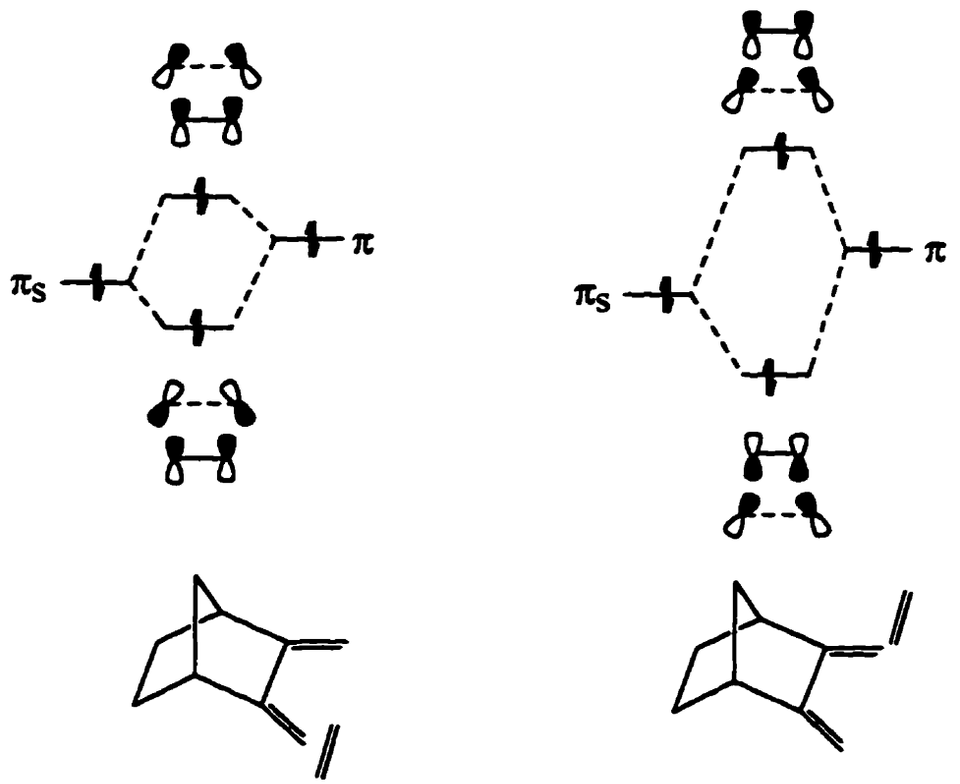


Figure 10. Representation of Paquette's theory of orbital bending in norbornene systems

anticipated when discussing its appropriateness in predicting another phenomenon of the same reaction.

Of the theories presented for the π-facial selectivities in the Diels-Alder reaction of substituted 1,3-cyclopentadienes and related systems none appears to be reliable as a tool for predicting the facial selectivity for 1,3-cyclopentadienes and other related systems. A part of the problem may be that many theories are based upon, and hold for, only a limited number of examples and are often developed in contradiction to all other theories previously presented.

It is obvious that if a thorough understanding of these systems is to be attained it will require a carefully measured, reliable and systematic set of facial selectivity results from relatively simple Diels-Alder reactions. This set of results must contain the reactions of a number of dienes with different dienophiles. The data presented in this thesis will go a significant way in meeting these requirements, and it is anticipated that these data will be very useful for helping to delineate the factor, or factors, that need to be considered in future computational research. Ultimately, it is hoped that the combined experimental and computational approach will provide a theory that will be predictive for facial selectivity for all diene and dienophile combinations.

Results

1,5-Sigmatropic rearrangement occurs quite readily with simple 5-substituted 1,3-cyclopentadienes at room temperature (Figure 11), and the thermodynamically least favoured isomer is the one with the substituent at the 5-position.[11] Low reaction temperatures, usually below 0 °C, are necessary when these dienes are used, so Diels-Alder reactions involving these dienes are restricted to only the more reactive dienophiles. The 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene-based dienes, on the other hand, do not readily undergo the sigmatropic rearrangement at normal reaction temperatures. They are therefore more flexible for use with less reactive dienophiles, which require higher reaction temperatures and longer reaction times.

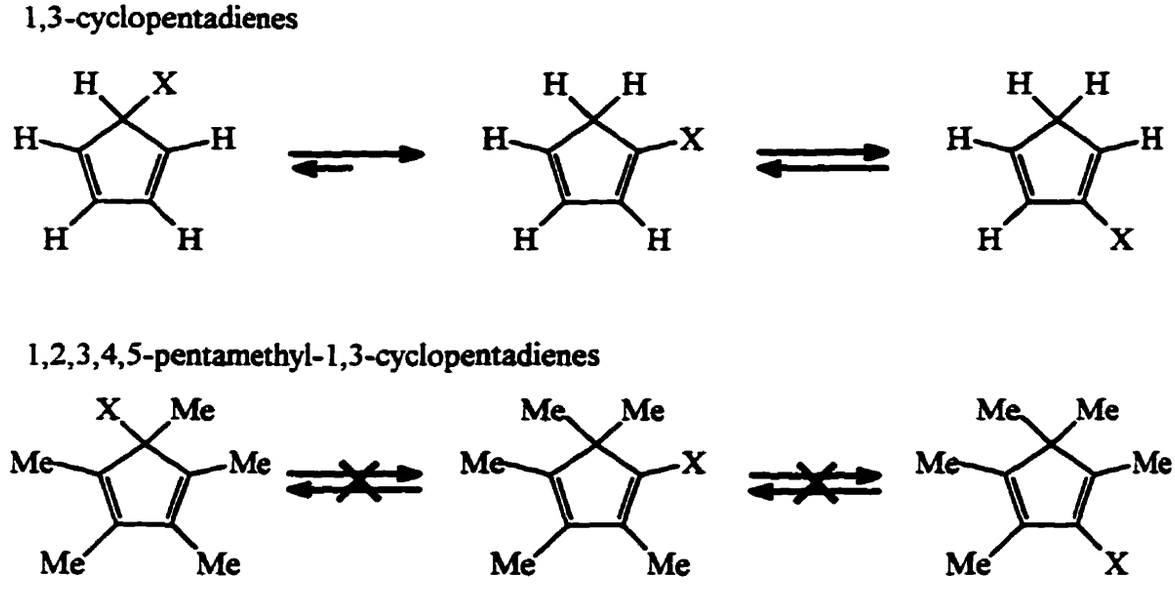
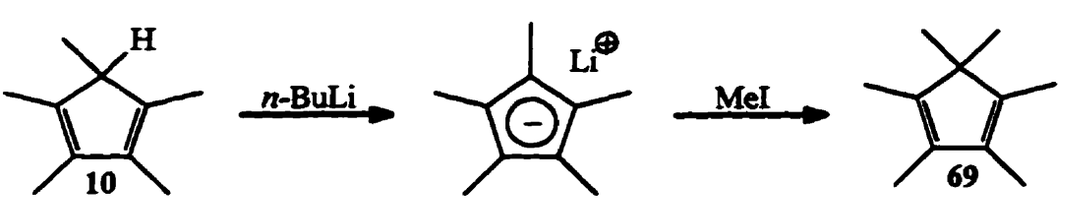


Figure 11. 1,5-Sigmatropic rearrangement of 1,3-cyclopentadienes

Hexamethyl-1,3-cyclopentadiene

Hexamethyl-1,3-cyclopentadiene adducts were synthesized in order to obtain the ^{1}H nmr chemical shifts of the *syn* and *anti* methyls on the C-8 carbon for each adduct. The chemical shifts of each of the methyls might serve as a useful tool for corroborating the stereochemistry of adducts from 5-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes. Table 7 (page 68) lists the chemical shifts of these methyls for all the adducts of *N*-phenylmaleimide, 4-phenyl-1,2,4-triazoline-3,5-dione and 1,1,2,2-tetracyanoethene studied.

Hexamethyl-1,3-cyclopentadiene **69** was prepared in one step by generation of the pentamethylcyclopentadienyl anion, at 0° C, by dropwise addition of an excess of *n*-butyllithium to a solution of **10** in anhydrous tetrahydrofuran. Two equivalents of iodomethane were added to the anion to give diene **69** in 75% yield. Diene **69** proved to be quite volatile, which accounted for some loss of product.



Scheme 12. Synthesis of hexamethyl-1,3-cyclopentadiene **69**

N-Phenylmaleimide was added to a solution of diene **69** in ether at room temperature. The single adduct **70** and some unreacted *N*-phenylmaleimide were inseparable by column chromatography, but recrystallization of the product from hexane gave a sample of adduct **70** that was homogeneous by ^{1}H and ^{13}C nmr spectroscopy.

It had been anticipated that the stereochemistry of the adducts derived from plane-nonsymmetric dienes might be determined by measuring nuclear Overhauser enhancements (nOe) in the ^{1}H nmr spectra. The nOe data for **70** were fairly typical of many of the adducts. Diagnostically useful enhancements of signals were small for saturation of methyl signals and observation of other methyl signals. This proved to be a general difficulty with the use of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene derivatives, and in some instances x-ray crystallography was necessary to reveal the relative stereochemistry of Diels-Alder adducts. In the particular case of adduct **70**, saturation of the singlet at δ 1.60 (due to the methyls on C-5 and C-6) led to an nOe of only 0.4% of the singlet at δ 0.66 due to the methyl at C-8 (Figure 12).

Addition of 1,1,2,2-tetracyanoethene to a solution of **69** in ether at room temperature gave adduct **71**. Column chromatography of the crude adduct followed by washing the crystals with ether gave **71** as colourless crystals. A 0.6% enhancement of the signal at δ 0.81 resulted from saturation of the signals corresponding to the C-5 and C-6 methyls. The enhancement indicates that this methyl is *syn* to the double bond in **71**.

The reaction of diene **69** with 4-phenyl-1,2,4-triazoline-3,5-dione proceeded within minutes, as noted by the rapid dissipation of the characteristic red colour of the 4-phenyl-1,2,4-triazoline-3,5-dione to give adduct **72**. Column chromatography and subsequent recrystallization gave **72** as colourless crystals in 90% yield. The ^{1}H nOe analysis of **72** showed a 0.6% enhancement of the signal corresponding to the C-6 and C-7 methyls (δ 1.75) upon saturation of the methyl signal at δ 0.68 ppm. The

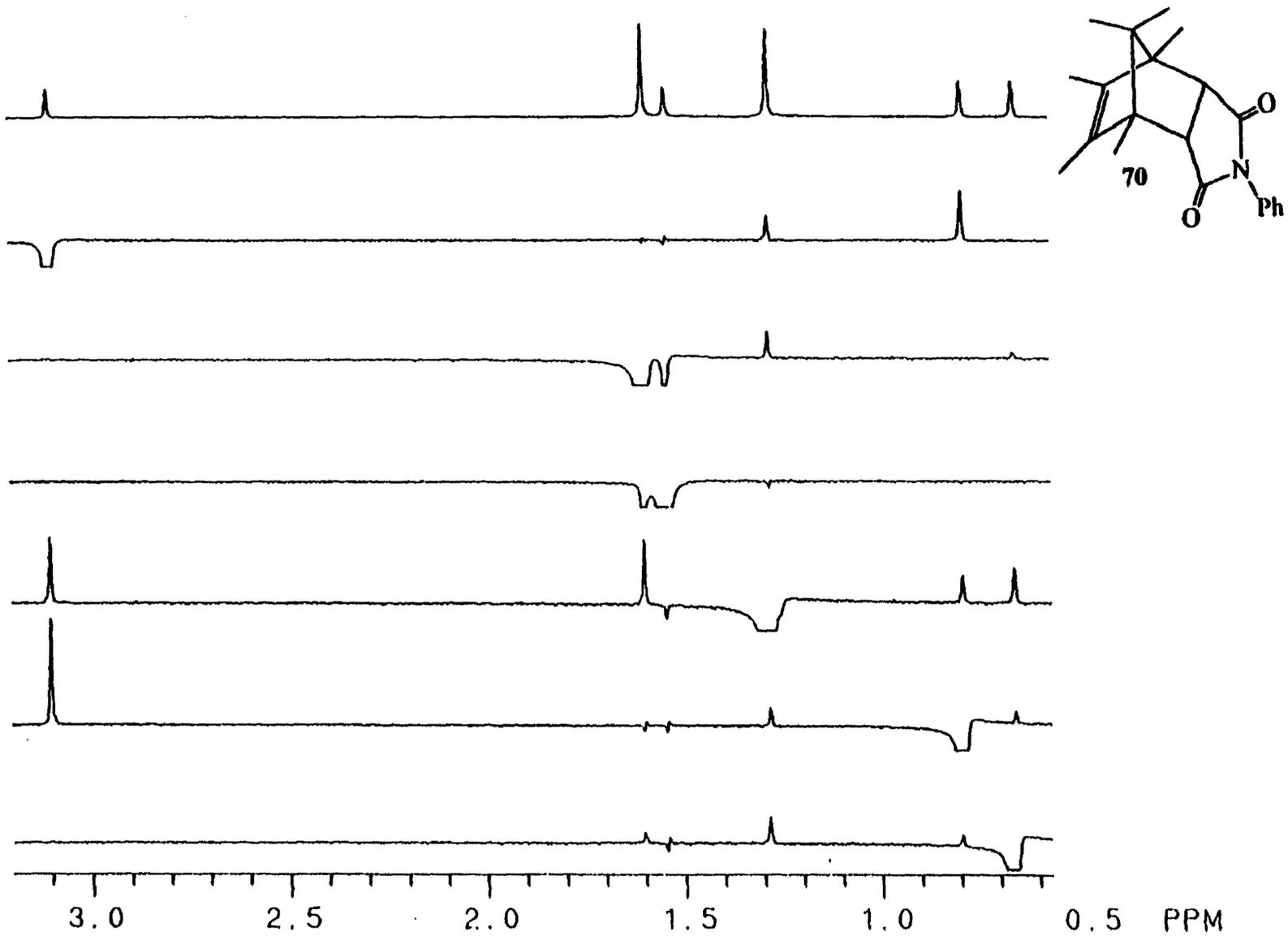
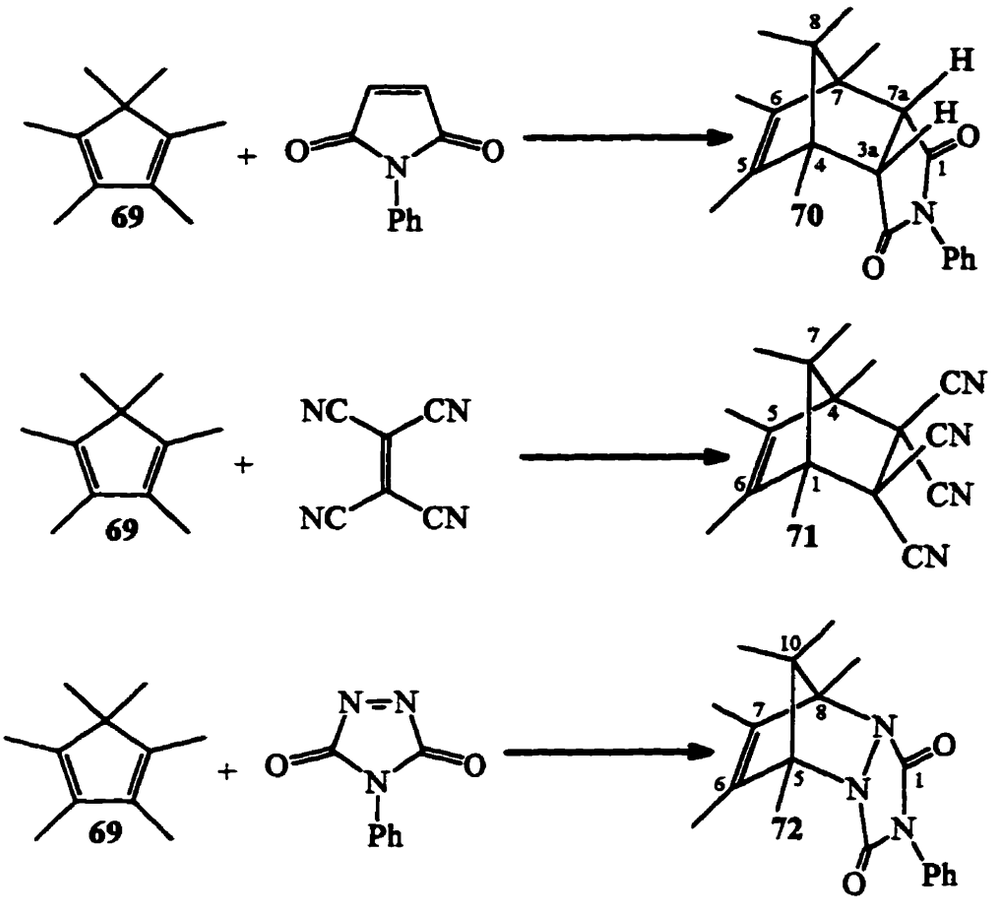


Figure 12. NOe of adduct **70**

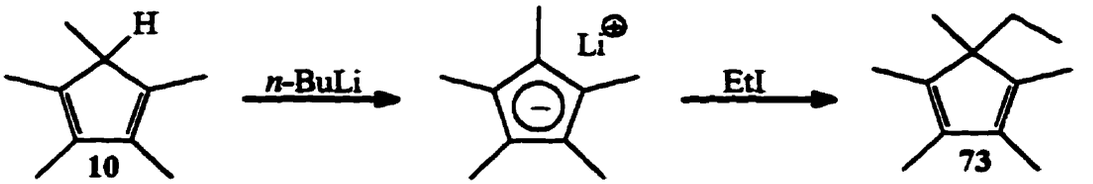
enhancement indicated that the saturated methyl was *syn* to the double bond of the norbornene moiety.



Scheme 13. Diels-Alder reactions of hexamethyl-1,3-cyclopentadiene **69**

5-Ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

The first plane-nonsymmetric diene that we examined was 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **73**, which was prepared in a fashion similar to that for **69** by first forming the pentamethylcyclopentadienyl anion at 0 °C and subsequent dropwise addition of 1.2 equivalents of iodoethane.



Scheme 14. Synthesis of 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **73**

A-values are a measure of the effective size derived from the axial versus equatorial energies in cyclohexanes.[40] Methyl and ethyl groups have A-values that are not significantly different, so A-values would suggest that diene **73** should have almost no facial selectivity. Since other results from this laboratory with 5-methyl- and 5-ethyl-1,3-cyclopentadiene were consistent with this prediction[41] then diene **73** might be expected to have facial selectivity that would reflect this very small difference in steric hindrance rather than a stereoelectronic phenomenon.

Addition of *N*-phenylmaleimide to a solution of **73** in ether at room temperature did result in the production of two adducts **74** and **75**, but in a ratio of 96 : 4, respectively. (To ensure that the adduct ratios reported in this thesis were kinetically derived rather than thermodynamically derived, solutions of isolated or enriched mixtures of the adducts in $CDCl_3$ were heated to 60 °C overnight and the composition of the adducts were reassessed. Unless specifically noted, the compositions did not change.) Column chromatography provided some of the major adduct **74** in homogeneous form. Due to the small proportion of **75**, it was not recovered in homogeneous form from the column fractions. Therefore, its spectral data were extracted from the spectra of the crude adduct mixture. The nOe analysis of **74** showed a 2.5% enhancement of the signal corresponding

to the C-8 methyl (δ 0.82) upon saturation of the signals due to the C-3a and C-7a hydrogens (δ 3.06). This enhancement was indicative of addition of the *N*-phenylmaleimide *endo* and *anti* to the face of the diene with the ethyl group.

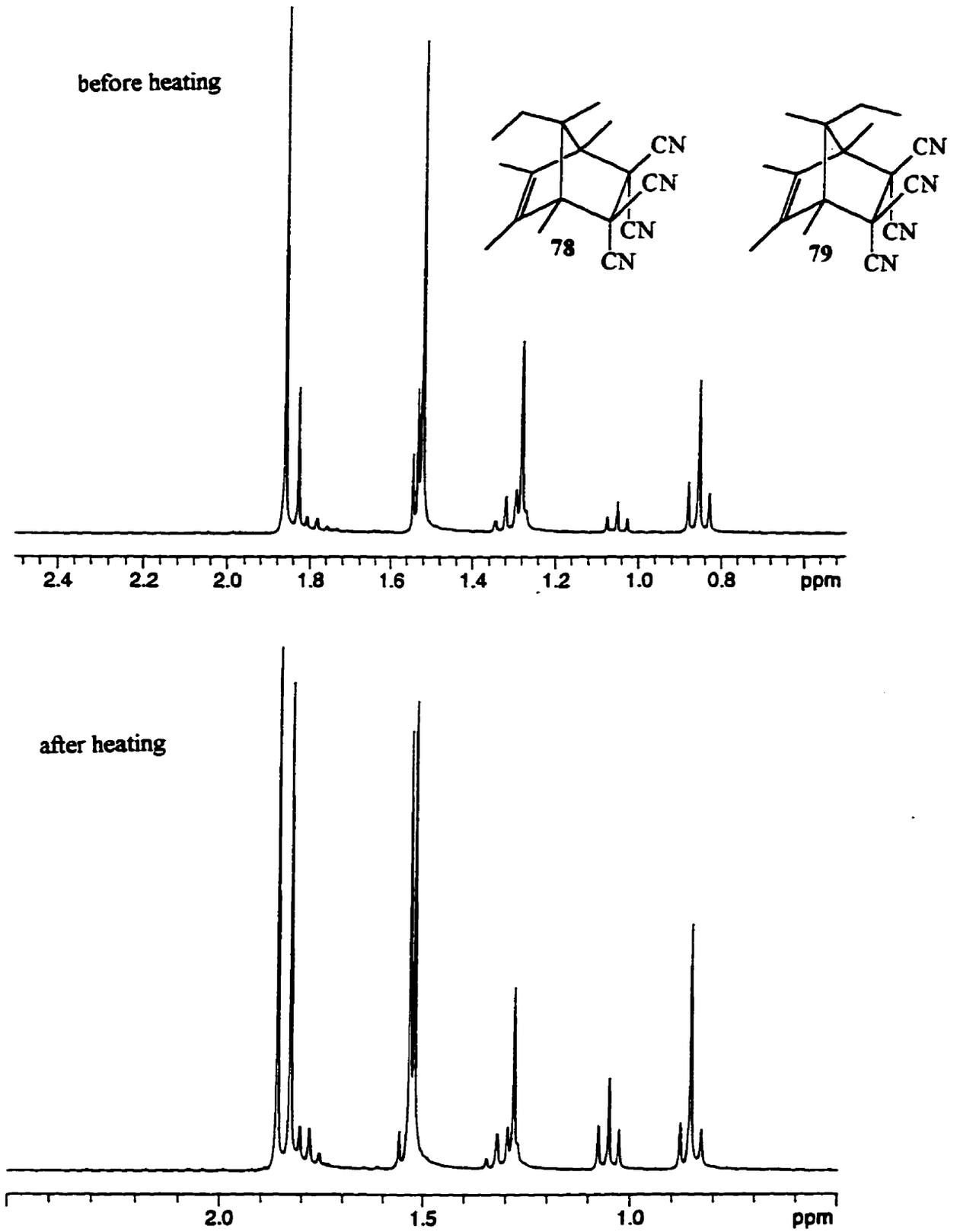
The rate of the reaction of diene **73** was compared with that of an equimolar amount of diene **69** in a competitive experiment with a limiting amount of *N*-phenylmaleimide. A 2.3 : 1 ratio of adducts **70** and **74**, respectively, was obtained. There are twice as many *syn*-to-methyl faces on **69** as on **73**, therefore the ratio observed was indicative of the methyl-bearing face of **73** being of about the same reactivity as **69**.

1,4-Naphthoquinone, added to an ether solution of **73**, gave a mixture of adducts **76** and **77** in a ratio of 95 : 5, respectively, after 16 hours at room temperature. The adduct mixture contained some unreacted 1,4-naphthoquinone, which proved to be inseparable from the adducts by column chromatography. Refluxing a solution of the adduct mixture with 2,3,4,5-tetraphenyl-2,4-cyclopentadien-1-one in diethyl ether removed the excess dienophile, and column chromatography of this reaction mixture provided a homogeneous sample of **76**. The ^{1}H nOe data for **76** included a 6% enhancement in the signal corresponding to the C-11 methyl (δ 0.46) upon saturation of the signal due to the C-4a and C-9a hydrogens (δ 2.83). Conversely, saturation of the C-11 methyl signal resulted in a 16% enhancement of the C-4a and C-9a hydrogens. These enhancements were indicative of **76** being an *anti*-addition product. The *syn*-addition product **77** was not obtained in homogeneous form, but its spectral data were obtained from spectra of the crude adduct mixture. A sample containing a mixture of

adducts **76** and **77**, in a ratio of 93 : 7 was heated at 60 °C for 20 hours in $CDCl_3$ and the nmr spectra of the heated sample revealed that the ratio of **76** and **77** had changed to 71 : 29. The relative amount of **77** formed over this 20 hour period was comparatively small, and it was felt that very little equilibration would have occurred during the time needed for the Diels-Alder reaction. Hence, the observed ratio was very likely a fair indication of the kinetically rather than thermodynamically derived products.

Addition of 1,1,2,2,-tetracyanoethene to a solution of **73** in ether at room temperature gave a mixture of **78** and **79** in a ratio of 90 : 10, respectively. The adducts were inseparable by column chromatography on silica gel. The nmr analysis of these diastereomers was carried out with the diastereomeric mixture. The nOe data for **78** included a 1.2% enhancement in the signal corresponding to the C-5 and C-6 methyls (δ 1.86) upon saturation of the ethyl CH_3 (δ 0.86), which was consistent with **78** being the product of addition *anti* to the ethyl group.

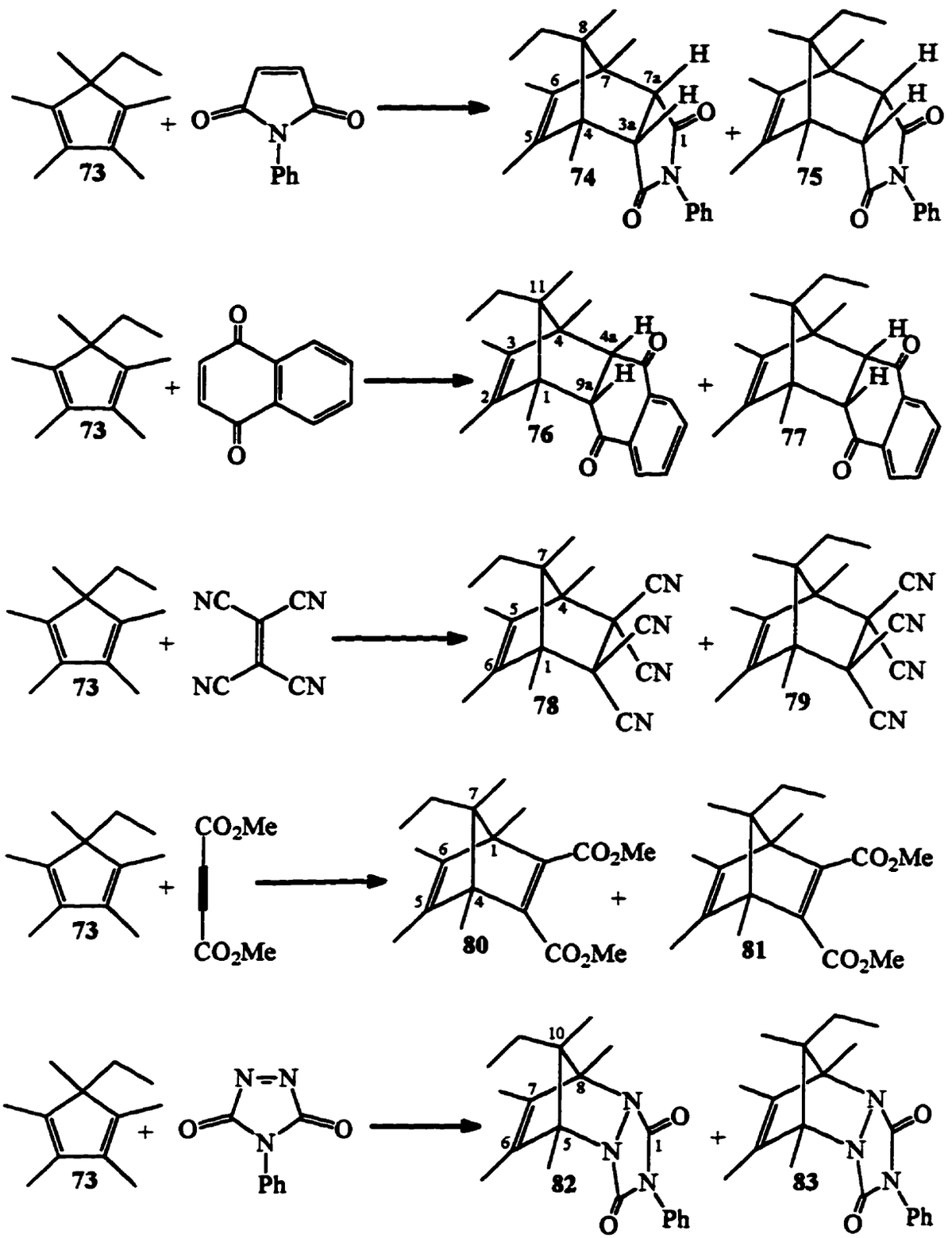
Heating of the mixture of **78** and **79** in $CDCl_3$ at 40 °C overnight resulted in an adduct ratio of 50 : 50. In this instance we felt that the original 90 : 10 ratio may have underestimated the facial selectivity due to some equilibration. Therefore, the reaction of **73** with 1,1,2,2-tetracyanoethene was repeated, and the reaction's progress was monitored carefully by ^1H nmr. After only five minutes the product ratio was found to be 97 : 3. Since we know that the product equilibrates to a 50 : 50 mixture, we can say that the kinetically-derived facial selectivity was equal to at least the highest observed ratio (Figure 13).



Figurue 13. ^{1}H nmr spectra of a mixture of adducts **78** and **79** before and after heating

Addition of dimethyl acetylenedicarboxylate to a solution of diene **73** in ether yielded, after seven days at room temperature, adducts **80** and **81** in a ratio of 81 : 19, respectively. The adducts were separated from unreacted dienophile by Kugelrohr distillation at 150 °C, and the residue was subjected to preparative thin layer chromatography (TLC). Due to the small amount of **81** formed it was not recovered from the TLC plate, however its nmr signals were extracted from spectra of the crude adduct mixture. The nOe data for **80** were inconclusive, and, due to its liquid state at room temperature, the relative stereochemistry of adduct **80** could not be determined by x-ray crystallography. The addition of diene **73** with dimethyl acetylenedicarboxylate might be expected to follow the trend observed for the other dienophiles. For this reason, we have tentatively assigned the stereochemistry of the major adduct to be the result of addition *anti* to the ethyl group. The reaction of diene **73** and dimethyl acetylenedicarboxylate was repeated at reflux in ether for 20 hours and no difference in the adduct ratio was observed.

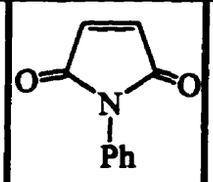
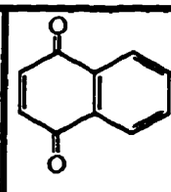
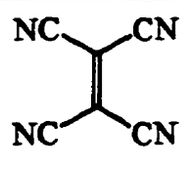
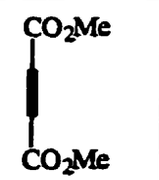
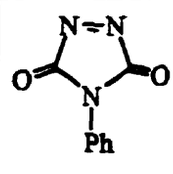
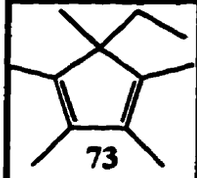
A mixture of adducts **82** and **83** in a ratio of ≥ 97 : 3, respectively, resulted from addition of 4-phenyl-1,2,4-triazoline-3,5-dione to a solution of **73** in ether at room temperature. Signals in the ^{1}H nmr which may have been attributable to the minor adduct were integrated to get the stated adduct ratio, however it could not be proven conclusively that they belonged to the minor adduct. Column chromatography gave **82** as Figurue 13. ^{1}H nmr spectra of a mixture of adducts **78** and **79** before and after heating a colourless solid (70%). The nOe analysis of **82** gave inconclusive results, therefore the



Scheme 15. Diels-Alder reactions of 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **73**

structure of **82** was determined by x-ray analysis (Figure 14). The facial selectivities with diene **73** are summarized in Table 1.

Table 1. Ratios of *anti* to *syn* addition for 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **73**

					
 **73**	96 : 4	95 : 5	≥ 97 : 3	81 : 19*	≥ 95 : 5

* assignment is tentative

5-Methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

5-Methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **84** was brought into the study due to the fact that it contained a heteroatom functionality that was not bonded directly to the C-5 carbon but was separated from it by a methylene group. An examination of the facial selectivity with this diene would serve two purposes. Firstly, it would demonstrate whether the *syn*-directing effect of first row heteroatoms is restricted to those directly bonded to the C-5 carbon or if the heteroatom serves simply to guide the dienophile onto the *syn* face and does not necessarily have to be a C-5 substituent. Secondly, this diene might give an indication of the steric difference between methyl and methoxy groups when compared to diene **73** if stereoelectronic control could be ruled out.

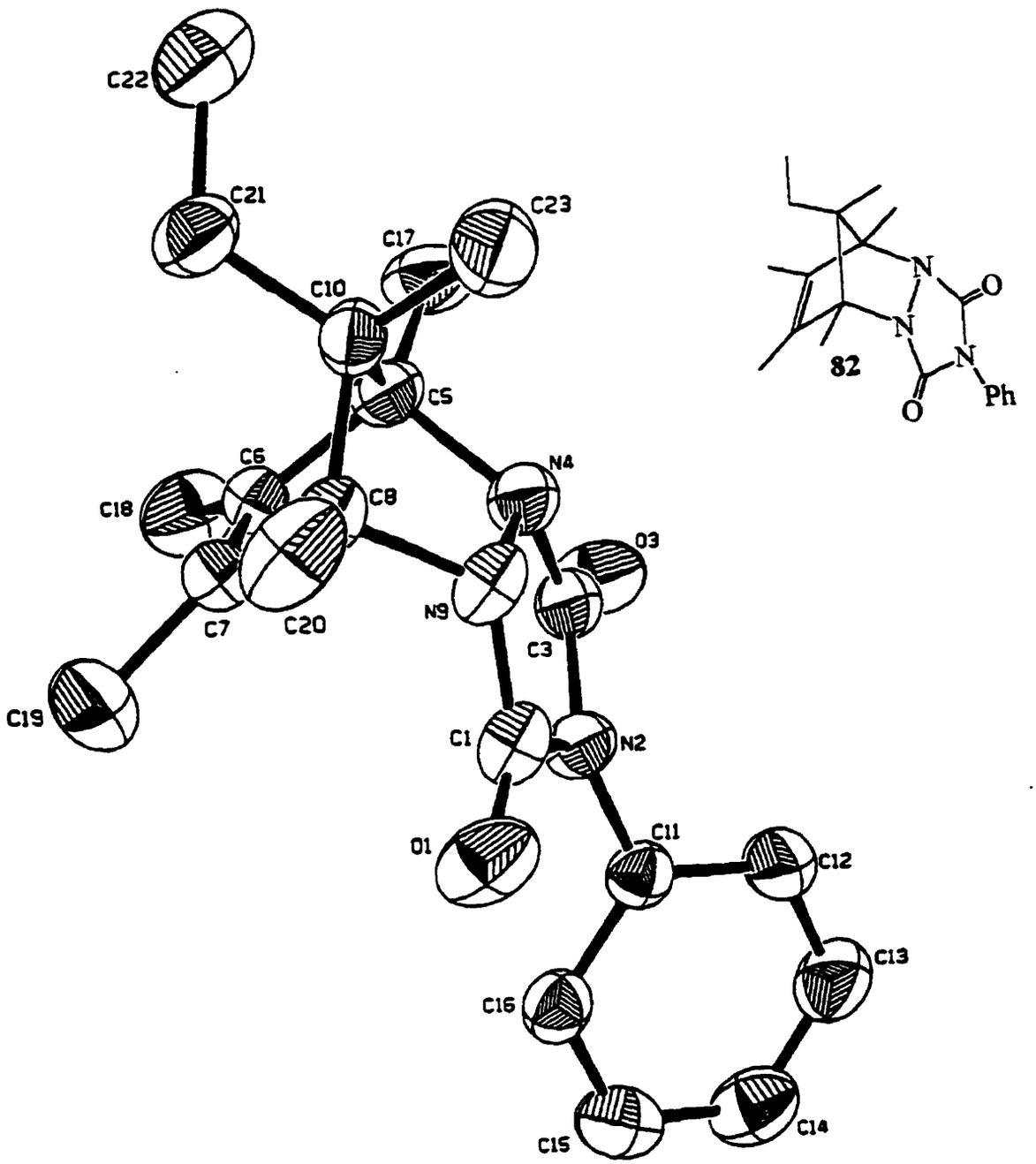
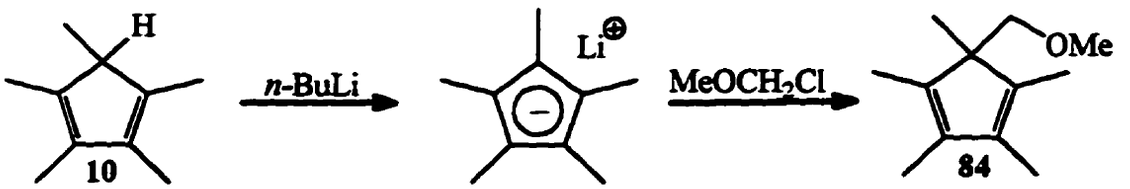


Figure 14. X-ray crystal structure of adduct **82**

The synthesis of diene **84** was carried out via the anionic intermediate and subsequent treatment with one equivalent of chloromethoxymethane as the alkylating agent to give the desired diene as a yellow oil in 86% yield (Scheme 16).



Scheme 16. Synthesis of 5-methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **84**

A solution of diene **84** in ether was treated with an equivalent of *N*-phenylmaleimide at room temperature to give a mixture adducts **85** and **86** in a ratio of 86 : 11, respectively. Column chromatography provided an analytical sample of adduct **85**. Adduct **86** was recovered as part of a three-part mixture of **85**, **86**, and unreacted *N*-phenylmaleimide. Therefore, its nmr data were obtained from the crude adduct mixture. An 11% nOe enhancement of the signal corresponding to the C-3a and C-7a hydrogens (δ 3.09) was observed upon saturation of the C-8 methyl (δ 0.95) of **85**. This enhancement demonstrated that **85** was the product of *endo* addition, *anti* to the methoxymethyl group.

Adducts **87** and **88** in a ratio of 84 : 12, respectively, were the outcome of addition of 1,4-naphthoquinone at room temperature to an ether solution of diene **84**. Preparative TLC of the crude adduct mixture gave **87** as a yellow solid (68%), however the minor

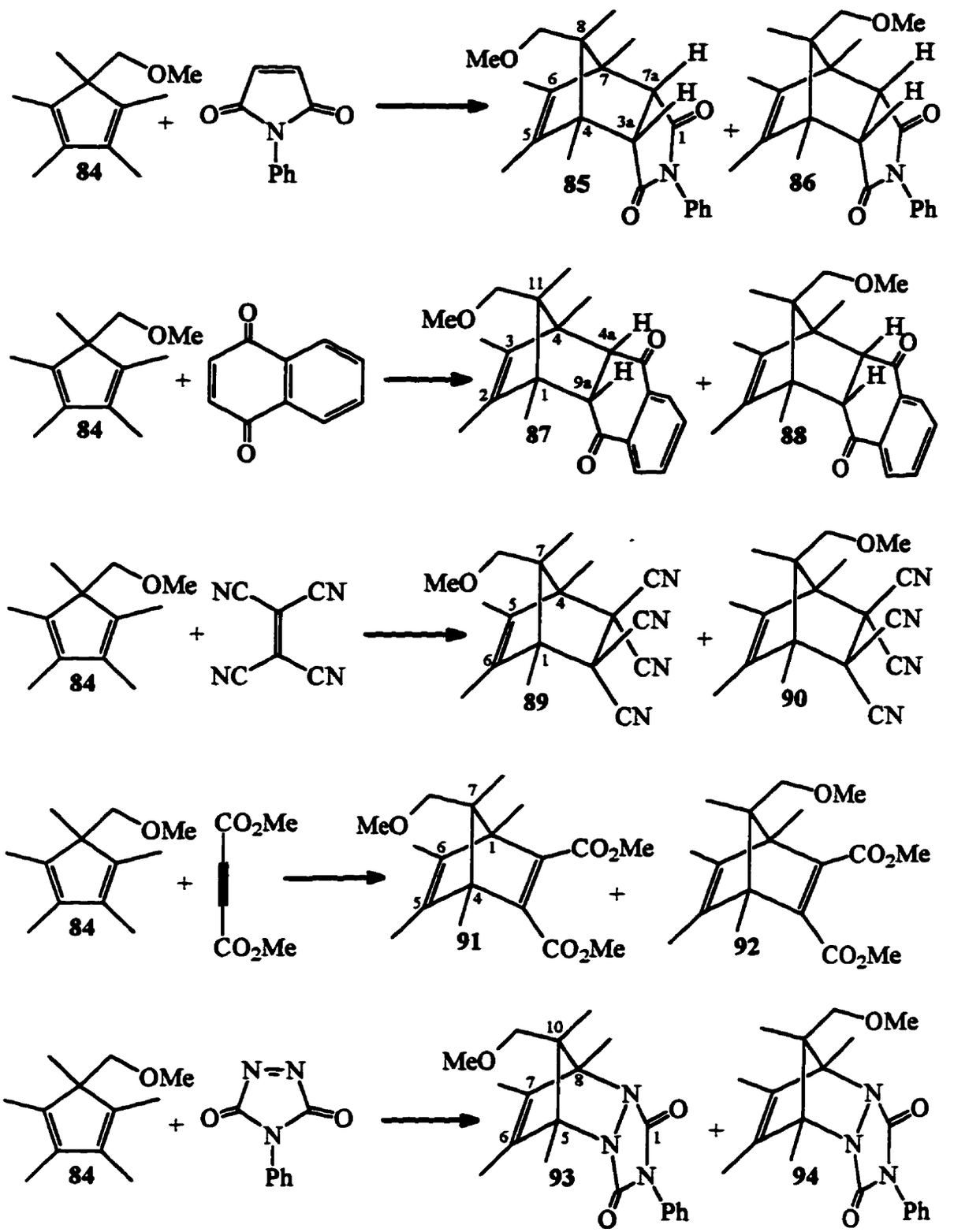
adduct **88** was not obtained in homogeneous form. The relative stereochemistry of **87** was determined on the basis of a 17% enhancement of the singlet corresponding to the C-4a and C-9a hydrogens (δ 3.17) upon saturation of the singlet for the C-11 methyl at δ 0.94. This enhancement was indicative of **87** being the *anti*-addition product.

An equimolar amount of 1,1,2,2-tetracyanoethene was added to a solution of diene **84** in ether, which afforded a 93 : 7 ratio of adducts **89** and **90**, respectively. Column chromatography failed to separate the adducts, and nmr analysis was done on the diastereomeric mixture, for which there was a 57% recovery from the column. Saturation of the singlet at δ 1.87 corresponding to the C-5 and C-6 methyls of **89** showed a 0.9% nOe enhancement of the singlet at δ 3.07 corresponding to the methylene attached to C-7. Conversely, saturation of the methylene signal gave a 0.5% enhancement of the signal for the C-5 and C-6 methyls. These enhancements showed that the major adduct **89** was the product of addition *anti* to the methoxymethyl group.

A sample containing a 58 : 42 mixture of adducts **89** and **90**, respectively (as measured by integration of the ^{1}H nmr), was heated to 60 °C in $CDCl_3$ for 20 hours and the ^{1}H nmr spectrum of the heated sample revealed that the ratio of **89** and **90** had changed to 61 : 39. The relative amount of epimerization over this 20 hour period was comparatively small, so it appeared that very little equilibration could have occurred during the time needed for the Diels-Alder reaction. Hence, the observed ratio was very largely a result of kinetic rather than thermodynamic control.

