Ottawa, Canada
K1A 0N4

CANADIAN THESES

THÈSES CANADIENNES

NOTICE

The quality of this microfiche is heavily dependent upon the quality of the original thesis submitted for microfilming. Every effort has been made to ensure the highest quality of reproduction possible.

If pages are missing, contact the university which granted the degree.

Some pages may have indistinct print especially if the original pages were typed with a poor typewriter ribbon or if the university sent us an inferior photocopy.

Previously copyrighted materials (journal articles, published tests, etc.) are not filmed.

Reproduction in full or in part of this film is governed by the Canadian Copyright Act, R.S.C. 1970, c. C-30.

AVIS

La qualité de cette microfiche dépend grandement de la qualité de la thèse soumise au microfilmage. Nous avons tout fait pour assurer une qualité supérieure de reproduction.

S'il manque des pages, veuillez communiquer avec l'université qui a conféré le grade.

La qualité d'impression de certaines pages peut laisser à désirer, surtout si les pages originales ont été dactylographiées à l'aide d'un ruban usé ou si l'université nous a fait parvenir une photocopie de qualité inférieure.

Les documents qui font déjà l'objet d'un droit d'auteur (articles de revue, examens publiés, etc.) ne sont pas microfilmés.

La reproduction, même partielle, de ce microfilm est soumise à la Loi canadienne sur le droit d'auteur, SRC 1970, c. C-30.

THIS DISSERTATION
HAS BEEN MICROFILMED
EXACTLY AS RECEIVED

LA THÈSE A ÉTÉ
MICROFILMÉE TELLE QUE
NOUS L'AVONS REÇUE

NL-339 (r.86/06)

Canada

THE UNIVERSITY OF ALBERTA

2-DIETHYLPHOSPHORYLOXY-1,3-BUTADIENE AND TRANS-2-DIETHYLPHOSPHORYLOXY-1,3-PENTADIENE IN LEWIS ACID CATALYZED DIELS-ALDER REACTIONS

by

WAISENG MARTIN FENG

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE
OF MASTER OF SCIENCE

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

SPRING 1986

ISBN 0-315-30214-3

THE UNIVERSITY OF ALBERTA

RELEASE FORM

NAME OF AUTHOR WAISENG MARTIN FENG

TITLE OF THESIS 2-DIETHYLPHOSPHORYLOXY-1,3-BUTADIENE AND TRANS-2-DIETHYLPHOSPHORYLOXY-1,3-PENTADIENE IN LEWIS ACID CATALYZED DIELS-ALDER REACTIONS

DEGREE FOR WHICH THESIS WAS PRESENTED M.Sc.

YEAR THIS DEGREE GRANTED 1986

Permission is hereby granted to THE UNIVERSITY OF ALBERTA LIBRARY to reproduce single copies of this thesis and to lend or sell such copies for private, scholarly or scientific research purposes only.

The author reserves other publication rights, and neither the thesis nor extensive extracts from it may be printed or otherwise reproduced without the author's written permission.

(Signed)

PERMANENT ADDRESS:

#6 Quie Kong 4th Road
Tongshan, Canton City
China

DATED March 12 1986

THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled 2-DIETHYLPHOSPHORYLOXY-1-3,BUTADIENE AND TRANS-2-DIETHYLPHOSPHORYLOXY-1,3-PENTADIENE IN LEWIS ACID CATALYZED DIELS-ALDER REACTIONS submitted by WEISENG MARTIN FENG in partial fulfilment of the requirements for the degree of MASTER OF SCIENCE

H.J. Liu, Supervisor

M. Cowie

D.D. Tanner

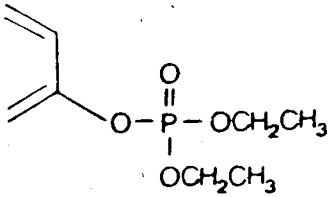
T.J. Danielson (Pharmacy)

DATE March 12, 1986

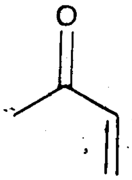
for my parents, my wife,
my sister and my brothers

ABSTRACT

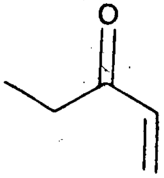
The Lewis acid catalyzed Diels-Alder reactions of 2-diethylphosphoryloxy-1,3-butadiene **i** were studied. This diene phosphate was found to react with a variety of α,β-unsaturated carbonyl compounds under Lewis acid catalysis to give synthetically useful cyclohexene derivatives, with excellent regioselectivity. The adducts were produced in accordance with the normal rules governing the Diels-Alder addition. In the presence of stannic chloride, acyclic α,β-unsaturated ketones such as methyl vinyl ketone **ii** and ethyl vinyl ketone **iii** reacted rapidly with diene phosphate i to afford exclusively the <u>para</u>-oriented adducts **iv** and v in excellent yields. Even with <u>trans</u>-3-penten-2-one **vi**, which is known to be a relatively poor dienophile, the cycloaddition reaction proceeded smoothly with complete regioselectivity to give adduct **vii** in good yield. Diene phosphate i was also found to undergo cycloaddition reaction with 3-butyn-2-one **viii** under stannic chloride catalysis to produce the expected enone **ix** in good yield along with small amounts of the regioisomer **x**. In cases of cyclic α,β-unsaturated ketones, the stannic chloride catalyzed addition of diene **i** to <u>p</u>-benzoquinone **xi** gave readily aromatic enol-phosphate **xii**. Similarly,when diene **i** was treated with cyclic enone-ester **xiii** in the presence of ferric chloride



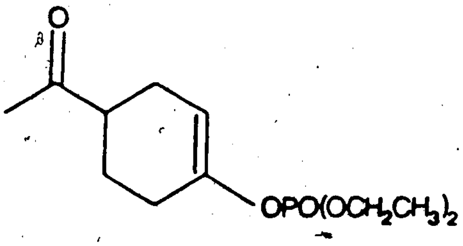
i



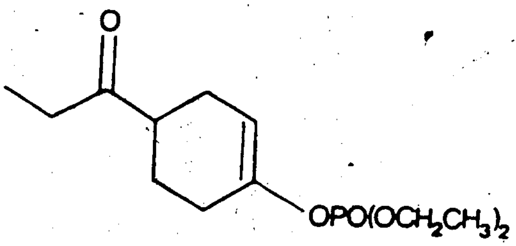
ii



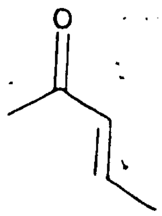
iii



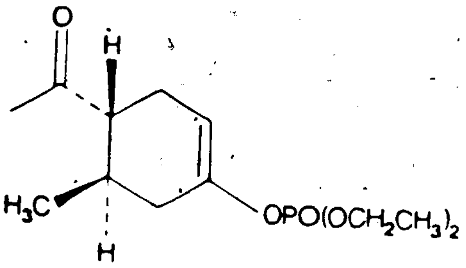
iv



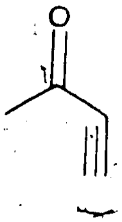
v



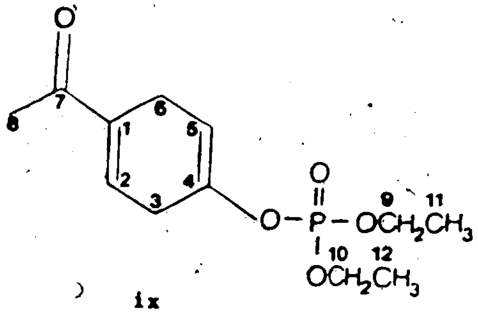
vi



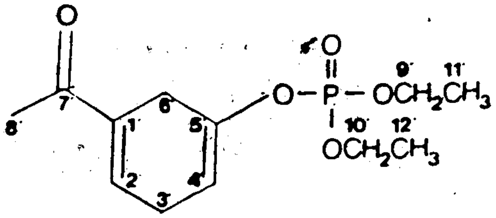
vii



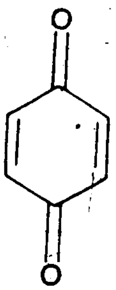
viii



ix



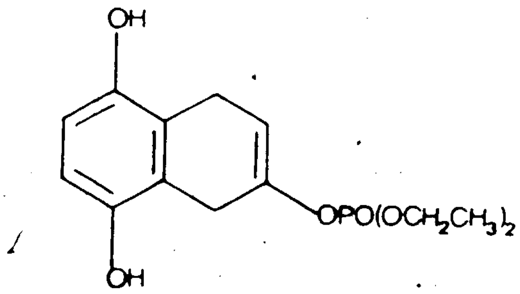
x



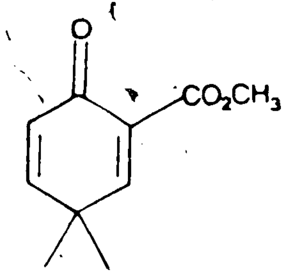
xi

a single adduct **xiv** was obtained in good yield. In this particular case, ferric chloride was shown to be a much better catalyst than boron trifluoride etherate and stannic chloride. The Diels-Alder reactions of diene **i** with 2-cyclopenten-1-one **xv** and 2-cyclohexen-1-one **xvi** were also examined using stannic chloride as a catalyst. These reactions were found to be less facile and the desired adducts **xvii** and **xviii** were obtained only in low yields.