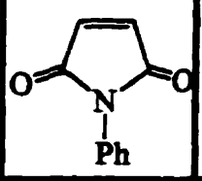
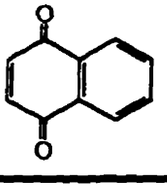
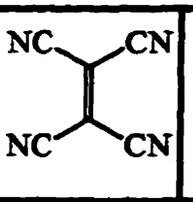
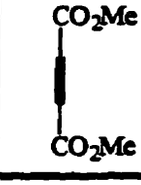
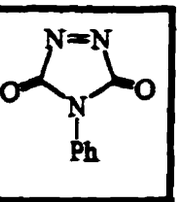
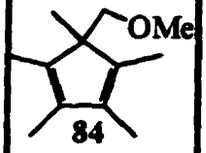
Addition of an excess of dimethyl acetylenedicarboxylate to a solution of **84** in ether, after 14 days at room temperature, gave adducts **91** and **92** in a ratio of 72 : 28, respectively. Column chromatography provided a small amount of homogeneous **91** as a yellow oil, but the spectral data for adduct **92** had to be obtained from the nmr spectra of a mixture of adducts. The nOe analysis of **91** included a 1.1% enhancement of the signal corresponding to the methylene attached at C-7 (δ 1.67) upon saturation of the C-5 and C-6 methyls (δ 3.30). This was indicative of **91** being the product of addition *anti* to the methoxymethyl group.

Adducts **93** and **94** were obtained in a ratio of 74 : 26, respectively, upon addition of 4-phenyl-1,2,4-triazoline-3,5-dione to an ether solution of **84** at room temperature. Column chromatography gave homogeneous samples of both **93** and **94** in 58% and 22% isolated yields, respectively. The relative stereochemistry of adduct **93** was established based upon an observed 0.4% nOe enhancement of the signal corresponding to the C-6 and C-7 methyls (δ 1.77) upon saturation of the singlet for the C-10 methylene (δ 3.04). This enhancement was consistent with **93** being the product of addition *anti* to the methoxymethyl group. Similarly, the relative stereochemistry of **94** was suggested by a modest 0.3% nOe enhancement of the signal corresponding to the C-6 and C-7 methyls (δ 1.73) upon saturation of the C-10 methyl (δ 0.80). This enhancement was consistent with **94** being the product of addition *syn* to methoxymethyl group. The facial selectivities with diene **84** are summarized in Table 2.



Scheme 17. Diels-Alder reactions of 5-methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **84**

Table 2. Ratios of *anti* to *syn* addition for 5-methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **84**

					
 **84**	86 : 14	88 : 22	93 : 7	73 : 27	74 : 26

1,2,3,4,5-Pentamethyl-1,3-cyclopentadiene

Although some additions to 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **10** had been reported previously,[10] additions with 4-phenyl-1,2,4-triazoline-3,5-dione and 1,1,2,2-tetracyanoethene had not been examined. We felt that these additions should be repeated because the adducts had not been separated in the previous work, and the data would provide a better comparison for the adducts of the previously unexamined dienophiles.

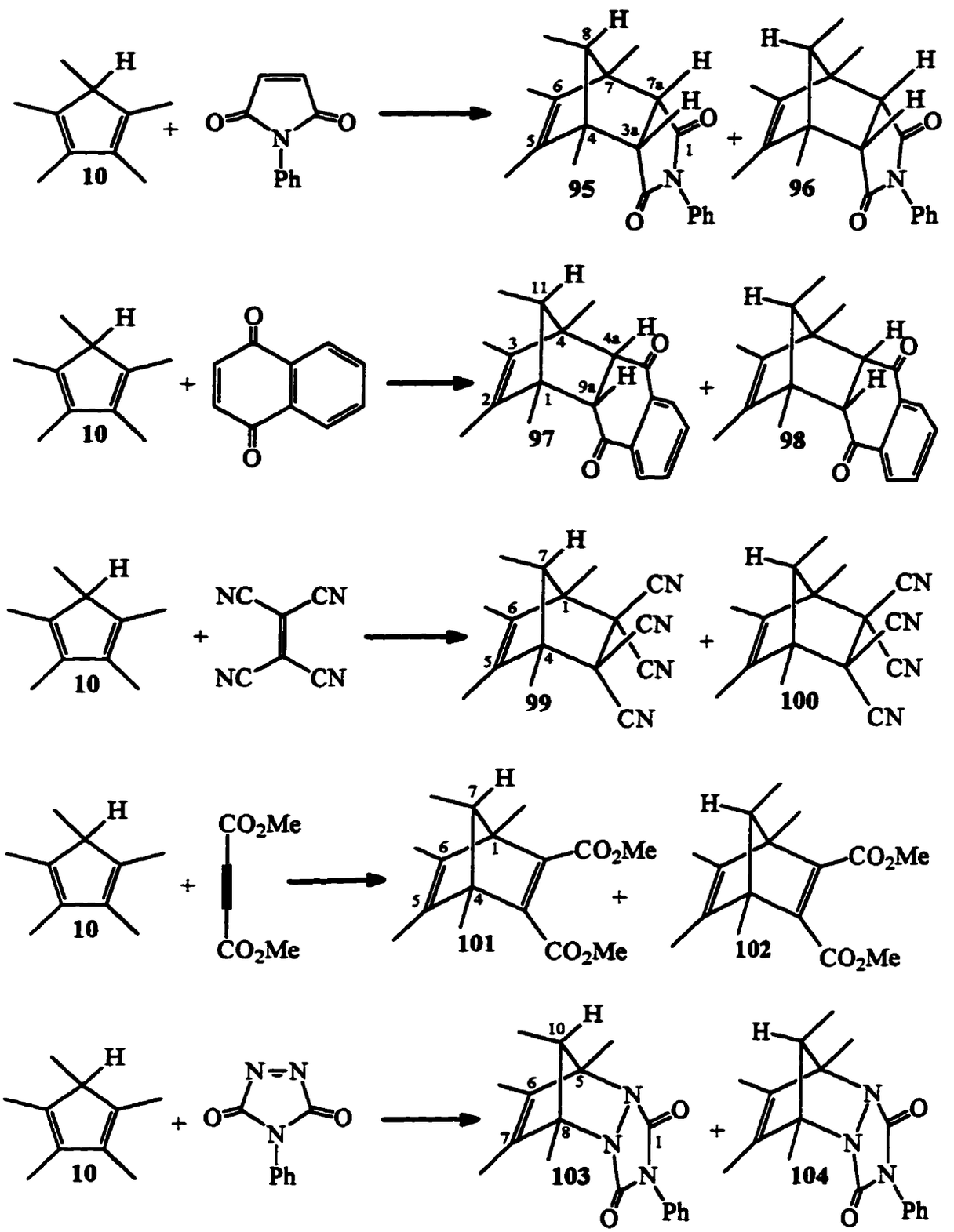
Adducts **95** and **96** were obtained in a ratio of 82 : 18, respectively upon addition of an equivalent of *N*-phenylmaleimide to a solution of diene **10** in ether. Column chromatography gave a homogeneous sample of **95**, however **96** remained in the mixture of diastereomers. The relative stereochemistry of adduct **95** was established based upon the observed 2% nOe enhancement of the signal corresponding to the C-8 hydrogen (δ 1.60) upon saturation of the C-3a and C-7a hydrogens (δ 3.04). This was consistent with **95** being the product of addition *anti* to the methyl group.

A solution of **10** in ether was treated with an equivalent of 1,4-naphthoquinone giving, after 24 hours at room temperature, a mixture of **97** and **98** in a ratio of 84 : 16, respectively. Column chromatography of the mixture gave an analytical sample of the minor adduct **98** as a colourless solid. As a result of the difficulty in separation of the diastereomers, **97** was not isolated from column fractions. The spectral data for **97** were gleaned from spectra of a mixture of the two adducts. The nOe analysis of **97** showed a 3% enhancement of the signal corresponding to the C-11 hydrogen (δ 1.53) upon saturation of the C-4a and C-9a hydrogens (δ 3.11), but with **98** there was a 5% enhancement of the signal corresponding to the C-11 methyl (δ 0.76) upon saturation of the C-4a and C-9a hydrogens (δ 3.09). The enhancements indicated that the major adduct **97** was the product of addition *anti* to the C-5 methyl and adduct **98** was the product of addition *syn* to the C-5 methyl.

1,1,2,2-Tetracyanoethene was added to an ether solution of diene **10** giving a mixture of adducts **99** and **100** in a ratio of 97 : 3, respectively. Column chromatography failed to separate the adducts, but crystallization from methanol gave some needle-like crystals of the major adduct **99**. The nmr signals for adduct **100** were educed from spectra of the crude adduct mixture. Elucidation of the stereochemistry of adduct **99** was done using nOe measurements, which included a 0.3% enhancement of the signal corresponding to the C-5 and C-6 methyls (δ 1.83) upon saturation of the signal for the C-7 methyl (δ 0.81). This was indicative of **99** being the product of addition *anti* to the C-5 methyl group.

A solution of **10** in ether was treated with an equivalent of dimethyl acetylenedicarboxylate resulting in the formation of a mixture of **101** and **102** in a ratio of 76 : 24, respectively, after seven days at room temperature. The adducts proved to be inseparable by flash chromatography on silica gel, and the nmr analysis was done on the mixture of diastereomers which was recovered in 60% yield from the flash column. Hydrolysis of the methyl esters of the product during chromatography may account for the low recovery of adducts by chromatography. (Samples which were allowed to stand at room temperature for several weeks showed signals in nmr spectra which were indicative of carboxylic acids.) ^{1}H nmr spectrum of **101** showed a 0.7% enhancement for the singlet corresponding to the C-7 methyl (δ 0.71) upon saturation of the singlet due the C-5 and C-6 methyls, indicating that **101** was the product of addition *anti* to the C-5 methyl group.

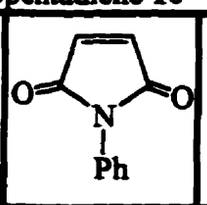
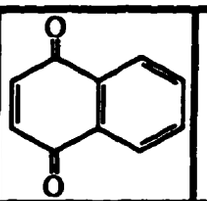
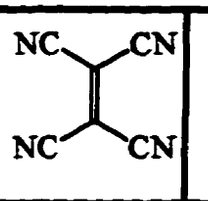
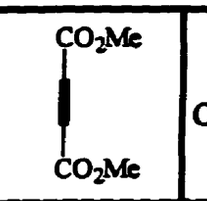
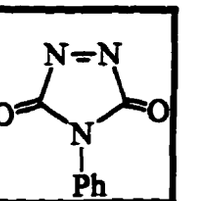
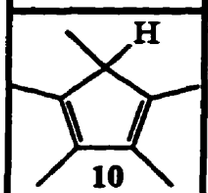
Addition of an equivalent of 4-phenyl-1,2,4-triazoline-3,5-dione to a solution of **10** in ether afforded a mixture of **103** and **104** in a ratio of 75 : 25, respectively. The mixture proved to be inseparable by flash chromatography, and a mixture of diastereomers was recovered from column fractions in 95% yield. The adducts were therefore analysed as a mixture . The nOe data for **103** showed a 2% enhancement in the signal corresponding to the C-6 and C-7 methyls (δ 1.50) upon saturation of the C-8 methyl (δ 0.21). Conversely, a 0.9% enhancement of the signal corresponding to the C-8 methyl was seen upon saturation of the singlet for the C-6 and C-7 methyls. These data were consistent with



Scheme 18. Diels-Alder reactions of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene 10

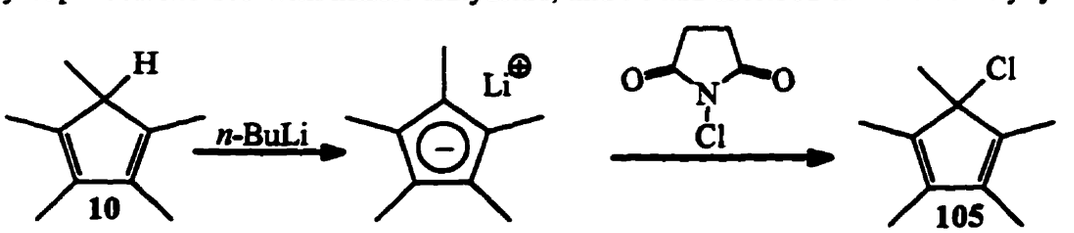
103 being the result of the dienophile adding *anti* to the face of **10** bearing the C-5 methyl. The facial selectivities with diene **10** are summarized in Table 3.

Table 3. Ratios of *anti* to *syn* addition for 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **10**

					
 **10**	82 : 18	84 : 16	97 : 3	76 : 24	75 : 25

5-Chloro-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

Halogen-substituted dienes were prepared in order to study the effects of substitution by heteroatoms on the facial selectivity of these 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene systems. These are the types of dienes that previous workers suggested might demonstrate steric and electronic effects in the facial selectivity of their Diels-Alder reactions. Fallis[31] had examined the addition of 5-chloro-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **105** with maleic anhydride, and he had ascribed the exclusively *syn* to



Scheme 19. Synthesis of 5-chloro-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **105**

chlorine facial selectivity to an "electronic" effect, the Cieplak theory. (Following his precedent, the terms *syn* and *anti* used to describe the additions of the halo-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes will be with respect to the halogen substituent.) However, he failed to see the utility of studying other halogen-substituted-pentamethyl-1,3-cyclopentadienes, such as the bromo- and iodo-dienes **106** and **107**, to see if any trends existed within the group, and maleic anhydride was the only dienophile that was used with diene **105**. Clearly, a systematic study should have involved the addition products of a number of dienophiles. This would have ensured that the result obtained was truly indicative of the selectivity of the diene rather than some feature particular to the dienophile.

In a method analogous to that used for the previous dienes, diene **105** was synthesized by formation of the pentamethylcyclopentadienyl anion and subsequent treatment with *N*-chlorosuccinimide at 0 °C. From the ^{1}H nmr spectrum of the crude product mixture, it was evident that only about 50% conversion of **10** to the chloro-diene **105** had been accomplished. Addition of the *N*-chlorosuccinimide at room temperature, rather than at 0 °C, and longer reaction times did not lead to an improvement in the yield of **105**. Furthermore, attempts to separate unreacted **10** from the 5-chloro-diene **105** by column chromatography did not prove effective. Fortunately, the ^{1}H nmr signals for the adducts derived from **105** and from diene **10** did not overlap, so analysis of crude mixtures of adducts, containing also adducts of **10**, was carried out without difficulty.

Addition of an equivalent of *N*-phenylmaleimide to an ether solution containing diene **105** gave, after 24 hours at room temperature, adduct **108** as the exclusive product from **105**. Column chromatography gave homogeneous **108** as a colourless solid. The relative stereochemistry of adduct **108** was not elucidated by nOe techniques due to inconclusive enhancements. The structure of **108** was determined to be product of *syn* addition by x-ray crystallography (Figure 15).

Treatment of an ether solution containing diene **105** with an equivalent of 1,4-naphthoquinone, after 16 hours at room temperature, yielded **109** as the only detectable product from **105**. Column chromatography gave homogeneous **109** as a colourless solid. The nOe experiments with **109** did not provide any stereochemically diagnostic information. For each of the dienes studied, the facial selectivity results for *N*-phenylmaleimide and 1,4-naphthoquinone have been very similar, so the stereochemistry of adduct **109** has been tentatively assigned as the *syn* to chlorine addition product, consistent with the results observed for the addition of diene **106** with *N*-phenylmaleimide.

An equivalent of 1,1,2,2-tetracyanoethene was added to a solution containing diene **105** in ether giving, after 16 hours at room temperature, adduct **110** as the only observed product from **105**. Column chromatography gave homogeneous **110** as colourless solid. The stereochemistry of **110** followed from the nOe data, which showed a 0.5% enhancement of the signal corresponding to the C-7 methyl (δ 1.39) upon saturation of the singlet for the C-5 and C-6 methyls (δ 1.90). Conversely, a rather modest 0.3%

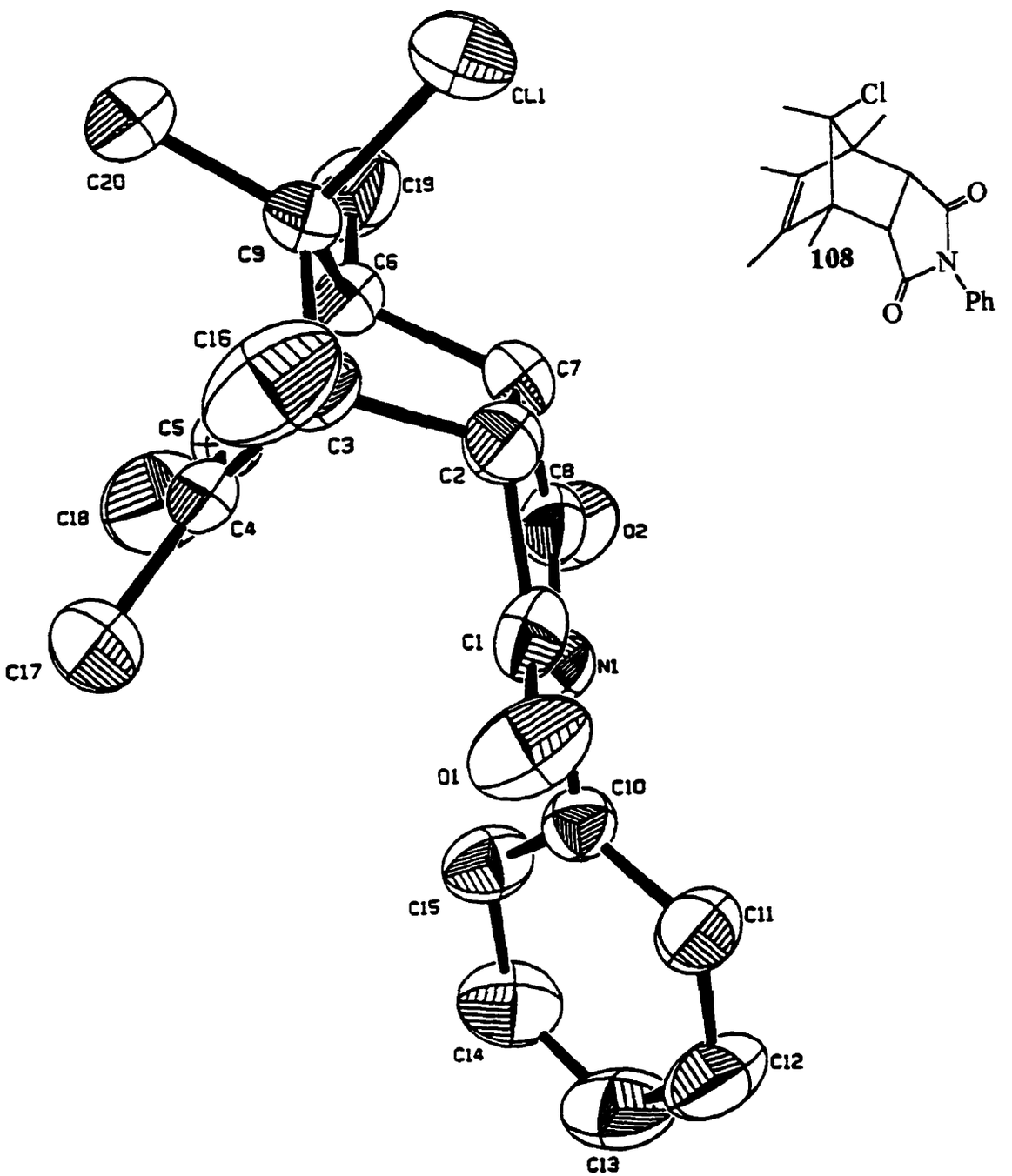


Figure 15. X-ray crystal structure of adduct **108**

enhancement of the signal corresponding to the C-5 and C-6 methyls was noted upon saturation of the signal for the C-7 methyl. These enhancements indicate that **110** was the product of addition of 1,1,2,2-tetracyanoethene to the face of **105** *syn* to the chlorine atom. The structure of **110** was confirmed by x-ray crystallography (Figure 16).

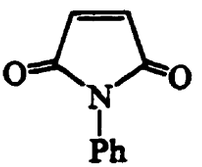
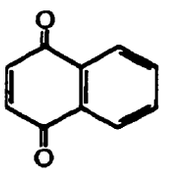
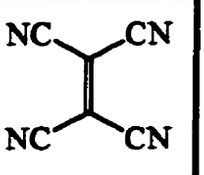
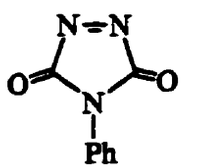
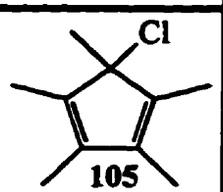
The addition of dimethyl acetylenedicarboxylate to diene **105** gave a black tarry substance, in which no addition products could be discerned by ^{1}H nmr. It was believed that diene **105** as well as the other 5-halogen -substituted pentamethyl-1,3-cyclopentadienes did not survive the long reaction times required for reaction with this dienophile.

Treatment of a solution containing **105** in ether with an equivalent of 4-phenyl-1,2,4- triazoline-3,5-dione yielded, after 16 hours at room temperature, adduct **111** as the only observed product of **105**. Column chromatography gave an analytical sample of adduct **111** as colourless crystals. The nOe analysis of adduct **111** failed to provide any diagnostically useful enhancements. However, the result of an x-ray analysis showed that adduct **111** was the product of addition *anti* to the chlorine. The facial selectivities with diene **105** are summarized in Table 4.

5-Bromo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

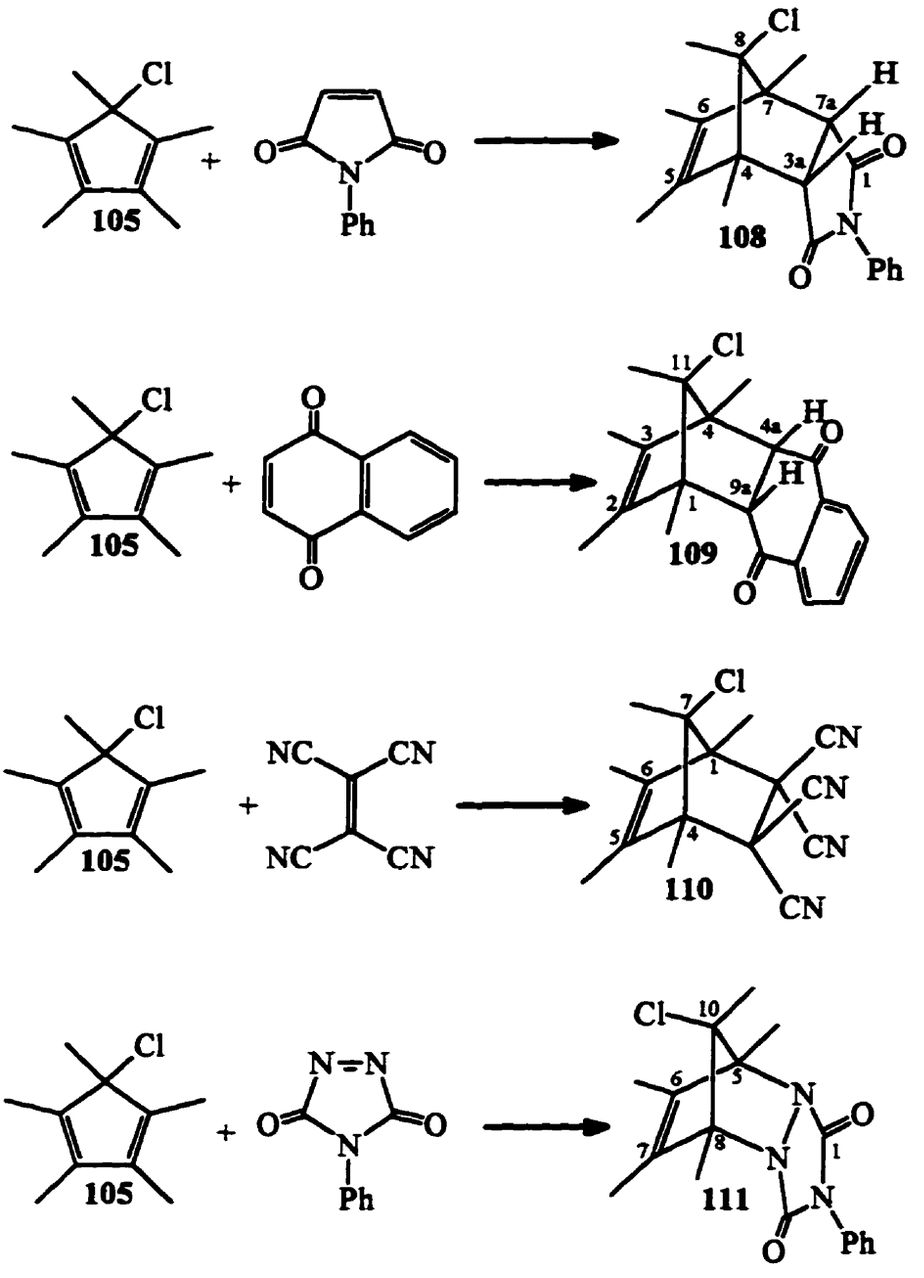
Formation of 5-bromo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **106** proceeded by addition of an equivalent of *N*-bromosuccinimide to the pentamethylcyclopentadienyl anion. Formation of the bromo-substituted diene proved to be more efficient than the chloro-analogue. Nevertheless, impurities resulting from degradation of the succinimide

cyclopentadiene **105**

				
 **105**	100% *syn*	100% *syn*	100% *syn*	100% *anti*

were often present in the diene, but purification of the diene by normal flash chromatography proved to be impossible due to a vigorous reaction when the crude product came into contact with the silica gel. The succinimide-derived impurities, however, did not impede analysis of the crude adduct mixtures. The bromo-substituted diene **106**, due to its instability at room temperature, could be used with only the more reactive dienophiles.

Addition of *N*-phenylmaleimide to a solution of diene **106** in ether gave, after 24 hours at room temperature, a mixture of two adducts **112** and **113** in a 50 : 50 ratio. Column chromatography gave a homogeneous sample of **112**, however **113** was recovered from column fractions in a three part mixture of **112**, **113**, and unreacted *N*-phenylmaleimide. The elucidation of the stereochemistry of adduct **112** was done by interpretation of nOe enhancement measurements that included a 3% enhancement of the signal corresponding to the C-8 methyl (δ 1.11) upon saturation of the signal due to the



Scheme 20. Diels-Alder reactions of 5-chloro-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **105**

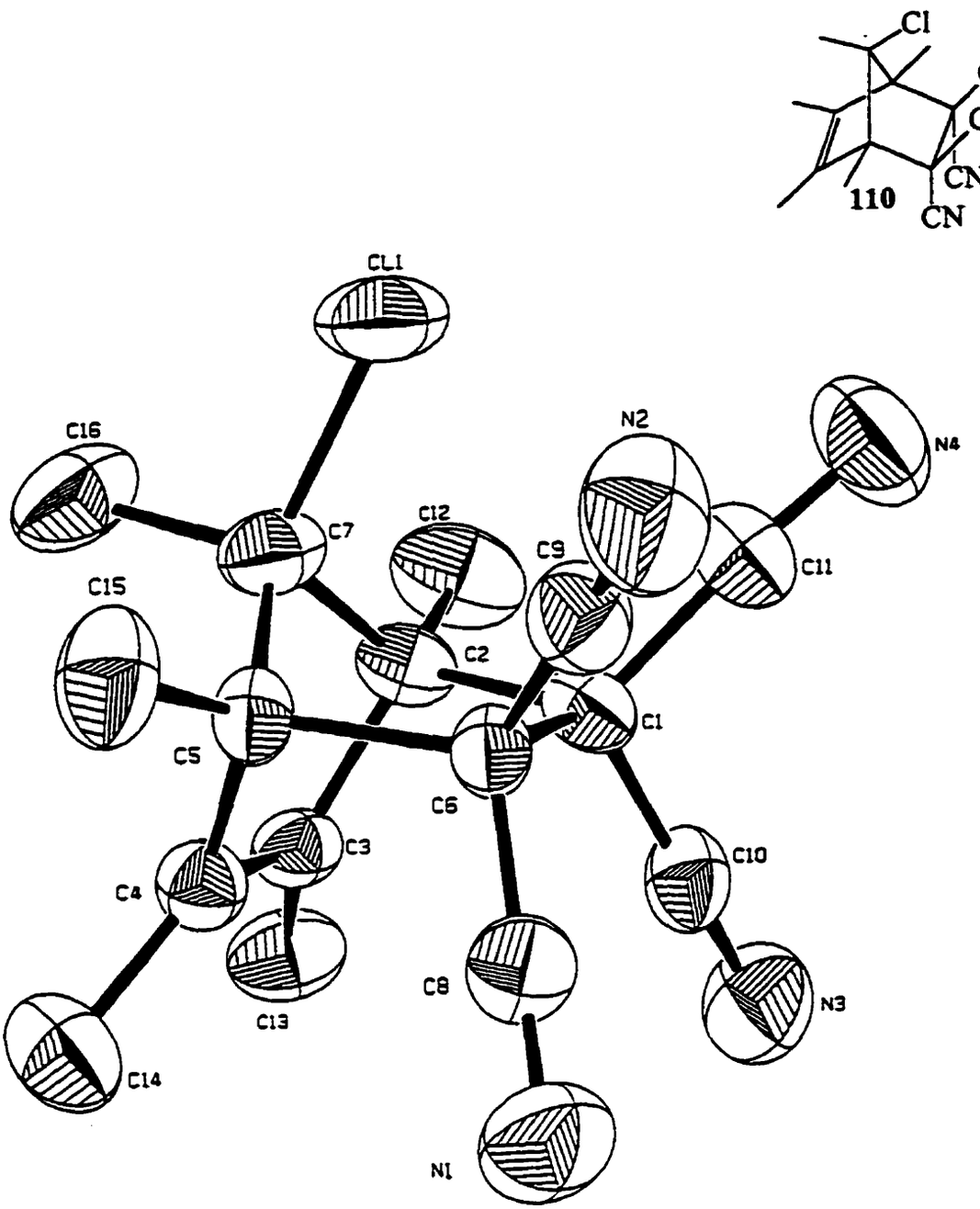
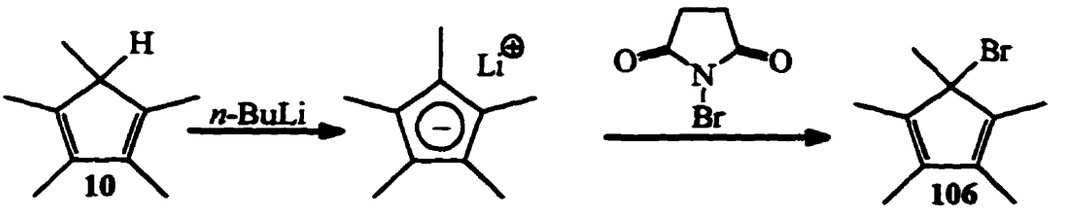


Figure 16. X-ray crystal structure of adduct **110**

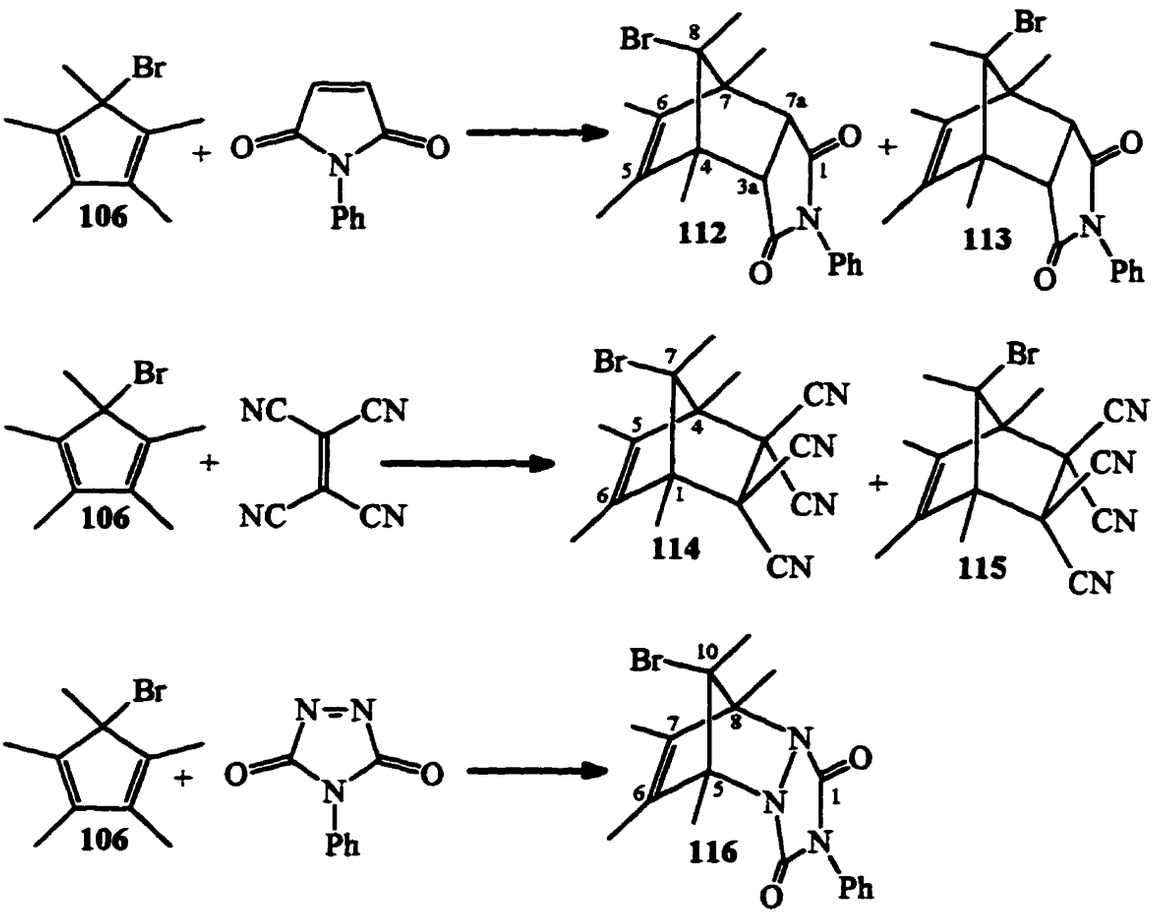


Scheme 21. Synthesis of 5-bromo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **106**

C-3a and C-7a hydrogens (δ 2.24). Also, an 11% enhancement of the signal corresponding to the C-3a and C-7a methyls was observed upon saturation of the signal for the C-8 methyl. The enhancements indicate that adduct **112** was the product of addition of *N*-phenylmaleimide to diene **106** *syn* to the bromine. Not only was the diene **106** unstable, but its adducts also decomposed quite quickly in $CDCl_3$ solution. This instability led to poor recoveries of adducts from the flash columns. The adducts were stable for reasonable periods as benzene solutions.

Addition of an equivalent of 1,4-naphthoquinone to a solution of **106** in ether gave, after 24 hours at room temperature, a black tarry substance. The black tar contained no observable addition products by ^1H nmr.

An equivalent of 1,1,2,2-tetracyanoethene was introduced into an ether solution of **106**. After 24 hours at room temperature, a mixture of adducts **113** and **114** in a ratio of 95 : 5, respectively was obtained. Preparative TLC gave a homogeneous sample of **113** as a colourless solid. However, due to the small proportion of adduct **114**, it was not isolated, so the nmr data for adduct **114** were excerpted from spectra of the crude adduct mixture. The nOe enhancements of adduct **113** failed to provide conclusive evidence for the stereochemistry of adduct **113**. The stereochemistry of the major adduct was



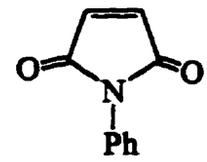
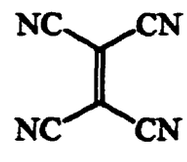
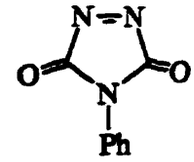
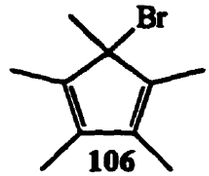
Scheme 22. Diels-Alder reactions of 5-bromo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **106**

tentatively assigned to be the product of addition of the dienophile *anti* to the bromine. This assignment has been made pending final verification by x-ray crystallography.

Treatment of a solution of **106** in ether with 4-phenyl-1,2,4-triazoline-3,5-dione resulted in adduct **116** as the only observed addition product. Passage through a silica plug gave an analytical sample of **116** as a colourless solid. Again, attempts to gain evidence for the stereochemistry of **116** by the measurement of nOe enhancements proved

fruitless. Therefore, the structure was determined to be the product of addition *anti* to the bromine by x-ray crystallography (Figure 17). The facial selectivities with diene **106** are summarized in Table 5.

Table 5. Ratios of *anti* to *syn* addition for 5-bromo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

			
 **106**	50 : 50	95 : 5	100% *anti*

5-Iodo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

5-Iodo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **107** was produced in a slightly different manner than the other halogen-substituted dienes. Rather than using *N*-iodosuccinimide as the iodine source, iodine crystals were used instead. This was done to eliminate the residual impurity caused by the succinimide, and, also, the disappearance of the characteristic brown colour of the iodine provided a good indication of when formation of the diene was complete. However, **107** and its adducts were even more unstable than **106** and its adducts in $CDCl_3$ and **107** decomposed quickly over silica gel.

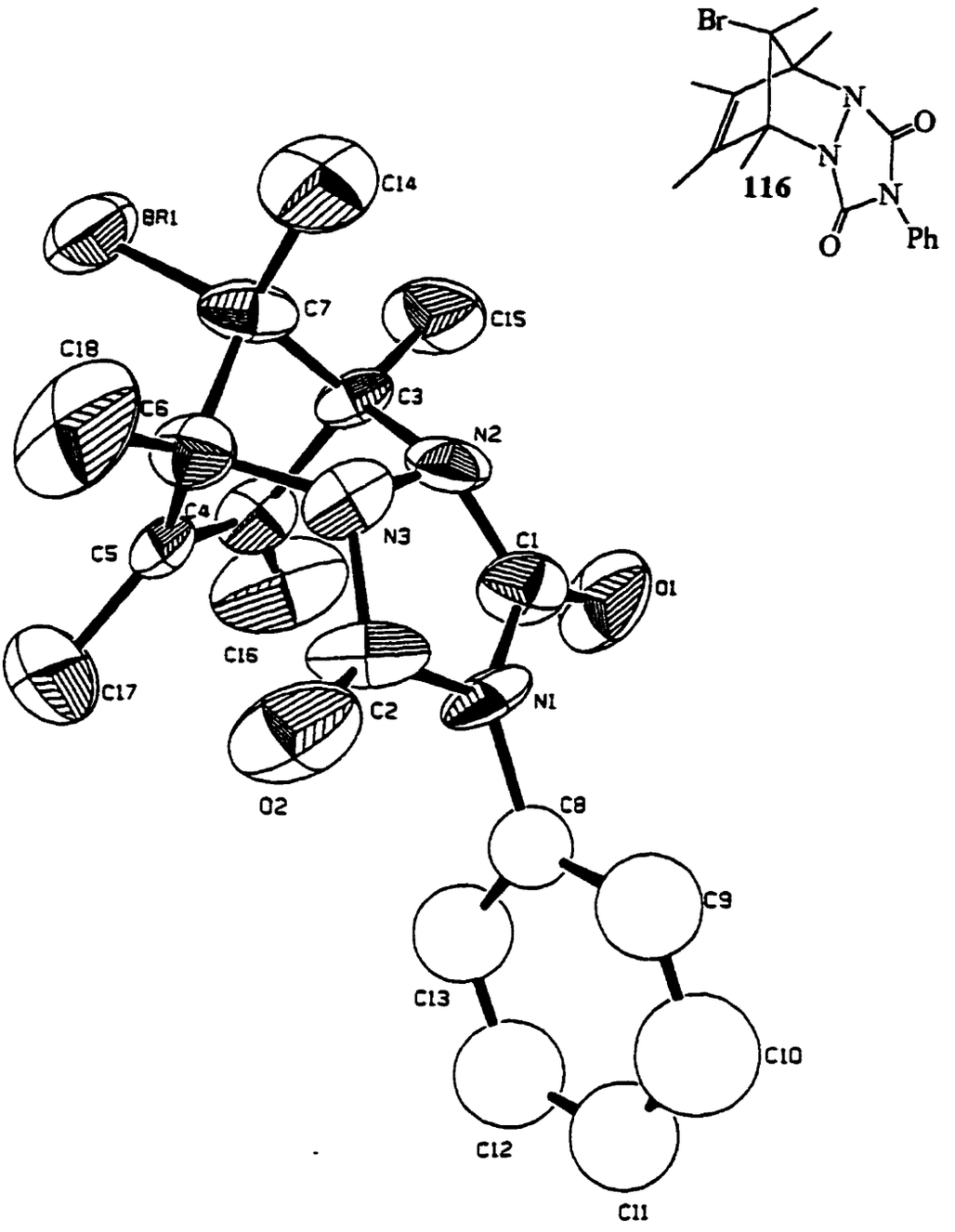
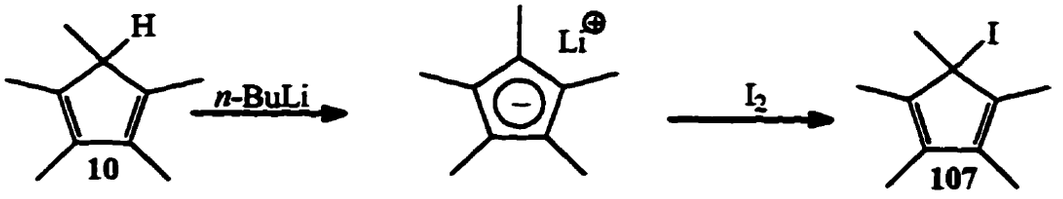


Figure 17. X-ray crystal structure of adduct **116**



Scheme 23. Synthesis of 5-iodo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **107**

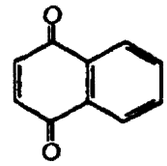
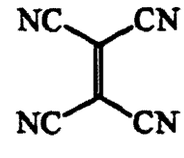
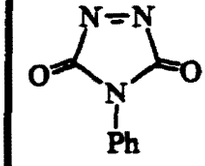
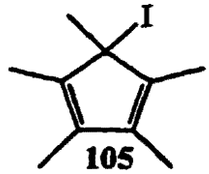
An equivalent of *N*-phenylmaleimide was added to a solution of **107** in ether giving, after 8 hours at room temperature, adduct **117** as the only detectable product. Rapid passage through a silica plug followed by column chromatography gave **117** as a pale yellow solid. The relative stereochemistry of adduct **117** was evident from a 0.7% enhancement of the signal corresponding to the C-8 methyl (δ 1.81) upon saturation of the singlet corresponding to the C-3a and C-7a hydrogens (δ 3.13). Also, saturation of the singlet corresponding to the C-8 methyl resulted in a 12% enhancement of the signal corresponding to the C-3a and C-7a hydrogens. These enhancements were strong evidence that adduct **117** was the *anti*-addition product (Figure 18).

Addition of an equivalent of 1,1,2,2-tetracyanoethene to a solution of diene **107** in ether gave, after 16 hours at room temperature, adduct **118** as the only observed product. Adduct **118** proved to be very unstable, and it decomposed even when refrigerated. This instability precluded nOe and x-ray analysis. It is expected that the selectivity in this addition should be consistent with that observed for the reaction between diene **107** and *N*-phenylmaleimide. For this reason, the stereochemistry of adduct **118** has been

tentatively assigned as the product of addition of 1,1,2,2-tetracyanoethylene *anti* to the iodo-substituent.

Treatment of a solution of diene **107** in ether with 4-phenyl-1,2,4-triazoline-3,5-dione gave, after 16 hours at room temperature, **119** as the only adduct. Adduct **119** also decomposed quickly. Due to its unstable nature, x-ray analysis was not practical, and, unfortunately, nOe enhancements failed to provide evidence for the relative stereochemistry of adduct **119**. The results of dienes **105** and **106** with 4-phenyl-1,2,4-triazoline-3,5-dione both showed that addition proceeded exclusively *anti* to the substituent. It would be expected that diene **107** would also follow this trend of *anti* addition. Thus the structure of adduct **119** was tentatively assigned as the product of addition *anti* to the iodine. The addition results for diene **107** are presented in Table 6.

Table 6. Addition results for 5-iodo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **107**

			
 **105**	100% *anti*	100% *anti*	100% *anti*

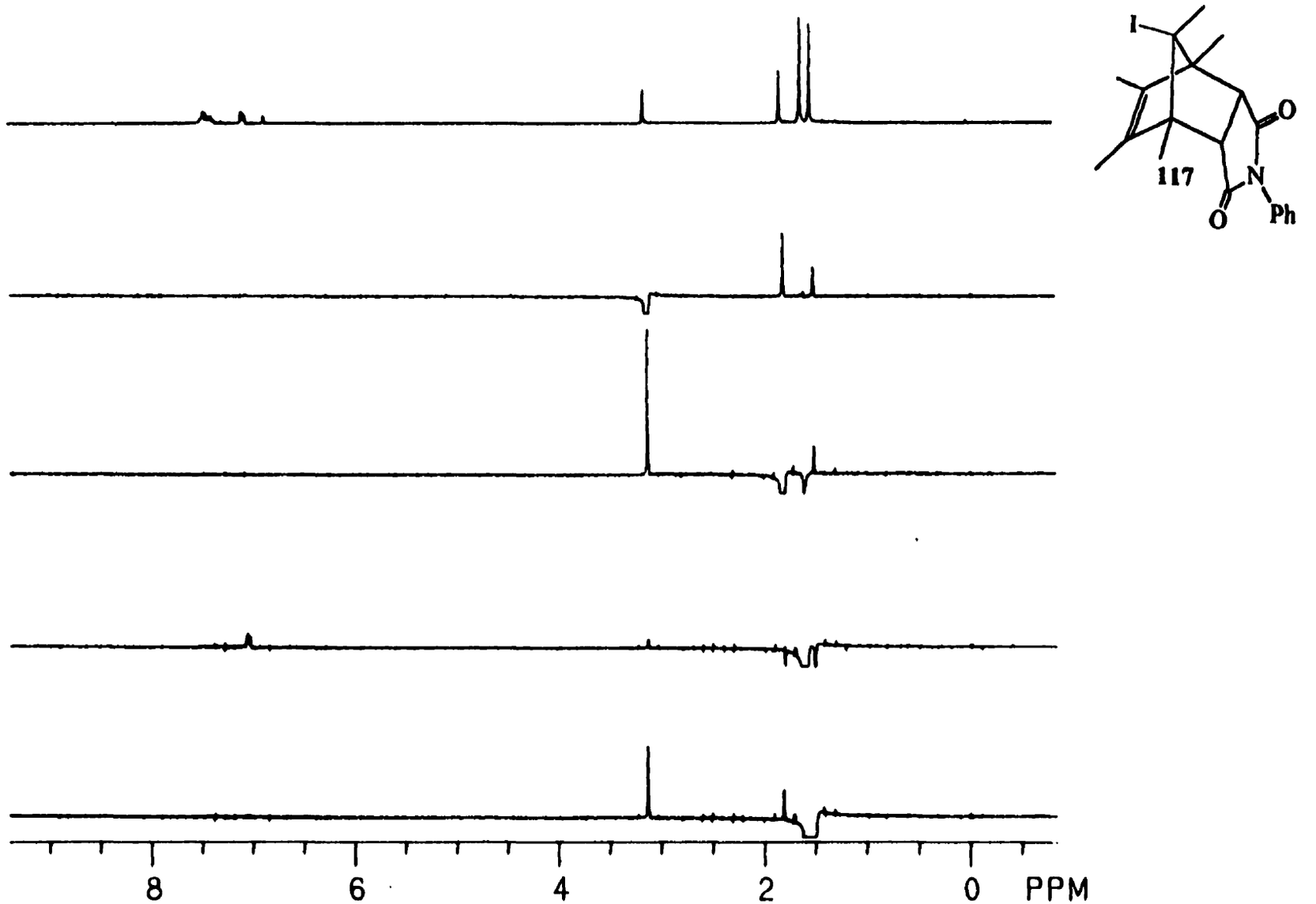
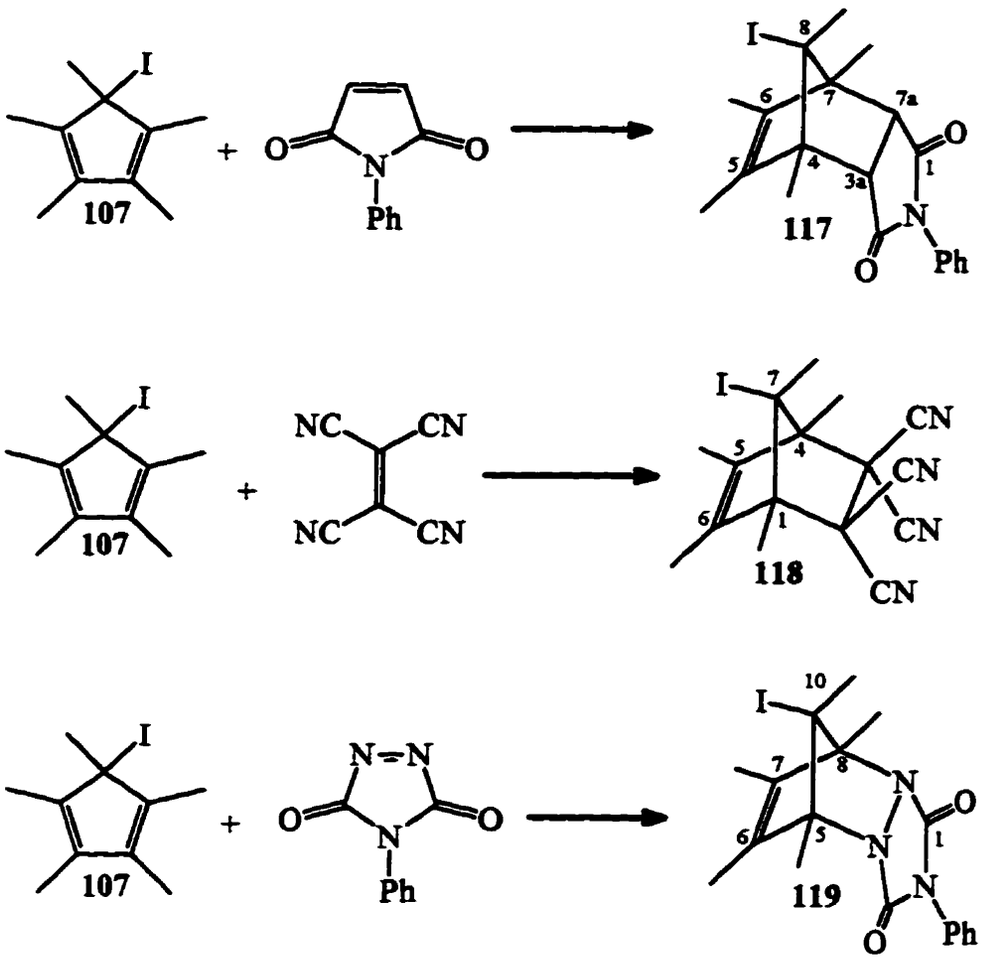


Figure 18. NOe spectra of adduct 117



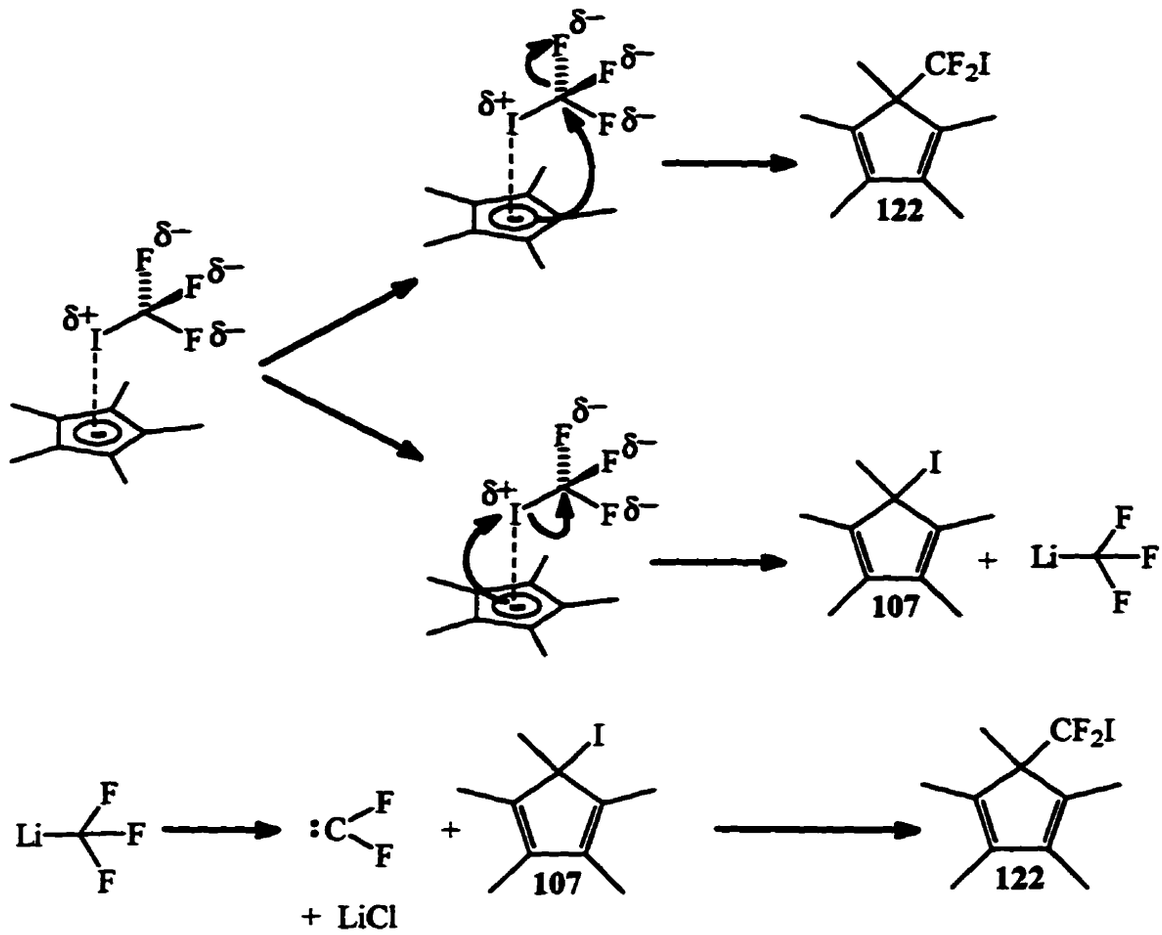
Scheme 24. Diels-Alder reactions of 5-iodo-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **107**

trifluoromethyl-1,3-cyclopentadiene **120** would be an excellent way to determine the effect of electron-withdrawing groups on the facial selectivity. Due to the similarity in size between methyl and trifluoromethyl groups, the faces of **120** should be sterically very similar and so the facial selectivity might be mainly the result of the difference in electronegativity or another "electronic" difference between the two groups. The

synthesis was attempted in the usual way: generation of the pentamethylcyclopentadienyl anion and then the addition of trifluoroiodomethane. Without isolation of the product, the reaction mixture was added to a solution of *N*-phenylmaleimide in ether. The crude product mixture was analysed by ^{1}H nmr spectroscopy. The spectrum showed signals for adduct **117**, which we had seen derived from diene **107**, but there were also signals for a second adduct, which appeared similar to those expected for the adduct of diene **120**. However, in the ^{1}H nmr spectrum of this second adduct a signal corresponding to the methyl situated on C-8 appeared as a triplet (J = 1.5 Hz). Considering the ability of fluorine to couple with hydrogens, some coupling was expected, but three fluorines should have resulted in a quartet rather than the observed triplet. It was noted that a homogeneous sample of the second adduct slowly turned pink upon standing in solution, and this solution gave a positive test by starch-iodide. The high resolution mass spectral analysis showed a parent ion which corresponded to the molecular formula $C_{20}H_{22}F_2INO_2$. This, coupled with the nmr evidence, which was indicative of the addition product of a 5-substituted 1,2,3,4,5- pentamethyl-1,3-cyclopentadiene, revealed that this was compound **121**, the adduct of 5-difluoroiodomethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **122** and *N*-phenylmaleimide. Furthermore, nOe enhancements of 5% for the signal corresponding to the C-8 methyl (δ 1.18) upon saturation of the C-3a and C-7a (δ 3.10) hydrogens and a 10% enhancement of the signals corresponding to the C-3a and C-7a hydrogens upon saturation of the C-8 methyl showed that **121** was a result of addition of the dienophile *anti* to the difluoroiodomethyl substituent.

To our knowledge the formation of diene **122** or any difluoroiodomethyl derivative, by an anionic process from trifluoroiodomethane is without precedent in the literature. However, we can rationalize this chemistry in the two ways shown in Scheme 25. The strong electron-withdrawing properties of the fluorines of trifluoroiodomethane must cause the iodine to be significantly polarized, so the iodine carries a significant partial positive charge. (This would be consistent with the formation of **107** as the other product.) Upon addition to the pre-formed cyclopentadienyl anion, there may be a pre-association of this partial positive centre (the iodine) with the anion. The electrostatic attraction between the iodine and the anion might make it impossible for the anion also to attack the alkylating agent while expelling iodine as a leaving group in a concerted S_N2 process. The result is the displacement of the poorer leaving group, fluoride, by the S_N2 mechanism to give diene **122**.

The second rationalization is as follows. Trifluoroiodomethane is known to form difluorocarbenes in the presence of alkyllithium reagents.[42] Cao *et. al* noted that the difluorocarbene could attack iodide ion in solution to form CF_2I^-.[43] While this cannot lead to diene **122**; it does suggest an affinity of difluorocarbene for iodide. Thus, it is possible that difluorocarbene is also able to insert itself into the C-5-to-iodine bond of diene **107** (formed by the S_N2 process) to give diene **122**. Further investigation into this diene was abandoned due to the fact that the large substituent size would be expected to force additions to proceed exclusively *anti* and would not fit into the study.



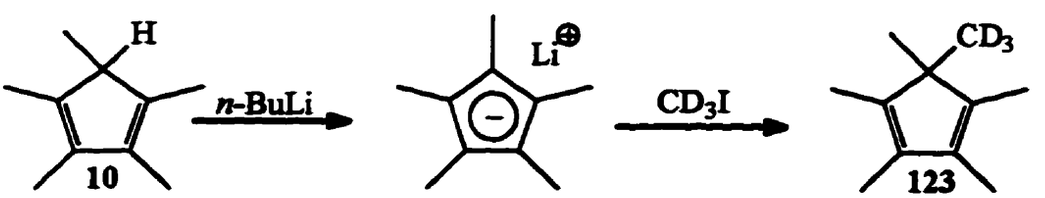
Scheme 25. Formation of difluoroiodomethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **122**

5-Trideuteromethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

Calculations were done using 3-21G-optimized structures of a 1,3-cyclopentadiene substituted with both methyl and trideuteromethyl at the C-5 position. The computational results suggested that Diels-Alder reactions with this diene in its staggered-staggered conformation should show a considerable secondary deuterium isotope effect.[44] The implication was that a diene such as 5-trideuteromethyl-1,2,3,4,5-pentamethyl-1,3-

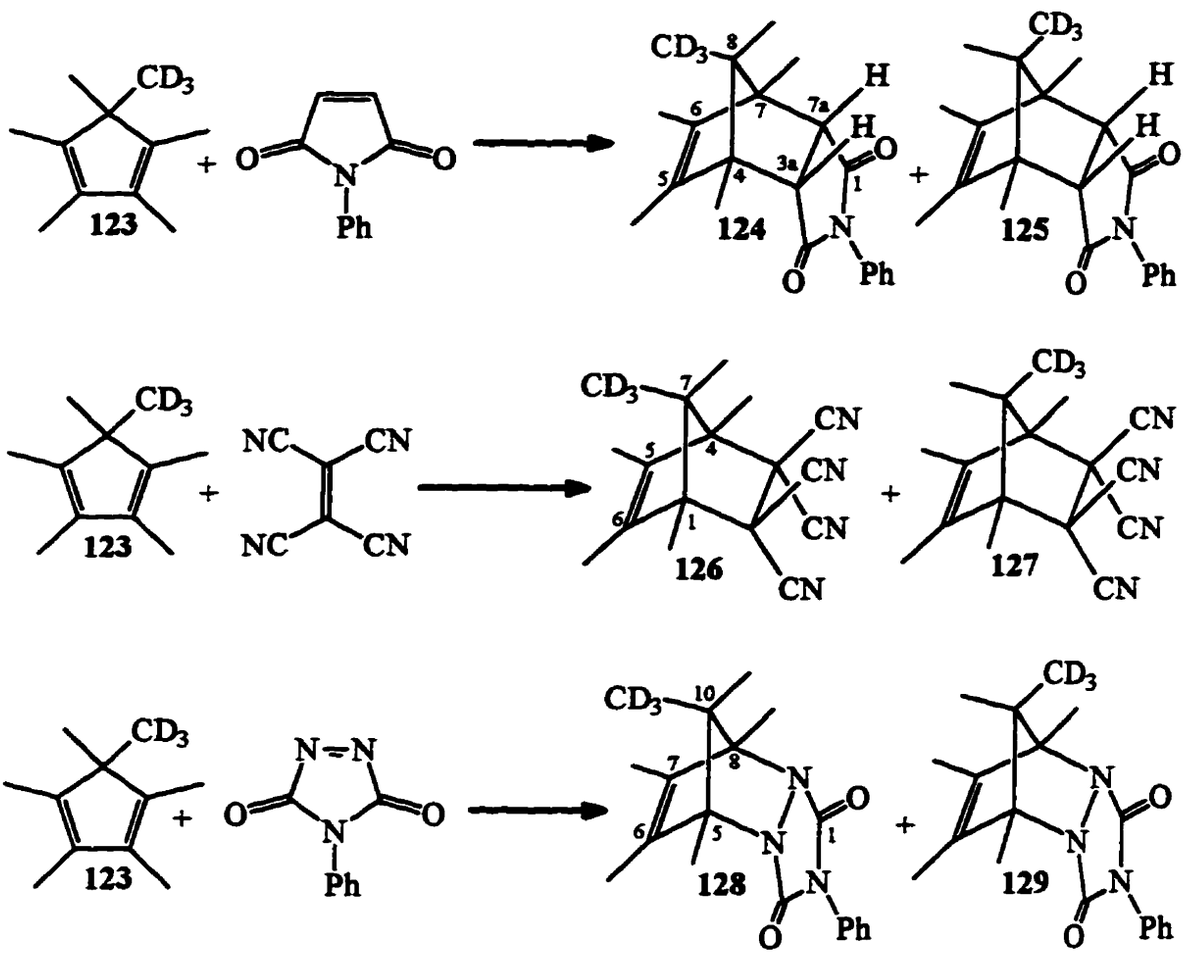
cyclopentadiene **123** should show facial selectivity measurable even by nmr in its additions with various dienophiles.

Diene **123** was produced by treatment of the pentamethylcyclopentadienyl anion with 1.2 equivalents of iodomethane-d_3 at 0 °C. Products of addition to diene **123** with *N*-phenylmaleimide, 4-phenyl-1,2,4-triazoline-3,5-dione and 1,1,2,2-tetracyanoethene were formed, but in no reaction was any facial selectivity evident.



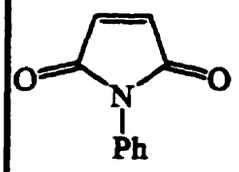
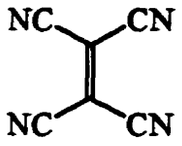
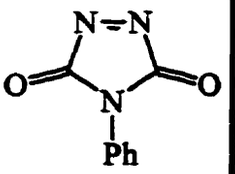
Scheme 26. Synthesis of 5-trideuteromethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **123**

Additions of diene **123** with 4-phenyl-1,2,4-triazoline-3,5-dione were done at several different temperatures from room temperature to -78 °C. The crude adduct mixtures were analysed by both ^{1}H nmr and ^{2}H nmr, however integration of these spectra did not reveal facial selectivity for any of the additions (Figure 30). This negative result led to a further computational investigation, which revealed that the facial selectivity and the sign of the isotope effect were highly dependant upon the conformations of the C-5 methyl and trideuteromethyl groups.



Scheme 27. Diels-Alder reactions of 5-trideuteromethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **123**

Table 7. Summary of ^{1}H nmr chemical shifts of bridge methyls for the Diels-Alder adducts of 5-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes

dienophile	adduct	*syn* methyl†	adduct	*anti* methyl†
	**70**	0.79	**70**	0.66
	74	0.82	**75**	0.70
	85	0.95	**86**	0.79
	96	0.76	**95**	0.64
	-	-	**108**	1.30
	112	1.11	**113**	1.58
	117	1.81	-	-
	**71**	1.25	**71**	0.81
	78	1.28	**79**	0.85
	89	1.40	**90**	0.97
	100	0.98	**99**	0.81
	-	-	**110**	1.39
	114	2.00 ($CDCl_3$) 1.51 (C_6D_6)	**115**	1.66 ($CDCl_3$)
	118	1.57 (C_6D_6)	-	-
	**72**	1.05	**72**	0.68
	82	1.07	**83**	
	93	1.19	**94**	0.80
	104	0.75	**103**	0.21
	111	1.59	-	-
	116	1.82	-	-
	119	1.75 (C_6D_6)	-	-

†*syn* and *anti* refer to the orientation of the bridge methyl with respect to the dienophile moiety of the adduct

Discussion

There are many proposals in the literature that suggest that the facial selectivity in 5-substituted-1,3-cyclopentadienes is very largely governed by some stereo-electronic phenomenon. On the other hand, steric hindrance has been invoked as a significant factor in determining the facial selectivity with surprisingly few plane-nonsymmetric dienes. The best-known examples of Diels-Alder facial selectivities that do not seem to be controlled by steric hindrance involve cyclopentadienes substituted by heteroatoms. Various electronic properties of the heteroatom have been used to explain this facial selectivity.

A measure of the steric influence of various groups would be necessary for any argument based primarily upon steric considerations. A relationship between steric hindrance and the facial selectivity in the Diels-Alder reaction could be made once the effective sizes of various substituent groups are known.

It is more difficult to determine the size of a group and its steric influence than it may at first appear. For example, from Van der Waal's radii[45] it seems obvious that an iodine must occupy more space than does a chlorine, and this might reasonably translate into iodine being more sterically hindering than chlorine. On the other hand, experimental values, known as A-values, are available that purport to define steric effects. The A-value is defined as the free energy difference between chair forms of cyclohexane with the atom or group in the equatorial and in the axial position (Figure 19). Some relevant A-values,[40] corresponding Van der Waal's radii and bond lengths[46] are given in Table 8.

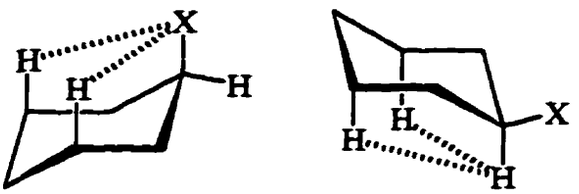


Figure 19. Steric interactions for the determination of A-values

Table 8. A-values and Van der Waal's radii for selected groups

Group	A-value (kJ/mole)	Van der Waal's radius (Å)	Bond length (Å)
H	0	1.2	1.09
CN	0.6 - 1.0	1.4	1.43††
F	1.0	0.71	1.40
I	2.0 - 2.6	2.15	2.16
Br	2.15	1.95	1.97
Cl	3.0	1.8	1.79
OAc	3.0	1.4†	1.43††
OMe	3.1	1.4†	1.43††
OH	3.8 - 4.1	1.4†	1.43††
CO_2Me	5.3 - 5.5	1.4†	1.47††
CO_2H	5.7 - 6.1	1.4†	1.47††
NH_2	5.9	1.5†	1.47††
Me	7.28	2.0	1.53††
Et	~7.3	>2.0	1.53††

† where group radii are not available sizes stated are of the C-5-bonded atom
†† stated values refer to the C-5-to-atom bond length

From Table 8 it is clear that steric hindrance correlates poorly with the space that the group occupies. In fact, the smaller chlorine atom has a larger A-value, and thus is

more sterically hindering, than the larger iodine. Furthermore, both chlorine and iodine appear to be less sterically hindering than is a methyl group.

For groups with similar cyclohexane-to-group bond lengths, such as CN, CH_3, F, NH_2 and OMe, the A-values do reflect the relative sizes of the groups. This accounts for the increase in A-values for carbon-based groups that follow the trend $sp < sp^2 < sp^3$ due to increasing size. This also explains the similarities among the oxygen-based groups such as OAc, OMe and OH. What is not immediately evident is why iodine should be less sterically hindering than either chlorine or bromine, and why a methyl group is among the more sterically hindering groups listed. The anomalies apparent in A-values cannot be attributed to simple size since, from Van der Waal's radii, an iodine is larger than a chlorine; therefore, at least one other factor must also be a significant component. Better sense can be made of A-values if bond lengths are taken into consideration. As the length of the bond that joins the substituent to cyclohexane increases, the substituent gets further away from the interacting axial hydrogens of the cyclohexane rings, decreasing the corresponding A-value (Figure 20).

If Diels-Alder facial selectivity is governed by steric interactions, then it would be reasonable to expect a good correlation with A-values. However, the facial selectivities of dienes **130**, **131** and **132** indicate a range of facial selectivities that do not correlate with A-values.[41] Can these Diels-Alder reactions still be controlled by simple steric interactions?

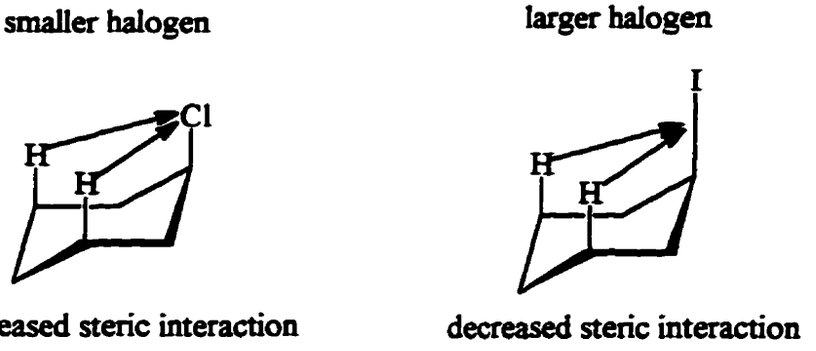


Figure 20. Relative steric influences for A-values.

130 **131** **132**

The geometry and atomic relationships for the Diels-Alder reactions are not the same as those used for A-values. In the Diels-Alder reaction, the steric influences that affect the facial selectivity result from the interaction of the C-5-substituent and the incoming dienophile in the *syn* transition state versus the interaction of the C-5 hydrogen and the incoming dienophile in the *anti* transition state. With simple 1,3-cyclopentadiene, the C-5 hydrogen is well situated to hinder the incoming dienophile (Figure 21), and *anti* transition states with 5-substituted cyclopentadienes have the same relationship (Figure 22). This is plausible because in the *syn* transition states (Figure 22) the substituent-to-C5-bond length is longer than that of the C-H. Indeed, with X = F, O, or N the steric influence of the group might be less than hydrogen resulting in a greater propensity for addition *syn* to these substituents, but when the substituent is even larger, such as with

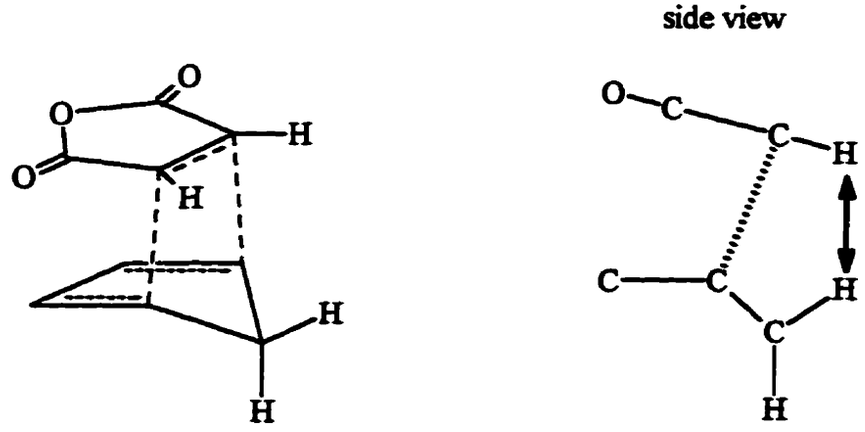


Figure 21. Relative distances in the transition state of the Diels-Alder reaction of 1,3-cyclopentadiene and maleic anhydride

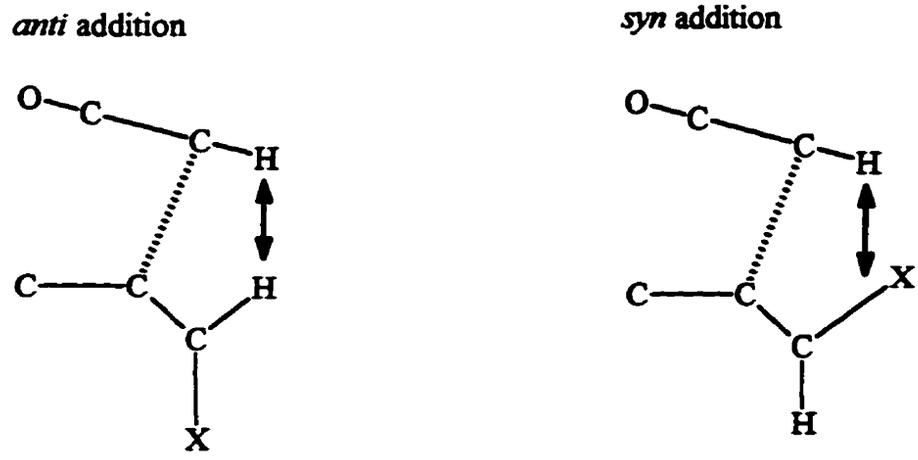
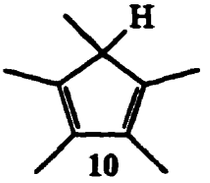


Figure 22. Side views of the transition states of 5-substituted-1,3-cyclopentadienes

methyl, bromine, or iodine, the size of the group will play a more pronounced role in the facial selectivity pushing the selectivity more toward *anti* addition.

From the A-values in Table 8, it can be seen that one traditionally thinks of the hindering ability of a hydrogen to be much less than that of a methyl group. As a result, for the Diels-Alder reaction of **10**, one should expect the selectivity to reflect a large

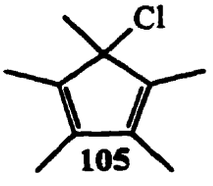
difference in size. Additions of a number of dienophiles to this diene showed preferential approach *anti* to the methyl group. However, the selectivities (Table 3) were rather modest. (The selectivity being as low as 75 : 25 for the reaction of **10** with 4-phenyl-1,2,4-triazoline-3,5-dione.) Even more dramatically, the reaction between diene **133** and *N*-phenylmaleimide gives a *syn* to *anti* ratio of only 1 : 1.5.[41] These selectivities would be consistent with a pronounced hindering ability of the hydrogen. This in turn may be evidence for an important interplay between the C-5-to-substituent bond length and the effective size of the substituent in determining the steric hindrance.



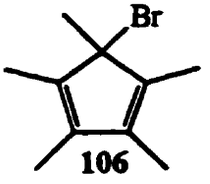
10

133

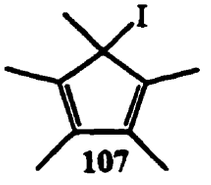
The results of additions involving the 5-halogen-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes **105**, **106** and **107** are very important in corroborating the idea of bond length and size in determining the steric contribution. Additions to the chloro-substituted diene, **105**, indicate that the two effects, namely the shorter C-5-to-methyl bond length and the larger Van der Waal's radius of the methyl group, are both causing additions to proceed *anti* to the methyl, and thus *syn* to the chlorine. These factors are evident in the A-values of the respective substituents which also show a methyl group to be more sterically hindering than chlorine.



105



106



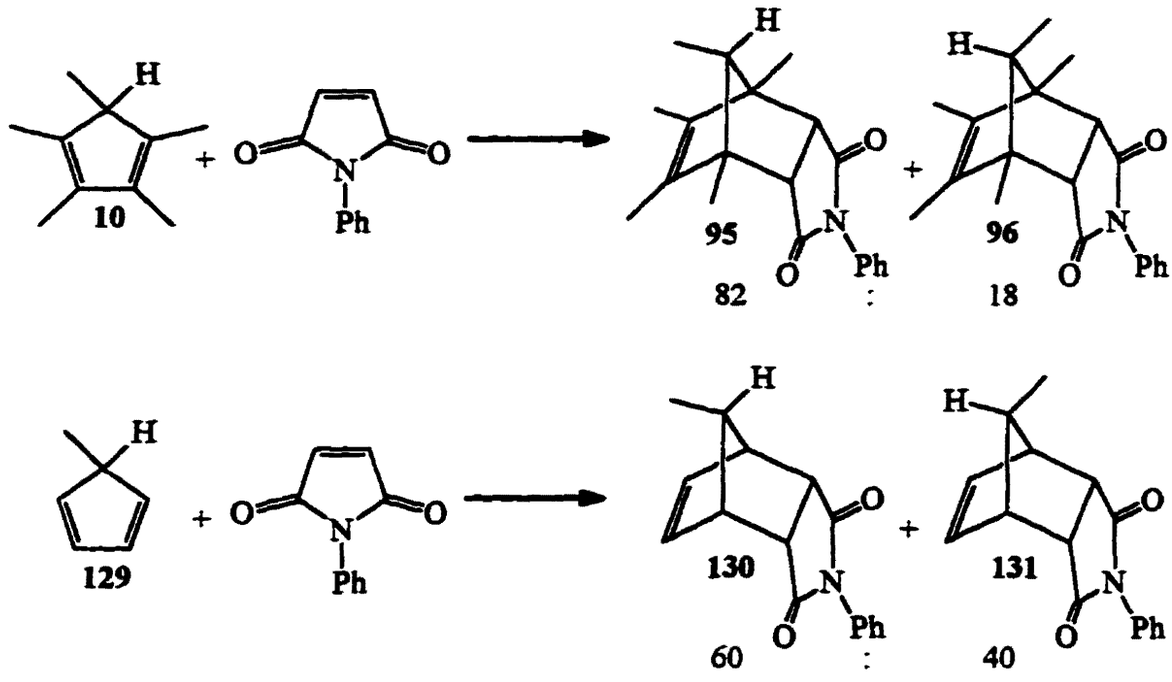
107

The addition of *N*-phenylmaleimide to the bromine-substituted diene, **106**, is probably the most significant in the halogen series since it provides us with an equivalence point for two steric entities. The 50 : 50 ratio of addition products indicates that the effect of the difference in Van der Waal's radii of the groups is exactly balanced by the opposing effect of the difference in the bond lengths of the two substituents.

The results with the iodine-substituted diene, **107**, demonstrate that, in dienes where the substituent has a very large Van der Waal's radius, the steric interaction between the dienophile and the substituent itself dominates the control of the selectivity despite the longer bond length.

When the results obtained for the addition of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **10** are compared with the results obtained for the additions of 5-methyl-1,3-cyclopentadiene, **129**, it might be expected that the facial selectivities would be the same since both involve selectivity that opposes a hydrogen to a methyl. The selectivities were, in fact, not the same with the **10** and **129** giving *syn* : *anti* ratios of 18 : 82 and 40 : 60, respectively, in their additions to *N*-phenylmaleimide (Scheme 28).

The Hammett equation gives a relationship between the ratio of products obtained in a given reaction and the difference in the Gibbs free energy of their transition states. The difference in Gibbs free energy of the *syn* and *anti* transition states ($\Delta\Delta G^{\ddagger}_{(Me\text{-}H)}$) can be calculated to be 0.91 kJ/mol from the ratio of adducts obtained from diene **129**. The same treatment for diene **10**, leads to a difference in the Gibbs free energy, $\Delta\Delta G^{\ddagger}_{(Me^{a}\text{-}H^{a})}$, of 3.8 kJ/mol. The difference in the transition state energies for the two dienes may be a result



Scheme 28. Diels-Alder additions of **10** and **129** with *N*-phenylmaleimide

of another steric or torsional interaction present in the transition state of **10** which is not present in the less substituted diene **129**. In the transition state of cyclopentadiene systems, the C-5 carbon is forced out of the plane of the diene. When this change occurs for diene **10**, the C-5 methyl is forced into a position where it is roughly coplanar with the methyls on C-1 and C-4 of the diene (Figure 23).[47] The closer contact with these methyls may translate into the 2.9 kJ/mol difference in the *syn* activation energies between additions *syn* to methyl in **10** and *syn* to methyl in **129**,assuming that the *anti* transition state energies are the same.[47]

If the energy difference observed is due to a steric interaction then it should be present in all additions *syn* to the methyl with **10**, regardless of the other C-5 substituent.

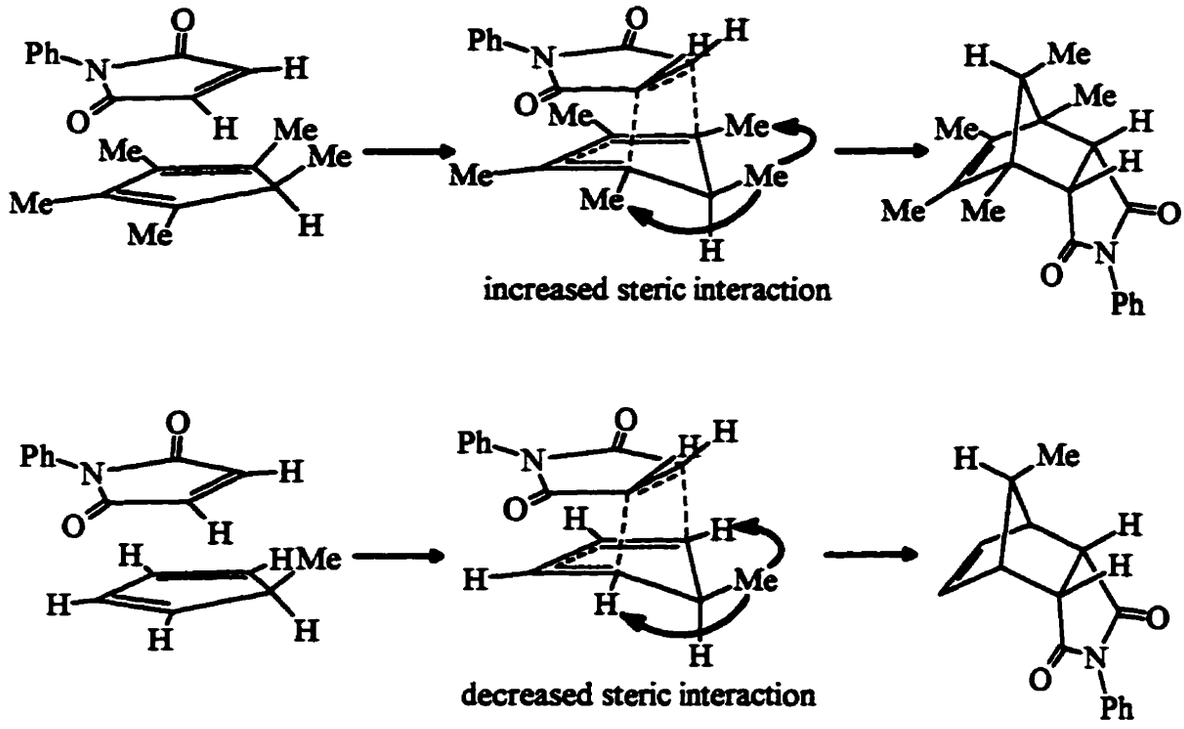


Figure 23. Comparison of *syn* to methyl attacks of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene and 1,3-cyclopentadiene with *N*-phenylmaleimide

With this in mind, the difference in the Gibbs free energies for *syn* and *anti* additions, $\Delta\Delta G^{\ddagger}_{(X\text{-}H)}$, can be calculated for any of the 5-substituted-1,3-cyclopentadiene results. For steric control of the facial selectivity, the effects should be additive and the difference in the Gibbs free energies at the transition states, $\Delta\Delta G^{\ddagger}_{(Me^{a}\text{-}X^{a})}$, for 5-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes can be predicted using the results from 5-substituted-1,3-cyclopentadienes.

The facial selectivity depends on the difference in the Gibbs free energies of the two transition states:

$$\Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}X^{\bullet})} = \Delta G^{\ddagger}_{(Me^{\bullet})} - \Delta G^{\ddagger}_{(x^{\bullet})} \qquad (1)$$

where $\Delta G^{\ddagger}_{(Me^{\bullet})}$ is the activation energy for additions *syn* to methyl for 5-substituted-1,2,3,4,5-pentamethyl-1,3-cyclopentadienes, and $\Delta G^{\ddagger}_{(x^{\bullet})}$ is the activation energy for additions *syn* to the substituent for 5-substituted-1,2,3,4,5-pentamethyl-1,3-cyclopentadienes. When the substituent is hydrogen, i.e.; X = H:

$$\Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}H^{\bullet})} = \Delta G^{\ddagger}_{(Me^{\bullet})} - \Delta G^{\ddagger}_{(H^{\bullet})} \qquad (2)$$

Then, because rearranging (2) gives (3):

$$\Delta G^{\ddagger}_{(Me^{\bullet})} = \Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}H^{\bullet})} + \Delta G^{\ddagger}_{(H^{\bullet})} \qquad (3)$$

in which $\Delta G^{\ddagger}_{(H^{\bullet})}$ is the activation energy for additions *syn* to hydrogen for **10**. Making the substitution gives:

$$\Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}X)} = \Delta G^{\ddagger}_{(H^{\bullet})} + \Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}H^{\bullet})} - \Delta G^{\ddagger}_{(x^{\bullet})} \qquad (4)$$

For the simple 5-substituted-1,3-cyclopentadienes,

$$\Delta\Delta G^{\ddagger}_{(X\text{-}H)} = \Delta G^{\ddagger}_{(x)} - \Delta G^{\ddagger}_{(H)} \qquad (5)$$

It can be assumed that addition *syn* to the hydrogen at C-5 of **10**, $\Delta G^{\ddagger}_{(H^{\bullet})}$, and *syn* to the C-5 hydrogen of 5-substituted-1,3-cyclopentadienes, $\Delta G^{\ddagger}_{(H)}$, require very similar energy, hence

$$\Delta G^{\ddagger}_{(H^{\bullet})} = \Delta G^{\ddagger}_{(H)} \qquad (6)$$

For substituents with relatively long C-5-to-substituent bond lengths, it might be assumed that the energy required for addition *syn* to a substituent of 5-substituted-1,2,3,4,5-penta-

methyl-1,3- cyclopentadienes, $\Delta G^{\ddagger}_{(x^{\bullet})}$, and 5-substituted-1,3-cyclopentadienes, $\Delta G^{\ddagger}_{(x)}$, will also require very similar energies, i.e.:

$$\Delta G^{\ddagger}_{(x^{\bullet})} = \Delta G^{\ddagger}_{(x)} \qquad (7)$$

Making the required substitutions gives:

$$\Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}X)} = \Delta G^{\ddagger}_{(H)} + \Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}H^{\bullet})} - \Delta G^{\ddagger}_{(x)} \qquad (8)$$

and taking into account (5):

$$\Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}X^{\bullet})} = \Delta\Delta G^{\ddagger}_{(Me^{\bullet}\text{-}H^{\bullet})} - \Delta\Delta G^{\ddagger}_{(X\text{-}H)} \qquad (9)$$

Thus, the equation is reduced to variables that can be obtained experimentally. Table 9 lists the selectivities observed for various additions, the corresponding $\Delta\Delta G^{\ddagger}$ values, and the calculated $\Delta\Delta G^{\ddagger}$ using the above equation.

Several of the 5-substituted-1,2,3,4,5-pentamethyl-1,3-cyclopentadienes presented in Table 9 do not have reliable $\Delta\Delta G^{\ddagger}_{(X\text{-}H)}$ values. For examples such as the chloro- and iodo-substituted dienes, the observed 100% selectivities cause a problem in the estimation of the difference in energy for the *syn* and *anti* transition states. Whenever possible, experimental values of $\Delta\Delta G^{\ddagger}$ were used in our calculations in Table 9 but unfortunately, certain dienes such as 5-cyano- and 5-amino-1,3-cyclopentadiene, have yet to be synthesized and therefore addition results are unavailable. In cases where experimental facial selectivity results were not available, ratios calculated by Poirier *et al.* were used.[47] Poirier *et al.* predicted ratios by computational methods that showed excellent correlation with the available experimental facial selectivity results. It was therefore felt that their

results would also provide reasonable predictions for the dienes that have yet to be synthesized.