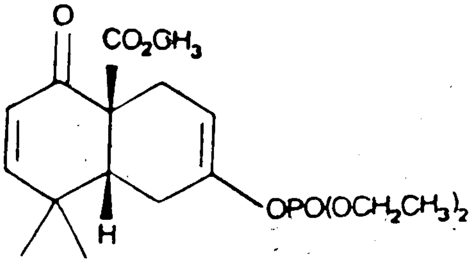
The stannic chloride catalyzed Diels-Alder reactions of trans-2-diethylphosphoryloxy-1,3-pentadiene **xix** were also studied. Diene phosphate **xix** was found to react efficiently with a number of acyclic α,β-unsaturated ketones such as methyl vinyl ketone **ii**, ethyl vinyl ketone **iii** and trans-3-penten-2-one **vi** with complete regio- and stereoselectivity to give cyclohexene derivatives **xx**, **xxi** and **xxii**. The addition of diene **xix** to p-benzoquinone **xi** was shown to be equally facile resulting in the formation of aromatic enol-phosphate **xxiii** in synthetically useful yield.



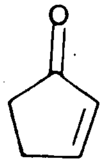
xii



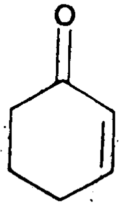
xiii



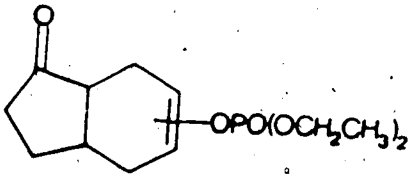
xiv



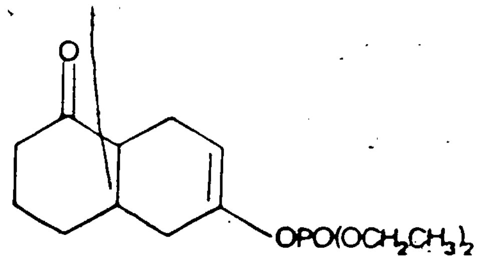
xv



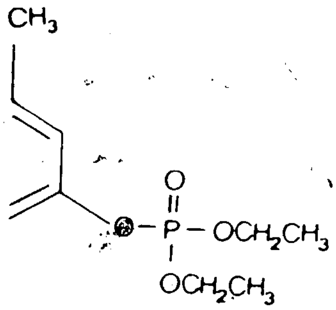
xvi



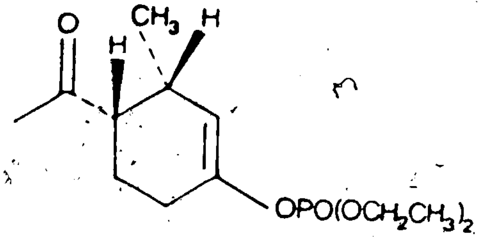
xvii



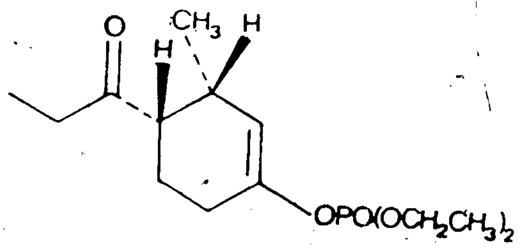
xviii



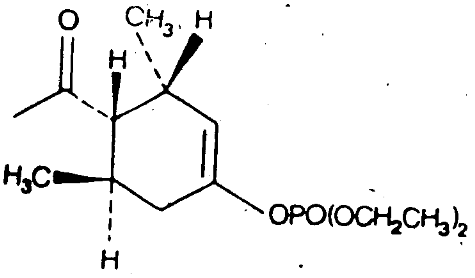
xix



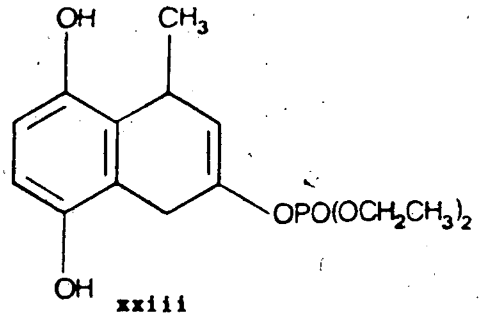
xx



xxi



xxii



xxiii

ACKNOWLEDGEMENTS

The author wishes to express his utmost gratitude to his research director, Dr. H.J. Liu, for his invaluable guidance during the course of this work and also for his interest and assistance in the preparation of this thesis.

The author would also like to thank the technical staff of this department; Dr. A.M. Hogg and his staff for the mass spectra, the staff of the microanalytical laboratory for the elemental analyses, Dr. T. Nakashima and R.N. Swindlehurst and their associates, especially G. Bigam and L. Kong for their excellent high-field ^1H nmr and ^{13}C nmr spectra, J. Hoyle for recording the ftir spectra and also to Annabelle Wiseman for typing the thesis.

Special thanks also go to Mr. B. Ramani for the preparation of 2-carbomethoxy-4,4-dimethyl-2,5-cyclohexadien-1-one.

TABLE OF CONTENTS

LIST OF TABLES

TABLE PAGE

CHAPTER 1

INTRODUCTION*

The cycloaddition of dienes with olefins (dienophiles) to give cyclohexenes was first observed and correctly formulated by Diels-Alder[13] to be a general process in 1928. Since then, the Diels-Alder reaction has been studied extensively. Now it is one of the most common and elegant methods for the construction of six-membered ring systems and has been used for the total syntheses of natural products. However, the detailed nature of the mechanism of this reaction still remains in question.[5,14] The formulation of the cycloaddition as a concerted electrocyclic process[15] has recently received support from Frontier Orbital Calculations,[14,16,17] which successfully predict the regioselectivity of the reaction. On the other hand, MINDO/3 calculations,[18] indicate a highly unsymmetrical transition state in which the two new σ bonds are formed at two different "stages" of the cycloaddition.[19] An understanding of the characteristic features of the Diels-Alder reaction has led to the

---

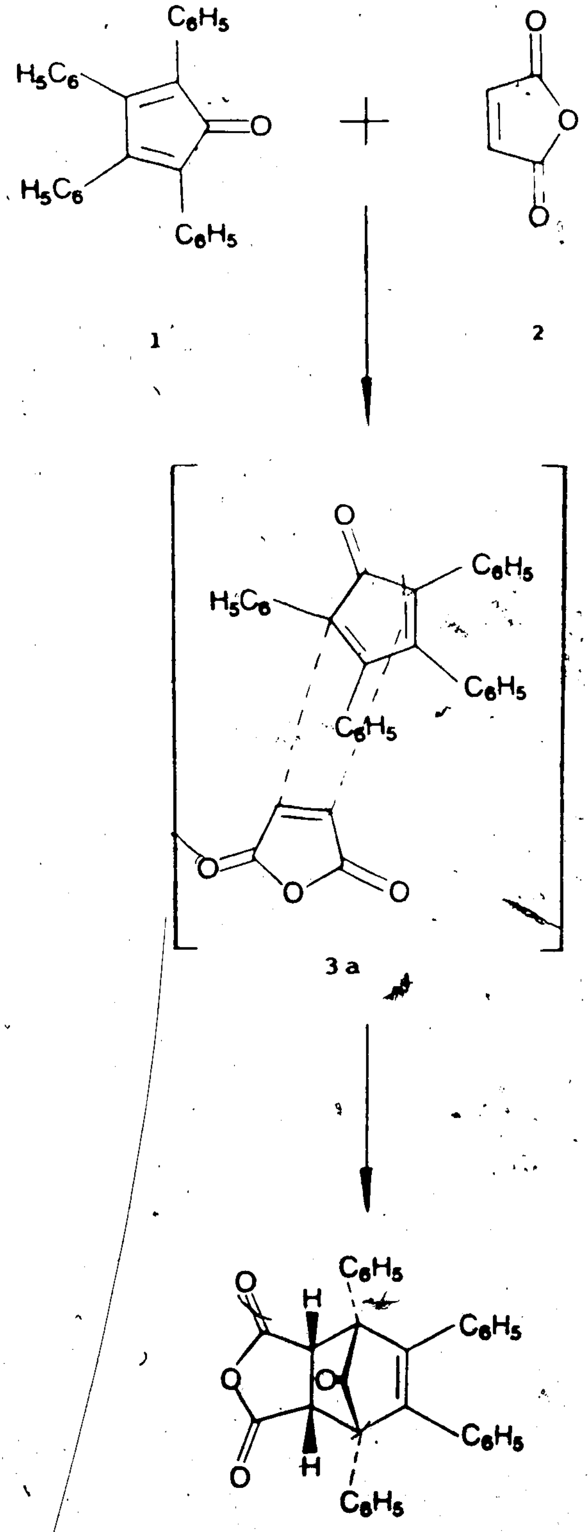
*For general references on the Diels-Alder reaction see references 1-12.

development of a series of empirical rules which easily predict the structural outcome of the reaction.