For diene **105** the calculated $\Delta\Delta G^{\ddagger}$ is 6.8 kJ/mol, which corresponds to a product ratio of 93 : 7 at 25 °C. This is quite close to the observed selectivity if the detection limits of the method used for determining product ratios is taken into account. For diene **106**, the calculated $\Delta\Delta G^{\ddagger}$ is 0.12 kJ/mol, which is very close to the experimental value of 0 kJ/mole. Dienes **105**, **106** and **107** are of particular importance here since the calculations are very close to the experimental values. The correlation observed for the halogen-substituted dienes provides strong evidence that the π-facial selectivity may be controlled by steric factors despite the fact that these substituents were traditionally implicated in stereoelectronic control arguments.

For the examples which do not correlate well, one of the assumptions made must not hold. Computational evidence provided by Poirier *et al.* suggests that the assumption that $\Delta G^{\ddagger}_{(H^{\bullet})} = \Delta G^{\ddagger}_{(H)}$ is valid since they found little difference in the diene deformation energies for addition *syn* to a hydrogen atom, regardless of the *anti* substituent. The breakdown must be with the assumption that $\Delta G^{\ddagger}_{(x^{\bullet})} = \Delta G^{\ddagger}_{(x)}$ for all 5-substituted-1,2,3,4,5-pentamethyl-1,3-cyclopentadienes.

When the facial selectivities of dienes **10** and **129** were compared, the difference in the activation energies of the *syn* to methyl additions was attributed to the steric influence of the C-5 methyl of diene **10** becoming roughly coplanar with the C-1 and C-4 methyls of the diene ring. For substituents with relatively long C-5-to-substituent bond lengths the

effect of the substituent-to-C1 and C-4 methyls must be relatively small. The assumption, however may not necessarily hold for shorter C-5-to-substituent bond lengths. For

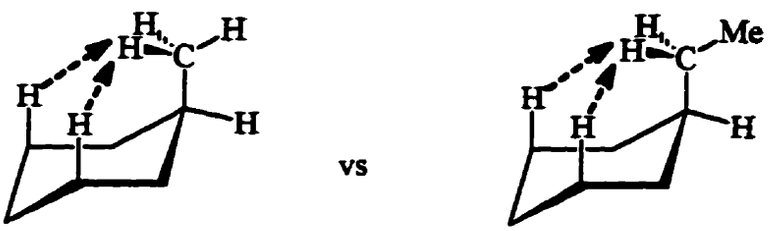
Table 9. $\Delta\Delta G^{\ddagger}$ Values for selected Diels-Alder additions

5-substituted cyclopentadienes		5-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes		
substituent	published $\Delta\Delta G^{\ddagger}$(kJ/mole)		experimental $\Delta\Delta G^{\ddagger}$(kJ/mole)	calculated $\Delta\Delta G^{\ddagger}$(kJ/mole)
NH_2[a]	-17	NH_2[c]	>11	21
CN[a]	-5.5	CN[d]	>11	9.3
CH_2OMe[b]	-3.8	CH_2OMe[e]	-3.0	7.5
Cl[b]	-3.0	Cl[e]	>11	6.8
Me[b]	0.91	H[e]	3.8	3.8
SH[a]	1.0	SH[e]	0.50	2.8
SPh[c]	1.0	SPh[c]	-8.7	2.8
Et[b]	1.8	Et[e]	-7.9	2
Br[b]	3.9	Br[e]	0	-0.12
I[a]	26	I[e]	<-11	-22

(a) reference 47; (b) reference 41; (c) reference 31; (d) reference 50; (e) work presented in this thesis

substituents with shorter C-5-to-substituent bond lengths, the substituent must be closer C-1 and C-4 methyls. This proximity may cause additions *syn* to the substituent to be less energetically favorable than in the corresponding 5-substituted 1,3-cyclopentadiene for which no such eclipsing interaction would be present. Also, for more complex substituents such as CH_2OMe, Et and SPh, the conformation of the substituent must play a role in determining the facial selectivity.

The importance of conformation is illustrated clearly by the additions of 5-ethyl- and 5-methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, **73** and **84**, respectively. The A-values for methyl and ethyl are almost the same (Table 8), and presumably, the



methylcyclohexane ethylcyclohexane

Figure 24. Relative steric influences for the A-values of methyl- and ethylcyclohexane

A-value for methoxymethyl must also be similar. Similarities in these A-values results from the ability of the ethyl group of ethylcyclohexane to adopt a conformation that presents a size that is very similar to that of methyl (Figure 24).

For dienes which are doubly substituted at the 5-position, such as 5-ethyl or 5-methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, **73** and **84**, and where both of the C-5 substituents are carbons, the facial selectivity appears to be governed by the conformation of the substituents rather than just differences in C-5-to-substituent bond length.

73 **84**

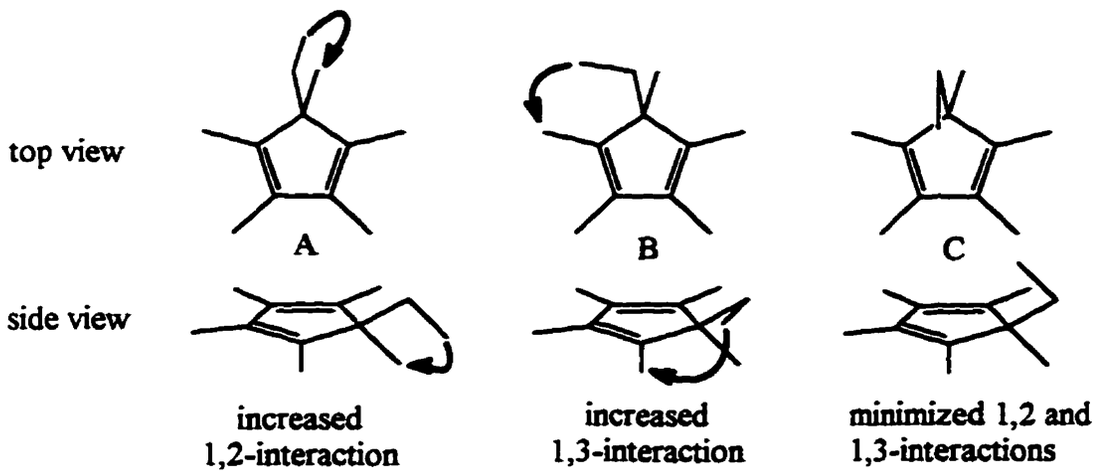


Figure 25. Possible conformations of 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **73**

The result of a calculation to find the lowest-energy conformation of **73** using *ab initio* 3-21G basis set[48] was the same as by using the semi-empirical *Power Search*[49] software for personal computers. The ethyl-substituted diene adopts the conformation "C" depicted in Figure 25 that is very much favoured over other conformations. The conformation "C" was found to be 28 KJ/mol lower in energy than the "A" conformer at 3-21G. The predicted conformation is further corroborated by the high upfield shift of the CH_3 of the ethyl group. The upfield shift (δ 0.24) is a result of the shielding effect of the diene π-system. This type of shielding can only occur if the diene adopts conformation "C" in solution. In this conformation, the ethyl group minimizes its steric interactions not only with the C-5 methyl, but also with the C-1 and C-4 methyls. Indeed, the *ab initio* data showed that the energy necessary to rotate the ethyl out of this conformation would not be available at ambient temperatures. The conformation of the ethyl group effectively

blocks the face *syn* to ethyl such that the dienophile must approach from the face *anti* to ethyl. This demonstrates the necessity of examining conformation, not only in the Diels-Alder reaction but in all reactions in which steric hindrance might play a role in

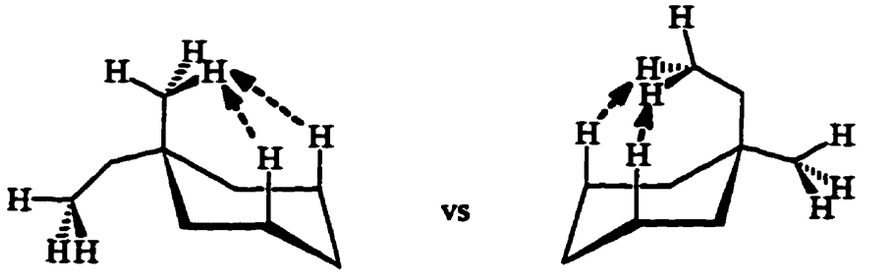


Figure 26. Chair conformers of 1-ethyl-1-methylcyclohexane

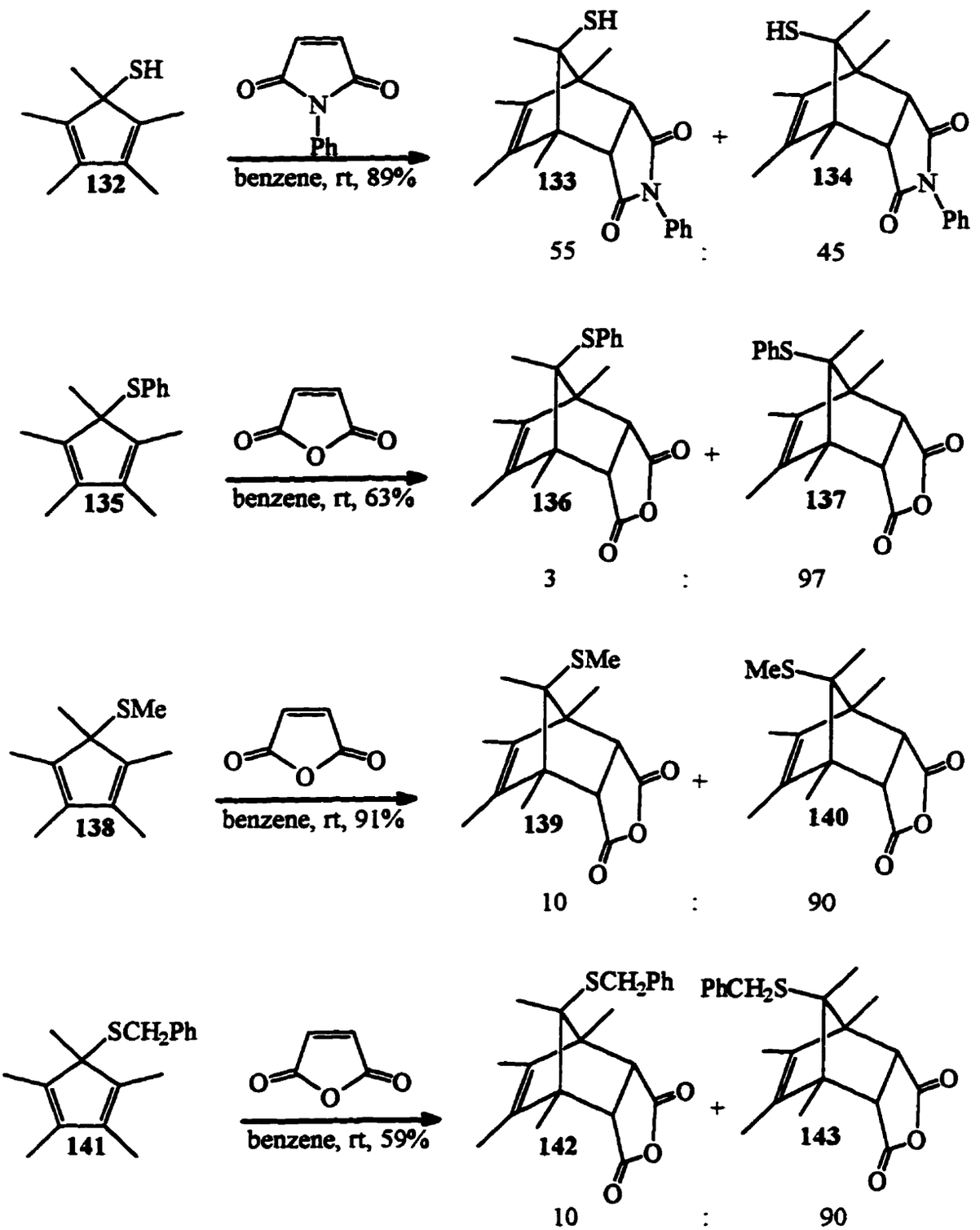
governing the outcome. Furthermore, it can be anticipated that 1-ethyl-1-methyl-cyclohexane would have one preferred conformer in which the ethyl group is in the equatorial position, in spite of negligible difference in the A-values between methyl and ethyl (Figure 26).

The possible conformations of **84** were calculated in the same fashion as for the ethyl-substituted diene using *ab initio* and *Power Search*. It was found that this diene adopts a conformation similar to the ethyl-substituted diene, with the methoxy group pointing out over the diene's π-system. Although computations using diene **84** were not done directly, this conformer was predicted to be 26 KJ/mol lower in energy than the conformer analogous to "A" when the OMe was replaced with OH in order to simplify the calculation. The facial selectivity results demonstrate that contrary to Anh's theory of donation from the substituent heteroatom into the dienophile LUMO, this group is not at

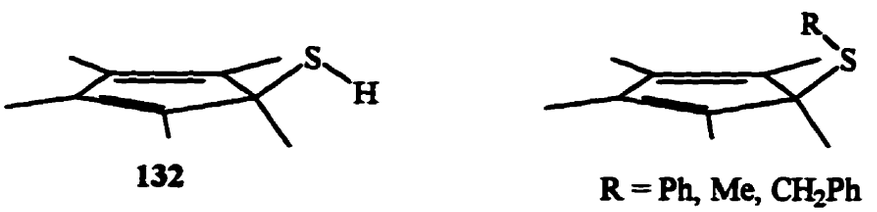
all *syn* directing. It is only slightly less *anti* directing than an ethyl group. The decrease in the *anti* directing abilities when compared to the 5-ethyl substituted diene is due to a decrease in the energy necessary to rotate the methoxy group away from the π-system. The decrease in rotational energy is a result of a smaller effective size of a methoxy group in **84** compared to a methyl in **73**. Again, one could predict that 1-methoxymethyl-1-methyl-cyclohexane would have a preferred conformation in which the methoxymethyl group is in the equatorial position, for the same reason as for the ethyl example. It would be expected, however, that, due to the smaller size of the oxygen of the methoxy group compared to a methyl, that the $\Delta\Delta G^{\circ}$ of the two conformers would be less than that of the 1-ethyl-1-methyl-cyclohexane.

This view might also explain the selectivities observed by Fallis[32] where they compared a number of sulfur-substituted 1,2,3,4,5-pentamethyl-1,3- cyclopentadienes (Scheme 29). They noted that the selectivity was very largely *anti* to the sulfur atom, regardless of its substitution. However, the simple unsubstituted mercaptan, **132**, showed almost no selectivity. The similarities in the selectivities for **135**, **138** and **141** are not surprising considering that the size of the sulfur and C-5-to-substituent bond length will be the same for all. The difference in the selectivity for **132** is most likely due to the fact that substituted sulfur substituents are able to adopt conformations that cause them to be somewhat more sterically hindering despite the other similarities (Figure 27).

Competitive Diels-Alder reactions can often give significant insight into the forces governing the facial selectivity. From the competitive reaction between **10** and **69**, it was



Scheme 29. Cycloadditions of 5-sulfur-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes [32]



132 R = Ph, Me, CH_2Ph

Figure 27. Postulated preferred conformations of 5-sulfur-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes

found that the hydrogen-bearing face of **10** is much more reactive than is **69**. If one subscribes to the theory that additions are stabilized by better σ-donating *anti* substituents, as proposed by Fallis,[32] then **69** should be of about the same reactivity as the

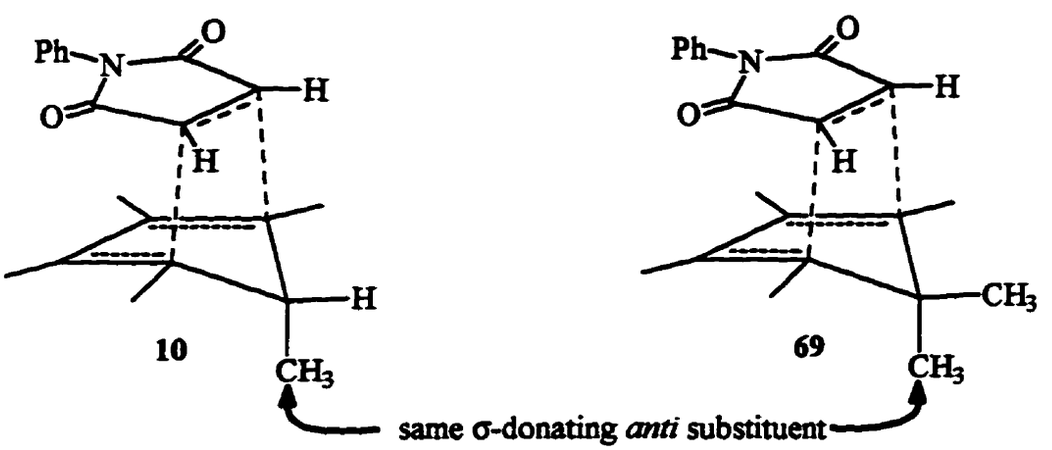


Figure 28. Competitive reaction between diene **10** and diene **69**

hydrogen-bearing face of **10** because both have the same *anti* substituent (Figure 28).

For the competitive reaction between hexamethyl-1,3-cyclopentadiene and 5-ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, the product mixture showed that the reactivity of **69** is approximately the same as the face of **73** *anti* to the ethyl group. This

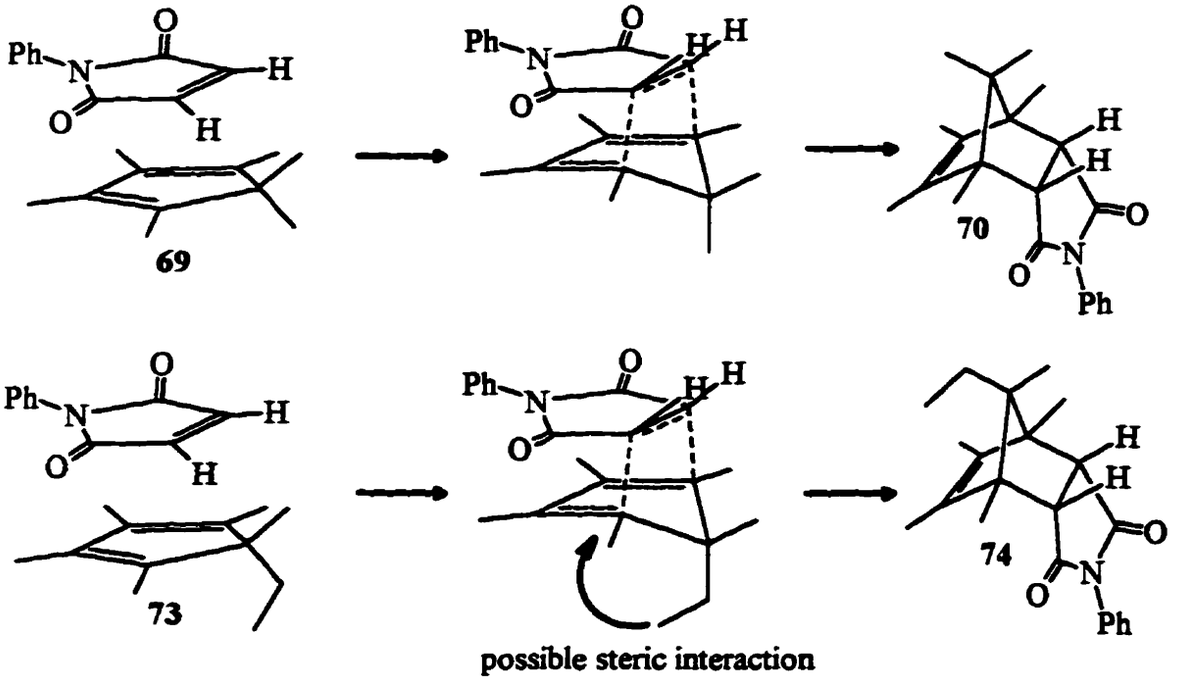


Figure 29. Comparison of *syn*-to-methyl attacks on diene **69** and diene **73** by *N*-phenylmaleimide

result indicates that, as reported by Poirier *et al.*,[47] the facial selectivity in the Diels-Alder reaction is largely independent of the *anti* substituent. Due to the preferred conformation of **73**, it might be expected that some steric interaction might result within the diene moiety from additions *anti* to the ethyl group (Figure 29). For this to be true, addition *anti* to ethyl with **73** should require more energy than addition to **69**. The competitive reaction however, indicates that both additions proceed at the same rate and therefore must require the same energy.

Certain groups have attempted to relate the facial selectivity of Diels-Alder additions to the reactivity of the diene/dienophile combination. In particular, Inagaki[50] recently published results that suggested a strong correlation between the reactivity of

dienophiles and their facial selectivity. Inagaki proposed that 4-phenyl-1,2,4-triazoline-3,5-dione should be more selective than *N*-phenylmaleimide due to an estimated 227-fold increase in the reactivity.

For the 5-alkyl substituted dienes that we studied, the product ratios indicated that the facial selectivity was relatively independent of the dienophile used. The data in Table 3 shows that 4-phenyl-1,2,4-triazoline-3,5-dione is less selective than *N*-phenylmaleimide despite its greater reactivity. Other dienophiles such as dimethyl acetylenedicarboxylate are sterically unencumbering, but are much less reactive, with reactions requiring days at room temperature, yet even its facial selectivity was only slightly less than that of *N*-phenylmaleimide.

Selectivity seemed more dependent on the shape of the dienophile and thus on steric hindrance. For all of the alkyl substituted dienes that we investigated, the trend of selectivity was:

1,1,2,2-tetracyanoethene > *N*-phenylmaleimide ≈ 1,4-naphthoquinone > 2-phenyl-1,2,4-triazoline-3,5-dione > dimethyl acetylenedicarboxylate.

It was not surprising that 1,1,2,2-tetracyanoethene was the most selective of the dienophiles since the nitriles would exhibit more steric influence in the direction of the plane-nonsymmetry of the dienes than would any other dienophile studied. The vinylic hydrogens on *N*-phenylmaleimide and 1,4-naphthoquinone would be less sterically hindering than the nitriles of 1,1,2,2-tetracyanoethene, however they would be expected to provide more steric influence than either the lone pairs of 2-phenyl-1,2,4-triazoline-3,5-

dione or the π-electrons of dimethyl acetylenedicarboxylate. The latter dienophiles provided similar selectivities, as might be expected from a lack of sterically hindering substitution.

The reactions of the 5-halogen-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes appeared to have a much greater dependence on the nature of the dienophile than with the alkyl-substituted dienes. For instance, the reaction of **106** and *N*-phenylmaleimide proceeded with almost no selectivity. However, when the same diene reacted with its heteroatom analogue, 2-phenyl-1,2,4-triazoline-2,5-dione, the addition proceeded with very high *anti* selectivity. The difference in the selectivity in these cases might be attributed to electrostatic repulsion between the lone pair electrons of the halogen and the lone pair electrons of the nitrogens of the 4-phenyl-1,2,4-triazoline-3,5-dione. Similar electrostatic repulsions are likely to be responsible for the reversal in selectivity when the additions of **105** with *N*-phenylmaleimide and 4-phenyl-1,2,4-triazoline-3,5-dione are compared. Addition to the ethylene-based dienophile proceeded with addition exclusively *syn* to the heteroatom, whereas, due to the electrostatic repulsions, addition to the heteroatom analogue proceeded with exclusively *anti* selectivity. Inagaki[50] made no mention of electrostatic repulsions in his explanation of the proposed reactivity-enhanced selectivity (RES) theory despite the fact that the results for 5-phenylthio-1,3-cyclopentadiene were used as the chief argument for the RES theory. It might be expected that greater *anti* selectivity would be observed when this diene was added to 4-phenyl-1,2,4-triazoline-3,5-dione as a result of these electrostatic repulsions.

In summary, the syntheses of 5-ethyl-, 5-methoxymethyl-, 5-chloro-, 5-bromo-, 5-iodo-, 5-difluoroiodomethyl- and 5-trideuteromethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene were accomplished. The Diels-Alder reactions of these dienes, as well as 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene, with various dienophiles were studied. The results obtained suggest that the facial selectivity in the Diels-Alder reaction of 5-substituted-1,2,3,4,5-pentamethyl-1,3-cyclopentadienes is controlled primarily by steric interactions between the C-5 substituent and the incoming dienophile.

The difference in the facial selectivity for dienes **10** and **129** has been related to a steric interaction between the C-5 methyl and the C-1 and C-4 methyls during *syn* addition. This steric interaction has been shown to be present for all additions *syn* to methyl for 5-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes. It has also been shown that a relationship between the facial selectivity of these dienes and 5-substituted 1,3-cyclopentadienes exists.

It has been found that the facial selectivity in the Diels-Alder reaction of 5-substituted 1,2,3,4,5-pentamethyl-1,3-cyclopentadienes correlates poorly with the A-values of the C-5 substituent. Despite this poor correlation, the facial selectivity in the Diels-Alder reaction of 5-substituted-1,2,3,4,5-pentamethyl-1,3-cyclopentadienes is believed to be governed primarily by steric interactions between the C-5 substituent of the diene and the incoming dienophile. We have reasoned that the poor correlation between A-values and facial selectivity in the Diels-Alder reaction is due to the difference in the geometry of the steric interactions for the two phenomena.

Experimental

General

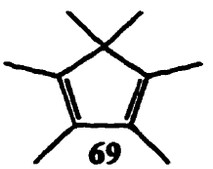
The term "ether" refers to diethyl ether. All solvents were purified by distillation prior to use. Tetrahydrofuran was distilled from sodium metal/benzophenone. Most reagents were not purified prior to use. An exceptions was 1,4-naphthoquinone which was obtained by flash chromatography on silica gel using 30% ethyl acetate in hexanes as the eluting solvent. Brine refers to an aqueous, saturated NaCl solution. Where an inert atmosphere was required, reactions were run under an atmosphere of dry nitrogen. Reactions were monitored by thin layer chromatography (TLC) using Baker-Flex silica gel plates, which were visualized by UV fluorescence, or by spraying with a solution of phosphomolybdic acid, ceric sulphate and sulphuric acid followed by heating. Preparative TLC was done using EM Separations Silica Gel 60 commercial plates with a 1 mm plate thickness. Flash chromatography was performed on Merck type 60 silica gel, 230-400 mesh. Melting points were performed on a Fisher-Johns apparatus and are uncorrected. Infrared (ir) spectra were recorded on a Mattson FT (Fourier transform) instrument as transmittance spectra. Nuclear magnetic resonance (nmr) spectra were obtained on a General Electric GE 300-NB (300 MHz for ^{1}H) instrument. The ^{1}H nmr shifts of $CDCl_3$ solutions were measured relative to a tetramethylsilane internal standard, but in other solvents the shifts were calibrated to a solvent resonance. Multiplicities are described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet). The ^{13}C nmr

shifts are relative to internal solvent resonance ($CDCl_3$ = δ 77.0, C_6D_6 = δ 128.0). The ^1H and ^{13}C nmr assignments were aided by ^1H-^{13}C correlation (HET-CORR) 2-D spectra and nuclear Overhauser effect (nOe) enhancement measurements, which in most cases led to the assignment of stereochemistry. The nOe measurements were made from sets of interleaved ^1H experiments (16K) of 8 transients cycled 12 to 16 times through the list of frequencies to be saturated. The decoupler was gated on continuous wave mode for 6 seconds with sufficient attenuation to give a 70-90% reduction in intensity of the irradiated signal. Frequency changes were preceded by a 60 second delay. Four scans were used to equilibrate spins before data acquisition, but a relaxation delay was not applied between scans at the same frequency. The nOe difference (nOed) spectra[51] were obtained from zero filled 32K data tables to which a 1 to 2 Hz exponential line-broadening function had been applied. The nOe results are reported in the following format: δ saturated signal (enhanced signal, % enhancement). Mass spectral (ms) data were from a V.G. Micromass 7070 HS instrument. Data for x-ray structures were collected using a Rigaku AFC6S diffractometer, and the structures were determined by D. O. Miller or Dr. J. N. Bridson of this Department. Elemental analyses were performed by the Canadian Microanalytical Service Ltd., Vancouver, BC.

General procedure for Diels-Alder reactions

To a solution of freshly prepared diene in ether at room temperature was added the dienophile, in one portion. After 16 to 20 hours the reaction mixture was

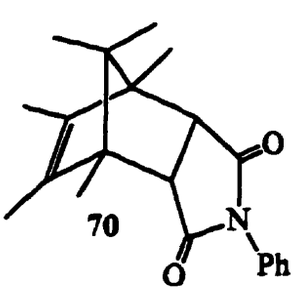
concentrated under vacuum. The mass of the residue was always very similar to the sum of the expected mass of the diene and the dienophile, and, in every instance, the ^{1}H nmr spectrum of the crude product was consistent with very high conversion of the addends into one or more Diels-Alder adducts. The adduct ratios were determined by careful integration of the ^{1}H nmr spectra of these crude adduct mixtures. However, it should be added that the synthesis of some dienes from 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene **10** was only of moderate yield, so some of the adducts were derived from **10** also. Not all reactions were repeated, but when reactions were repeated the adduct ratios proved to be very similar. In most instances, a sample of the major adduct was isolated by careful chromatography and crystallization. Our emphasis was on obtaining a sample homogeneous by ^{1}H and ^{13}C nmr, so the "isolated" yields quoted below do not reflect the extent of adduct formation but rather the ease of purification. When Homogeneous samples were available, the assignment of the relative stereochemistry was made on these. Nevertheless, many minor adducts, due to their relatively small quantities, were not recovered in homogeneous form, so their nmr data were extracted from spectra of adduct mixtures. In order to ensure that the observed adduct ratios were a result of kinetic rather than thermodynamic reaction outcomes, solutions of isolated adducts in $CDCl_3$were heated to reflux for 24 hours and the samples were examined by ^{1}H nmr to determine if thermal equilibration had occurred.



69

1,2,3,4,5,5-Hexamethyl-1,3-cyclopentadiene 69

To a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (1.00 g, 7.34 mmol) in tetrahydrofuran (30 mL), at 0 °C under N_2 was added *n*-butyllithium (Aldrich; 3.5 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred for 10 min. To the slurry was added iodomethane (0.55 mL, 8.0 mmol) over 3 min, and the mixture was stirred for 4 h at rt. The mixture was diluted to twice its volume with ether, and the solution was washed with water (3 x 20 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under vacuum to give **69** as a yellow oil (826 mg, 75%): ^{1}H nmr δ: 1.76 (6H, s), 1.65 (6H, s), 0.88 (6H, s).

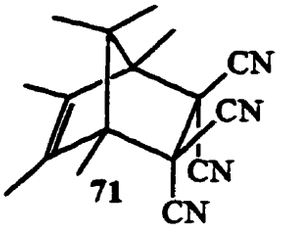


70

(3*a*α,4α,7α,7*a*α)-3*a*,4,7,7*a*-Tetrahydro-4,5,6,7,8,8-hexamethyl-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 70

To a solution of **69** (159 mg, 1.05 mmol) in ether (15 mL) was added *N*-phenylmaleimide (184 mg, 1.05 mmol) in one portion, and the solution was stirred for

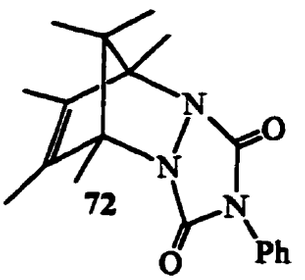
36 h at rt. The ether was removed under vacuum to provide crude **70**, a yellow solid, essentially quantitatively. The colour was removed by flash chromatography on silica gel using 5% ethyl acetate in hexanes as the eluting solvent and subsequent recrystallization from hexane gave an analytically homogeneous sample of **70**: mp: 125-126 °C; ir (thin film) ν_{max}: 1711 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.38 (3H, m, C-3'H, C-4'H and C-5'H), 7.06 (2H, m, C-2'H and C-6'H), 3.10 (2H, s, C-3aH and C-7aH), 1.60 (6H, s, C-5Me and C-6Me), 1.28 (6H, s, C-4Me and C-7Me), 0.79 (3H, s, C-8Me *anti* to norbornene double bond), 0.66 (3H, s, C-8Me *syn* to norbornene double bond); nOe data: 1.60 (1.28, 0.9%; 0.79, 5%), 1.60 (1.28, 1.0%; 0.66, 0.8%), 1.28 (3.10, 7%; 1.60, 2%; 0.79, 2%; 0.66, 3%), 0.79 (3.10, 12%; 1.28, 0.8%; 0.66, 1.1%), 0.66 (1.60, 0,4%; 1.28, 1.1%, 0.79, 1.0%); ^{13}C nmr ($CDCl_3$) δ: 177.1 (C-1 and C-3), 135.2 (C-5 and C-6), 132.1 (C-1'), 129.0 (C-2' and C-6'), 128.3 (C-4'), 126.6 (C-3' and C-5'), 64.3 (C-8), 60.0 (C-4 and C-7), 51.6 (C-3a and C-7a), 17.3 (C-4Me and C-7Me), 16.9 (C-5Me and C-6Me), 11.5 (both C-8Me's); ms: 323 (M^+, 8), 173 (1), 150 (100), 135 (17). Exact mass calculated for $C_{21}H_{25}NO_2$: 323.1884; found 323.1880.



71

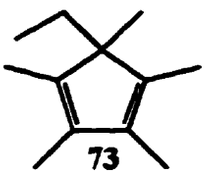
2,2,3,3-Tetracyano-1,4,5,6,7,7-hexamethylbicyclo[2.2.1]hept-5-ene 71

To a solution of **69** (149 mg, 1.00 mmol) in ether (15 mL) was added 1,1,2,2-tetracyanoethene (127 mg, 1.00 mmol) in one portion, and the solution was stirred at rt for 4 h. The solvent was removed under vacuum to give crude **71** as a yellow solid. Flash chromatography on silica gel using 20% ethyl acetate in hexanes as the eluting solvent and washing with ether gave **71** as a colourless solid (207 mg, 75%): mp: 170 °C (decomposes); ir (thin film) ν_{max}: 2244 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 1.85 (6H, s, C-5Me and C-6Me), 1.49 (6H, s, C-1Me and C-4Me), 1.25 (3H, s, C-7Me *anti* to double bond), 0.81 (3H, s, C-7Me *syn* to double bond); nOe data: 1.85 (1.49, 1.1%; 1.25, 0.3%; 0.81, 0.6%), 1.49 (1.85, 2%; 1.24, 21%; 0.81, 3%); ^{13}C nmr ($CDCl_3$) δ: 141.2 (C-5 and C-6), 111.5 (C-2CN and C-3CN), 111.0 (C-2CN and C-3CN), 68.5 (C-2 and C-3), 62.1 (C-1 and C-4), 50.7 (C-7), 20.5, 18.9, 12.1, 9.5; ms: (M^+ not present),150 (100), 135 (74), 128 (41), 119 (21), 76 (26).



5,8-Dihydro-5,6,7,8,10,10-hexamethyl-2-phenyl-5,8-methano-1*H*-(2,4,9)triazolo-(1,2-*a*)pyridazine-1,3(2*H*)-dione 72

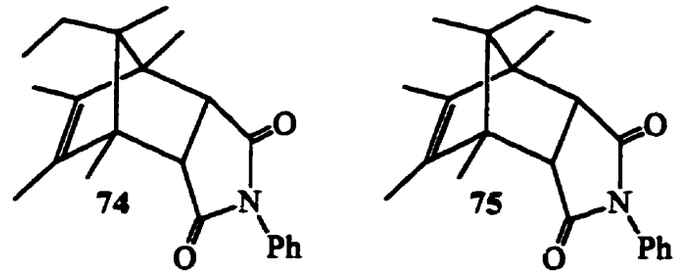
To a solution of diene **69** (86 mg, 0.57 mmol) in benzene (15 mL) was added 4-phenyl-1,2,4-triazoline-3,5-dione (100 mg, 0.57 mmol) in one portion, and the mixture was stirred at rt for 16 h. The solvent was removed under vacuum to give crude **72** as a colourless solid. Flash chromatography on silica gel using 5% ethyl acetate in hexanes as the eluting solvent and subsequent recrystallization from hexanes gave **72** as colourless crystals (167 mg, 90%): mp: 171-172 °C; ir (thin film) ν_{max}: 1714 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.41 (2H, m, C-2'H and C-6'H), 7.32 (3H, m, C-3'H, C-4'H and C-5'H), 1.75 (6H, s, C-6Me and C-7Me), 1.65 (6H, s, C-5Me and C-8Me), 1.05 (3H, s, C-10Me *anti* to double bond), 0.68 (3H, s, C-10Me *syn* to double bond); nOe data: 1.05 (1.65, 1.0%; 0.68, 1.6%), 0.68 (1.75, 0.6%; 1.65, 1.2%; 1.05, 2%); ^{13}C nmr ($CDCl_3$) δ: 159.4 (C-1 and C-3), 132.7 (C-6 and C-7), 131.5 (C-1'), 129.0 (C-3' and C-5'), 128.0 (C-4'), 125.4 (C-2' and C-6'), 81.6 (C-5 and C8), 59.9 (C-10), 17.2, 17.0, 11.3, 10.4; ms: 325 (M^+, 6), 310 (2), 256 (3), 150 (100), 135 (23).



73

5-Ethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene 73

To a solution of **10** (500 mg, 3.67 mmol) in 25 mL of tetrahydrofuran at 0 °C under N_2 was added *n*-butyllithium (Aldrich; 1.7 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred for 15 min. To the slurry was added iodoethane (0.35 mL, 4.4 mmol) dropwise causing the mixture to become clear. The solution was stirred at 0 °C for 3 h. The mixture was diluted to 50 mL with ether, and the organic solution was washed with water (50 mL) and brine (50 mL). The organic layer was dried (anhydrous $MgSO_4$), and the solvent was removed under vacuum to obtain **73**[52] as a yellow oil (575mg, 95%): ^{1}H nmr ($CDCl_3$) δ: 1.76 (6H, s), 1.65 (6H), 1.41 (2H, q, J = 7.2 Hz, C-5Et), 0.85 (3H, s, C-5Me), 0.24 (3H, t, J = 7.2 Hz, C-5Et); ^{13}C nmr ($CDCl_3$) δ: 139.6, 133.7, 56.1, 27.9, 21.9, 10.9, 9.6, 8.0.



(3*a*α,4α,7α,7*a*α,8*r*)-8-Ethyl-3*a*, 4,7,7*a*-tetrahydro-4,5,6,7,8-pentamethyl-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 74 and **(3*a*α,4α,7α,7*a*α,8*s*)-8-ethyl-3*a*,4,7,7*a*-tetrahydro-4,5,6,7,8-pentamethyl-2-phenyl- 4,7-methano-1*H*-isoindole-1,3-dione 75**

To an solution of diene **73** (230 mg, 1.40 mmol) in ether (15 mL) was added *N*-phenylmaleimide (242 mg, 1.40 mmol) in one portion, and the mixture was stirred at rt for 144 h. The ether was removed under vacuum to give a yellow oil which crystallized upon scratching. The ^{1}H nmr analysis revealed two adducts, **74** and **75**, in a ratio of 96 : 4, respectively. Recrystallization from hexane gave some **74** as a colourless solid (230 mg, 49%). Unfortunately, due to the small proportion of **75**, it was not isolated. The nmr data for **75** were extracted from the nmr spectrum of the crude adduct mixture.

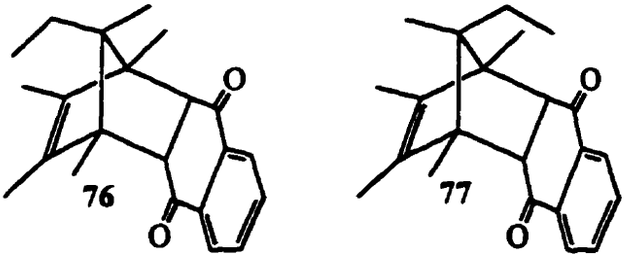
For **74**: mp 105-106 °C; ir (thin film) ν_{max}: 1704 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.37 (3H, m, C-1'H, C-3'H and C-4'H), 7.06 (2H, m, C-2'H and C-6'H), 3.06 (2H, s, C-3aH and C-7aH), 1.62 (6H, s, C-5Me and C-6Me), 1.32 (6H, s, C-4Me and C-7Me), 1.28 (2H, q partially overlapped, J = 7.7 Hz, C-8Et), 0.82 (3H, s, C-8Me), 0.81 (3H, partially overlapped t, J = 7.7 Hz, C-8Et); nOe data: 3.06 (1.32, 1.0%; 0.82, 2.5%), 1.62 (1.38, 1.1%; 1.28, 1.7%; 0.81, 0.5%); ^{13}C nmr ($CDCl_3$) δ: 177.1 (C-1 and C-3), 135.1 (C-5 and

C-6), 132.1 (C-1'), 129.0 (C-2' and C-6'), 128.3 (C-4'), 126.6 (C-3' and C-5'), 66.9 (C-8), 60.7 (C-4 and C-7), 51.5 (C-3a and C-7a), 24.0 (C-8Et), 14.1 (C-4Me and C-7Me), 12.6 (C-8Et), 11.5 (C-5Me and C-6Me), 10.1 (C-8Me); ms: 337 (M^+, 5), 308 (1), 173 (2), 164 (100), 149 (19). Exact mass calcd. for $C_{22}H_{27}NO_2$: 337.2040; found 337.2039.

For **75** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 7.37 (3H, m, C-1'H, C-3'H and C-4'H), 7.06 (2H, m, C-2'H and C-6'H), 3.13 (2H, s, C-3aH and C-7aH), 1.58 (6H, s, C-5Me and C-6Me), 1.27 (6H, s, C-4Me and C-7Me), 1.21 (2H, q, J = 6.4 Hz, C-8Et), 0.83 (3H, t, J = 6.4 Hz, C-8Et), 0.70 (3H, s, C-8Me).

Competitive reaction between **69** and **73**

To a solution of diene **69** (89 mg, 0.59 mmol) and diene **73** (113 mg, 0.69 mmol) in ether was added *N*-phenylmaleimide (100 mg, 0.58 mmol) in one portion, and the solution was stirred at rt for 16 h. The solvent was removed under vacuum to give a yellow oil. The ^{1}H nmr analysis revealed adducts **70** and **74** in a ratio of 2.3 : 1, respectively.



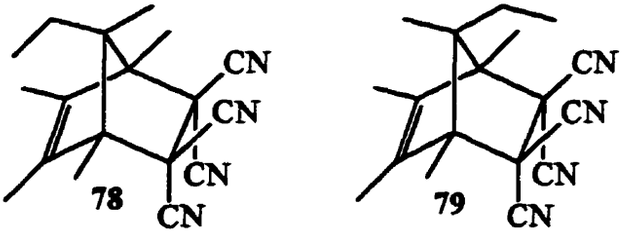
(1α,4α,4aα,9aα,11*r*)-11-Ethyl-1,4,4a,9a-tetrahydro-1,2,3,4,11-pentamethyl-1,4-methanoanthracene-9,10-dione 76 and **(1α,4α,4aα,9aα,11*s*)-11-ethyl-1,4,4a,9a-tetrahydro-1,2,3,4,11-pentamethyl-1,4-methanoanthracene-9,10-dione 77**

1,4-Naphthoquinone (290 mg, 1.83 mmol) was added to a solution of diene **73** (300 mg, 1.83 mmol) in ether (15 mL) in one portion, and the solution was stirred at rt for 24 h. The solvent was removed under vacuum, and the crude product was obtained as a yellow solid. Analysis by ^{1}H nmr revealed **76** and **77** in a ratio of 95 : 5, respectively. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent provided **76** as a white solid in a yield of 320 mg (54%) from **10**. Due to the small proportion of **77** it was not isolated, but its nmr data were obtained from the nmr spectrum of the crude adduct mixture.

For **76**: mp 132-133 °C; ir (thin film) ν_{max}: 1677 cm^{-1}; ^{1}H nmr (C_6D_6) δ: 7.96 (2H, m, C-5H and C-8H), 7.00 (2H, m, C-6H and C-7H), 2.83 (2H, s, C-4aH and C-9aH), 1.25 (6H, s, C-1Me and C-4Me), 1.06 (2H, q, J = 7.7 Hz, C11Et), 1.02 (6H, s, C-2Me and C-3Me), 0.65 (3H, t, J = 7.7 Hz, C-11Et), 0.46 (3H, s, C-11Me); nOe data: 2.83 (1.25, 0.9%; 0.46, 6%), 1.25 (2.83, 8%; 1.06, 3%; 1.02, 1.5%; 0.65, 3%; 0.46, 2%), 1.06 (0.65, 1.5%; 0.46, 0.8%),1.02 (2.83, 0.3%; 1.25, 1%; 0.65, 1%), 0.65 (1.25, 0.4%; 1.06,

1.6%; 1.02, 0.3%; 0.46, 0.7%), 0.46 (2.83, 16%; 1.25, 0.8%; 1.06, 3%; 0.65, 2%); ^{13}C nmr (C_6D_6) δ: 197.5 (C-9 and C-10), 137.4 (C-2 and C-3), 135.8 (C-8a and C-10a), 133.4 (C-6 and C-7), 126.2 (C-5 and C-8), 64.7 (C-2Me and C-3Me), 63.0 (C-1 and C-4), 55.9 (C-4a and C-9a), 24.1 (C-11Et), 14.5 (C-1Me and C-4Me), 12.3 (C-11Et), 11.8 (C-2Me and C-3Me), 11.0 (C-11Me); ms: (M^+ not found), 164 (96), 158 (63), 149 (100), 135 (31), 121 (26), 104 (39).

For **77** (from mixture): ^{1}H nmr (C_6D_6) δ: 7.96 (2H, m, C-5H and C-8H), 7.00 (2H, m, C-6H and C-7H), 3.24 (2H, s, C-4aH and C-9aH), 1.19 (6H, s, C-1Me and C-4Me), 1.05 (2H, q, J = 7.1 Hz, C11Et), 0.76 (3H, t, J = 7.1 Hz, C-11Et), 0.50 (6H, s, C-2Me and C-3Me), 0.46 (3H, s, C-11Me).



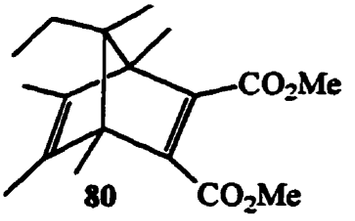
(7*r*)-2,2,3,3-Tetracyano-7-ethyl-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 78 and **(7*s*)-2,2,3,3-tetracyano-7-ethyl-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 79**

To a solution of diene **73** (230 mg, 140 mmol) in ether (15 mL) was added 1,1,2,2-tetracyanoethene (179 mg, 140 mmol) in one portion, and the mixture was stirred at rt for 24 h. The solvent was removed under vacuum to give a dark yellow solid. The ^{1}H nmr analysis revealed two products, **78** and **79**, in a ratio of 90 : 10, respectively. (The

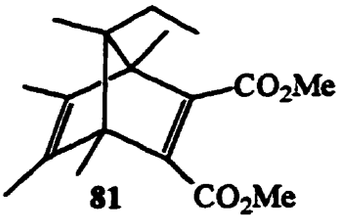
reaction was repeated and the ratio of adducts was checked after 5 min which showed a 97 : 3 ratio of **78** and **79**, respectively. Heating a mixture of **78** and **79** to 40 °C in $CDCl_3$ for 20 h resulted in a 50 : 50 ratio of adducts.) Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent and column chromatography on Florisil using 17% ethyl acetate in hexanes as the eluting solvent both failed to separate the adducts. For the mixture of adducts: ir (KBr) ν_{max}: 2245 cm^{-1}; ms: (M^+ not found), 164 (100), 149 (78), 135 (25), 128 (42), 119 (25).

For **78** (from mixture): ^1H nmr ($CDCl_3$) δ: 1.86 (6H, s, C-5Me and C-6Me), 1.52 (6H, s, C-1Me and C-4Me), 1.31 (2H, q, J = 7.7 Hz, C-7CH_2), 1.28 (3H, s, C-7Me), 0.86 (3H, t, J = 7.7 Hz, C-7Et); nOe data: 1.86 (1.52, 4%), 1.52 (1.86, 3%; 1.31, 0.7%; 1.28, 1.6%; 0.86, 2%), 0.86 (1.86, 1.2%; 1.52, 3%; 1.31, 1.9%; 1.28, 1.1%); ^{13}C nmr ($CDCl_3$) δ: 141.1 (C-5 and C-6), 111.6 (C-2CN and C-3CN), 111.1 (C-2CN and C-3CN), 69.3 (C-7), 64.5 (C-1 and C-4), 50.8 (C-2 and C-3), 27.0 (C-7Et), 16.0 (C-7CH_2), 12.2 (C-5Me and C-6Me), 10.7 (C-1Me and C-4Me), 9.6 (C-7Me).

For **79** (from mixture): ^1H nmr ($CDCl_3$) δ: 1.82 (6H, s, C-5Me and C-6Me), 1.79 (2H, q, J = 7.3Hz, C-7CH_2), 1.53 (6H, s, C-1Me and C-4Me), 1.05 (3H, t, J = 7.3Hz, C-7Et), 0.85 (3H, s, C-7Me); ^{13}C nmr δ: 141.5 (C-5 and C-6), 111.6 (C-2CN and C-3CN), 111.1 (C-2CN and C-3CN), 69.2 (C-7), 64.9 (C-1 and C-4), 50.6 (C-2 and C-3), 26.1 (C-7Et), 16.4 (C-7CH_2), 12.2 (C-1Me and C-4Me), 10.8 (C-5Me and C-6Me), 9.1 (C-7Me).



80



81

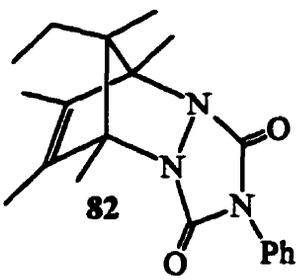
(7*s*)-7-Ethyl-1,4,5,6,7-pentamethyl-2,3-bis(methoxycarbonyl)-bicyclo[2.2.1]hepta-2,5-diene 80 and **(7*r*)-7-ethyl-1,4,5,6,7-pentamethyl-2,3-bis(methoxycarbonyl)-bicyclo[2.2.1]hepta-2,5-diene 81**

To a solution of diene **73** (230 mg, 1.40 mmol) in ether (15 mL) was added dimethyl acetylenedicarboxylate (199 mg, 1.40 mmol) in one portion, and the mixture was stirred at rt for 5 d. The ether was removed under vacuum to give a yellow oil. ^{1}H nmr analysis revealed two adducts, **80** and **81**, in a ratio of 81 : 19, respectively. Kugelrohr distillation removed excess dimethyl acetylenedicarboxylate and preparative TLC of the residue using 17% ethyl acetate in hexanes as the eluting solvent gave **80** as a colourless oil (137 mg, 32%). Adduct **81** was not isolated but its was analyzed from the crude mixture.

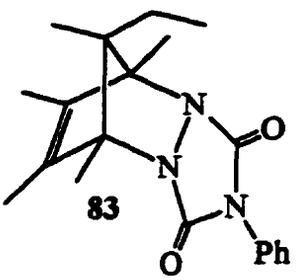
For **80**: ir (thin film) ν_{max}: 1732, 1620 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 3.73 (6H, s, 2 x CO_2Me), 1.66 (6H, s, C-5Me and C-6Me), 1.45 (2H, q, J = 7.7 Hz, C-7Et), 1.21 (6H, s, C-1Me and C-4Me), 1.00 (3H, s, C-7Me), 0.82 (3H, t, J = 7.7 Hz, C-7Et); nOe data: 1.66 (1.21, 1.2%), 1.45 (1.00, 0.7%; 0.82, 1.7%), 1.21 (1.66, 2.0%; 1.45, 3.1%; 1.0, 2.3; 0.82, 2.1%), 1.00 (1.45, 1.9%; 1.21, 0.6%; 0.82, 2.2%), 0.82 (1.45, 1.6%; 1.21, 0.6%; 1.00, 0.9%); ^{13}C nmr ($CDCl_3$) δ: 166.7 (2 x CO_2Me carbonyl), 153.5 (C-2 and C-3), 142.6 (C-5

and C-6), 84.5 (C-7), 67.1 (C-1 and C-4), 51.6 (2 x CO_2methyl), 25.7 (C-7CH_2), 15.1 (C-7Me), 11.9 (C-5Me and C-6Me), 10.6 (C-7Et), 9.4 (C-1Me and C-4Me); ms: 306 (M^+, 13), 291 (16), 275 (12), 259 (100), 247 (72), 219 (72), 217 (26), 215 (84), 187 (48), 91 (20), 87 (24), 55 (20); Exact mass calculated for $C_{18}H_{26}O_4$: 306.1830; found 306.1835.

For **81** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 3.74 (6H, s, C-2CO_2Me and C-3CO_2Me), 3.73 (6H, s, 2 x CO_2Me), 1.63 (6H, s, C-5Me and C-6Me), 1.60 (2H, q, J = 7.4 Hz, C-7Et), 1.21 (6H, s, C-1Me and C-4Me), 0.87 (3H, t, J = 7.4 Hz, C-7Et), 0.85 (3H, s, C-7Me).



82



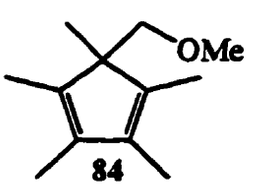
83

(10*r*)-10-Ethyl-5,8-dihydro-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*-(1,2,4) triazolo(1,2-*a*)pyridazine-1,3(2*H*)-dione 82 and **(10*s*)-10-ethyl-5,8-dihydro-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*-(1,2,4)triazolo(1,2-*a*)pyridazine-1,3(2*H*)-dione 83**

To an solution of diene **73** (235 mg, 1.72 mmol) in ether (15 mL) was added 4-phenyl-1,2,4-triazoline-3,5-dione (250 mg, 1.43 mmol) in one portion, and the mixture was stirred at rt for 18 h even though the characteristic red colour of the dienophile had dissipated within minutes. The ether was removed under vacuum to give the crude

product as a white solid. The ^{1}H nmr analysis revealed two adducts, **82** and **83**, in a ratio of ≥97 : 3, respectively. Flash chromatography on silica gel using 5% ethyl acetate in hexanes as the eluting solvent gave **82** as a colourless solid (338 mg, 70%). Small peaks along the baseline of the nmr spectrum suggested the presence of a minor adduct however its presence could not be confirmed.

For **82**: mp: 114-115 °C; ir (thin film) ν_{max}: 1770, 1717 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.34 (5H, m, aromatics), 1.76 (6H, s, C-6Me and C-7Me), 1.68 (6H, s, C-5Me and C-8Me), 1.19 (2H, q, J = 7.6 Hz, C-10Et), 1.07 (3H, s, C-10Me), 0.85 (3H, t, J = 7.6 Hz, C-10Et); ^{13}C nmr ($CDCl_3$) δ: 159.3 (C-1 and C-3), 132.4 (C-6 and C-7), 131.5 (C-1'), 128.9 (C-3' and C-5'), 127.9 (C-4'), 125.3 (C-2' and C-6'), 82.3 (C-5 and C8), 62.3 (C-10), 24.1, 13.9, 11.3, 11.2, 9.7; ms: 339 (M^+, 7), 324 (3), 256 (7), 164 (100), 149 (26). Elemental analysis: calculated for $C_{20}H_{25}N_3O_2$: C 70.77%, H 7.42%, N 12.38; found: C 70.88%, H 7.51%, N 12.38%. The structure of **82** was determined by x-ray analysis.

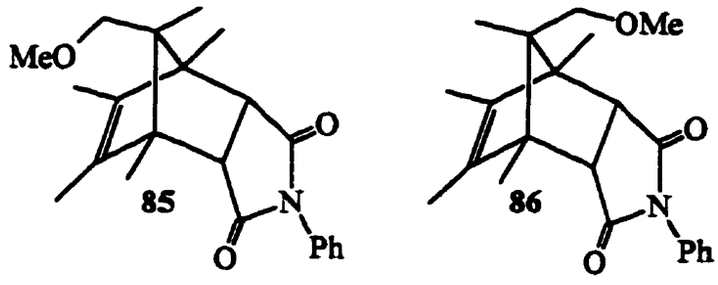


84

5-Methoxymethyl-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene 84

To a solution of **10** (500 mg, 3.67 mmol) in tetrahydrofuran (25 mL) at 0 °C under N_2, was added *n*-butyllithium (Aldrich; 1.7 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred for 10 min at rt. To the slurry was added chloromethoxy-

methane (295 mg, 3.66 mmol) dropwise, causing the mixture to become clear and the solution was stirred at 0 °C for 1 h. The solution was diluted to twice its volume with ether, and the solution was washed with water (50 mL) and brine (50 mL), and the combined washings were re-extracted with hexanes (50 mL). The organic layers were combined, dried (anhydrous $MgSO_4$), and the solvents were removed under vacuum to provide **84** as a yellow oil (520 mg, 86%): ^{1}H nmr ($CDCl_3$) δ: 3.25 (2H, s, C-5CH_2), 3.24 (3H, s, OMe), 1.77 (6H, s, C-1Me and C-4Me), 1.75 (6H, s, C-2Me and C-3Me), 0.89 (3H, s, C-5Me); ^{13}C ($CDCl_3$) δ: 139.4 (C-1 and C-4), 133.9 (C-2 and C-3), 76.8 (C-5OCH_2), 59.2 (C-5OMe), 56.6 (C-5), 11.1, 10.1.



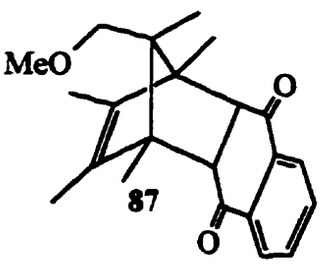
(3*a*α,4α,7α,7*a*α,8*r*)-3*a*,4,7,7*a*-Tetrahydro-8-methoxymethyl-4,5,6,7,8-pentamethyl-2-phenyl-4,7-methano-1*H*- isoindole-1,3-dione 85 and **(3*a*α,4α,7α,7*a*α,8*s*)-3*a*,4,7,7*a*-tetrahydro-8-methoxymethyl-4,5,6,7,8-pentamethyl-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 86**

To a solution of diene **84** (260 mg, 1.44 mmol) in ether (15 mL) was added *N*-phenylmaleimide (240 mg, 1.39 mmol) in one portion, and the mixture was stirred at rt

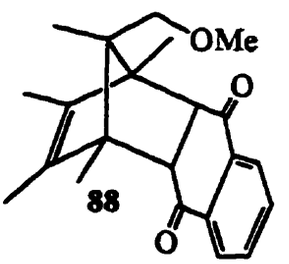
for 48 h. The ether was removed under vacuum to give a yellow solid. The ^{1}H nmr analysis revealed two adducts, **85** and **86**, in a ratio of 86 : 14, respectively. Flash chromatography on silica gel using 4% ethyl acetate in hexanes as the eluting solvent gave an analytical sample of **85** as a white solid. Due to the small proportion of **86**, it was not isolated but its nmr data were obtained from the nmr spectrum of the crude adduct mixture.

For **85**: mp 105-106 °C; ir (thin film) ν_{max}: 1711 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.38 (3H, m, C-3'H, C-4'H and C-5'H), 7.06 (2H, d, J = 7.1 Hz, C-2'H and C-6'H), 3.22 (3H, s, OMe), 3.16 (2H, s, C-8CH_2), 3.09 (2H, s, C-3a and C-7a), 1.63 (6H, s, C-5Me and C-6Me), 1.33 (6H, s, C-4Me and C-7Me), 0.95 (3H, s, C-8Me); nOe data: 1.63 (3.16, 1.2%; 3.09, 0.4%; 1.33, 1.0%), 1.33 (3.22, 0.4%; 3.16, 4%; 3.09, 7%; 1.62, 1.8%; 0.95, 2%), 0.95 (3.22, 0.4%; 3.16, 1.8%; 3.09, 11%; 1.33, 0.8%); ^{13}C nmr ($CDCl_3$) δ: 176.8 (C-1 and C-3), 132.0 (C-1'), 135.4 (C-5 and C-6), 129.1 (C-2' and C-6'), 128.3 (C-4'), 126.6 (C-3' and C-5'), 75.0 (OMe), 67.6 (C-8), 59.7 (C-4 and C-7), 59.2 (C-8CH_2), 51.5 (C-3a and C-7a), 12.9, 12.7, 11.5; ms: 353 (M^+, 7), 308 (2), 180 (100), 173 (7), 165 (21), 148 (29), 135 (20).

For **86** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 7.38 (3H, m, C-3'H, C-4'H and C-5'H), 7.06 (2H, m, C-2'H and C-6'H), 3.31 (3H, s, OMe), 3.23 (2H, s, C-8CH_2), 3.18 (2H, s, C-3a and C-7a), 1.58 (6H, s, C-5Me and C-6Me), 1.34 (6H, s, C-4Me and C-7Me), 0.79 (3H, s, C-8Me).



87



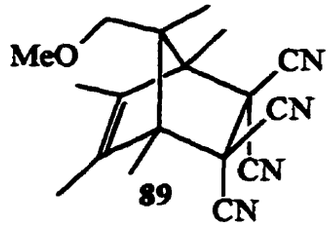
88

(1α,4α,4aα,9aα,11*r*)-1,4,4*a*,9*a*-Tetrahydro-11-methoxymethyl-1,2,3,4,11-pentamethyl-1,4-methanoanthracene-9,10-dione 87 and **(1α,4α,4aα,9aα,11*s*)-1,4,4*a*,9*a*-tetrahydro-11-methoxymethyl-1,2,3,4,11-pentamethyl-1,4-methanoanthracene-9,10-dione 88**

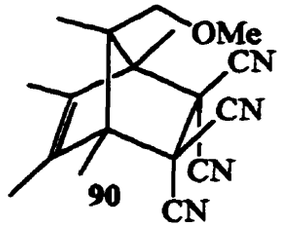
To a solution of **10** (150 mg, 1.10 mmol) in tetrahydrofuran (15 mL) at 0 °C under N_2 was added *n*-butyllithium (Aldrich; 0.88 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred at 0° C for 10 min. To the slurry was added chloromethoxy-methane (1.06 mg, 1.32 mmol) dropwise, and the mixture was stirred at 0° C for 1 h. The solution of **84** was diluted to twice its volume with ether, washed with water (3 x 20 mL) and then transferred to a second flask. To this solution was added 1,4-naphthoquinone (174 mg, 1.10 mmol) in one portion. The solution was stirred at rt for 20 h. The mixture was dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum to give a yellow solid. The ^1H nmr analysis revealed two products, **87** and **88**, in a ratio of 88 : 12, respectively. Peparative TLC on a silica plate using 17% ethyl acetate in hexanes as the eluting solvent gave **87** as a yellow solid (254 mg, 68%) and the nmr data for **88** were obtained from the spectra of the mixture of adducts.

For **87**: mp: 132-133 °C; ir (thin film)ν_{max}: 1677, 1586 cm^{-1} ^1H nmr ($CDCl_3$) δ: 7.92 (2H, m C-5H and C-8H), 7.63 (2H, m, C-6H and C-7H), 3.19 (3H, s, C-11OMe), 3.17 (2H, s, C-4aH and C-9aH), 3.12 (2H, s, C-11CH_2), 1.24 (6H, s, C-1Me and C-4Me), 1.10 (6H, s, C-2Me and C-3Me), 0.94 (3H, s, C-11Me); nOe data: 1.24 (3.19, 1.0%; 3.17, 9%; 3.12, 5%, 1.10, 3%; 0.94, 2%), 1.10 (3.12, 1.5%; 1.24, 1.6%), 0.94 (3.19, 0.6%; 3.17, 17%; 3.12, 2%; 1.24, 1.4%); ^{13}C nmr ($CDCl_3$) δ: 198.1 (C-9 and C-10), 136.6 (C-2 and C-3), 136 (C-8a and C-10a), 133.3 (C-6 and C-7), 125.7 (C-5 and C-8), 74.7 (C-11CH_2), 63.8 (C-11), 63.6 (C-1 and C-4), 59.2 (C-11OMe), 55.5 (C-4a and C-9a), 13.0 (C-11Me), 11.4 (C-2Me and C-3Me), 11.8 (C-1Me and C-4Me); ms: 331 (M^+, 1), 180 (100), 165 (26), 158 (37), 149 (22), 148 (26), 135 (30), 134 (21), 133 (88), 119 (27), 104 (22), 76 (20), 45 (29).

For **88** (from mixture): ^1H nmr ($CDCl_3$) δ: 7.92 (2H, m C-5H and C-8H), 7.63 (2H, m, C-6H and C-7H), 3.31 (3H, s, C-11OCH_3), 3.26 (2H, s, C-4aH and C-9aH), 3.22 (2H, C-11CH_2), 1.27 (6H, s, C-1Me and C-4Me), 1.06 (6H, s, C-2Me and C-3Me), 0.74 (3H, s, C-11Me).



89



90

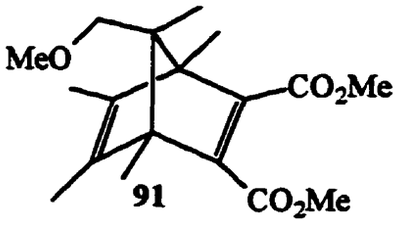
(7*r*)-2,2,3,3-Tetracyano-7-methoxymethyl-1,2,3,4,5-pentamethylbicyclo[2.2.1]-hept-5-ene 89 and **(7*s*)-2,2,3,3-tetracyano-7-methoxymethyl-1,2,3,4,5-pentamethylbicyclo [2.2.1]-hept-5-ene 90**

To a solution of diene **84** (330 mg, 1.83 mmol) in ether (15 mL) was added 1,1,2,2-tetracyanoethene (235 mg, 183 mmol) in one portion, and the solution was stirred at rt for 24 h. The solvent was removed under vacuum to give a white solid. Analysis of the crude product by ^{1}H nmr revealed the presence of two adducts, **89** and **90** in a ratio of 93 : 7, respectively. Flash chromatography on silica gel using 10% ethyl acetate in hexanes (500 mL) then 15% ethyl acetate in hexanes (500 mL) as the eluting solvents failed to separate the two adducts (320 mg, 57%). For the mixture: ir (thin film) ν_{max}: 2246 cm^{-1}; ms: (M^+ not found), 180 (38), 165 (22), 135 (33), 133 (100), 128 (79), 119 (36), 76 (66).

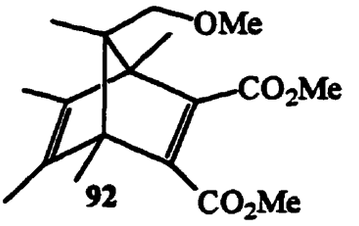
For **89** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 3.23 (C-7OMe), 3.07 (C-7CH_2), 1.87 (C-5Me and C-6Me), 1.51 (C-1Me and C-4Me), 1.40 (C-7Me); nOe data: 3.23 (3.07, 2%; 1.87, 0.2%; 1.40, 0.4%), 3.07 (3.23, 1.9%; 1.87, 0.5%; 1.51, 0.9%; 1.40, 1.3%), 1.87 (3.07, 0.9%; 1.51, 1.2%; 1.40, 0.2%), 1.51 (3.23, 0.6%; 3.07, 3%; 1.87, 2%; 1.40, 1.8%), 1.40 (3.23, 0.4%; 3.07, 2%; 1.87, 0.2%; 1.51, 0.3%); ^{13}C nmr ($CDCl_3$) δ: 141.7

(C-5 and C-6), 111.4 (C-2CN and C-3CN), 111.0 (C-5CN and C-6CN), 75.8 (C-7CH_2), 73.1 (C-7), 68.2 (C-1 and C-4), 65.3 (C-2 and C-3), 59.5 (C-7OMe), 14.9 (C-7Me), 12.2 (C-5Me and C-6Me), 10.8 (C-1Me and C-4Me).

For **90** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 3.61 (2H, s, C-7CH_2), 3.35 (3H, s, C-7OMe), 1.83 (6H, s, C-5Me and C-6Me), 1.54 (6H, s, C-1Me and C-4Me), 0.97 (3H, s, C-7Me); nOe data: 3.61 (3.35, 2%; 1.54, 0.6%), 3.35 (3.61, 3%), 1.54 (3.61, 2%; 1.83, 1.4%; 0.97, 1.9%), 0.97 (3.61, 0.9%); ^{13}C nmr ($CDCl_3$) δ: 141.4 (C-5 and C-6), 111.2 (C-2CN and C-3CN), 111.0 (C-2CN and C-3CN), 75.7 (C-7CH_2), 73.1 (C-7), 68.5 (C-1 and C-4), 64.3 (C-2 and C-3), 59.2 (C-7OMe), 15.8 (C-7Me), 12.1 (C-5Me and C-6Me), 10.7 (C-1Me and C-4Me).



91



92

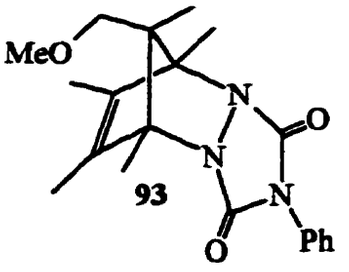
(7*s*)-7-Methoxymethyl-1,4,5,6,7-pentamethyl-2,3-*bis*-(methoxycarbonyl)-bicyclo [2.2.1]-hepta-2,5-diene 91 and **(7*r*)-7-methoxymethyl-1,4,5,6,7-pentamethyl-2,3-*bis*-(methoxycarbonyl)-bicyclo[2.2.1]hepta-2,5-diene 92**

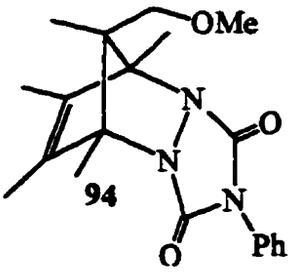
To a solution of **84** (662 mg, 3.67 mmol) in ether (20 mL) was added dimethyl acetylenedicarboxylate (1.44 g, 7.34 mmol) in one portion, and the mixture was stirred at rt for 14 d. The solvent was removed under vacuum to give a pale yellow oil. The ^{1}H nmr

analysis revealed two adducts, **91** and **92**, in a ratio of 72 : 28, respectively. Flash chromatography on silica gel using 3% ethyl acetate in hexanes as the eluting solvent gave an analytical sample of **91** as a yellow oil, but **92** was recovered only in a mixture of the two adducts.

For **91**: ir (thin film) ν_{max}: 1718 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 3.73 (6H, s, 2 x CO_2Me), 3.30 (2H, s, C-7CH_2), 3.21 (3H, s, OMe), 1.67 (6H, s, C-5Me and C-6Me), 1.22 (6H, s, C-1Me and C-4Me), 1.11 (3H, s, C-7Me); nOe data: 3.30 (1.22, 1.0%; 1.11, 1.6%), 1.67 (3.30, 1.1%; 1.22, 1.2%), 1.22 (3.30, 3%; 3.21, 0.6%; 1.67, 2%; 1.11, 1.6%), 1.11 (3.30, 1.5%; 3.21, 0.5%); ^{13}C nmr ($CDCl_3$) δ: 166.4 (2 x CO_2Me carbonyl), 153.3 (C-2 and C-3), 143.0 (C-5 and C-6), 83.2 (C-1 and C-4), 76.4 (C-7OMe), 65.9 (C-7), 59.2 (C-8CH_2), 51.7 (C-2CO_2Me and C-3CO_2Me), 14.0, 11.8, 9.5; ms: 322 (M^+, 5), 291 (4), 275 (15), 231 (23), 217 (43), 180 (2), 149 (8), 135 (11). Exact mass calculated for $C_{18}H_{26}O_5$: 322.1779; found, 322.1791.

For **92** (from mixture): ^1H nmr ($CDCl_3$) δ: 3.75 (6H, s, 2 x CO_2Me), 3.46 (2H, s, C-7CH_2), 3.26 (3H, s, C-7OMe), 1.63 (6H, s, C-5Me and C-6Me), 1.22 (6H, s, C-1Me and C-4Me), 0.96 (3H, s, C-7Me).





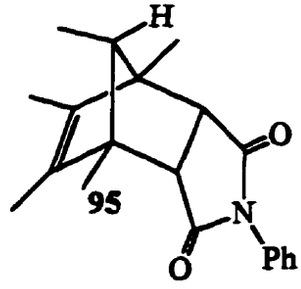
(10*r*)-5,8-Dihydro-10-methoxymethyl-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*-1,2,4-triazolo-(1,2-*a*)-pyridazine-1,3(2*H*)-dione 93 and (10*s*)-5,8-dihydro-10-methoxymethyl-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*-1,2,4-triazolo-(1,2-*a*)-pyridazine-1,3(2*H*)-dione 94

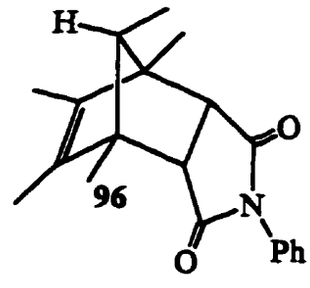
To a solution **84** (260 mg, 1.44 mmol) in ether (15 mL) was added, in one portion, the 4-phenyl-1,2,4-triazoline-3,5-dione (240 mg, 1.37 mmol), and the solution was stirred for 24 h even though the characteristic red colour of the dienophile disappeared within seconds of addition. The ether was removed under vacuum and to give a yellow oil which crystallized upon standing. The ^{1}H nmr analysis revealed the presence of two adducts, **93** and **94**, in a ratio of 74 : 26, respectively. Flash chromatography on silica gel using 5% ethyl acetate in hexanes gave **94** as a white solid (97 mg, 22%), but **93** was only recovered from flash fractions as a mixture of adducts.

For **93** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 7.36 (5H, m, aromatics), 3.23 (3H, s, OMe), 3.04 (2H, s, C-10CH_2), 1.77 (6H, s, C-6Me and C-7Me), 1.68 (6H, s, C-5Me and C-8Me), 1.19 (3H, s, C-10Me); nOe data: 3.23 (3.04, 2%), 3.04 (3.23, 1.8%; 1.77, 0.4%; 1.68, 0.8%; 1.19, 1.2%), 1.19 (3.23, 0.3%; 3.04, 1.6%; 1.68, 0.8%); ^{13}C nmr ($CDCl_3$) δ:

159.2 (C-1 and C-3), 132.6 (C-6 and C-7), 131.4 (C-1'), 129.0 (C-3' and C-5'), 128.1 (C-4'), 125.4 (C-2' and C-6'), 81.2 (C-5 and C-8), 74.3 (OMe), 63.4 (C-10), 59.4 ($C\text{-}10CH_2$), 13.1 (C-10Me), 11.6, 11.2.

For **94**: mp: 134.0-134.5 °C; ir (thin film) ν_{max}: 1718 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.36 (5H, m, aromatics), 3.50 (2H, s, $C\text{-}10CH_2$), 3.35 (3H, s, OMe),1.73 (6H, s, C-6Me and C-7Me), 1.70 (6H, s, C-5Me and C-8Me), 0.80 (3H, s, C-10Me); nOe data: 3.50 (3.35, 1.3%; 1.70, 0.9%; 0.80, 1.0%), 3.35 (3.50, 1.9%), 0.80 (3.50, 1.6%; 1.73, 0.3%; 1.70, 1.0%); ^{13}C nmr ($CDCl_3$) δ: 159.2 (C-1 and C-3), 132.8 (C-6 and C-7), 131.4 (C-1'), 129.0 (C-3' and C-5'), 128.1 (C-4'), 125.4 (C-2' and C-6'), 81.3 (C-5 and C-8), 73.6 (OMe), 62.3 (C-10), 59.3 ($C\text{-}10CH_2$), 12.0 (C-10Me), 11.4, 11.2; ms: 355 (M^+, 1), 180 (50), 177 (8), 165 (29), 149 (21), 135 (45), 133 (100), 119 (53).





(3*a*α,4α,7α,7*a*α,8*r*)-3*a*,4,7,7*a*-Tetrahydro-4,5,6,7,8-pentamethyl-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 95 and **(3*a*α,4α,7α,7*a*α,8*s*)-3*a*,4,7,7*a*-tetrahydro-4,5,6,7,8-pentamethyl-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 96**

To a solution of **10** (250 mg, 1.84 mmol) in ether (15 mL) was added *N*-phenylmaleimide (317 mg, 1.84 mmol) in one portion and the solution was stirred for 16 h at rt. The ether was removed under vacuum to give a yellow solid. The ^{1}H nmr spectrum revealed the presence of two adducts, **95** and **96**, in a ratio of 82 : 18, respectively. Flash chromatography using 5% ethyl acetate in hexanes as the eluting solvent to gave an analytical sample of **95** as a colourless crystals. Adduct **96** was not isolated but the nmr data were gleaned from the spectra of the mixture of adducts.

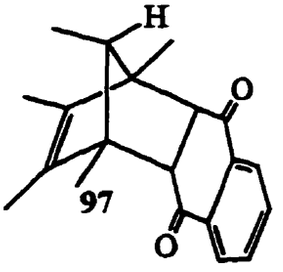
For **95**: mp 136-137 °C; ir (thin film) ν_{max}: 1712 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 7.38 (3H, m, C-3'H, C-4'H and C-5'H), 7.06 (2H, m, C-2'H and C-6'H), 3.04 (6H, s, C-3aH and C-7aH), 1.60 (1H, partially overlapped q, J = 6.7 Hz, C-8H), 1.59 (6H, partially overlapped s, C-5Me and C-6Me), 1.38 (6H, s, C-4Me and C-7Me), 0.64 (3H, d, J = 6.7 Hz, C-8Me); nOe data: 3.04 (1.60, 2%; 1.38, 0.7%), 1.38 (3.04, 6%; 1.60, 1.5%; 0.64, 2%), 0.64 (1.60, 0.5%; 1.38, 0.7%); ^{13}C nmr ($CDCl_3$) δ: 176.5 (C-1 and C-3), 133.6 (C-5 and C-6), 132.0 (C-1'), 129.1 (C-2' and C-6'), 128.3 (C-4'), 126.6 (C-3' and C-5'), 65.4 (C-8), 58.1 (C-4 and C-7), 53.1 (C-3a and C-7a), 14.7 (C-4Me and C-7Me), 11.3 (C-5Me and C-6Me), 7.5 (C-8Me); ms: 309 (M^+, 1), 173 (2), 136 (100), 121 (32); Elemental analysis for $C_{20}H_{25}NO_2$ required: C 77.64%, H 7.49%, N 4.53%; found: C 76.92%, H 7.59%, N 4.48%.

For **96** (from mixture): ^{1}H nmr (C_6D_6) δ: 7.44 (2H, m, C-2'H and C-6'H), 7.00 (2H, m,C-3'H and C-5'H), 6.88 (1H, m, C-4'H), 3.04 (2H, s, C-3aH and C-7aH), 1.57 (6H, s, C-5Me and C-6Me), 1.56 (6H, s, C-4Me and C-7Me), 0.94 (1H, q, J = 6.5 Hz,

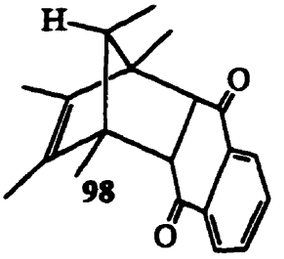
C-8H), 0.76 (3H, d, J = 6.5 Hz, C-8Me); ^{13}C nmr ($CDCl_3$) δ: 177.0 (C-1 and C-3), 132.0 (C-1'), 134.2 (C-5 and C-6), 129.0 (C-2' and C-6'), 128.3 (C-4'), 126.6 (C-3' and C-5'), 65.9 (C-8), 57.2 (C-4 and C-7), 51.2 (C-3a and C-7a), 14.1(C-4Me and C-7Me), 11.1 (C-5Me and C-6Me), 9.5 (C-8Me).

Competitive reaction between **10** and **73**

To a solution of diene **10** (63 mg, 0.46 mmol) and diene **73** (61 mg, 0.41 mmol) in ether was added *N*-phenylmaleimide (100 mg, 0.58 mmol) in one portion, and the solution was stirred at rt for 16 h. The solvent was removed under vacuum giving an oily yellow solid. The ^{1}H nmr analysis revealed only adduct **95** and unreacted diene **73**.



97



98

(1α,4α,4aα,9aα,11*r*)-1,4,4a,9a-Tetrahydro-1,2,3,4,11-pentamethyl-1,4-methano-anthracene-9,10-dione 97 and **(1α,4α,4aα,9aα,11*s*)-1,4,4a,9a-tetrahydro-1,2,3,4,11-pentamethyl-1,4-methanoanthracene-9,10-dione 98**

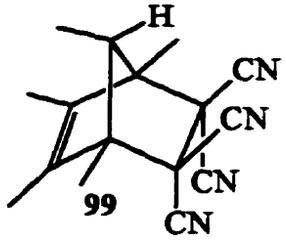
To a solution of diene **10** (250 mg, 1.83 mmol) in ether (15 mL) was added 1,4-naphthoquinone (240 mg, 1.51 mmol) in one portion, and the mixture was stirred at rt

for 24 h. The solvent was removed under vacuum to give a yellow solid. The ^{1}H nmr analysis revealed two adducts, **97** and **98**, in a ratio of 84 : 16, respectively. Flash chromatography on silica gel using 3% ethyl acetate in hexanes as the eluting solvent gave an analytical sample of **98** as a yellow solid, which became white after repeated washing with hexane. Adduct **97** was obtained only in a mixture of adducts.

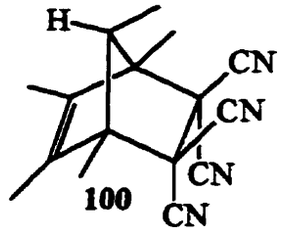
For **97** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 7.91 (2H, m, C-5H and C-8H), 7.63 (2H, m, C-6H and C-7H), 3.11 (2H, s, C-4aH and C-9aH), 1.53 (1H, q, J = 6.5 Hz, C-11H), 1.31 (6H, s, C-1Me and C-4Me), 1.06 (6H, s, C-2Me and C-3Me), 0.61 (3H, d, J = 6.5 Hz, C-11Me); nOe data: 3.11 (1.53, 3%; 1.31, 1.2%), 1.53 (3.11, 6%; 0.61, 1.3%), 1.31 (3.11, 10%; 1.06, 3%; 0.61, 3%), 1.06 (3.11, 0.6%; 1.31, 1.4%; 0.61, 0.8%) 0.61 (1.53, 0.6%; 1.31, 0.7%); ^{13}C nmr ($CDCl_3$) δ: 197.7 (C-9 and C-10), 136.4 (C-8a and C-10a), 133.8 (C-2 and C-3), 133.4 (C-6 and C-7), 125.9 (C-5 and C-8), 63.0 (C-11), 62.2 (C-1 and C-4), 58.1 (C-4a and C-9a), 14.0 (C-1Me and C-4Me), 11.3 (C-2Me and C-3Me), 7.4 (C-11Me).

For **98**: mp 143-144 °C; ir (thin film) ν_{max}: 1711 cm^{-1}; ^{1}H nmr ($CDCl_3/C_6D_6$) δ: 7.92/7.99 (2H, m, C-5H and C-8H), 7.63/7.01 (2H, m, C-6H and C-7H), 3.09/2.74 (2H, s, C-4aH and C-9aH), 1.30/1.30 (6H, s, C-2Me and C-3Me), 1.12/1.10 (6H, s, C-1Me and C-4Me), 1.22/0.93 (1H, q, J = 6.7 Hz, C-11), 0.76/0.40 (3H, d, J = 6.8 Hz, C-11Me); nOe data ($CDCl_3$): 3.09 (1.30, 1.7%; 1.12, 0.4%; 0.76, 5%), 1.30 (3.09, 10%; 1.12, 3%; 0.76, 0.9%), 0.76 (3.09, 4%; 1.12, 0.3%); ^{13}C nmr ($CDCl_3$) δ: 198.4 (C-9 and C-10), 138.7 (C-2 and C-3), 136.5 (C-8a and C-10a), 133.4 (C-6 and C-7), 125.8 (C-5 and C-8),

62.7 (C-11), 61.1 (C-1 and C-4), 55.1 (C-4a and C-9a), 13.5 (C-1Me and C-4Me), 11.1 (C-2Me and C-3Me), 9.6 (C-11Me); ms: (M^+ not found), 158 (2), 136 (24), 121 (27), 76 (100).



99



100

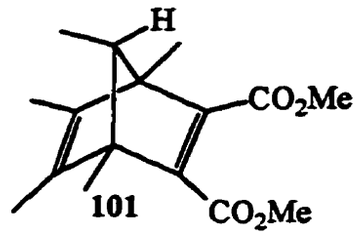
(7*s*)-2,2,3,3-Tetracyano-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 99 and **(7*r*)-2,2,3,3-tetracyano-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 100**

To a solution of diene **10** (250 mg, 183 mmol) in ether (10 mL) was added 1,1,2,2-tetracyanoethene (235 mg, 183 mmol) in one portion, and the mixture was stirred at rt for 2 h. The solvent was removed under vacuum to give a yellow solid. The ^{1}H nmr analysis revealed two adducts, **99** and **100**, in a ratio of 97 : 3, respectively. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent failed to separate the adducts. The mixture was recrystallized from methanol to give colourless needle-like crystals, which consisted exclusively of **99**. Due to the minute amounts of **100** formed, it was not isolated, but its nmr data were extracted from the nmr spectrum of the crude adduct mixture.

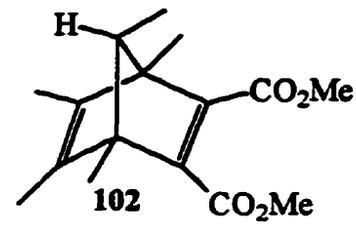
For **99**: mp 170-171 °C; ir (thin film) ν_{max}: 2245, 1547 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ: 2.11 (1H, q, J = 6.3 Hz, C-7H), 1.83 (6H, s, C-5Me and C-6Me), 1.54 (6H, s, C-1Me and C-4Me), 0.81 (3H, d, J = 6.3 Hz, C-7Me); nOe data: 2.11 (1.54, 0.4%; 0.81, 1.7%), 1.83

(1.54, 1.3%; 0.81, 0.5%), 1.54 (2.11, 9%; 1.83, 2%; 0.81, 2%), 0.81 (2.11, 7%; 1.83, 0.3%; 1.54, 0.7%); ^{13}C nmr ($CDCl_3$) δ: 137.9 (C-5 and C-6), 111.5 (C-2CN and C-3CN), 110.8 (C-2CN and C-3CN), 66.7 (C-2 and C-3), 57.5 (C-1 and C-4), 52.3 (C-7), 12.1 (C-5Me and C-6Me), 11.7 (C-1Me and C-4Me), 8.3 (C-7Me); ms: (M^+ not found), 136 (67), 128 (73), 121 (100), 105 (39), 76 (63). Elemental analysis for $C_{16}H_{16}N_4$ required: C 72.70, H 6.10, N 21.35; found: C 72.64, H 6.17, N 21.35.

For **100** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 2.29 (1H, q, J = 6.1 Hz C-7H), 1.61, 0.98 (3H, d, J = 6.1 Hz, C-7Me).



101



102

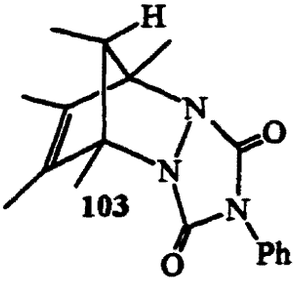
(7*s*)-1,4,5,6,7-Pentamethyl-2,3-bis(methoxycarbonyl)bicyclo[2.2.1]hepta-2,5-diene 101 and (7*r*)-1,4,5,6,7-pentamethyl-2,3-bis(methoxycarbonyl)bicyclo[2.2.1]hepta-2,5-diene 102

To a solution of diene **10** (200 mg, 1.47 mmol) in ether (15 mL) was added dimethyl acetylenedicarboxylate (187 mg, 1.47 mmol) in one portion, and the mixture was stirred at rt for 7 d. The ether was removed under vacuum to give a colourless oil. The ^{1}H nmr analysis revealed two adducts, **101** and **102**, in a ratio of 76 : 24, respectively.

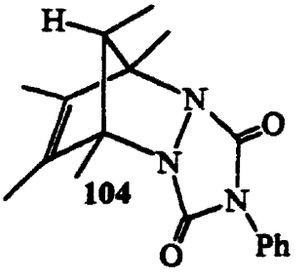
Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent failed to separate the two adducts (246 mg, 60%): ir (thin film) ν_{max}: 1716 cm^{-1}.