An important feature of the cycloaddition reaction is now embodied in the cis-principle. This principle predicts that the addition to the diene in the required cisoid conformation occurs from the same side at each end of the diene moiety and also that attack at both ends of the dienophilic double bond occurs from the same face of the dienophile. It further predicts that the relative configurations of the substituents in the transition states (for example, **3a**, Scheme I) are preserved in the products. Thus tetraphenylcyclopentadienone (**1**) reacts with maleic anhydride (**2**) to give adduct 3.[20,21] The cis-principle to which no violation has been observed to date, is expressed in the modern formulation of the reaction by Woodward and Hoffmann as a concerted $2\pi s + 4\pi s$ cycloaddition reaction.[15]

The endo-rule was originally formulated for the additions of cyclic dienes to dienophiles to predict that, of the two possible "sandwich-like" transition states (for example, **5a** and **6a**), the more preferred would be that with the "maximum concentration of double bonds".[3,5] Hence, the reaction of 1,3-cyclopentadiene (**4**) with maleic anhydride (**2**) proceeds to give only the endo-adduct 5 and not the exo-adduct 6[22] (Scheme II). The favoured

SCHEME I



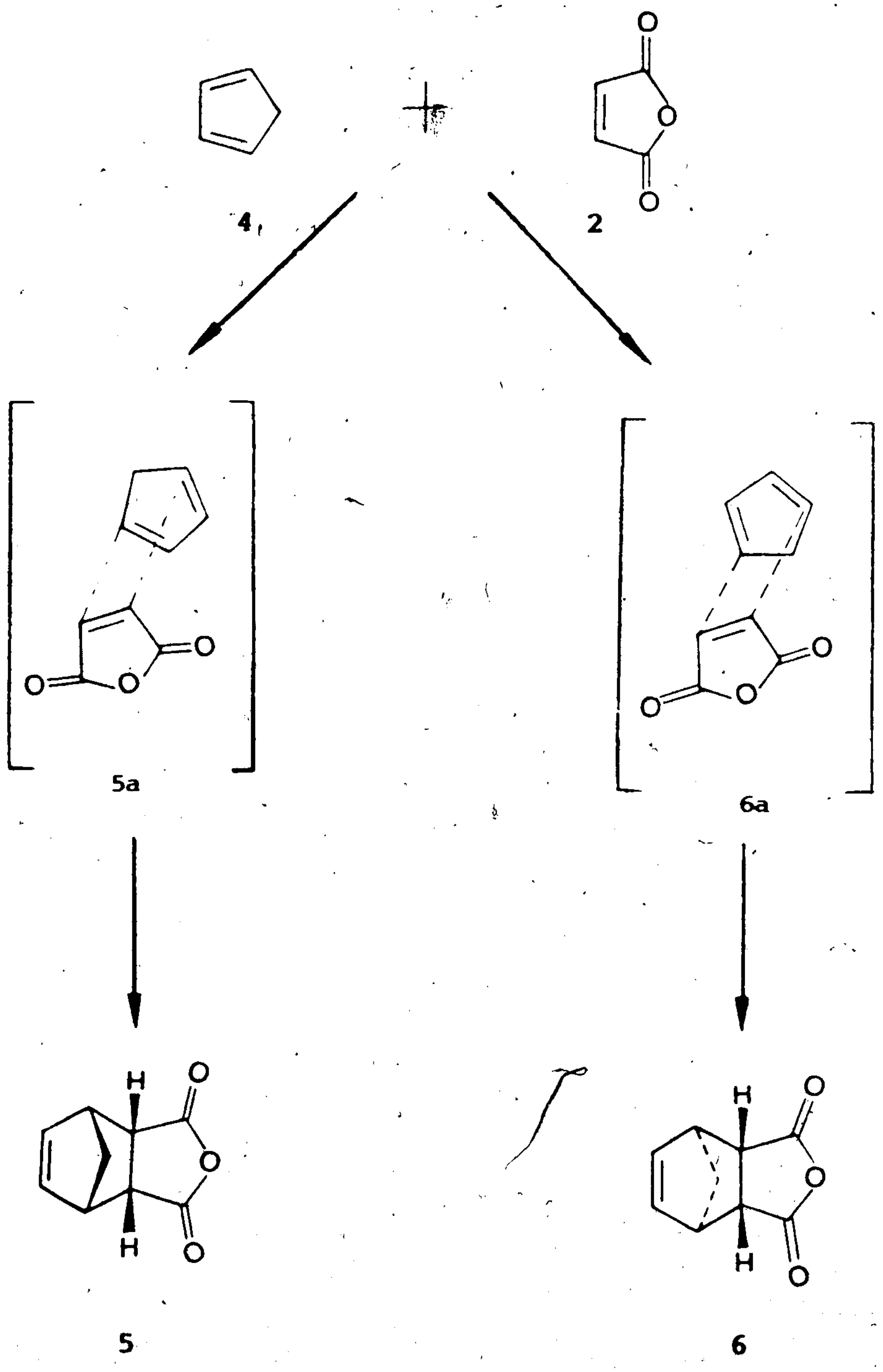
1

2

3 a

3

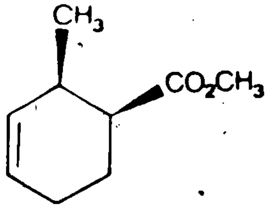
SCHEME II



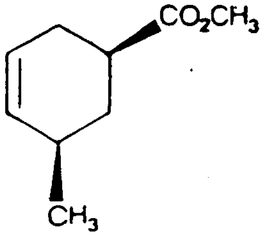
formation of the <u>endo</u>-adduct in the Diels-Alder reaction has been explained[15] by a stabilization of the transition state (for example, **5a**) in which secondary orbital overlap can occur between the π system of the diene and a π system in conjugation with the dienophilic double bond. The term "<u>exo</u>" therefore refers to the addition via the transition state (for example, **6a**) in which no secondary orbital overlap can occur. These explanations for the <u>endo</u>-rule can equally be applied to acyclic cases.

In the cases in which unsymmetrical dienes react with unsymmetrical dienophiles, regioisomeric adducts can, in principle, be obtained. Very often, a regioisomer is preferentially formed and such a bias in favour of one regioisomer is governed by a group of orientational rules which have greatly simplified prediction of the regiochemistry of the cycloaddition reaction. It has been shown that a 1-substituted diene combines with a dienophile to give the adduct in which the substituent of the diene component is adjacent (<u>ortho</u>) to the substituent of the dienophile. In accordance with this "<u>ortho</u>-rule", the principal product of the addition of <u>trans</u>-piperylene to methyl acrylate is adduct 7 rather than ester 8.

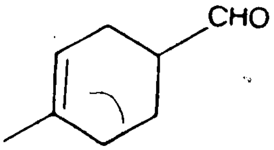
If a 2-substituted diene is used, the substituent promotes formation of the product having the two substituents in a <u>para</u>-relationship. In accordance with



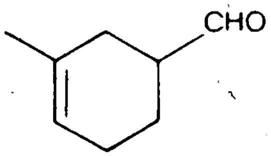
7



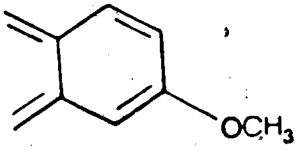
8



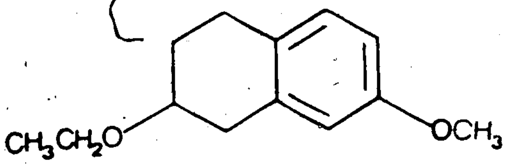
9



10



11



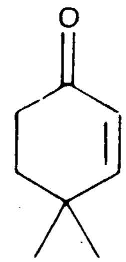
12

this "para-rule", it was observed that the addition of isoprene to acrolein led to the predominant formation of the adduct **9**.[23] The regioisomer **10** was obtained as a minor product.

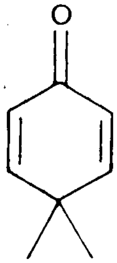
In the case of a 1,3-disubstituted diene, the ortho- and para-rules operate in a complementary fashion and give the adduct obeying both rules. However, it has been shown that, of the two competing ortho- and para-rules that can operate in the case of 1,2-disubstituted diene, the ortho-rule usually predicts the structural outcome of the cycloaddition reaction

Using Frontier Orbital Theory, Houk[16] predicted that, where substituents of both diene and dienophile are electron donating, the favoured product should have meta-orientated substituents. This "meta-rule" has since been observed experimentally by Fleming.[24] He found that the major product of addition of ethyl vinyl ether to the diene **11** was adduct **12**.[24]

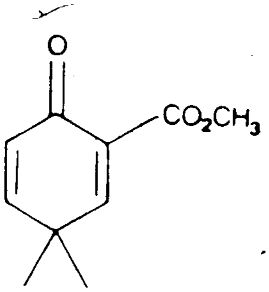
It is known that Lewis acids exert a strong catalyzing effect on the Diels-Alder reactions but solvent polarity seldom influences the cycloaddition reactions.[25] Lewis acid catalyzed Diels-Alder reactions are of great synthetic importance because they are not only faster[25,26,27,28] but also more stereoselective[25,29] and regioselective[25,30,31,32] than the uncatalyzed cycloaddition reactions. The observations that Lewis acid catalysis produces large increases in the rates of the Diels-Alder reactions have made available many adducts[26,27,28] which had previously been obtained with difficulty (high temperatures, sealed tubes, etc.). For example, the thermal cycloaddition of dienes to cyclohexenones is notoriously recalcitrant. And yet, it has recently been shown that Lewis acid can be applied to the Diels-Alder reaction of cyclohexanones. Kitahara[33] and co-workers reported the use of aluminum chloride as catalyst for the addition of several dienes to 2-methyl-2-cyclohexen-1-one. Aluminum chloride has also been used by Wenkert[34] and collaborators to catalyze the addition of 1,3-butadiene to a series of cycloalkenones and 2-methylcycloalkenones. In both cases adducts were obtained in synthetically useful yields. Liu and Browne conducted an extensive study[35] of the Diels-Alder reactions of 4,4-dimethyl-2-cyclohexen-1-one (**13**) and its derivatives **14** and **15**. They similarly observed improved yields with the use of Lewis acid catalysts.[35] Interestingly, regiochemical control was also found to be affected by the use of Lewis acids as illustrated by the reactions of isoprene with the dienone-ester **15**[35] (see Scheme III). This has led to the successful syntheses of α- and β-himachalene.[35] It is well known that stereoselectivity is enhanced by Lewis



13

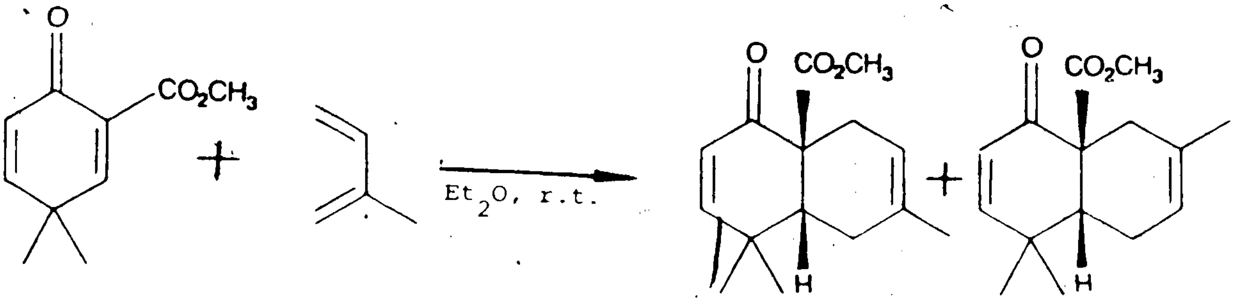


14



15

SCHEME III



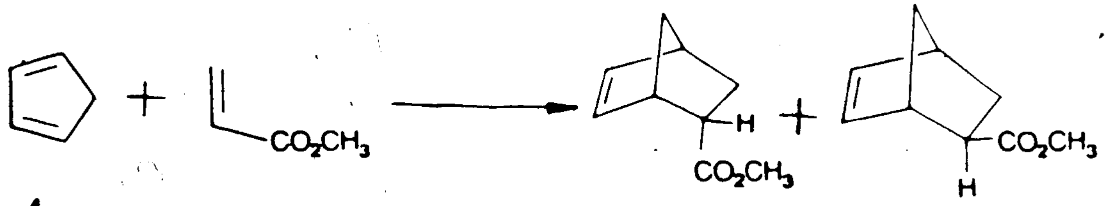
15

With $BF_3 \cdot Et_2O$	30%	70%
With $FeCl_3$	50%	50%
With $SnCl_4$	82%	18%

acids. This can be shown by the reactions of cyclopentadiene (**4**) with methyl acrylate[36] (see Scheme IV).

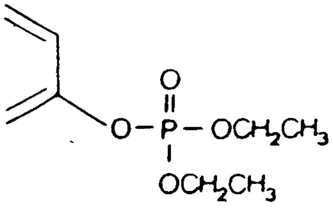
The Diels-Alder reaction of hetero-substituted 1,3-diene with dienophile has been increasingly developed as a valuable method for the syntheses of highly functionalized ring systems. The greater comprehension of the electronic and steric effects governing this reaction has resulted in the utilization of specifically functionalized dienes and dienophiles to produce hitherto unattainable substitution patterns regioselectively and stereoselectively. The introduction of hetero-substituents on the diene invariably has a dominant effect on the regiochemistry of the cycloaddition, and permits further transformations which take advantage of the relationship between the hetero-substituents and the newly-formed carbon-carbon double bonds. The use of such dienes has recently been an area of great synthetic activity.[37] For ~~example,~~ silyloxy-substituted butadienes[37] have come into widespread use in natural product syntheses. However, these types of dienes and the cycloaddition products derived from them are rather labile under acidic or basic conditions, or even in polar solvents. In a practical sense, the instability of these compounds is sometimes a serious problem in the Diels-Alder reaction as well as in the further transformations of the adducts. On the other

SCHEME IV

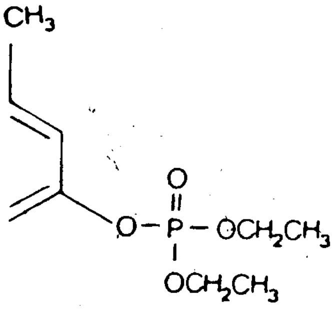


4

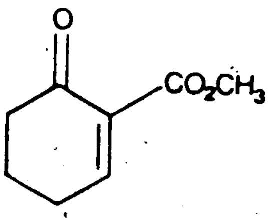
Without $AlCl_3$ at 0°C	88%	12%
With $AlCl_3$ at 0°C	96%	4%



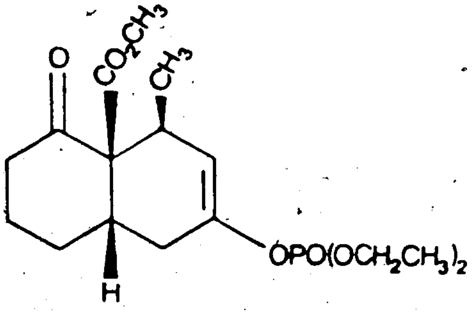
16



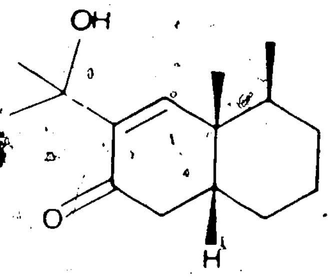
17



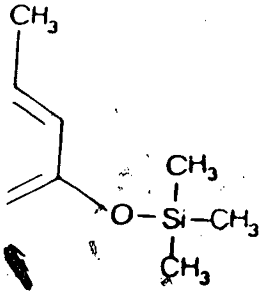
18



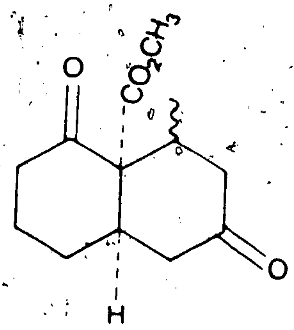
19



20



21



22

hand, diethyl 2-butadienyl phosphate (**16**)[38,39] was found to be an oxygen-substituted diene of unusual stability.[38] Liu and Ngooi used its analogue diethyl trans-1,3-pentadiene-2-yl phosphate (**17**)[40] to react with 2-carbomethoxy-2-cyclohexen-1-one (**18**).[40] The Diels-Alder adduct **19** was formed with excellent stereoselectivity. This has led to the successful synthesis of petasitolone (**20**).[40] At that time, they also found that the addition of trans-2-trimethylsilyloxy-1,3-pentadiene (**21**) to the dienone-ester (**18**) afforded the product as a mixture of two epimeric diketones **22** in much poorer yield. The diketones **22** resulted apparently from the hydrolysis of the expected Diels-Alder adducts.[40]

Diene phosphates, such as compounds **16** and **17**, represent themselves as attractive materials to serve as the diene component in the Diels-Alder reaction. In fact, phosphate **16** has been previously studied[38] briefly by Kienzle and Rosen as a diene in the cycloaddition reaction using thermal conditions. The potential use of diene phosphates in diene synthesis coupled with the observed stability of these compounds towards acid led us to undertake a study of the synthetic utility of compounds **16** and **17** in Lewis acid catalyzed Diels-Alder reactions. The details of this investigation are described in the next chapter.