For **101** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 3.74 (6H, s, 2 x CO_2Me), 2.35 (1H, q, J = 6.4 Hz, C-7H), 1.64 (6H, s, C-5Me and C-6Me), 1.27 (6H, s, C-1Me and C-4Me), 0.71 (3H, d, J = 6.4 Hz, C-7Me); nOe data: 3.74 (1.64, 0.2%; 1.27, 0.3%; 0.71, 0.2%), 2.35 (1.27, 0.4%; 0.71, 1.4%), 1.64 (2.35, 0.4%; 1.27, 0.8%; 0.71, 0.7%), 1.27 (3.74, 0.4%; 2.35, 6.4%; 1.64, 1.7%; 0.71, 2.6%), 0.71 (2.35, 7.1%; 1.64, 0.3%; 1.27, 0.8%); ^{13}C nmr ($CDCl_3$) δ: 166.4 (C-2CO_2Me and C-3CO_2Me), 155.7 (C-2 and C-3), 140.9 (C-5 and C-6), 80.6 (C-7), 63.0 (C-1 and C-4), 51.6 (C-2CO_2Me and C-3CO_2Me), 11.7, 11.2, 9.9.

For **102** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 3.75 (6H, s, 2 x 2CO_2Me), 2.14 (1H, q, J = 6.4 Hz, C-7H), 1.64 (6H, s, C-5Me and C-6Me), 1.27 (6H, s, C-1Me and C-4Me), 0.85 (3H, d, J = 6.4 Hz, C-7Me).



103



104

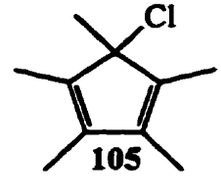
(10*r*)-5,8-Dihydro-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*-(1,2,4)triazolo-(1,2-*a*)pyridazine-1,3(2*H*)-dione 103 and **(10*s*)-5,8-dihydro-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*-(1,2,4)triazolo-(1,2-*a*)pyridazine-1,3(2*H*)-dione 104**

To a solution of diene **10** (200 mg, 1.47 mmol) in ether (15 mL) was added 4-phenyl-1,2,4-triazoline-3,5-dione (257 mg, 1.47 mmol) in one portion, and the solution was stirred for 4 h even though the characteristic red colour of the dienophile disappeared within seconds of addition. The ether was removed under vacuum to give a white solid. The ^{1}H nmr analysis revealed the presence of two adducts, **103** and **104**, in a ratio of 75 : 25, respectively. Chromatography on silica gel using 5% ethyl acetate in hexanes as the eluting solvent provided no separation of the adducts. For the mixture: ir (thin film) ν_{max}: 1767, 1716 cm^{-1}; ms: 311 (M^+, 1), 177 (14), 136 (100), 121 (87). Elemental analysis calculated for $C_{18}H_{21}N_3O_2$: C 69.43%, H 6.80%, N 13.49%; found: C 69.40%, H 6.87%, N 13.24%.

For **103** (from mixture): ^{1}H nmr (C_6D_6) δ: 7.43 (2H, m, C-2'H and C-6'H), 6.99 (2H, m, C-3'H and C-5'H), 6.87 (1H, m, C-4'H), 1.82 (1H, q, J = 6.6 Hz, C-10H), 1.59 (6H, s, C-5Me and C-8Me), 1.50 (6H, s, C-6Me and C-7Me), 0.21 (3H, d, J = 6.6 Hz, C-10Me); nOe data: 1.82 (1.59, 0.5%; 1.50, 0.5%; 0.21, 1.5%), 1.59 (1.82, 12%; 1.50, 1.3%; 0.21, 3%), 1.50 (1.59, 1.7%; 0.21, 0.9%), 0.21 (1.59, 2%; 1.50, 2%); ^{13}C nmr ($CDCl_3$) δ: 159.2 (C-1 and C-3), 135.3 (C-1'), 131.6 (C-7 and C-8), 128.9 (C-2' and C-6'), 128.1 (C-4'), 125.3 (C-3' and C-5'), 79.8 (C-5 and C-8), 60.3 (C-10), 13.2 (C-10Me), 11.2 (C-6Me and C-7Me), 8.0 (C-5Me and C-8Me);

For **104** (from mixture): ^{1}H nmr (C_6D_6) δ: 7.43 (2H, m, C-2'H and C-6'H), 6.99 (2H, m, C-3'H and C-5'H), 6.87 (1H, m, C-4'), 1.57 (1H, q, J = 6.5 Hz, C-10H), 1.56 (6H, s), 1.55 (6H, s), 0.75 (3H, d, J = 6.5 Hz, C-10Me); ^{13}C nmr ($CDCl_3$) δ: 159.2 (C-1

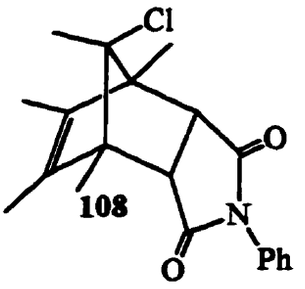
and C-3), 135.3 (C-1'), 131.4 (C-7 and C-8), 128.9 (C-2' and C-6'), 128.1 (C-4'), 125.3 (C-3' and C-5'), 78.7 (C-5 and C-8), 60.3 (C-10), 13.2, 11.2, 8.0.



105

5-chloro-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene

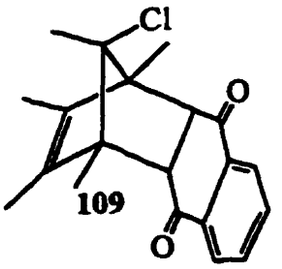
To a solution of diene **10** (270 mg, 1.98 mmol) in tetrahydrofuran (15 mL) at 0 °C under N_2 was added *n*-butyllithium (Aldrich, 0.95 mL of 2.5M in hexane), dropwise, and the resulting slurry was stirred at 0 °C for 1 h. To the slurry was added *N*-chloro-succinimide (320 mg, 2.39 mmol) in one portion, and the mixture was stirred at rt for 3 h. The mixture was diluted to twice its volume with ether, washed with water (2 x 20 mL), and dried over anhydrous $MgSO_4$, and the solvents were removed under vacuum. The diene was diluted to 10 mL in ether, and this was divided into two 5 mL portions. One half of the diene solution was used for reaction with 1,4-naphthoquinone and the other half was used for reaction with 4-phenyl-1,2,4-triazoline-3,5-dione.



(3*a*α,4α,7α,7*a*α,8*s*)-8-Chloro-3*a*, 4,7,7*a*-tetrahydro-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 108

To a solution of diene **10** (250 mg, 1.83 mmol) in tetrahydrofuran (25 mL), at 0 °C under N_2 was added *n*-butyllithium dropwise (Aldrich; 1.7 mL of 2.5M in hexane) and the resulting slurry was stirred for 15 min at 0 °C. To the slurry was added *N*-chlorosuccinimide (250 mg, 1.87 mmol) in one portion, and the solution was stirred at 0 °C for 2 h. The mixture was washed with a saturated aqueous solution $Na_2S_2O_3$ (20 mL), and the aqueous layer was extracted with ether (3 x 20 mL). The combined organic layers were dried (anhydrous $MgSO_4$) and the solvent was removed under vacuum. To a solution of **105** in ether (15 mL) was added *N*-phenylmaleimide (260 mg, 150 mmol) in one portion, and the mixture was stirred at rt for 24 h. The solvent was removed under vacuum to give a yellow solid for which the nmr spectrum showed signals attributable to **108** and to **95**. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent gave **108** as a white solid (220 mg, 35% from **10**): mp: 184-185°C; ir (thin film) ν_{max}: 1713 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.37 (3H, m, C-3'H, C-4'H and C-5'H), 7.06 (2H, d, J = 7.1 Hz, C-2'H and C-6'H), 3.42 (2H, s, C-3aH and C-7aH), 1.64 (6H, s, C-5Me and C-6Me), 1.43 (6H, s, C-4Me and C-7Me), 1.30 (3H, s, C-8Me); ^{13}C nmr

($CDCl_3$) δ: 176.3 (C-1 and C-3), 135.5 (C-5 and C-6), 131.9 (C-1'), 129.2 (C-2' and C-6'), 128.5 (C-4'), 126.5 (C-3' and C-5'), 92.6 (C-8), 61.3 (C-4 and C-7), 51.5 (C-3a and C-7a), 18.6 (C-8Me), 11.6, 11.4; ms: 343 (M^+, 9), 308 (3), 173 (8), 170 (100), 135 (43). Exact mass calcd. for $C_{20}H_{22}{}^{35}ClNO_2$: 343.1338; found 343.1339. The structure of **108** was determined by x-ray analysis.

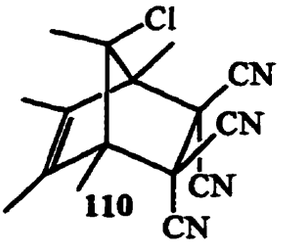


109

(1α,4α,4aα,9aα,11*s*)-11-Chloro-1,4,4*a*,9*a*-tetrahydro-1,2,3,4,11-pentamethyl-1,4-methanoanthracene-9,10-dione 109

1,4-Naphthoquinone (290 mg, 1.83 mmol) was added in one portion to the first 5 mL solution containing diene **105** (that had been diluted to 15 ml with ether) and the mixture was stirred at rt for 24 h. The solvent was removed under vacuum to give a yellow solid. The ^1H nmr analysis revealed a mixture of adducts **109** and **97**. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent to gave **109** as a white solid (80 mg, 13%); mp: 194-200 °C (decomposes while melting); ir (thin film) ν_{max}: 1672 cm^{-1}; ^1H nmr (C_6D_6) δ: 7.92 (2H, m, C-5H and C-8H), 7.08 (2H, m, C-6H and C-7H), 3.38 (2H, s, C-4aH and C-9aH), 1.39 (6H, s, C-1Me and C-4Me), 1.05

(3H, s, C-11Me), 0.95 (6H, s, C-2Me and C-3Me); ^{13}C nmr (C_6D_6) δ: 195.9 (C-9 and C-10), 136.1 (C-2 and C-3), 135.3 (C-8a and C-10a), 133.1 (C-6 and C-7), 125.8 (C-5 and C-8), 88.9 (C-11), 64.0 (C-1 and C-4), 54.8 (C-4a and C-9a), 17.7 (C-11Me), 11.0, 10.7; ms: (M^+ not found), 267 (3), 157 (15), 152 (100), 137 (49).

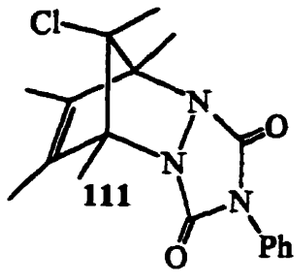


110

(7*r*)-7-Chloro-2,2,3,3-tetracyano-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 110

To a solution of **10** (200 mg, 1.47 mmol) in tetrahydrofuran (15 mL), under N_2 at 0°C, was added *n*-butyllithium (Aldrich, 1.17 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred at 0° C for 20 min. To the slurry was added *N*-chlorosuccinimide (392 mg, 2.94 mmol) in one portion, and the mixture was stirred at rt for 2 h. The mixture was diluted to twice its volume with ether, washed with saturated aqueous $Na_2S_2O_3$ (1 x 20 mL), and the aqueous layer was re-extracted with ether (20 mL). To the combined organic layers was added 1,1,2,2-tetracyanoethene (188 mg, 1.47 mmol) in one portion, and the mixture was stirred at rt for 6 h. The solution was dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum to give a dark purple oily solid. The ^1H nmr analysis revealed a mixture of adducts **97** and **110**. Passage through a Florisil plug using 50% ethyl acetate in hexanes as the eluting solvent then washing the

residue with a solution of 25% ethyl acetate in hexanes gave **110** as a white solid (152 mg, 35%): mp: 135 °C (decomposes); ir (thin film) ν_{max}: 2245 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 1.90 (6H, s, C-5Me and C-6Me), 1.64 (6H, s, C-1Me and C-4Me), 1.39 (3H, s, C-7Me); nOe data: 1.90 (1.64, 0.9%; 1.39, 0.5%), 1.64 (1.90, 1.7%; 1.39, 2%), 1.39 (1.90, 0.3%; 1.64, 0.7%); ^{13}C nmr ($CDCl_3$) δ: 141.0 (C-5 and C-6), 111.3 (C-2CN and C-3CN), 109.8 (C-2CN and C-3CN), 83.0 (C-7), 68.6 (C-1 and C-4), 50.9 (C-2 and C-3), 21.4 (C-7Me), 12.4, 9.6 ; ms: (M^+ not found), 263 (2), 170 (100), 135 (84), 119 (51).

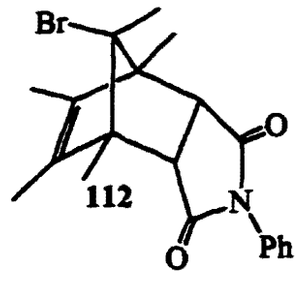


111

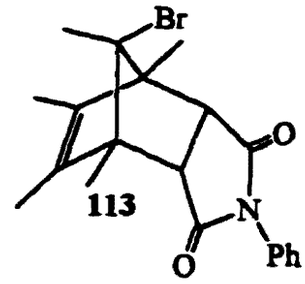
(10*r*)-10-Chloro-5,8-dihydro-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*-(1,2,4)-triazolo(1,2-*a*)pyridazine-1,3(2*H*)-dione 111

4-Phenyl-1,2,4-triazoline-3,5-dione (174 mg, 0.99 mmol) was added in one portion to the second 5 mL of solution of diene **105** (that had been diluted to 15 mL with ether) and the mixture was stirred at rt for 16 h. The solvent was removed under vacuum to give a dark yellow oil. The ^1H nmr analysis of the crude mixture revealed a mixture of **103** and **111**. Preparative TLC using 10% ethyl acetate in hexanes gave an analytical sample of **111**: mp: 127-127.5 °C; ir (thin film) ν_{max}: 1726 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.37

(5H, m, aromatics), 1.79 (6H, s, C-6Me and C-7Me), 1.77 (6H, s, C-5 and C-8), 1.59 (3H, s, C-10Me); ^{13}C nmr ($CDCl_3$) δ: 158.9 (C-1 and C-3), 133.1 (C-6 and C-7), 131.1 (C-1'), 129.1 (C-3' and C-5'), 128.4 (C-4'), 125.4 (C-2' and C-6'), 84.7 (C-10), 81.1 (C-5 and C-8), 19.8, 11.3, 10.4; ms: 347 (M^+, 1), 345 (M^+, 4), 330 (3), 256 (5), 170 (100), 135 (32), 119 (16). Exact mass calculated for $C_{18}H_{20}{}^{35}ClN_3O_2$: 345.1243; found 345.1242.



112



113

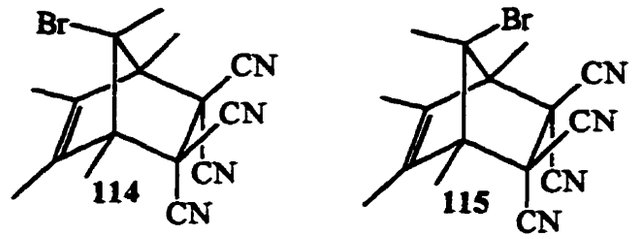
(3*a*α,4α,7α,7*a*α,8*s*)-8-Bromo-3*a*,4,7,7*a*-tetrahydro-4,5,6,7,8-pentamethyl-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 112 and **(3*a*α,4α,7α,7*a*α,8*r*)-8-bromo-3*a*,4,7,7*a*-tetrahydro-4,5,6,7,8-pentamethyl-2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 113**

To a solution of **10** (250 mg, 1.83 mmol) in tetrahydrofuran (25 mL), at 0°C under N_2, was added *n*-butyllithium dropwise (Aldrich; 1.7 mL of 2.5 M in hexane) and the resulting slurry was stirred for 20 min at 0 °C. To the slurry was added *N*-bromosuccinimide (327 mg, 1.83 mmol) in one portion. The solution was stirred at 0 °C for 2 h. The mixture was diluted to twice its volume with ether, washed with a saturated aqueous solution of $Na_2S_2O_3$ (20 mL) and the aqueous layer was re-extracted with ether (3 x 20 mL). The combined organic layers were dried (anhydrous $MgSO_4$) and

the solvent was removed under vacuum. To this solution of diene **106** in ether (15 mL) was added *N*-phenylmaleimide (260 mg, 150 mmol) in one portion, and the mixture was stirred at rt for 24 h. The ether was removed under vacuum to give a yellow solid. The ^{1}H nmr analysis revealed two adducts, **112** and **113**, in a ratio of 50 : 50. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent gave some homogeneous **112** as a white solid, but **113** was recovered still mixed with **112** so its nmr data were extracted from spectra of the mixture.

For **112**: mp 140-142°C; ir (thin film) ν_{max}: 1713 cm^{-1}; ^{1}H nmr (C_6D_6) δ: 7.41 (3H, m, C-3'H, C-4'H and C-5'H), 6.99 (2H, d, C-2'H and C-6'H), 2.24 (2H, s, C-3aH and C-7aH), 1.49 (6H, s, C-5Me and C-6Me), 1.38 (6H, s, C-4Me and C-7Me), 1.11 (3H, s, C-8Me); nOe data: 2.24 (1.38, 0.7%; 1.11, 3%), 1.38 (2.24, 5%; 1.11, 2%), 1.11 (2.24, 11%, 1.49, 0.7%); ^{13}C nmr ($CDCl_3$) δ: 175.3 (C-1 and C-3), 137.7 (C-5 and C-6), 132.1 (C-1'), 129.2 (C-2' and C-6'), 128.6 (C-4'), 126.5 (C-3' and C-5'), 94.1 (C-8), 61.5 (C-4 and C-7), 48.2 (C-3a and C-7a), 21.7 (C-8Me), 12.4, 11.6; ms: 389 (M^+, 6), 387 (M^+, 6), 308 (8), 216 (25), 214 (27), 173 (3), 135 (100).

For **113** (from mixture): ^{1}H nmr ($CDCl_3$) δ: 7.41 (3H, m, C-3'H, C-4'H and C-5'H), 7.05 (2H, m, C-2'H and C-6'H), 3.51 (2H, s, C-3aH and C-7aH), 1.65 (6H, C-5Me and C-6Me), 1.58 (6H, s, C-4Me and C-7Me), 1.49 (3H, s, C-8Me).

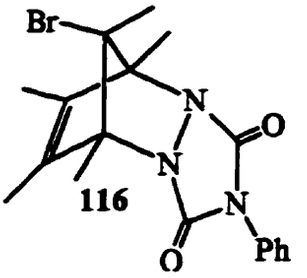


(7*s*)-7-Bromo-2,2,3,3-tetracyano-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 114 and (7*r*)-7-bromo-2,2,3,3-tetracyano-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 115

To a solution of **10** in tetrahydrofuran at 0°C under N_2 was added *n*-butyllithium (Aldrich, 1.0 mL of 2.5 M in hexane) dropwise, and the resulting slurry was stirred at 0 °C for 10 min. To the slurry was added *N*-bromosuccimide (327 mg, 1.83 mmol) in one portion, and the mixture was stirred at 0 °C for 10 min then at rt for 40 min. The mixture was washed with water (2 x 20 mL), and the combined aqueous layers were extracted with ether (20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was removed under vacuum. To a solution of the diene in ether (15 mL) was added 1,1,2,2-tetracyanoethene (235 mg, 1.83 mmol) in one portion, and the mixture was stirred at rt for 24 h. The solvent was removed under vacuum to give a yellow solid. The ^1H nmr analysis revealed two adducts, **114** and **115**, in a ratio of 95 : 5, respectively. Preparative TLC using 10% ethyl acetate in hexanes gave **114** as a white solid (110 mg, 17%). Due to the small proportion of **115**, it was not recovered from the TLC plate so its nmr spectrum was extracted from the spectrum of the crude adduct mixture.

For **114**: mp: >150 °C (decomposes); ir (thin film) ν_{max}: 2248 cm^{-1}; ^1H nmr ($CDCl_3/C_6D_6$) δ: 2.00/1.51 (3H, s, C-7Me), 1.86/2.29 (6H, s, C-5Me and C-6Me), 1.72/1.03 (6H, s, C-1Me and C-4Me); ^{13}C nmr (C_6D_6) δ: 144.2 (C-5 and C-6), 111.4 (C-2CN and C-3CN), 111.1 (C-2CN and C-3CN), 86.8 (C-7), 69.0 (C-1 and C-4), 48.1 (C-2 and C-3), 24.0 (C-7Me), 12.2, 10.1; ms: (M^+ not found), 216 (13), 214 (16), 135 (100), 128 (59), 119 (25), 81 (2), 79 (7).

For **115** (from mixture): ^1H nmr ($CDCl_3$) δ: 1.91 (6H, s, C-5Me and C-6Me), 1.83 (6H, s, C-1Me and C-4Me), 1.66 (3H, s, C-7Me).

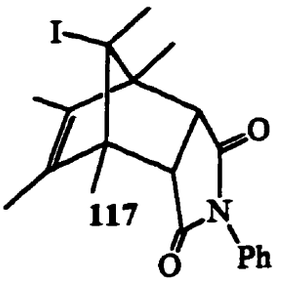


(10*r*)-10-Bromo-5,8-dihydro-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*(1,2,4)-triazolo(1,2-*a*)pyridazine-1,3(2*H*)-dione 116

To a solution of **10** (250 mg, 1.83 mmol) in of tetrahydrofuran (15 mL), at 0 °C under N_2 was added *n*-butyllithium (Aldrich; 1.7 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred at 0 °C for 1 h. To the slurry was added *N*-bromosuccinimide (327 mg, 1.83 mmol) in one portion, and the solution was stirred at 0 °C for 3 h. The reaction mixture was diluted to twice its volume with ether, washed with water (2 x 30

mL) and brine (30 mL), and the combined aqueous layers were re-extracted with ether (30 mL). The combined organic layers were dried (anhydrous $MgSO_4$), and the solvent was removed under vacuum to give diene **106** as an orange liquid.

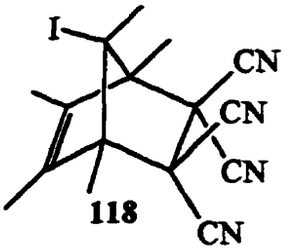
To a solution of **106** in ether (15 mL) was added 2-phenyl-1,2,4-triazoline-3,5-dione (160 mg, 0.97 mmol) in one portion, and the solution was stirred at rt for 24 h. The solvent was removed under vacuum to give a thick oil. The ^1H nmr analysis revealed **116** was the only adduct. Passage through a silica plug using 10% ethyl acetate in hexanes as the eluting solvent and preparative TLC on silica using 25% ethyl acetate in hexanes as the eluting solvent gave an analytical sample of **116** as a white solid: mp: >95 °C (decomposes); ir (thin film) ν_{max}: 1778, 1725 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.36 (5H, m, aromatics), 1.82 (6H, s, C-6Me and C-7Me), 1.75 (6H, s, C-5Me and C-8Me), 1.74 (3H, s, C-10Me); ^{13}C nmr ($CDCl_3$) δ: 158.9 (C-1 and C-3), 134.2 (C-6 and C-7), 131.1 (C-1'), 129.1 (C-2' and C-6'), 128.4 (C-4'), 125.4 (C-3' and C-5'), 81.5 (C-5 and C8), 21.7 (C-10Me), 11.4, 11.1; ms: 391 (1), 389 (1) both M^+, 256 (1), 216 (34), 214 (36), 135 (100). The structure of **116** was determined by x-ray crystal analysis.



(3*a*α,4α,7α,7*a*α,8*r*)-3*a*,4,7,7*a*-Tetrahydro-11-iodo-4,5,6,7,8-pentamethyl-4,7-methano-1*H*-isoindole-1,3-dione 117

To a solution of **10** (200 mg, 1.47 mmol) in tetrahydrofuran (15 mL), at 0°C under N_2, was added *n*-butyllithium (Aldrich, 1.17 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred at 0 °C for 20 min. To the slurry was added dropwise a solution of iodine (273 mg, 1.47 mmol) in tetrahydrofuran (5.0 mL). Addition of the iodine was stopped when an additional drop was added and the iodine colour persisted. The solution was stirred at 0 °C for 20 min. The mixture was diluted to twice its volume with ether, washed with a saturated aqueous solution of $Na_2S_2O_3$ (20 mL) and with water (20 mL). The combined aqueous layers were re-extracted with ether (20 mL), the organic layers were combined and the volume was reduced to 15 mL under vacuum. To the diene solution was added *N*-phenylmaleimide (254 mg, 1.47 mmol) in one portion, and the mixture was stirred at rt for 8 h. The mixture was dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum to give a dark yellow oil. The ^1H analysis revealed **117** was the only adduct. Passage through a Florisil plug using 25% ethyl acetate in hexanes as the eluting solvent then preparative TLC using 20% ethyl acetate in hexanes as the eluting solvent gave a homogeneous sample of **117** as a pale yellow solid: mp:

105-108 °C; ir (thin film) ν_{max}: 1717 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.43 (3H, m, C-1'H, C-3'H and C-4'H), 7.04 (2H, d, J = 7.3 Hz, C-2' and C-6'), 3.13 (2H, s, C-3aH and C-7aH), 1.81 (3H, s, C-8Me), 1.60 (6H, s, C-5Me and C-6 Me), 1.51 (6H, s, C-4Me and C-7Me); nOe data: 3.13 (1.81, 4.0%; 1.51, 0.9%), 1.81 (3.13, 12%; 1.51, 0.7%); ^{13}C nmr ($CDCl_3$) δ: 175.1 (C-1 and C-3), 140.8 (C-5 and C-6), 134.1 (C-1'), 129.1 (C-2' and C-6'), 128.6 (C-4'), 126.4 (C-3' and C-5'), 86.4 (C-8), 62.5 (C-4 and C-7), 45.9 (C-3a and C-7a), 25.3 (C-8Me),14.0, 11.7; ms: 435 (M^+, 1), 308 (14), 173 (100), 135 (35), 127 (2), 117 (22).

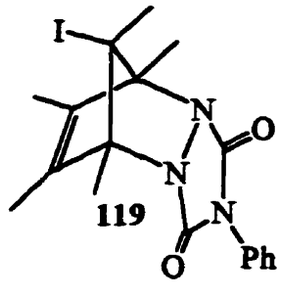


118

(7*s*)-2,2,3,3-Tetracyano-7-iodo-1,4,5,6,7-pentamethylbicyclo[2.2.1]hept-5-ene 118

To a solution of **10** (250 mg, 1.83 mmol) in tetrahydrofuran (15 mL) at 0 °C under N_2 was added *n*-butyllithium (Aldrich, 1.0 mL of 2.5 M in hexane) dropwise, and the resulting slurry was stirred for 10 min. Iodine (~400 mg, 1.88 mmol) was added to the slurry until the solution became a brown colour, indicating an excess of I_2. The mixture was stirred for 15 min. The mixture was diluted to twice its volume with ether, washed with water (2 x 15 mL) and the combined aqueous layers were re-extracted with ether (15 mL). The combined organic layers were dried over anhydrous $MgSO_4$. The solvents were reduced to approximately 30 mL under vacuum. 1,1,2,2-Tetracyanoethene (234 mg,

1.83 mmol) was added to the diene solution in one portion, and the mixture was stirred at rt for 16 h. The solvent was removed under vacuum to give a thick yellow oil. The ^1H nmr analysis of the crude product revealed that **118** as the only addition product. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent gave a homogeneous sample of **118** as a gray solid: mp: (decomposes before melting); ir (thin film) ν_{max}: 2247 cm^{-1}; ^1H nmr (C_6D_6) δ: 1.75 (3H, s, C-10Me), 1.27 (6H, s, C-5Me and C-6Me), 1.10 (6H, s, C-5Me and C-8Me); ^{13}C nmr (C_6D_6) δ: 147.8 (C-5 and C-6), 111.7 (C-2 CN and C-3 CN), 111.1 (C-2 CN and C-3 CN), 74.5 (C-7), 70.2 (C-1 and C-4), 44.8 (C-2 and C-3), 28.0 (C-7Me), 12.3, 11.6.

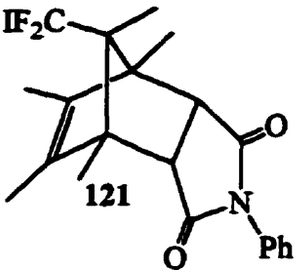


119

(10*r*)-5,8-Dihydro-10-iodo-5,6,7,8,10-pentamethyl-2-phenyl-5,8-methano-1*H*(1,2,4)-triazolo(1,2-*a*)pyridazine-1,3(2*H*)-dione 119

To a solution of **10** (250 mg, 1.83 mmol) in tetrahydrofuran (15 mL), at 0 °C under N_2, was added *n*-butyllithium (Aldrich, 1.0 ml of 2.5 M in hexane) dropwise and the resulting slurry was stirred for 10 min. Iodine (~400 mg, 1.88 mmol) was added to the slurry until the solution became a brown colour indicating an excess of I_2. The mixture

was stirred for 15 min. The mixture was washed with water (2 x 15 mL), and the combined aqueous layers were re-extracted with ether (15 mL). The combined organic layers were dried over anhydrous $MgSO_4$. The solvents were reduced to approximately 30 mL under vacuum. 4-Phenyl-1,2,4-triazoline-3,5-dione (200 mg, 1.14 mmol) was added to the diene solution in one portion, and the mixture was stirred at rt for 16 h. The solvent was removed under vacuum to give a thick yellow oil. The ^1H nmr analysis of the crude adduct mixture revealed that **119** was the only addition product. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent gave **119** as a gray solid (240 mg, 48%): ir (thin film) ν_{max}: 1777, 1723 cm^{-1}; ^1H nmr (C_6D_6) δ: 7.40 (2H, m, C-3'H and C-5'H), 7.01 (2H, m, C-2'H and C-6'H), 6.90 (1H, m, C-4'), 1.76 (6H, s, C-5Me and C-6Me), 1.75 (3H, s, C-10Me), 1.51 (6H, s, C-5Me and C-8Me); ^{13}C nmr (C_6D_6) δ: 159.5 (C-1 and C-3), 136.6 (C-6 and C-7), 131.9 (C-1'), 129.4 (C-2' and C-6'), 128.5 (C-4'), 126.0 (C-3' and C-5'), 82.8 (C-5 and C-8), 69.8 (C-10), 25.9 (C-7Me), 12.9, 11.8.

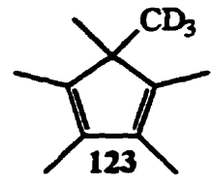


(3*aα*,4*a*,7*a*,7*aα*,8*r*)-8-(Difluoroiodomethyl)-3*a*,4,7,7*a*-tetrahydro-4,5,6,7,8-pentamethyl- 2-phenyl-4,7-methano-1*H*-isoindole-1,3-dione 121

To a solution of **10** (400 mg, 2.9 mmol) in tetrahydrofuran (20 mL) at 0 °C under N_2 was added *n*-butyllithium (Aldrich; 1.35 mL of 2.5M in hexane) dropwise, and the solution was stirred at 0 °C for 10 min. To the resulting slurry was added a solution of trifluoroiodomethane (670 mg, 3.4 mmol) in dry toluene (18 mL) and the solution was stirred at rt for 1 h. The solution was washed with water (2 x 30 mL) and brine (30 mL), dried over anhydrous $MgSO_4$ and the solvent was removed under vacuum. To a solution of the diene in ether (15 mL) was added *N*-phenylmaleimide (920 mg, 3.37 mmol) in one portion and the mixture was stirred at rt for 40 h. The solvent was removed under vacuum to give and ^1H nmr analysis of the residue revealed the presence of two adducts, **117** and **121**, in a ratio of 2.4 : 1, respectively. Flash chromatography on silica gel using 10% ethyl acetate in hexanes as the eluting solvent separated the two reaction products.

For **121**: mp: 166-167° C; ir (thin film) ν_{max}: 1715 cm^{-1}; ^1H nmr ($CDCl_3$) δ: 7.41 (3H, m, C-3'H, C-4'H and C-5'H), 7.06 (2H, m, C-2'H and C-6'H), 3.10 (2H, s, C-3aH and C-7aH), 1.64 (6H, s, C-5Me and C-6Me), 1.53 (6H, s, C-4Me and C-7Me), 1.18 (3H, apparent triplet, J = 1.5 Hz, C-8Me); nOe data: 3.10 (1.53, 0.6%; 1.18, 5%), 1.53 (3.10,

7%; 1.18, 1.8%), 1.18 (3.10, 10%); ^{13}C nmr ($CDCl_3$) δ: 175.3 (C-1 and C-3), 134.2 (C-1'), 129.2 (C-2' and C-6'), 128.6 (C-4'), 126.5 (C-3' and C-5'), 59.0 (C-4 and C-7), 51.3 (C-3a and C-7a), 14.9, 13.3, 11.8; ms: 486 (4), 485 (15) both M+, 357 (6), 338 (33), 312 (100), 185 (74), 173 (90), 135 (30). Exact mass for $C_{21}H_{22}F_2INO_2$ required: 485.0664; found 485.0662.



123

5-(Trideuteromethyl)-1,2,3,4,5-pentamethyl-1,3-cyclopentadiene 123

To a solution of 1,2,3,4,5-pentamethyl-1,3-cyclopentadiene (580 mg, 4.25 mmol) in tetrahydrofuran (30 mL), at 0 °C under N_2 was added *n*-butyllithium (Aldrich; 1.7 mL of 2.5M in hexane) dropwise, and the resulting slurry was stirred for 10 min. To the slurry was added iodomethane-d_3 (0.55 mL, 8.0 mmol) over 3 min, and the mixture was stirred for 4 h at rt. The mixture was diluted to twice its volume with ether and was washed with water (3 x 20 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under vacuum to give **69** as a yellow oil (575 mg, 88%). Addition of *N*-phenylmaleimide, 1,1,2,2,-tetracyanoethene and 4-phenyl-1,2,4-triazoline-3,5-dione were done in a manner analogous to the additions of diene **69**. All additions proceeded with no selectivity, giving 50 : 50 mixtures of *syn* : *anti* addition products. The nmr spectra of the adducts of **123** were virtually identical to the

corresponding adducts of diene **69**, the main difference being the integrals of the peaks corresponding to the methyls on the bridge. Since half of the methyls on the bridge in the adducts of diene **123** have been replaced by trideuteromethyls, the integrals of the corresponding peaks in the ^1H nmr are only half as big as the peaks for the same methyls of the non-deuterated adducts of **69** (Figure 30).

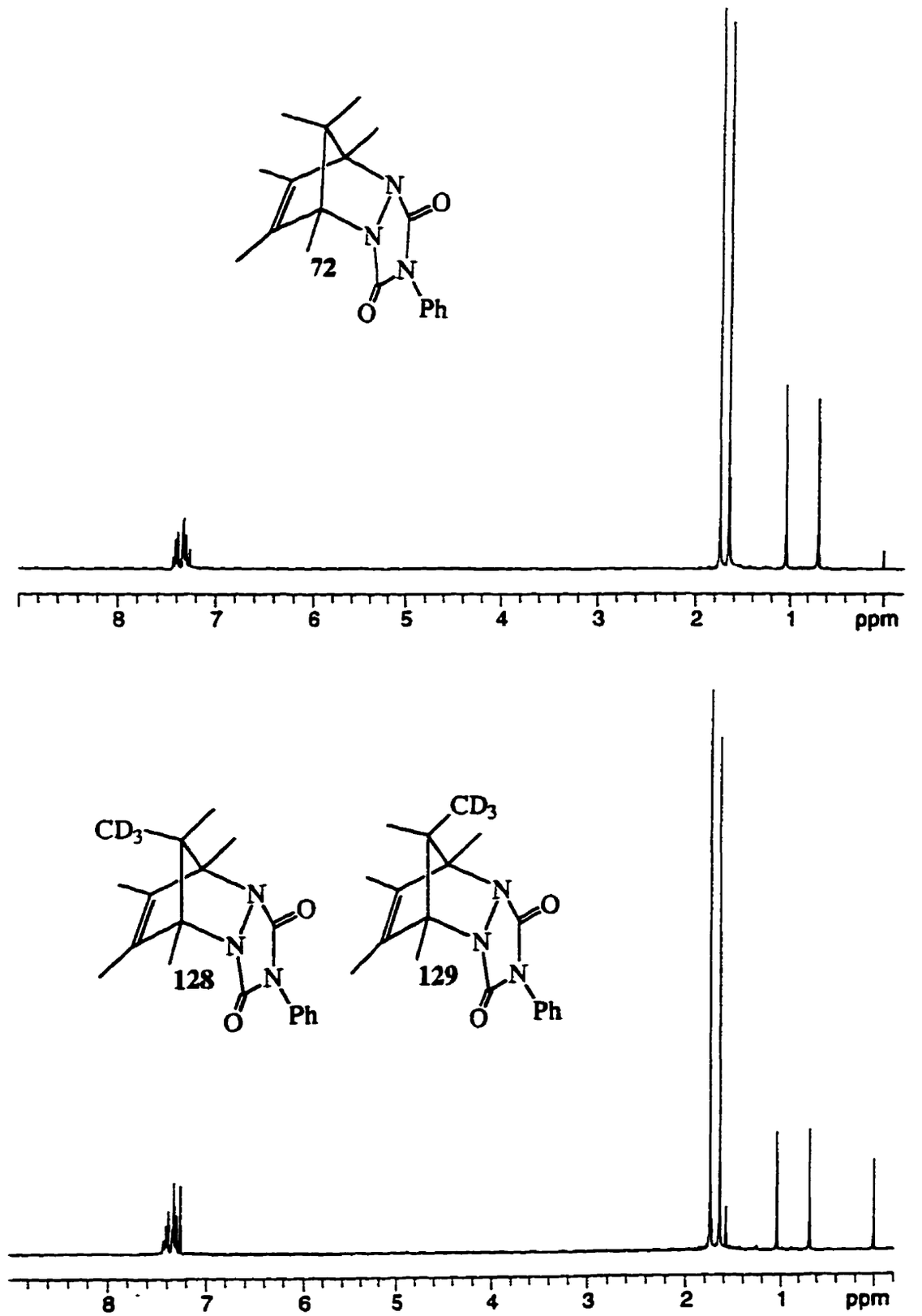


Figure 30. Comparison of the ^{1}H nmr spectra of adduct **72** and a mixture of adducts **128** and **129**

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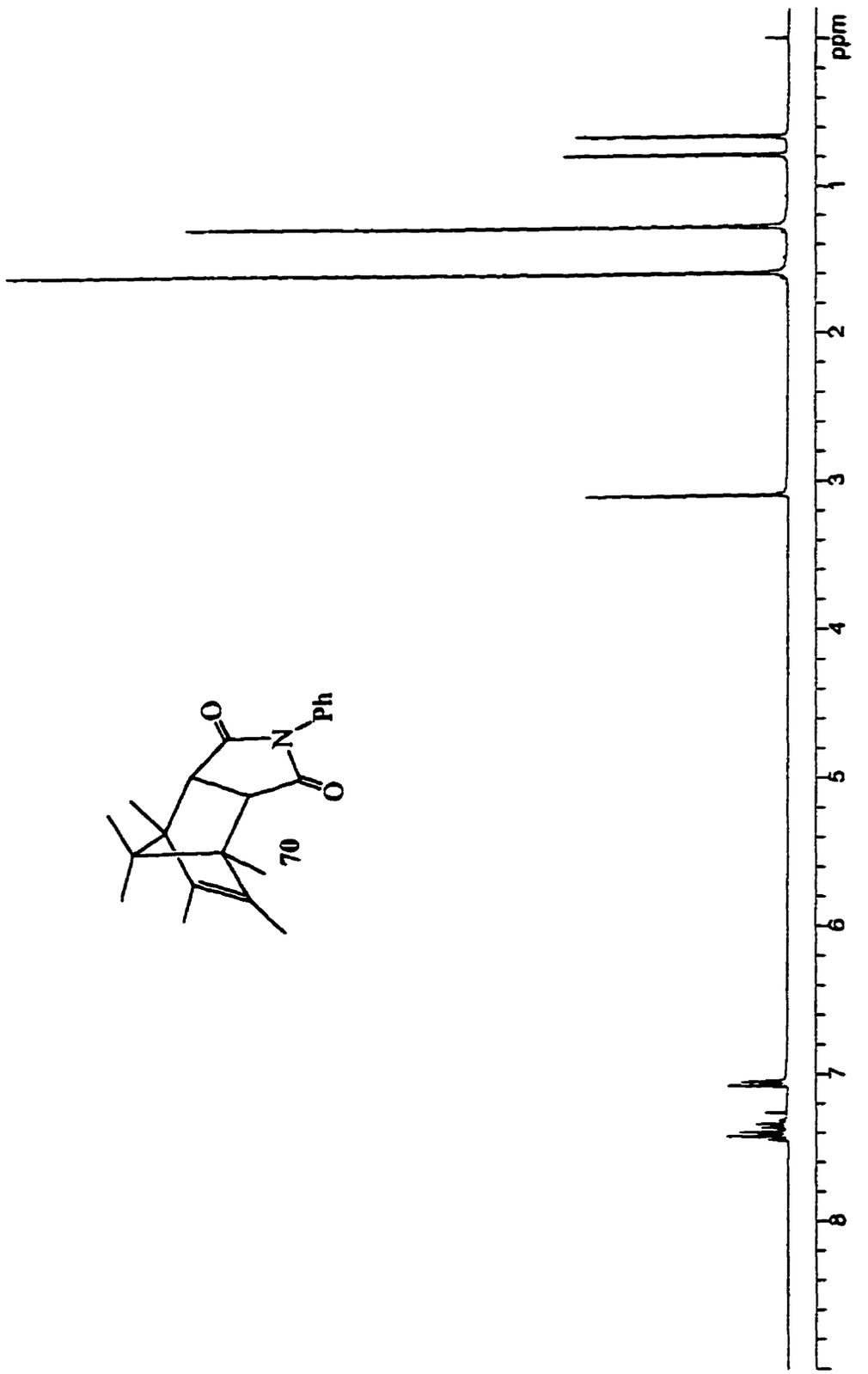
Appendix