CHAPTER 2

RESULTS AND DISCUSSION

2-Diethylphosphoryloxy-1,3-butadiene (**16**) was prepared from methyl vinyl ketone and diethyl chlorophosphate.[39] The reaction was carried out by treatment of methyl vinyl ketone with lithium diisopropylamide in tetrahydrofuran at -78°C, followed by trapping the enolate ion thus formed with diethyl chlorophosphate. After the distillation of the crude product at 82-84°C/1.2 torr, diene **16** was obtained as a colorless oil in 52% yield. Its mass spectrum showed a molecular ion at m/e 206.0707 corresponding to the molecular formula $C_8H_{15}PO_4$. The ir spectrum exhibited absorption bands at 1280 and 1045 cm^{-1} due to the phosphate moiety. The ^1H nmr spectrum showed a doublet of doublets of doublets (J = 17, J' = 10, J" = 3 Hz) at δ 6.20 due to the proton on C-3. Two multiplets at δ 4.20 (four protons) and 1.38 (six protons) were assigned to the methylene groups and the methyl groups respectively. Diene phosphate **16** can be stored at 0°C over a long period of time without apparent deterioration.

trans-2-Diethylphosphoryloxy-1,3-pentadiene (**20**) is also a stable compound at 0°C. It can be easily obtained[40] from trans-3-penten-2-one and diethyl chlorophosphate. Although trans-3-penten-2-one is commercially available, it is rather expensive. For the present studies, this compound was prepared[44] by ~~the~~ aluminum chloride catalyzed acylation of propylene with acetyl chloride followed by dehydrochlorination.[48] Treatment of trans-3-penten-2-one with lithium diisopropylamide followed by trapping the resulting enolate ion with diethyl chlorophosphate gave diene **17** (b.p. 84-86°C/0.5 torr) as a colorless oil in 41% yield. The mass spectrum indicated a molecular ion at m/e 220.0865 corresponding to the molecular formula $C_9H_{17}PO_4$. The ir spectrum showed the phosphate absorptions at 1275 and 1270 cm^{-1}. The ^1H nmr showed two multiplets at δ 4.82 and 4.60 due to the terminal vinylic protons. The remaining vinylic protons were found as a complex multiplet centered approximate~~ly~~ at δ 6. The four methylene protons appeared as a doublet of quartets (J = J' = 7 Hz) at δ 4.17. The six methyl protons of the phosphate moiety appeared as a triplet (J = 7 Hz) at δ 1.35. A doublet (J = 5.5 Hz) at δ 1.80 was assigned to the vinylic methyl group.

The Diels-Alder reactions of dienes **16** and **17** with a variety of dienophiles were carried out under Lewis acid catalysis. The results are discussed in the following sections.

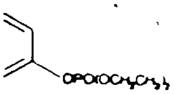
1. Diels-Alder Reactions of 2-Diethylphosphoryloxy-1,3-Butadiene (**16**)

Diene **16** was subjected to reactions with a number of α,β-unsaturated carbonyl compounds at temperatures ranging from 0°C to 20°C. Stannic chloride, ferric chloride, boron trifluoride etherate, aluminum chloride, and zinc chloride were used as catalysts. The results are summarized in Table I and Scheme V.

A. Addition to Ethyl Vinyl Ketone (Entry 1)

The Diels-Alder addition of diene phosphate **16** to ethyl vinyl ketone at 0°C and under stannic chloride catalysis proceeded rapidly to give a 1:1 adduct in 94% yield. The ^{13}C nmr analysis showed that it was a single compound. The mass spectrum showed a molecular ion at m/e 290.1278 corresponding to the molecular formula $C_{13}H_{23}PO_5$. The ir spectrum exhibited bands due to a ketone at 1710 cm^{-1}, an enol-phosphate at 1680 cm^{-1}, and a phosphate group at 1277 and 1035 cm^{-1}. The ^{1}H nmr spectrum showed a broad singlet at $\delta 5.52$ for the vinylic proton and a multiplet at $\delta 2.53$ due to the two methylene protons adjacent to the carbonyl group. The methyl group

Table I. Stannic Chloride Catalyzed Diels-Alder Reactions of Diene **16**

Dienophile + 

16

$\xrightarrow[CH_2Cl_2,\ 0^0C]{1\ equiv.\ SnCl_4}$ Adduct(s)

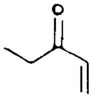
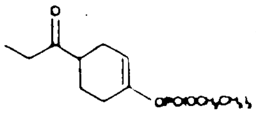
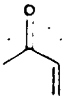
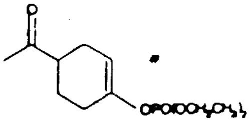
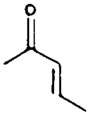
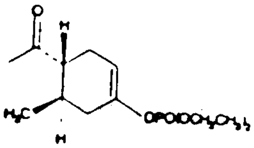
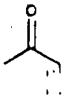
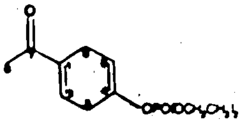
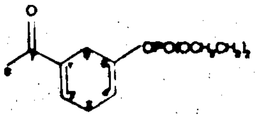
Entry[a]	Dienophile	Diene (equiv.)	Time (h)[b]	Yield[c]	Product(s) (ratio)
1		1.3	1	94%	 **23**
2		1.3	1.5	100%	 **28**
3		1.3	40	90%	 **32**
4		1.3	18	81%	 **36** (8:1)  **37**

Table I. (Continued)

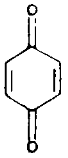
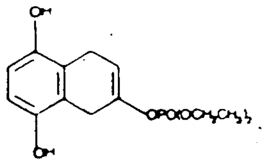
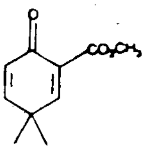
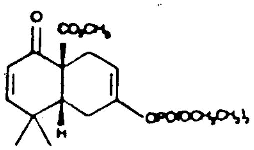
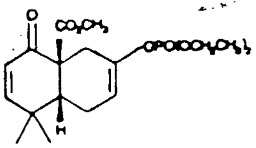
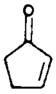
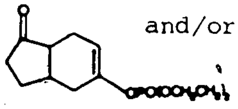
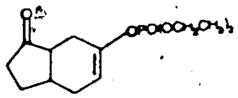
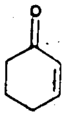
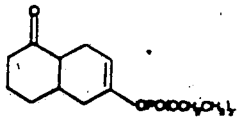
Entry^a	Dienophile	Diene (equiv.)	Time (h)^b	Yield^c	Product(s) (ratio)
5		1.3	5	93%	 41
6		1.3	65	23%^{d}	  45 (4.5:1) 46
7		3	54	12%	 and/or  53 54
8^e		4	34	34%	 55

Table I. (Footnotes)

[a] All reactions were carried out under a nitrogen or argon atmosphere.

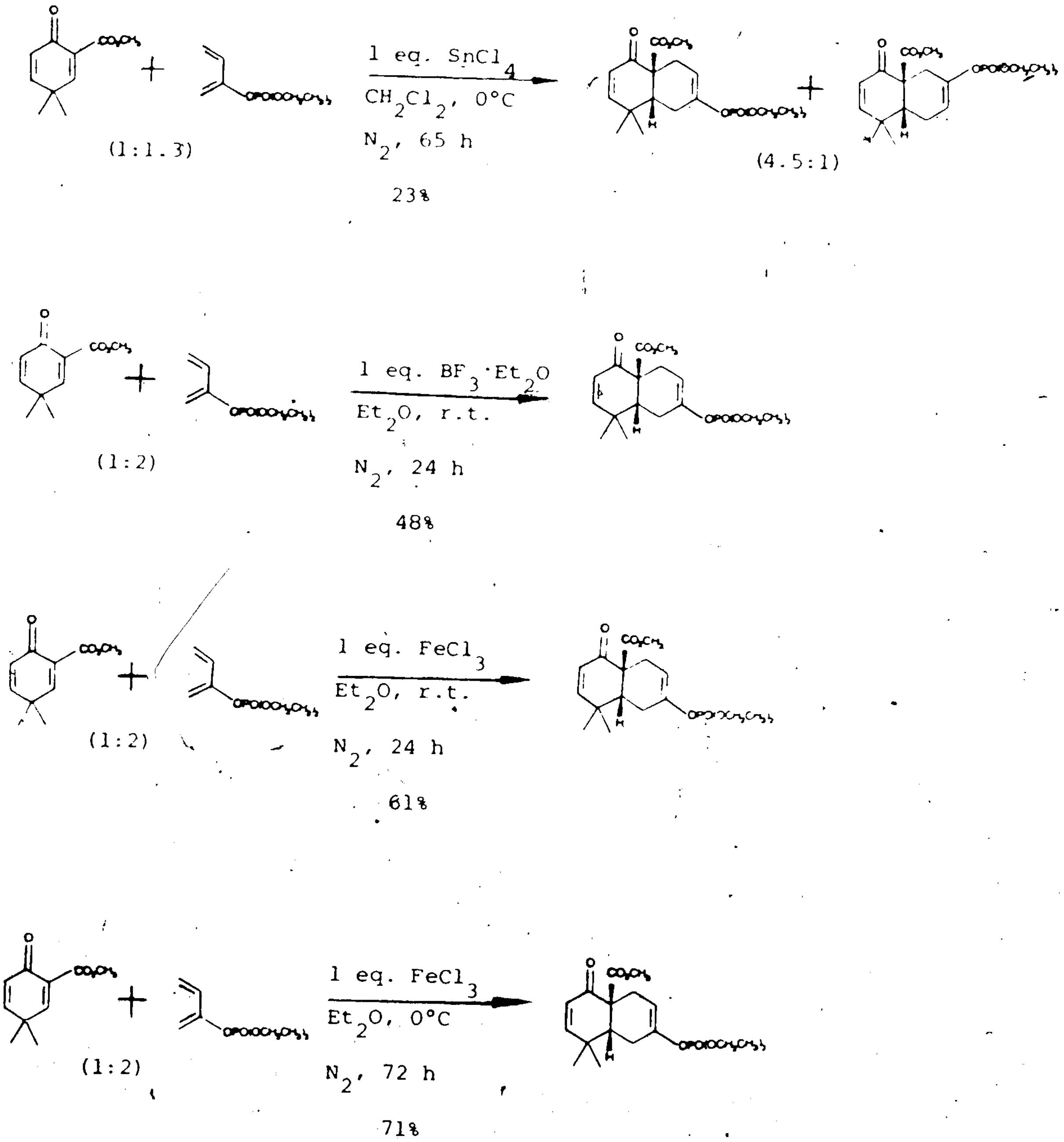
[b] The cited times reflect only the periods used to ensure the completion of the reaction.

[c] The yields were calculated based on the amounts of the dienophiles used.

[d] The yield was 72% based on the consumed starting material.

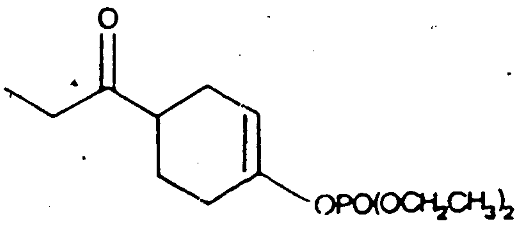
[e] This reaction was performed at room temperature instead of 0°C. The solvent system for the reaction was a 1:1 mixture of dichloromethane and diethyl ether.

SCHEME V

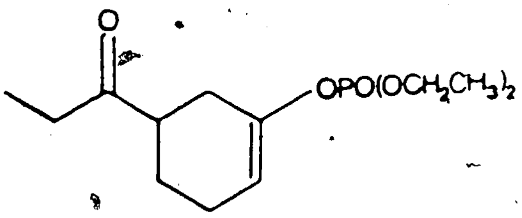

CO2CH3
OPO(OCH2CH3)2
(1:1.3)
1 eq. SnCl4
CH2Cl2, 0°C
N2, 65 h
23%
H
(4.5:1)
(1:2)
1 eq. BF3·Et2O
Et2O, r.t.
N2, 24 h
48%
(1:2)
1 eq. FeCl3
Et2O, r.t.
N2, 24 h
61%
(1:2)
1 eq. FeCl3
Et2O, 0°C
N2, 72 h
71%

of the ketone side-chain appeared as a triplet (J = 7 Hz) at δ1.08. Two multiplets at δ4.17 and 1.38 were assigned to the ethyl protons of the phosphate group. If the Diels-Alder addition followed the normal *para*-rule, then, these spectral data suggested that the structure **23** could be assigned to the adduct. However, it is known that the Diels-Alder reaction with a 2-substituted diene could lead to a mixture of regioisomers and orientational reversal in violation of the *para*-rule has also been observed.[41]

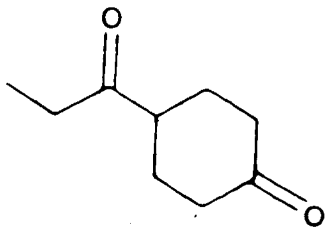
It was therefore possible that the addition of diene phosphate **16** to ethyl vinyl ketone could lead to the regioisomer **24**. To rule out this possibility, a more rigorous proof of the regiochemistry was warranted. A conclusive proof of the regiochemistry might be achieved by the conversion of this adduct to a diketone. Such a derivatization of the Diels-Alder adduct could lead to either the diketone **25** or the isomeric diketone **26**. The



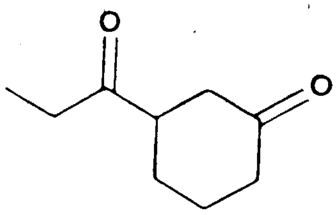
23



24



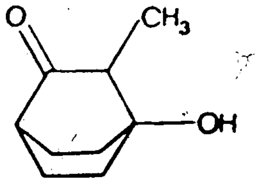
25



26

former compound must be derived from **23** while the latter from **24**. Distinguishing the two diketones should be possible by inspection of the ^{13}C nmr spectrum. The diketone **25** should show seven lines in the ^{13}C nmr spectrum because of its plane of symmetry, while compound **26** should show more than seven lines.

The Diels-Alder adduct was treated with sodium hydroxide in refluxing methanol in order to hydrolyze the phosphate group. Two compounds were obtained in 44% and 12% yields, respectively, after chromatography of the crude product on silica gel. The major compound, which was obtained as a white solid, showed in the mass spectrum a molecular ion at m/e 154.1002 corresponding to the molecular formula $C_9H_{14}O_2$. The ir spectrum showed a hydroxyl absorption at 3420 cm^{-1} and a ketone signal at 1710 cm^{-1}. The ^1H nmr spectrum showed a broad singlet (one proton) at δ 2.58 which disappeared upon addition of D_2O. A methyl signal appeared as a doublet (J = 7 Hz) at δ 1.16. Also observed was a multiplet at δ 2.25, integrating to two hydrogen atoms. This signal could be attributed to protons α to a ketone carbonyl. The ^{13}C nmr spectrum showed a set of 9 lines. The minor compound was a yellow oil. Its mass spectrum showed a molecular ion as the base peak at m/e 154.1000 indicating the molecular formula $C_9H_{14}O_2$. The ir spectrum showed a ketone absorption at 1711 cm^{-1}. The ^1H nmr showed a methyl group as a triplet (J = 7 Hz) at δ 1.10 and a methylene group as a quartet (J = 7 Hz) at δ 2.58. A methine proton appeared as a triplet of triplets (J = 10, J' = 4 Hz) at δ 2.82. Most importantly, the ^{13}C nmr showed a set of 7 lines. The above spectral data strongly suggested that the minor product was the diketone **25** and the major product was the hydroxy ketone **27**. The latter compound was apparently



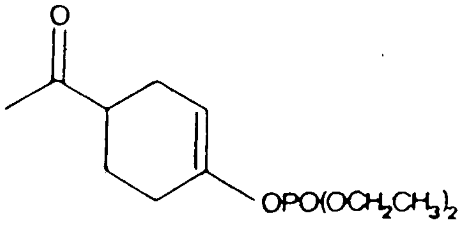
27

derived from the former one by an intramolecular aldol condensation reaction.

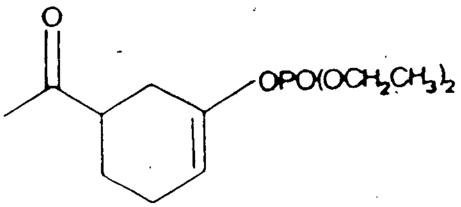
The isolation of compounds **25** and **27** indicated that the adduct must possess the regiochemistry defined by structure **23**, as a result of <u>para</u>-addition.

B. Addition to Methyl Vinyl Ketone (Entry 2)

The diene phosphate **16** was found to react rapidly with methyl vinyl ketone at 0°C in methylene chloride in the presence of stannic chloride to give a 1:1 adduct in quantitative yield. The ^{13}C nmr analysis indicated the presence of a single isomer. The mass spectrum showed a molecular ion at m/e 276.1125 corresponding to the molecular formula $C_{12}H_{21}PO_5$. The ir spectrum displayed absorptions due to a ketone (1710 cm^{-1}), an enol-phosphate (1685 cm^{-1}), and a phosphate group (1276 and 1035 cm^{-1}). The ^{1}H nmr spectrum showed a broad singlet at δ5.53 for a vinylic proton and a singlet at δ2.20 for a methyl group. Two multiplets at δ4.18 and 1.38 were assigned to the ethyl protons of the phosphate group. If the Diels-Alder reaction followed the normal <u>para</u>-rule, then these spectral data were in agreement with the structure **28** for the adduct. However, abnormal addition would lead to the regioisomer **29**.

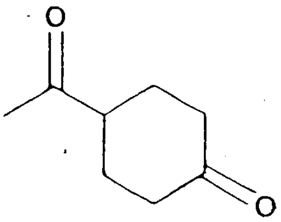


28

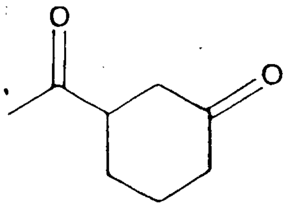


29

To determine the regiochemistry conclusively, the Diels-Alder adduct was treated with sodium hydroxide in refluxing methanol to give a diketone in 27% yield. The mass spectrum showed a molecular ion as the base peak at m/e 140.0844 indicating the molecular formula $C_8H_{12}O_2$. In the ^1H nmr spectrum, all the signals appeared above δ2.90 in the high field region, including a triplet of triplets (J = 10, J' = 4 Hz) at δ2.80 for a methine proton and a singlet at δ2.24 for a methyl group. The ir spectrum showed a ketone absorption at 1710 cm^{-1}. The ^{13}C nmr spectrum displayed four lines at δ48.46, 39.66, 27.99 and 27.76 (the two carbonyl signals failed to appear). The above spectral data indicated that the diketone must have the structure **30** and not **31**. Since diketone **30** was derived from the Diels-Alder product, it follows that the Diels-Alder product must possess the "<u>para</u>" regiochemistry as depicted in structure **28**.