Selected ^{1}H nmr spectra of isolated adducts are arranged in the order in which they appear in the text.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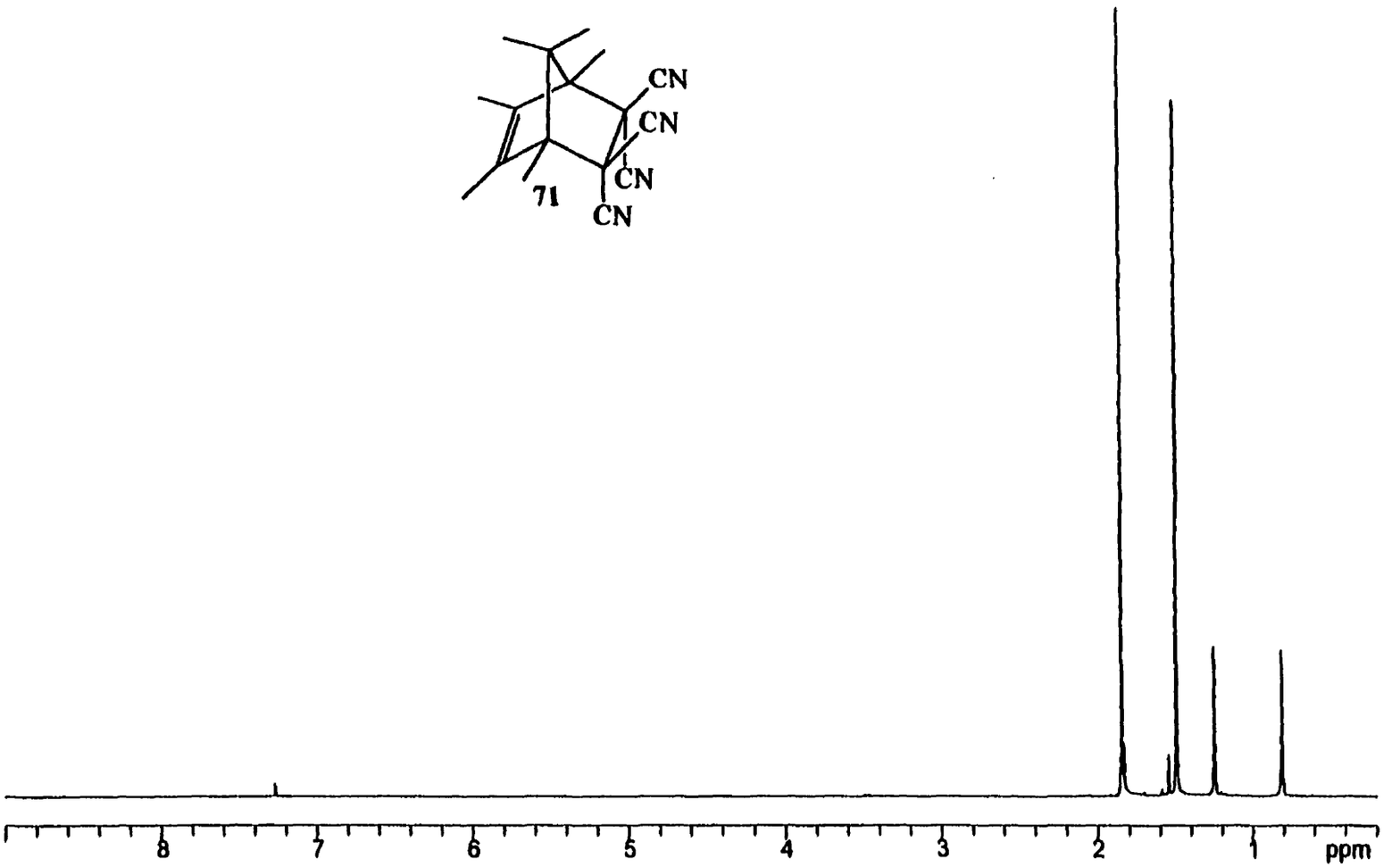
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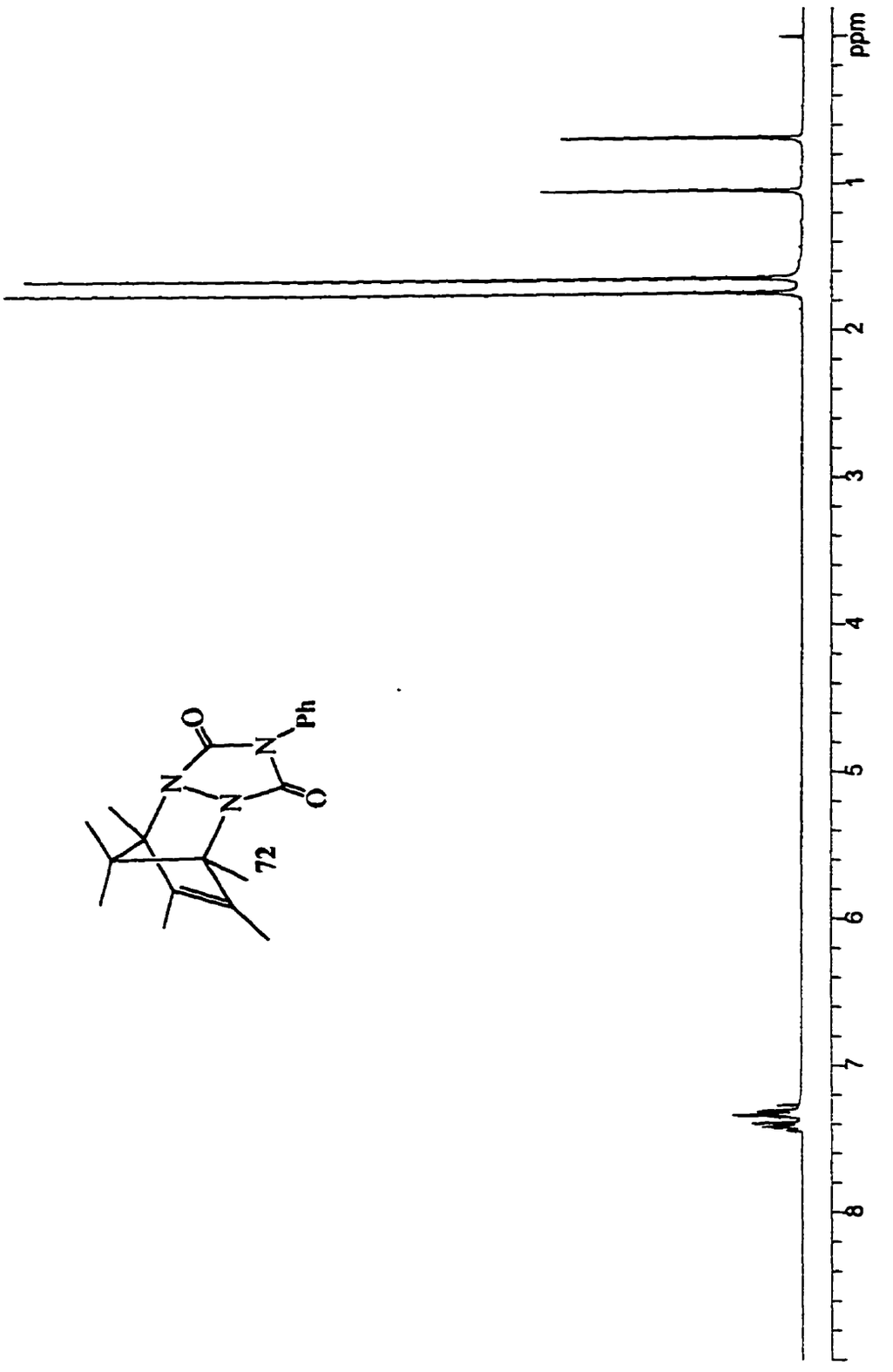
ppm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O
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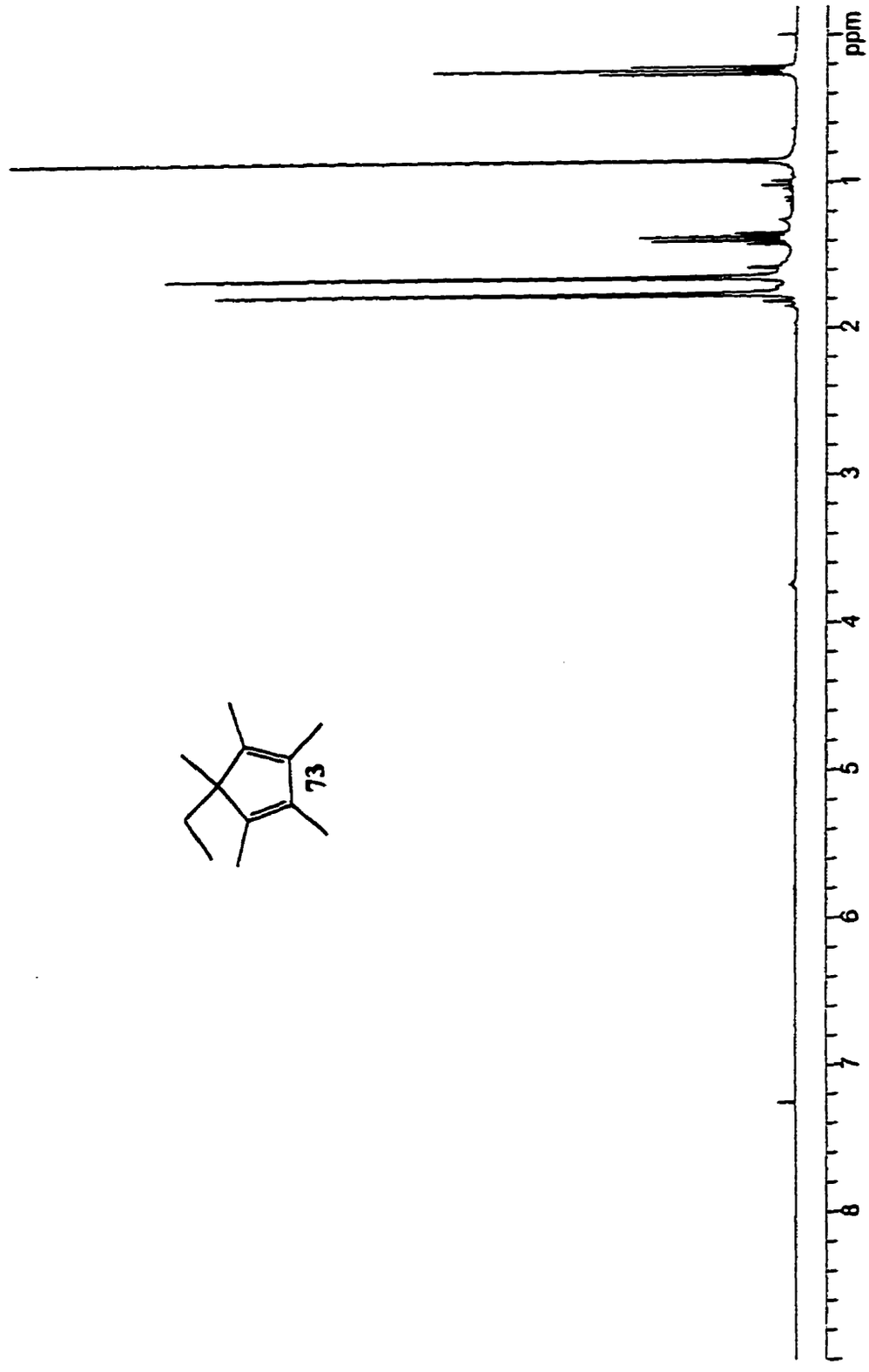
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3
4
5
6
7
8

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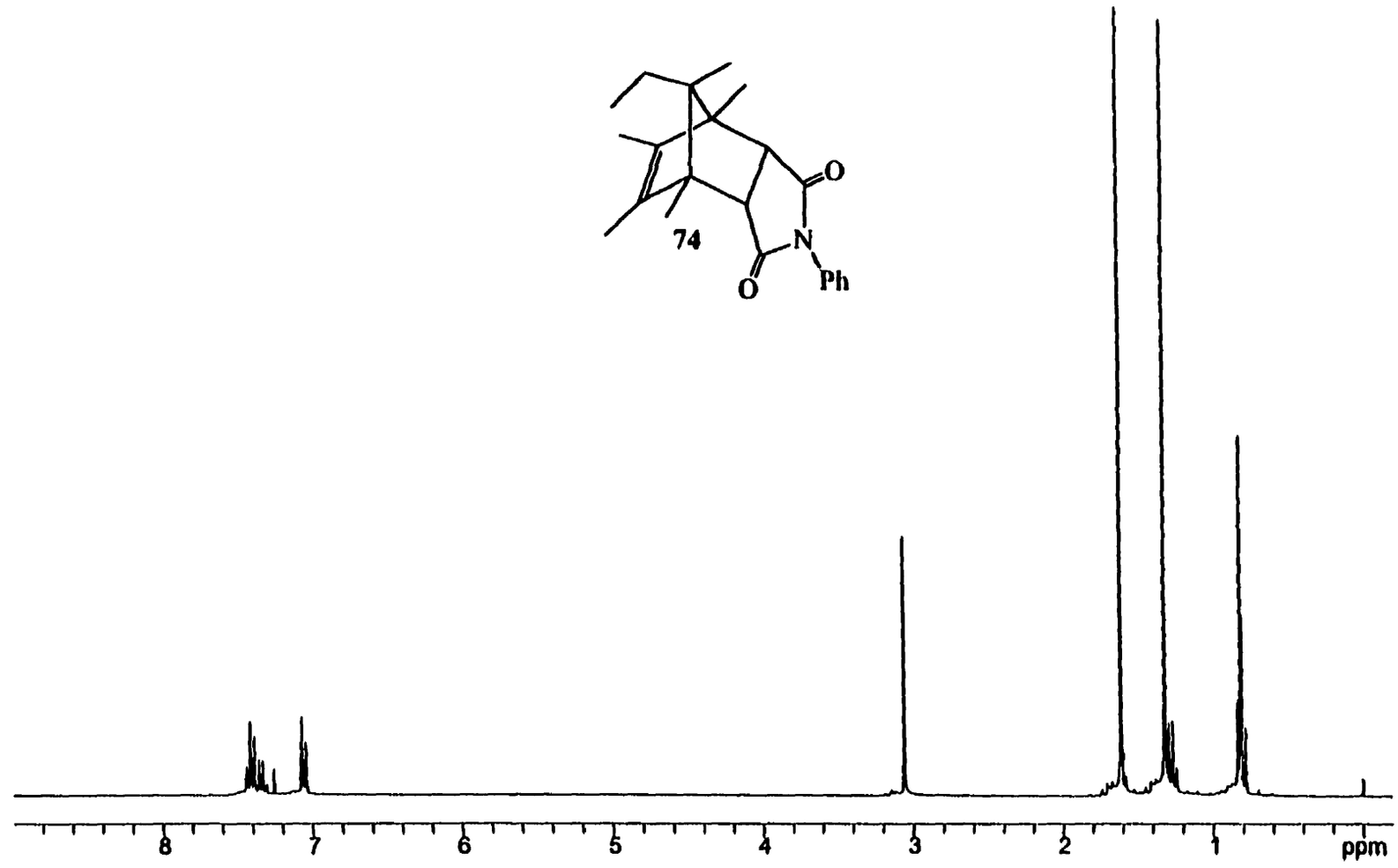
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3
2
1
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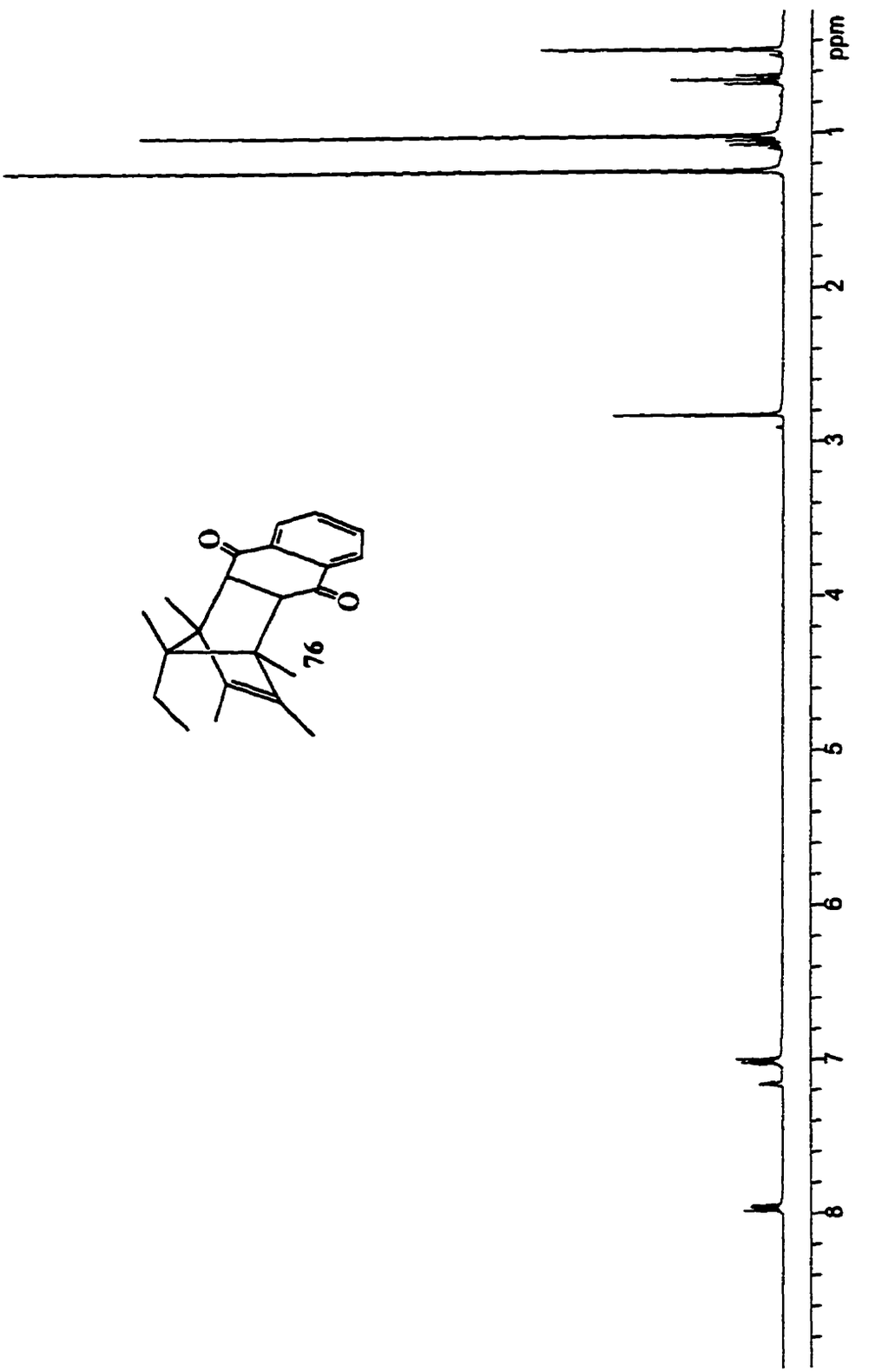
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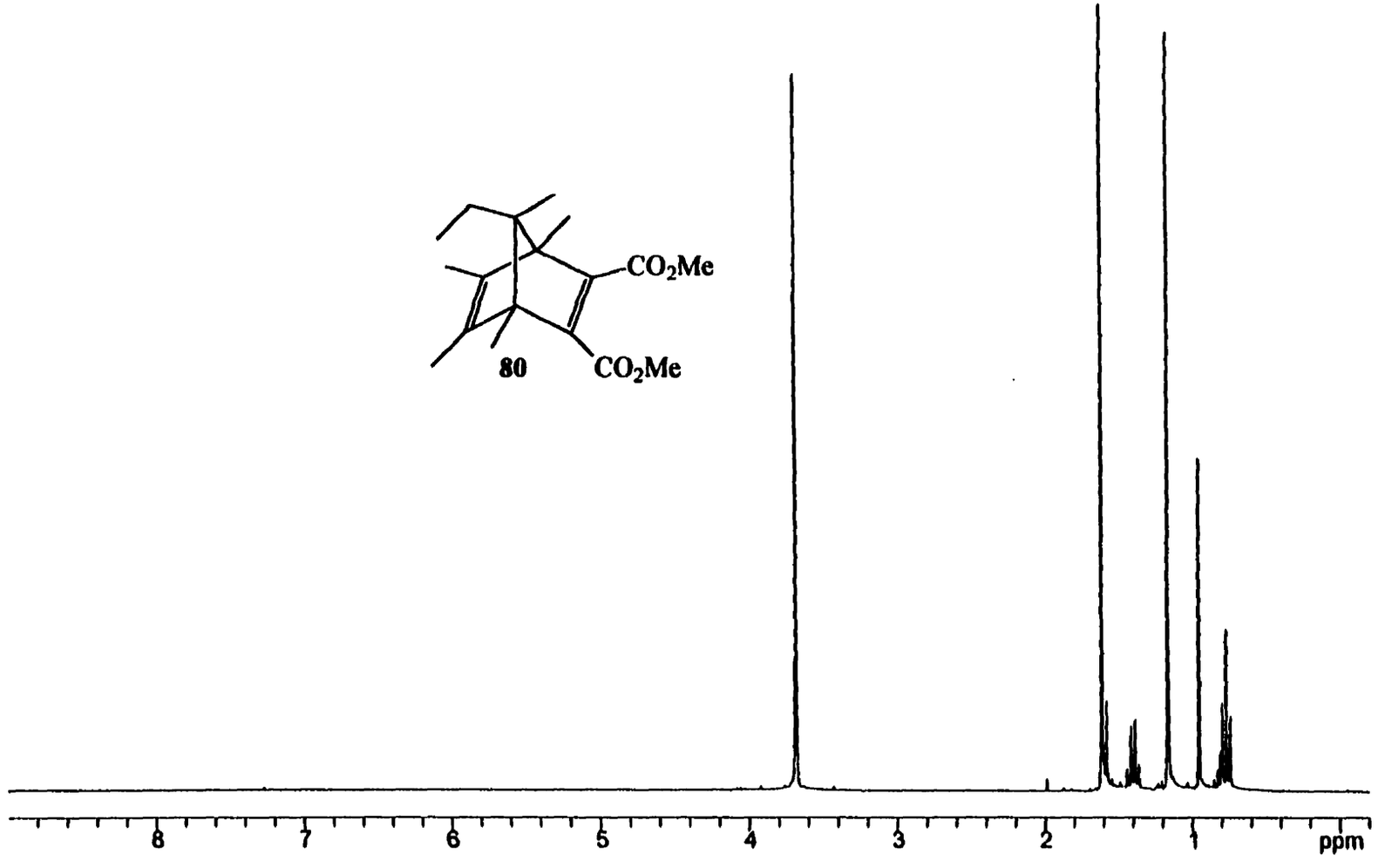
6
7
8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CO2Me
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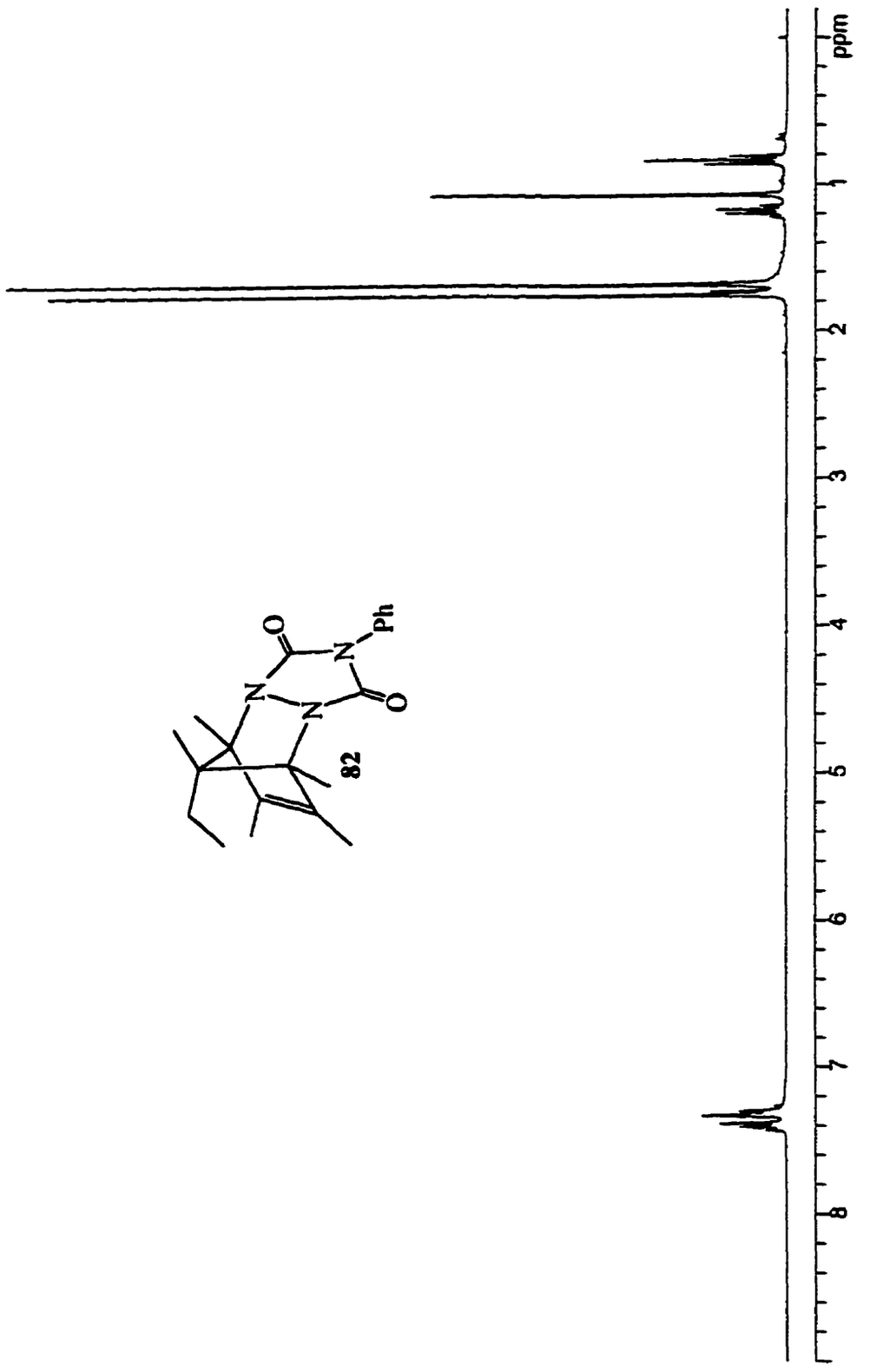
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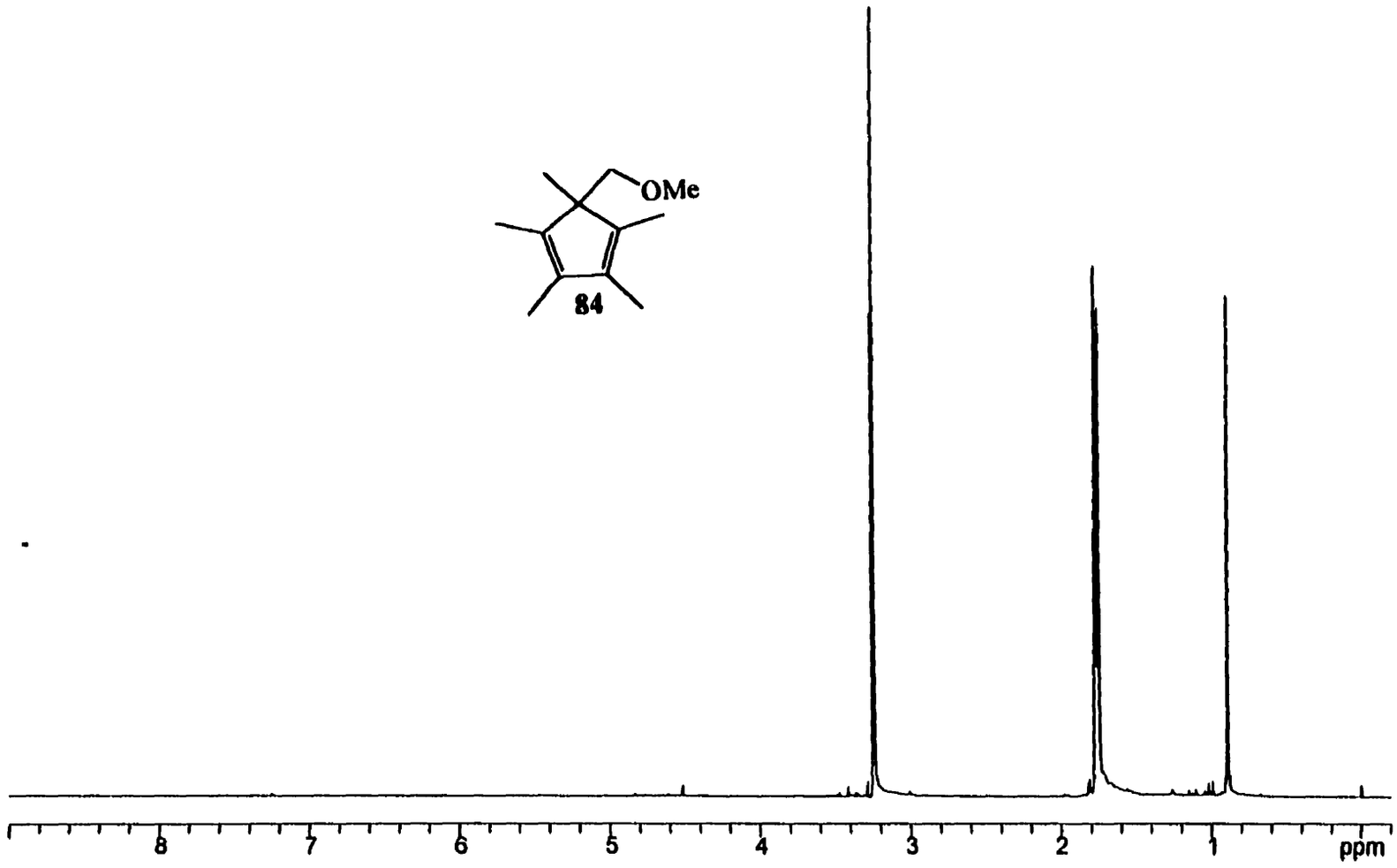
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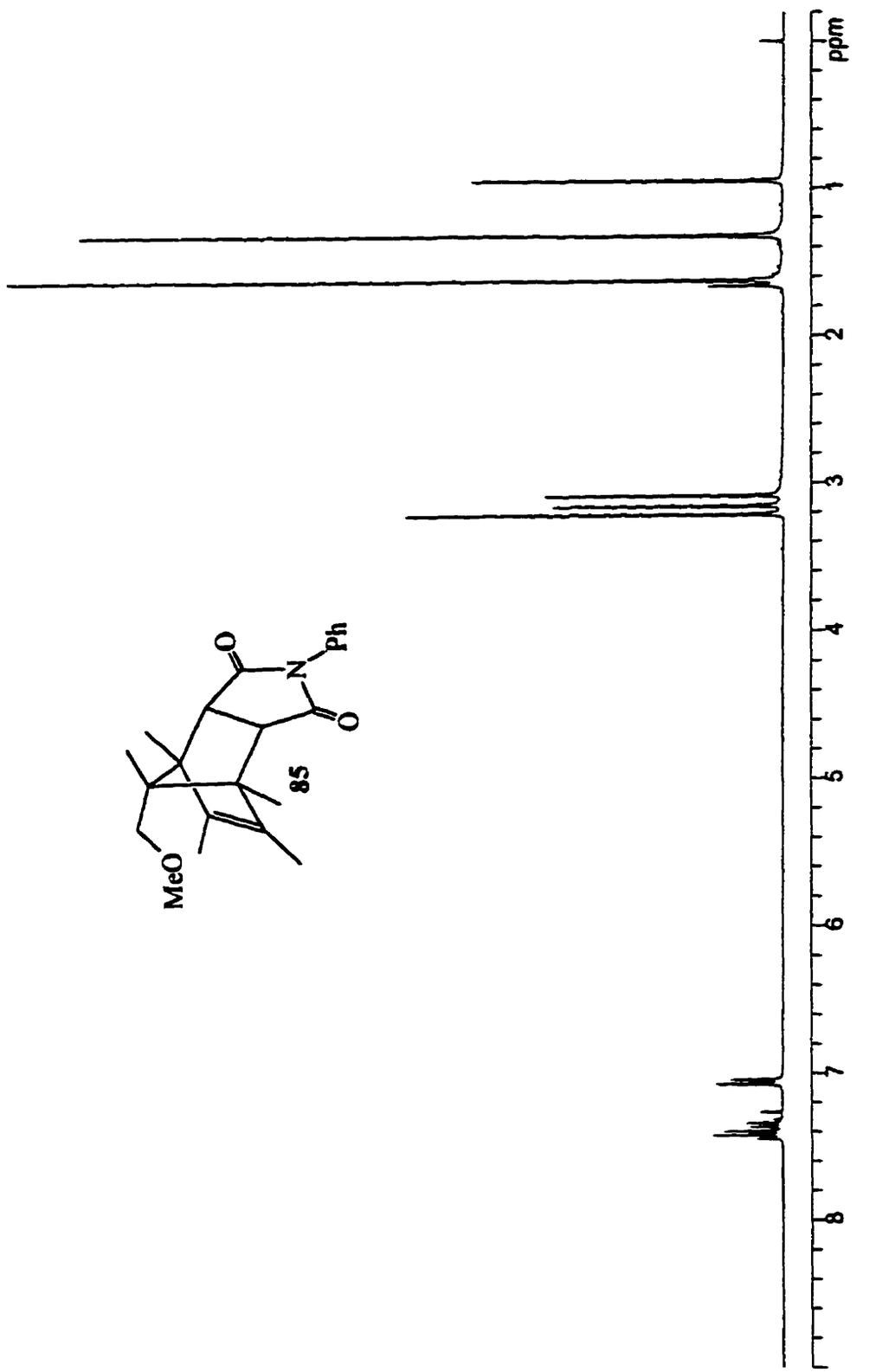
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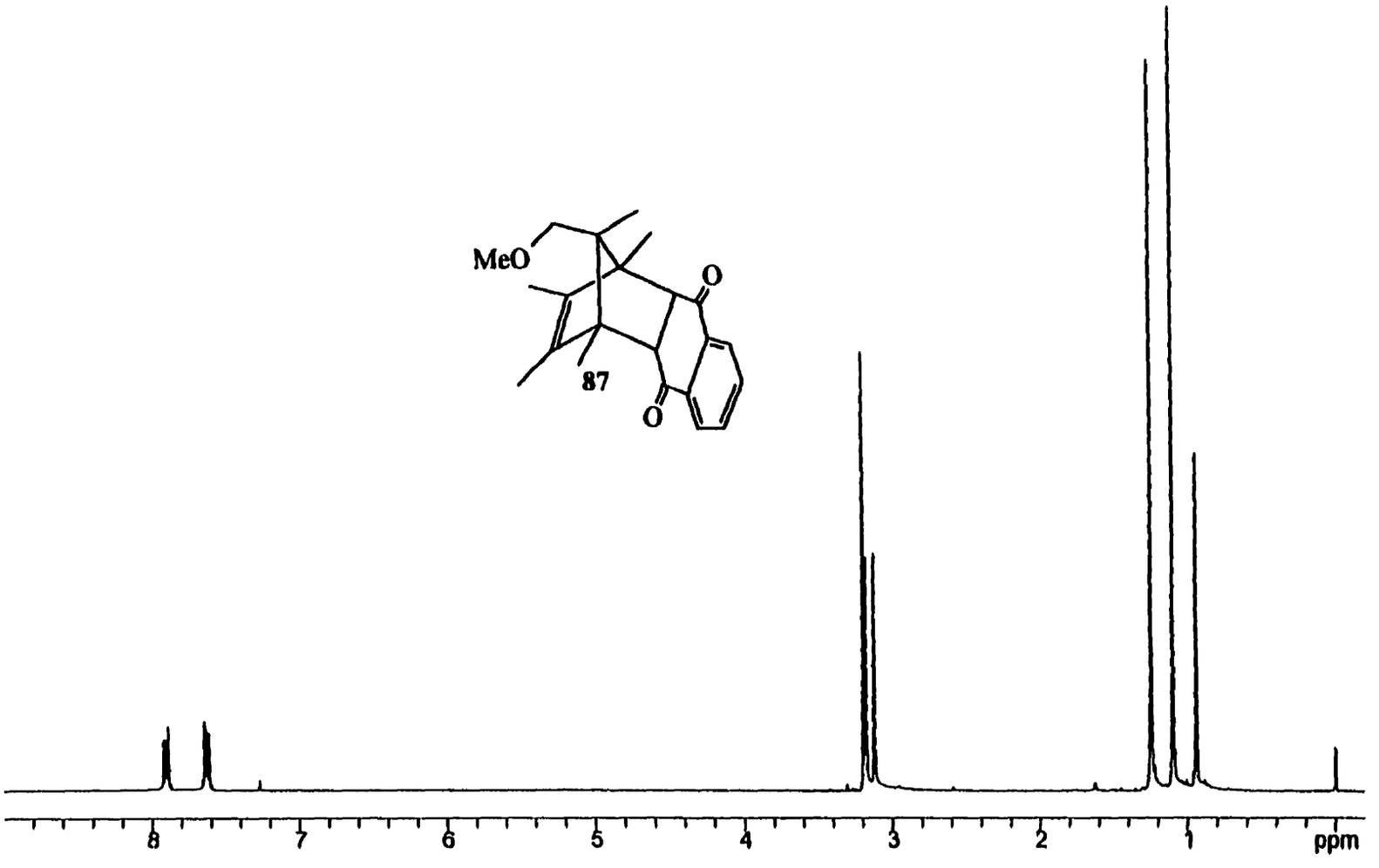
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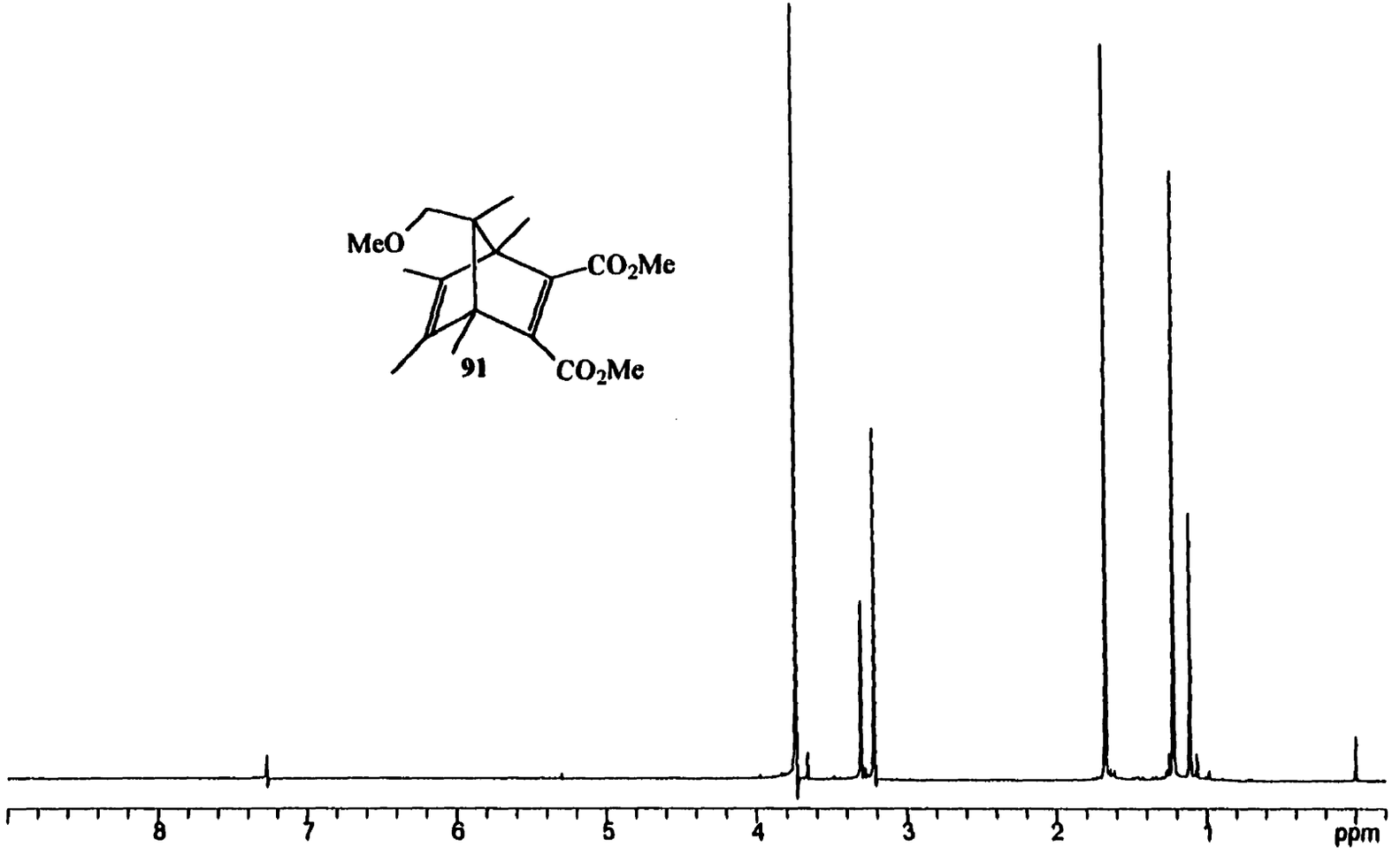
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2
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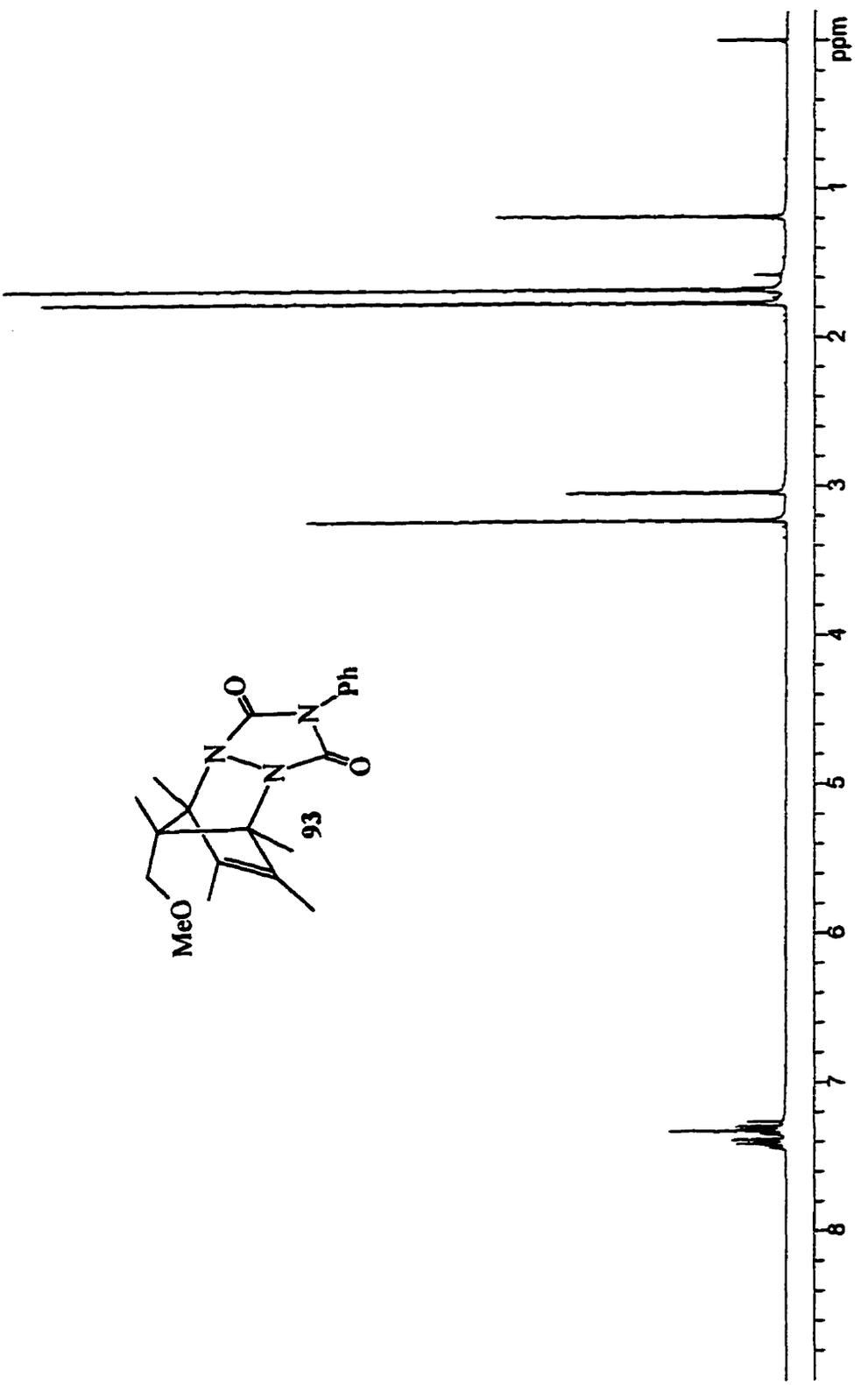
ppm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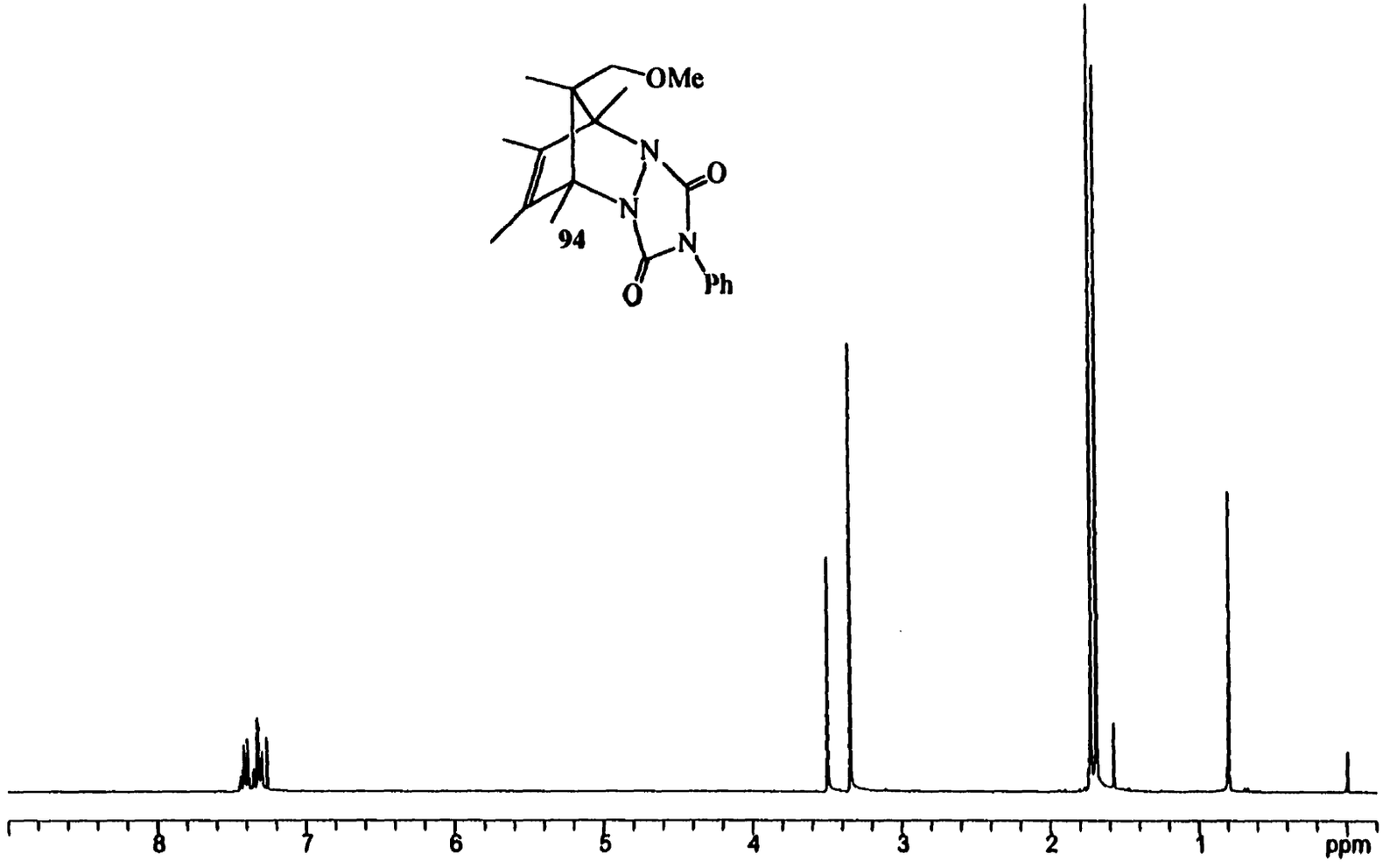
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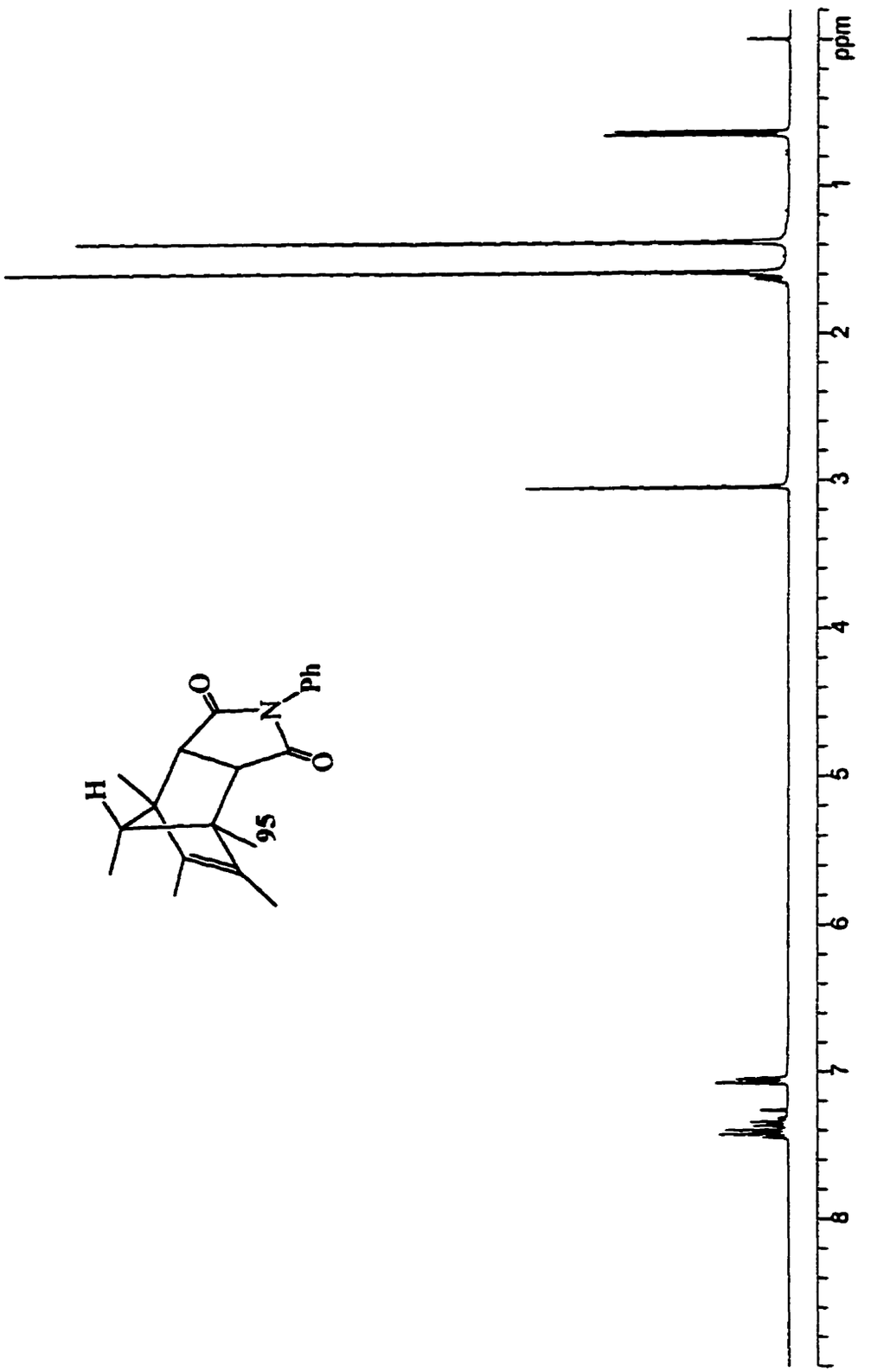
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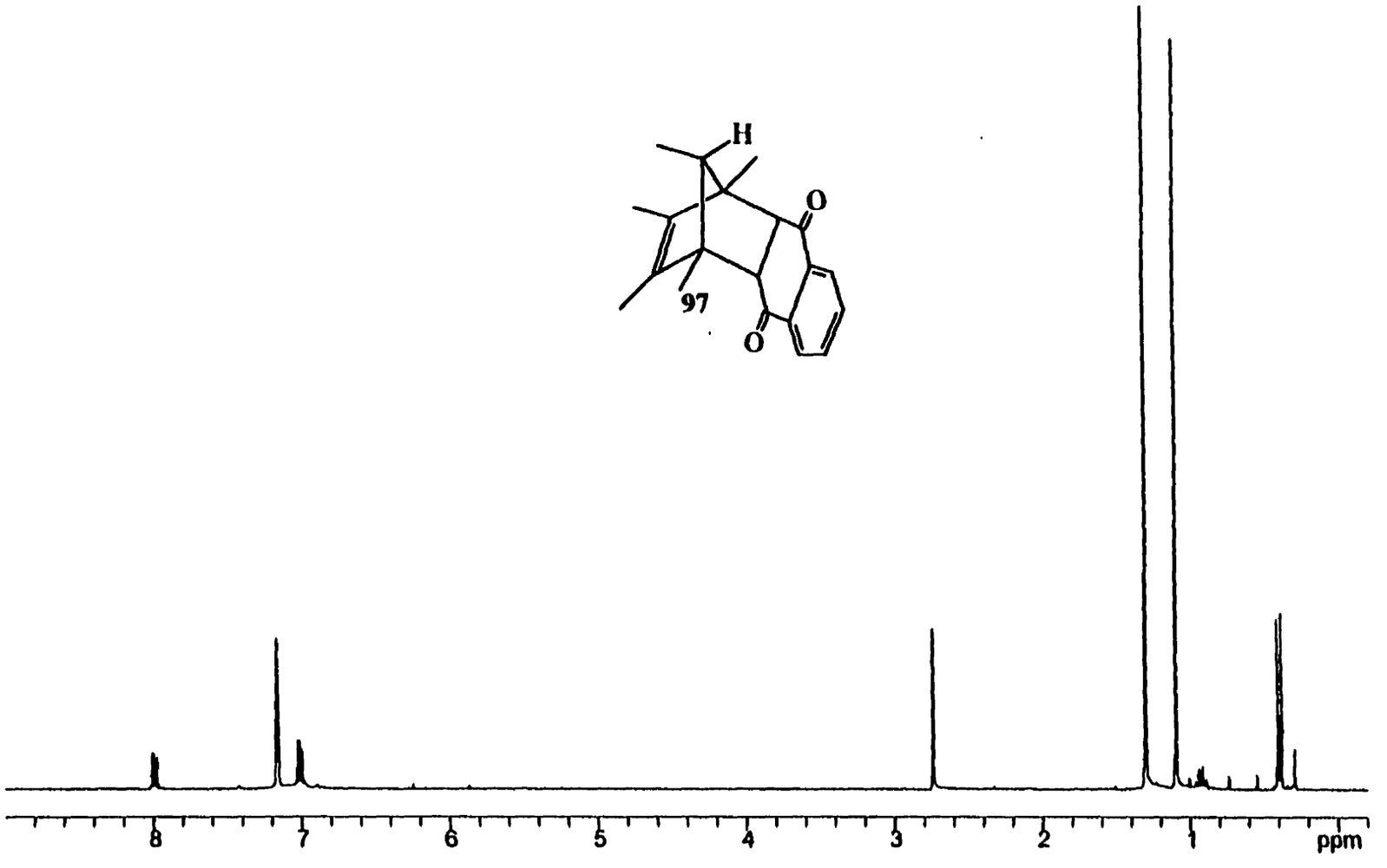
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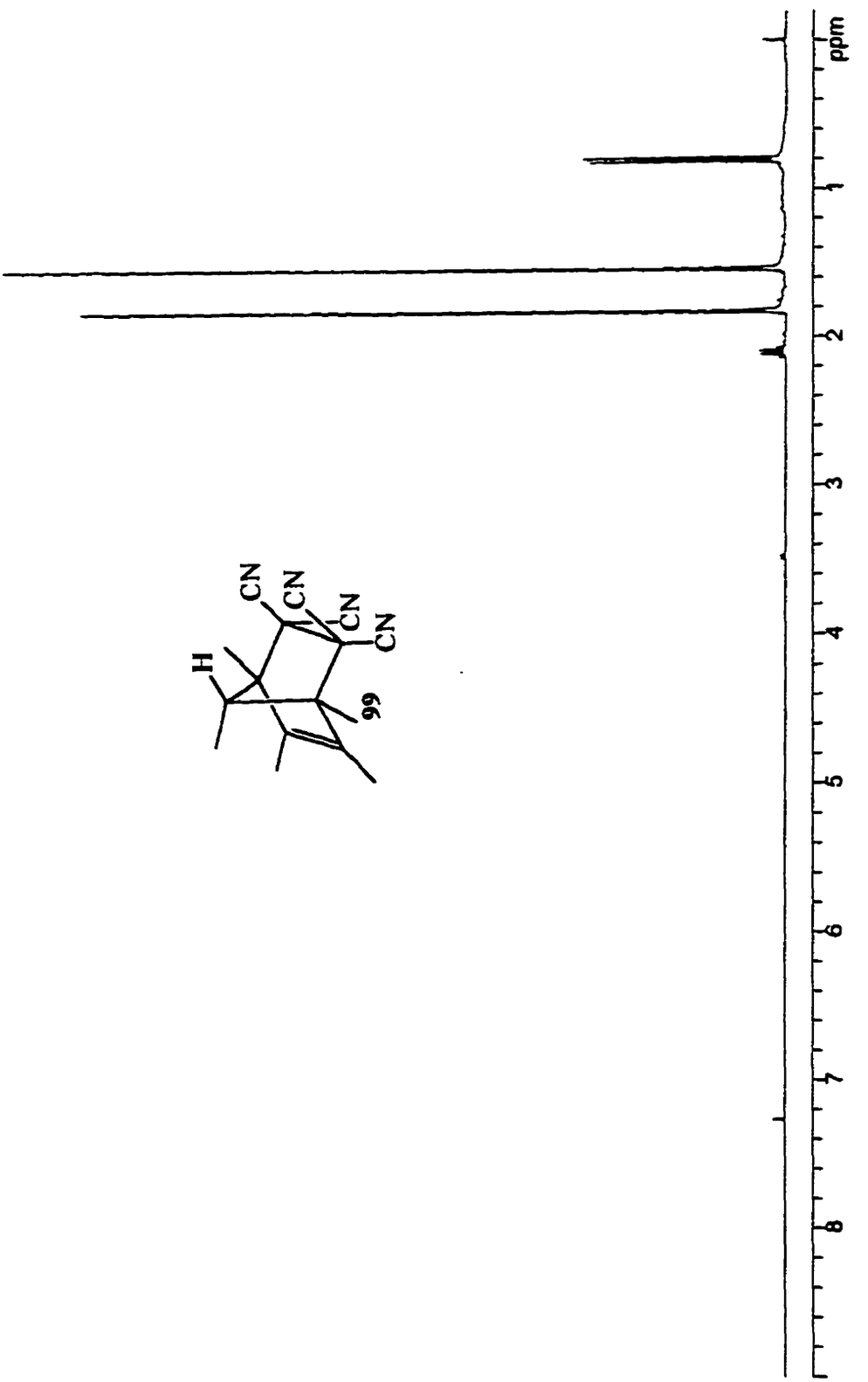
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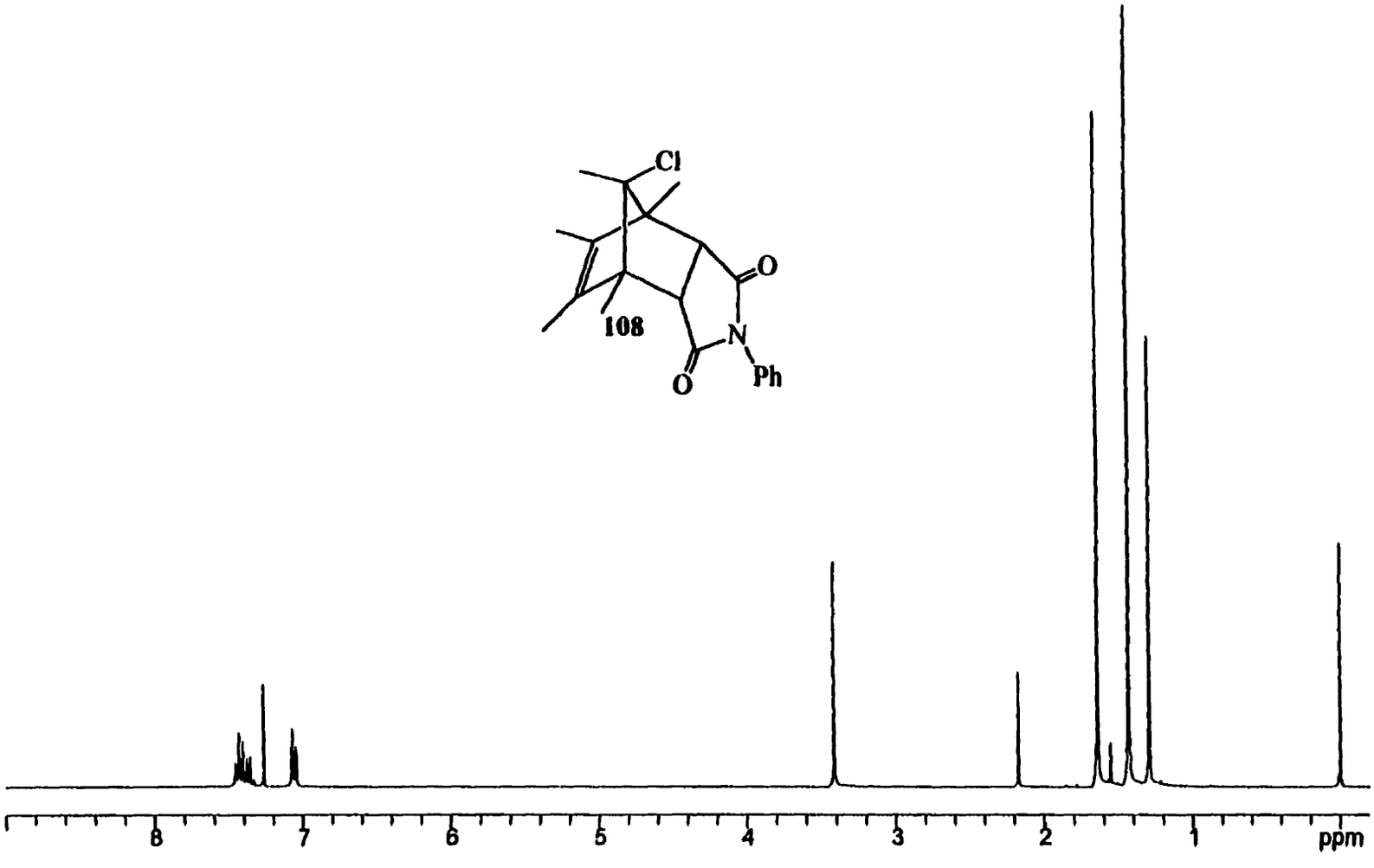
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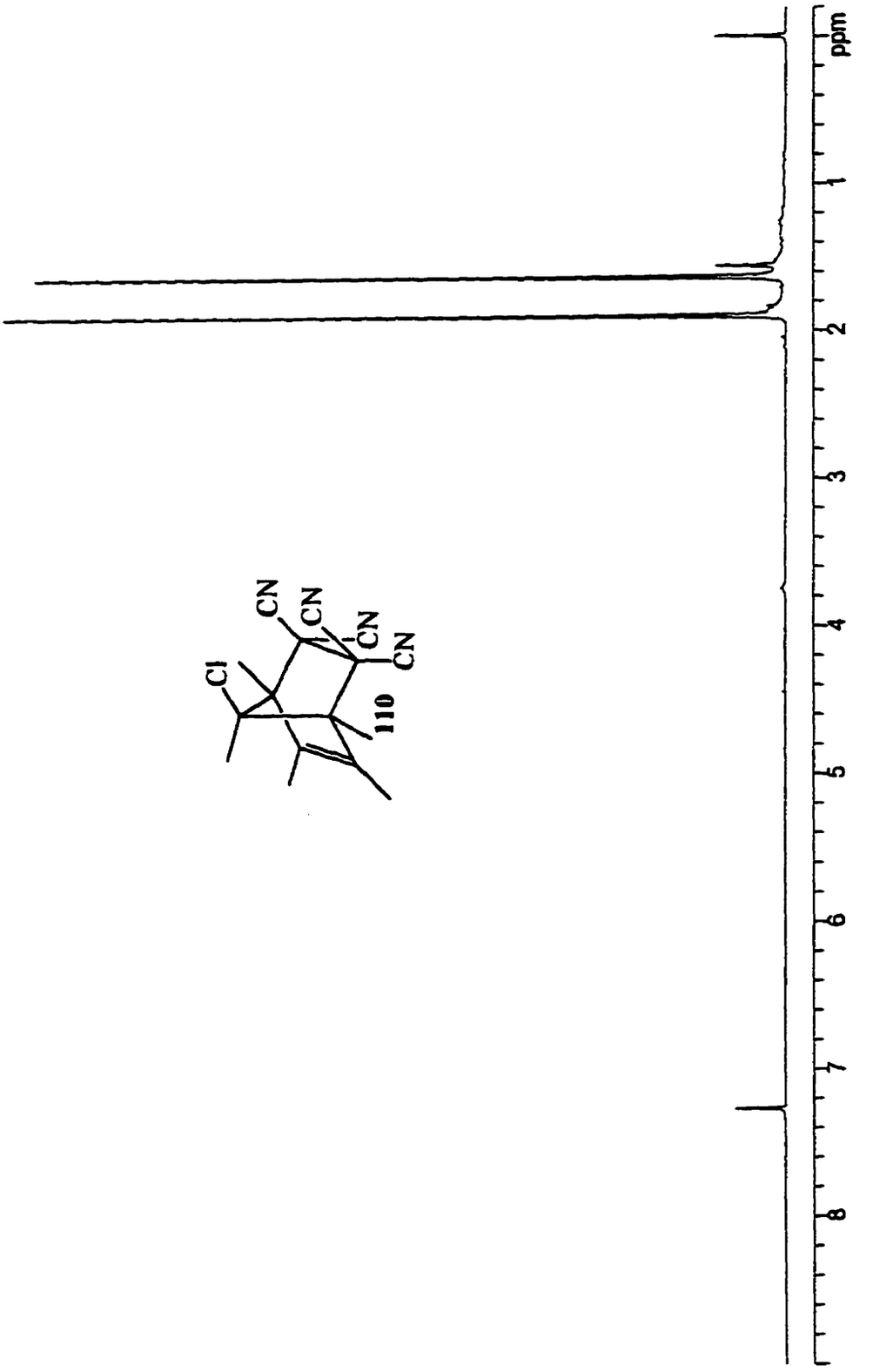
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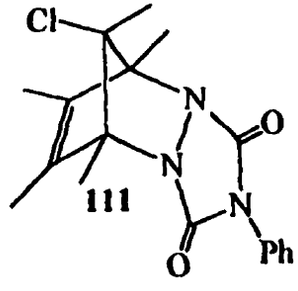