30



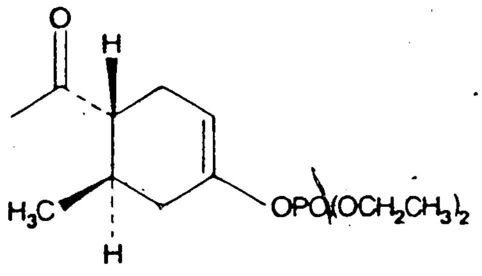
31

It is noteworthy that several outstanding features were observed for the stannic chloride catalyzed reaction of methyl vinyl ketone and the diene phosphate **16**, including the fast reaction rate, the excellent yield, and the complete regioselectivity. In the case of the thermal addition of methyl vinyl ketone to 2-dimethylphosphoryloxy-1,3-butadiene,[38] two inseparable regioisomers were isolated in a ratio of 2:1.

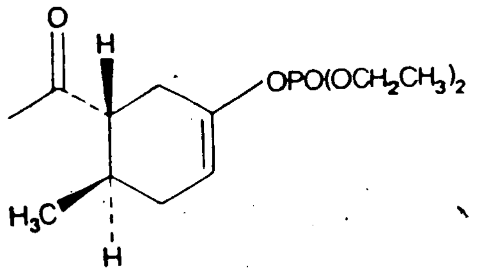
Addition to trans-3-Penten-2-one (Entry 3)

The diene phosphate **16** reacted smoothly with trans-3-penten-2-one under stannic chloride catalysis at 0°C to afford a 1:1 adduct in 90% yield. The ^{13}C nmr spectrum verified that the adduct was a single compound. The mass spectrum showed a molecular ion at m/e 290.1284 for the molecular formula $C_{13}H_{23}PO_5$. The ir spectrum showed bands due to a ketone at 1711 cm^{-1} and a phosphate group at 1275 and 1036 cm^{-1}. The ^{1}H nmr spectrum showed a broad singlet at δ5.48 for a vinylic proton. A methyl group attached to a carbonyl group appeared as a singlet at δ2.10. A doublet (J = 6 Hz) at δ0.98 was assigned to a methyl group attached to the β-carbon of a ketone. Two multiplets at δ4.16 and 1.36 were readily attributable to the ethyl protons of the phosphate group. A triplet of doublets (J = 10, J' = 5.5 Hz) at δ2.42 was assigned to a methine proton adjacent to the ketone.

Preliminary analysis of the spectral data indicated that the structure of the Diels-Alder adduct was either **32**, resulting from the normal addition, or **33**, resulting from the abnormal addition. The stereochemistry of the adduct could be easily assigned based on the *cis*-principle to which no violation has been observed. Thus, the tertiary proton α to the ketone should be *trans* to the β tertiary proton. This relationship was confirmed by the



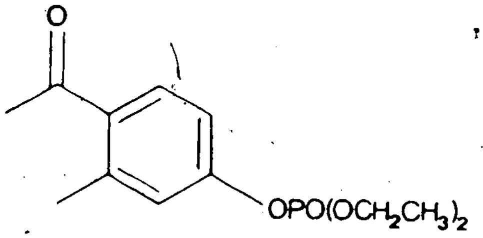
32



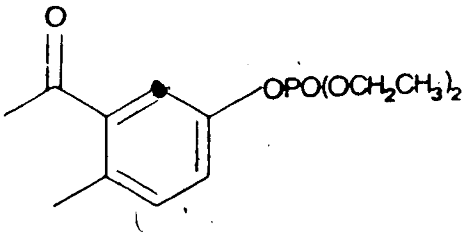
33

^{1}H nmr spectrum of the adduct which showed a doublet of doublets of doublets (J = J' = 10, J" = 5.5 Hz) at δ2.42 for the α methine proton. The appearance of two large trans-1,2-diaxial coupling constants of 10 Hz each is possible only when the two methine protons in question are trans to each other.

It remained to determine the regiochemistry of the Diels-Alder adduct. Due to the nonsymmetrical nature of this molecule, its conversion to a diketone would not lead to the successful determination of the regiochemistry. However, a conclusive proof of the regiochemistry might be achieved by aromatization of the Diels-Alder adduct. Such a derivatization could lead to either the aryl-ketone **34** or the regioisomeric aryl-ketone **35**. Distinguishing these



34



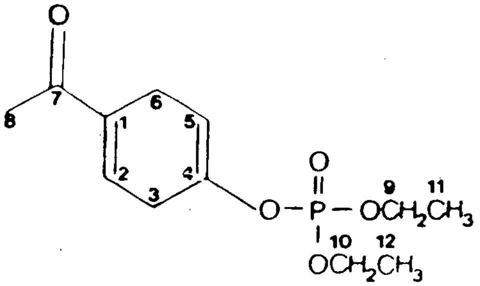
35

aryl-ketones should be possible by inspection of the ^{1}H nmr spectrum. The carbonyl group should cause the ^{1}H nmr signal of the β proton of either **34** or **35** to be shifted down-field significantly and the coupling pattern of this proton would provide evidence for the regiochemical assignment of the aromatic compound. Therefore, the regiochemistry of the Diels-Alder adduct could be determined.

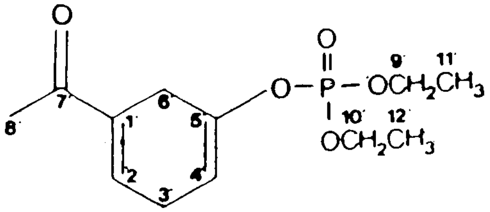
The cycloaddition adduct was aromatized with N-bromosuccinimide in carbon tetrachloride at reflux for 1 h. The reaction gave a rather complex mixture of products from which the aryl-ketone **34** was isolated in 19% yield. The mass spectrum of this compound showed a molecular ion at m/e 286.0974 corresponding to the molecular formula $C_{13}H_{19}PO_5$. The ir spectrum showed absorptions due to an aromatic ketone at 1684 cm^{-1}, a phosphate group at 1278 and 1031 cm^{-1} as well as an aromatic ring at 3060, 1610 and 1580 cm^{-1}. The ^1H nmr spectrum showed the aromatic proton adjacent to the acyl group as a doublet at δ 7.78 with a coupling constant of 8.5 Hz. The proton para to the methyl group appeared as a doublet of doublets (J = 8.5, J' = 2.5 Hz) at δ 7.18. The remaining aromatic proton appeared as a doublet (J = 2.5 Hz) at δ 7.14. Two singlets at δ 2.59 and 2.56 were attributed to the methyl groups and the multiplets at δ 4.27 and 1.38 were assigned to the ethyl protons of the phosphate group. The above spectral data, particularly the coupling pattern of the aromatic protons, agree only with the structure **34**. Hence the regiochemistry of the Diels-Alder adduct must be as defined by structure **32**.

D. Addition to 3-Butyn-2-one (Entry 4)

Diene **16** reacted with 3-butyn-2-one under stannic chloride catalysis to give an inseparable mixture of two isomeric adducts in 81% yield. The mixture showed ir absorptions at 1670 (α,β-unsaturated ketone), 1705 (enol-phosphate), 1277 and 1031 cm^{-1} (phosphate group). A molecular ion peak at m/e 274.0968 in the mass spectrum indicated the chemical formula as $C_{12}H_{19}PO_5$. The ^1H nmr spectrum showed two sets of signals in an integral ratio of 8:1. One set, due to the major product, showed two vinylic protons as multiplets at δ6.82 (β to ketone) and 5.58 (enol-phosphate). A methyl group appeared as a singlet at δ2.33. Two multiplets at δ3.16 and 3.03 were assigned to the methylene groups of the cyclohexadiene ring. Ethyl protons of the phosphate group appeared as multiplets at δ4.18 and 1.36. The other set, due to the minor product, consisted of multiplets at δ6.86 and 5.52 due to two vinylic protons, as well as a singlet at δ2.34 due to a methyl group. The ^{13}C nmr spectrum also showed two sets of signals. These spectral data indicated that a mixture of the enol-phosphate **36** and the regioisomeric enol-phosphate **37** was formed. However, the structures of the major and the minor products remained to be determined. According to the <u>para</u>-rule of the Diels-Alder reaction, adduct **36** is expected to be the major product and **37** to be the minor product. This expectation was



36



37

supported by the ^{13}C nmr spectral data listed in Table II.