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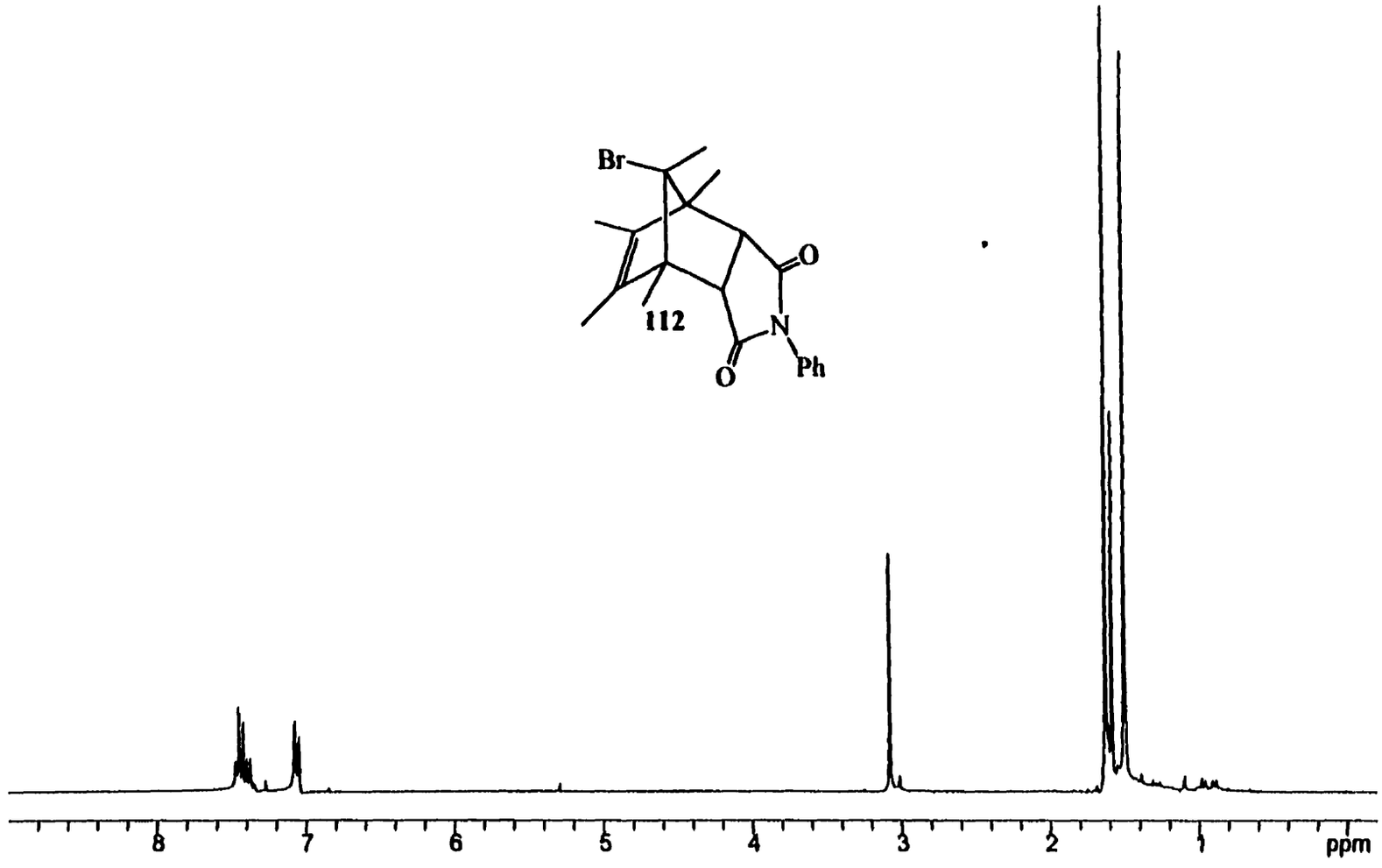
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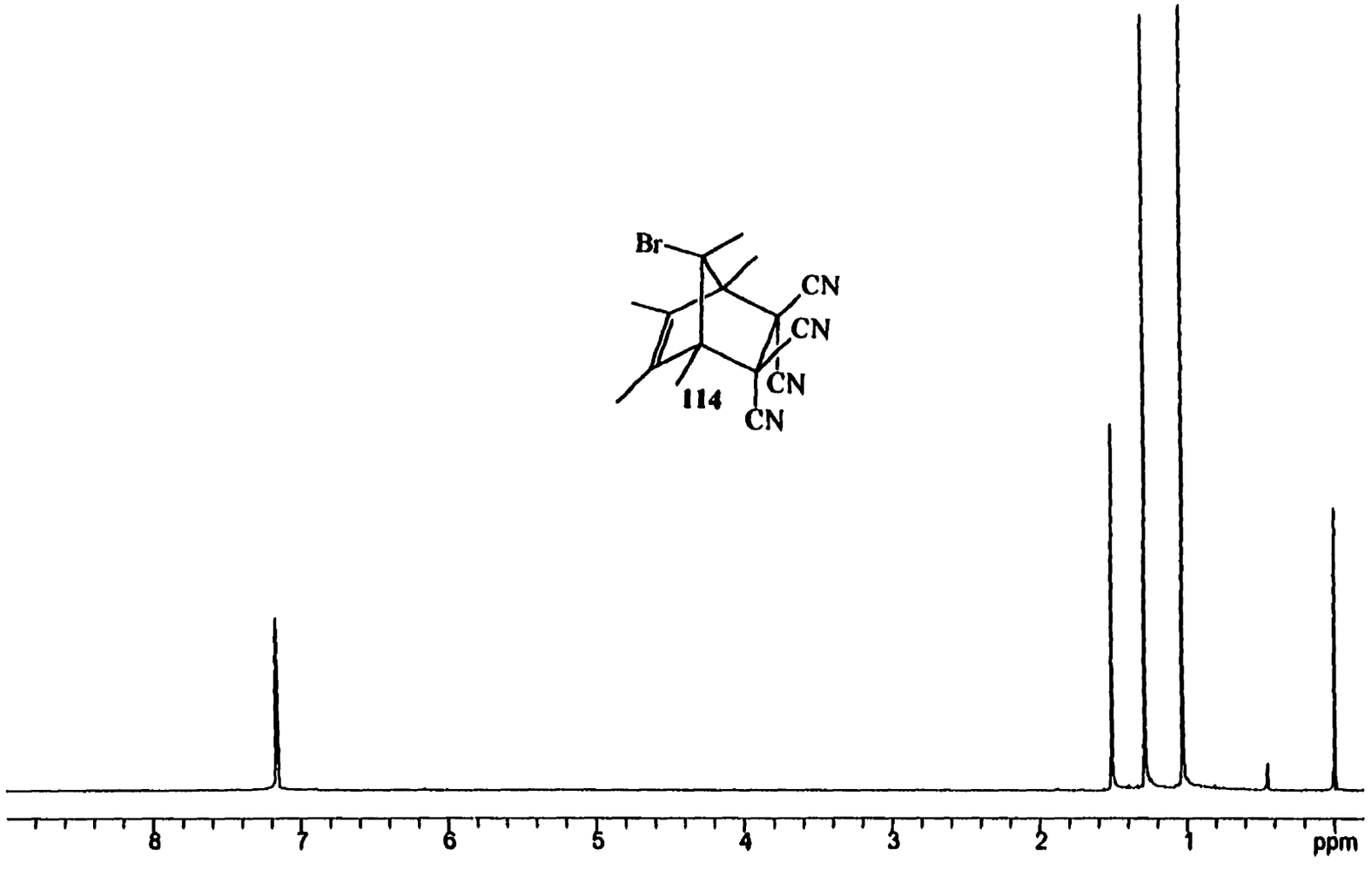
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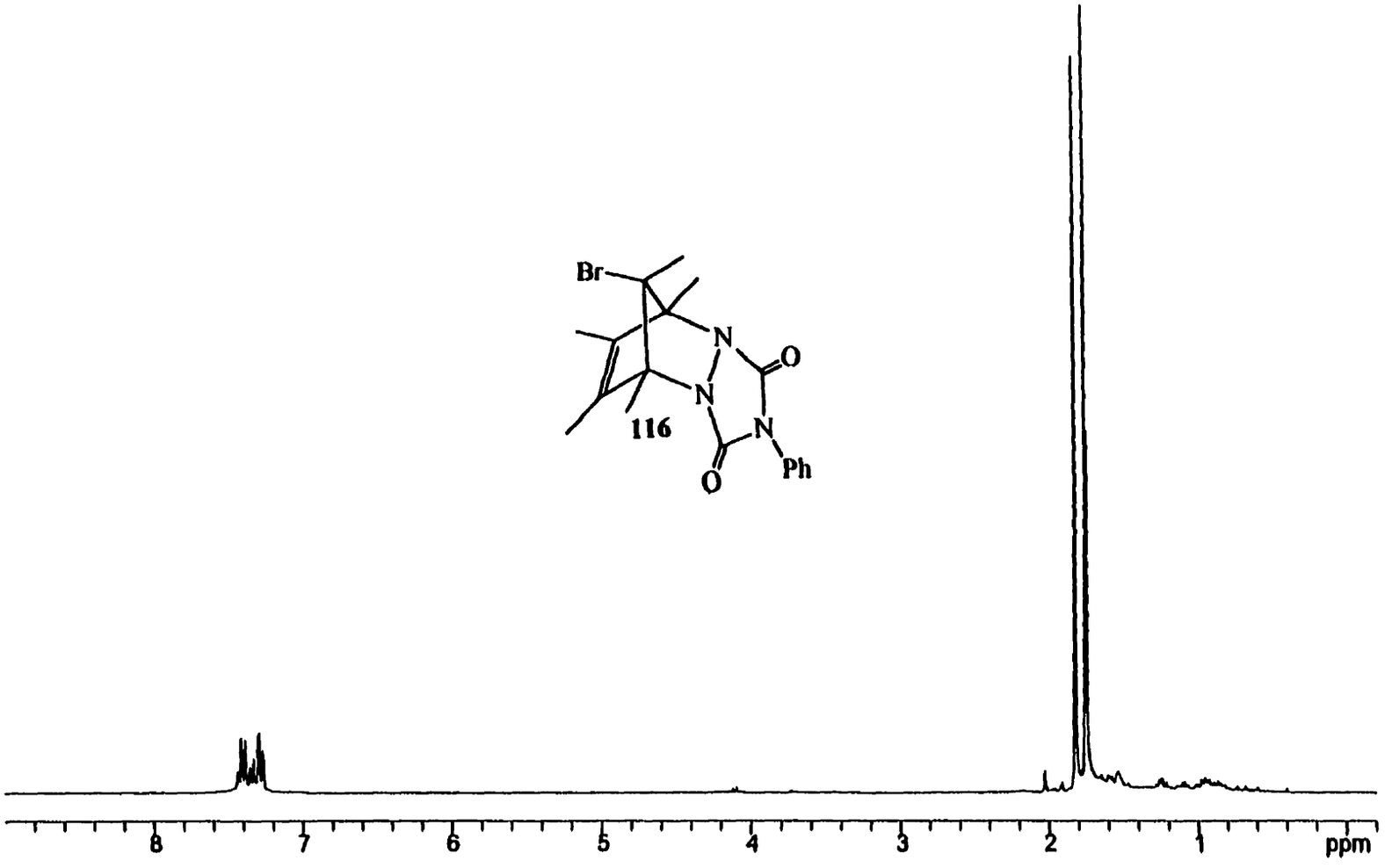
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1
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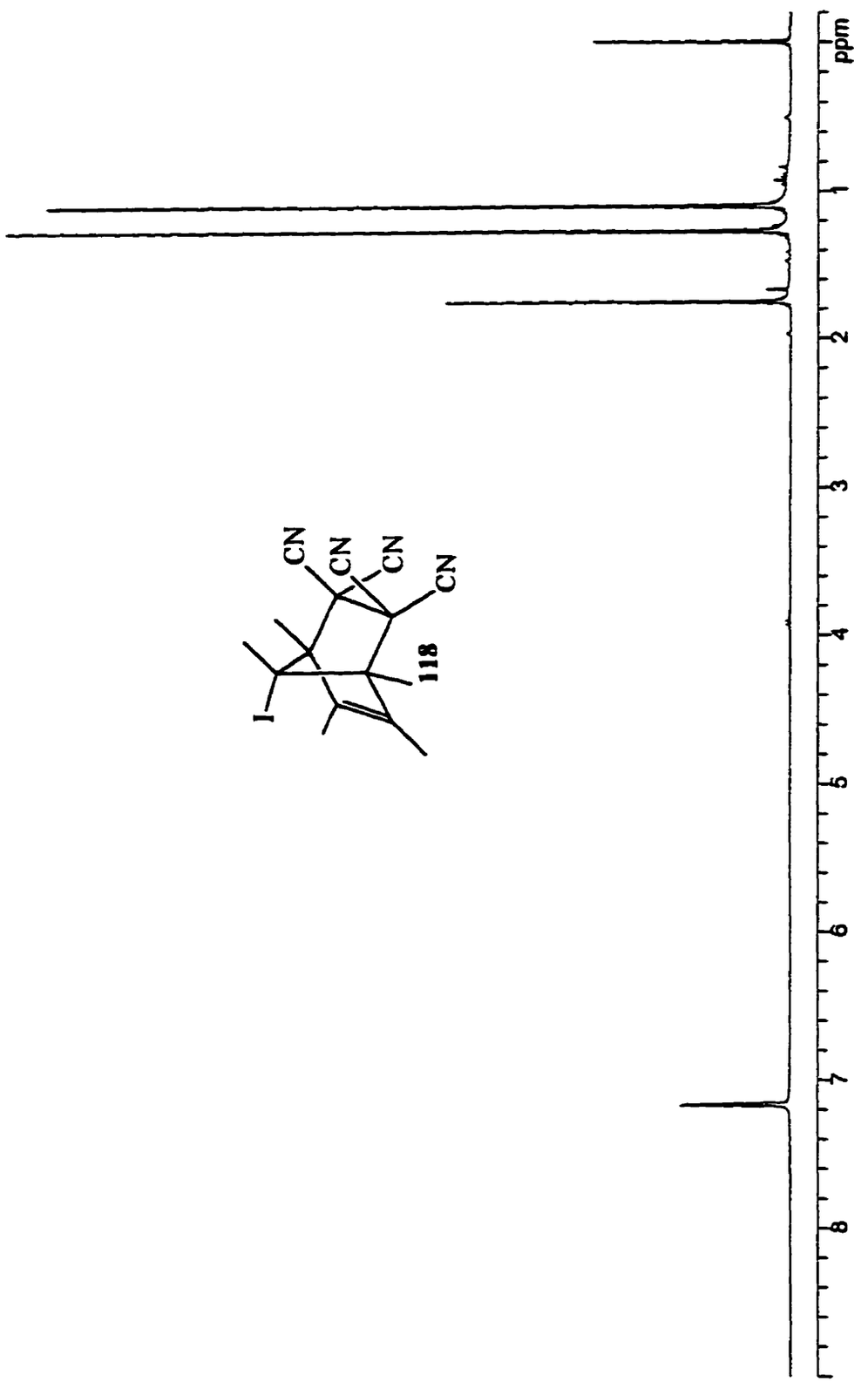
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CN
CN
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I
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ppm
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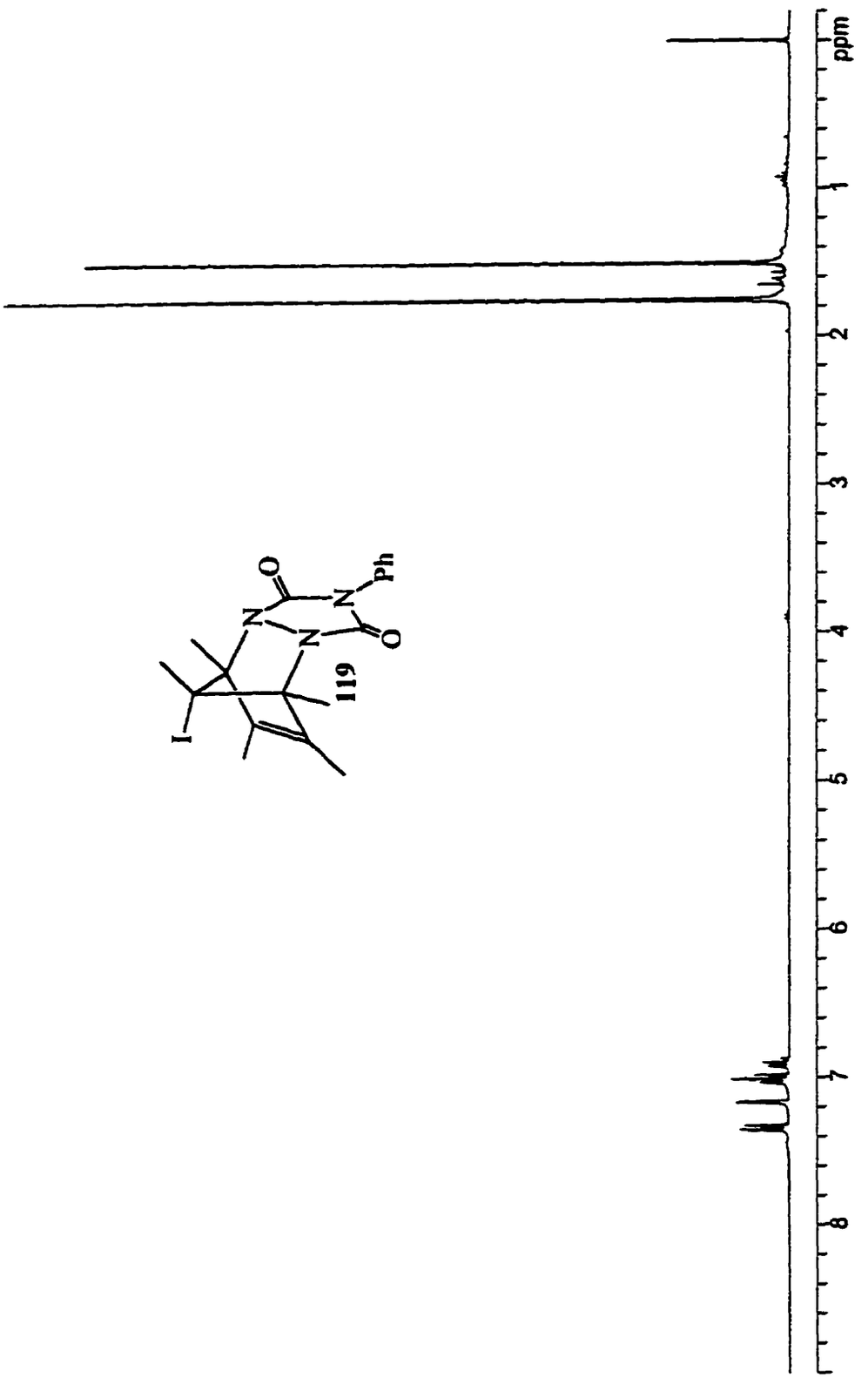
6
7
8


ppm
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2
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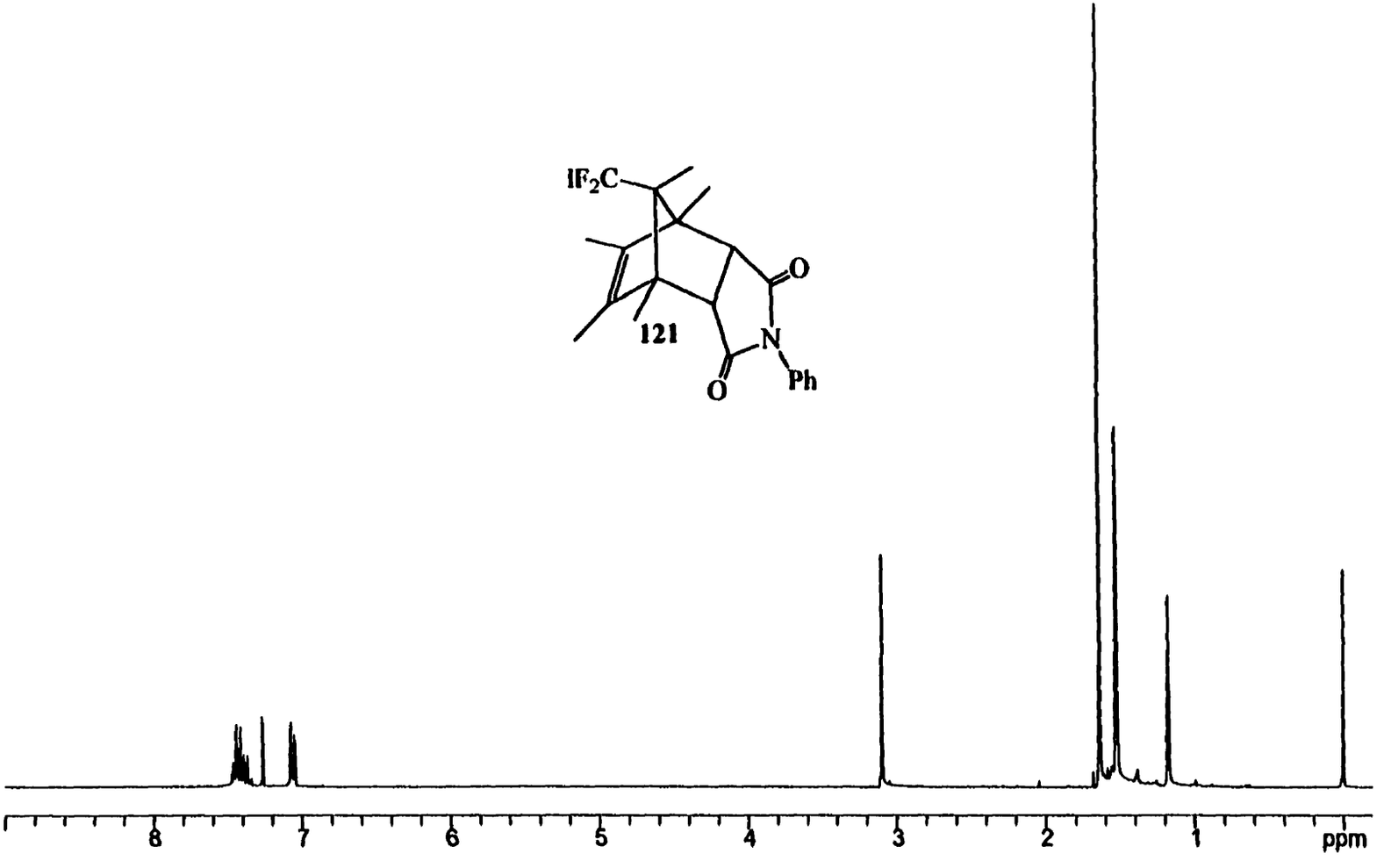
6
7
8
O
N
Ph
N
N
O
I
119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O
N
Ph
O
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7
6
5
4
3
2
1
ppm