In the ^{13}C nmr spectrum of compound **36**, the signal corresponding to C-3, which is linked to a center (C-2) of greater electron deficiency, is expected to appear at lower field than the signal of C-6 attached to a carbon (C-1) which is electronically less deficient. It is further expected that C-3 of compound **36** should appear as a doublet due to the carbon-phosphorus coupling while a singlet should be observed for C-6. Similarly, in the ^{13}C spectrum of **37**, C-3' signal is expected to appear in the lower field relative to that of C-6'. In this case, however, a doublet is anticipated for the C-6' signal due

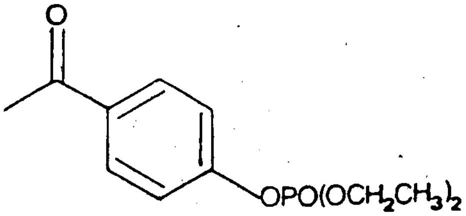
Table II. ^{13}C nmr Data of Adducts **36** and **37**

	1	2	3*	4*	5*	6	7	8	9*,10*	11*,12*
major (δ)	135.41	134.64	28.79 28.76	142.62 142.53	107.15 107.10	23.96	196.60	24.28	63.48 63.41	15.23 15.16
	1'	2'	3'	4'*	5'*	6'*	7'	8'	9',10'*	11',12'*
minor (δ)	135.27	135.66	26.92	104.83 104.78	145.05 144.96	26.20 26.15	196.38	24.28	63.48 63.41	15.23 15.16

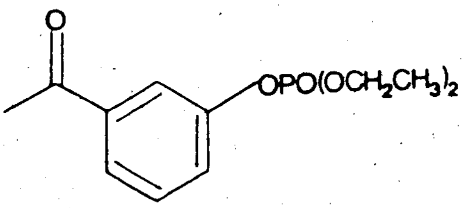
*Because of carbon-phosphorus coupling, a doublet was observed for each of these carbons.

to the carbon-phosphorus coupling. An examination of the ^{13}C nmr spectral data (Table II) reveals that the major signals are consistent with those expected for structure **36** while the minor signals agree with those expected for the structure **37**. Consequently, structures **36** and **37** were assigned respectively to the major and the minor adducts obtained from the Diels-Alder reaction of 3-butyn-2-one and diene phosphate **16**.

Rigorous proof of the regiochemistry of the adducts **36** and **37** might be achieved by aromatization. Dehydrogenation of the mixture obtained from the Diels-Alder reaction would afford aryl-ketones **38** and **39**. Distinguishing these aryl-ketones should be feasible by inspection of the ^{13}C nmr and ^{1}H nmr spectra. In the ^{13}C nmr spectrum, compound **38** should show 8 signals while **39** should display more than 8 signals. In the ^{1}H nmr spectrum, compound **38** should show a pair of doublets in the aromatic region, while **39** should show a more complex splitting pattern for the aromatic protons.



38

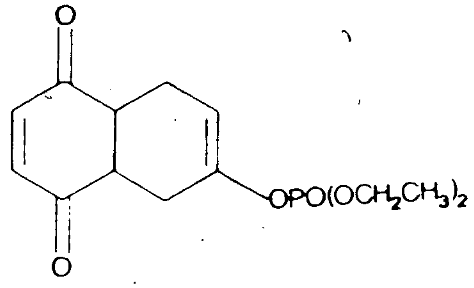


39

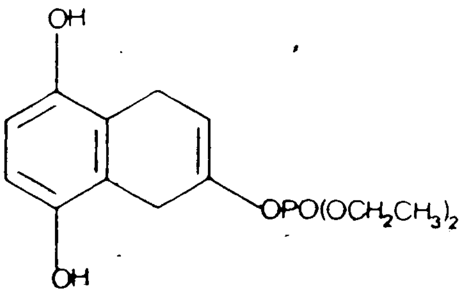
The mixture of the Diels-Alder adducts was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in benzene at reflux for 2 h. An inseparable mixture of two isomeric aryl-ketones was obtained in 79% yield. The mass spectrum of the mixture showed a molecular ion at m/e 272.0816 indicating the molecular formula $C_{12}H_{17}PO_5$. The ir spectrum exhibited an α,β-unsaturated ketone band at 1686 cm^{-1} and aromatic absorptions at 3060, 1600 and 1050 cm^{-1}. The ^1H nmr showed two sets of signals in an integral ratio of 11:1. The major set of signals showed a doublet (J = 9 Hz) at δ7.79 due to the aromatic protons ortho to the acyl group and a doublet of doublets [J = 9, J' = 1 Hz (carbon-phosphorus coupling)] at δ7.32 for the remaining aromatic protons. A sharp singlet at δ2.58 was assigned to the methyl ketone protons. Two multiplets at δ4.24 and 1.36 due to the ethyl groups were also observed. The minor set consisted of two multiplets at δ7.78 and 7.47 for the aromatic protons and a singlet at δ2.60 due to the methyl-ketone group. The ^{13}C nmr spectrum of the mixture showed mainly one set of signals consisting of four singlets and four doublets due to carbon-phosphorus coupling. The corresponding signals of the minor aromatic compound were too weak to be detected. The preceeding spectral data indicated conclusively that the aryl-ketone **38** was the major product and **39** the minor product. Since aryl-ketones **38** and **39** were derived from the enol-phosphates **36** and **37** respectively, the assignments of the major Diels-Alder adduct to **36** and the minor adduct to **37** were confirmed.

E. Addition to 1,4-Benzoquinone (Entry 5)

The addition of diene **16** to *p*-benzoquinone under stannic chloride catalysis proceeded smoothly and rapidly to give an aromatic compound in 93% yield. The mass spectrum showed a molecular ion peak at m/e 314.0921 indicating the molecular formula $C_{14}H_{19}PO_6$. The ir spectrum showed a hydroxyl absorption at 3320 cm^{-1}, an enol-phosphate band at 1705 cm^{-1}, aromatic absorptions at 3010, 1615, and 1491 cm^{-1}, as well as phosphate bands at 1287 and 1038 cm^{-1}. The ^1H nmr spectrum (CD_3OD) showed a sharp singlet at δ 6.50 due to two aromatic protons. A vinylic proton appeared as a multiplet at δ 5.64. A slightly broad singlet at δ 3.36 was attributed to four allylic protons. Two multiplets at δ 4.18 and 1.36 were attributed to the ethyl protons of the phosphate group. The above spectral data indicated that the initially formed Diels-Alder cycloaddition product **40** had undergone further isomerization under the influence of the acidic conditions to the aromatic enol-phosphate **41**.



40

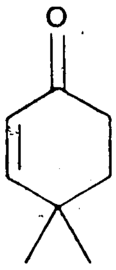


41

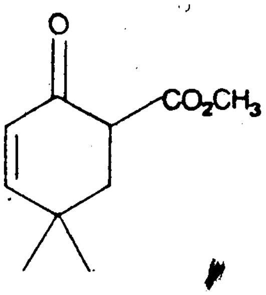
This structural assignment was further confirmed by the ^{13}C nmr spectrum which indicated the presence of eight sp^2 carbons.

F. Addition to 2-Carbomethoxy-4,4-Dimethyl-2,5-Cyclohexadiene-1-one (**44**) (Entry 6)

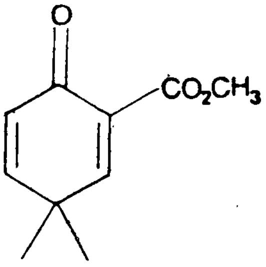
Dienone-ester **44** was easily prepared from enone **42** via intermediate **43**.[42] It can be seen that there are in



42

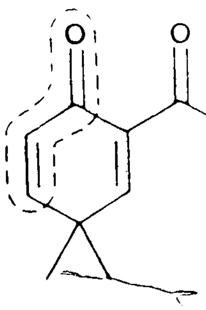


43

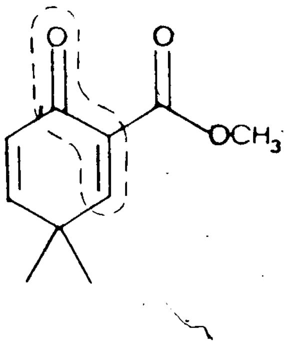


44

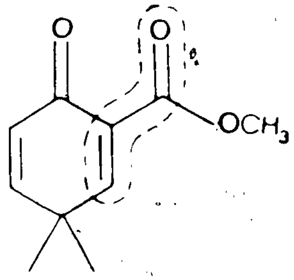
fact three dienophilic moieties in **44** as illustrated by **44a**, **44b** and **44c**. On the basis of the Alder-rule,* the unsubstituted enone system of **44a** is expected to be relatively unreactive. Ordinarily it would be unnecessary to distinguish the relative reactivities of the two moieties **44b** and **44c** except in the case where the <u>endo</u>-rule comes into effect. The presence of a carbomethoxy as an activating group offers several interesting features.



44a



44b



44c

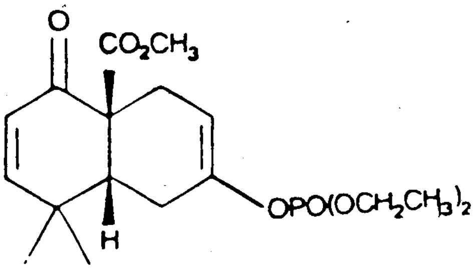
It can be easily removed from the resulting keto-esters by

---

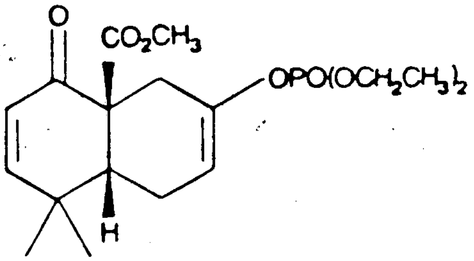
*The Alder-rule predicts that substitution of an electron-withdrawing substituent on the dienophilic double bond increases the reactivity of that bond and that substitution of electron-donating substituents on the diene increases the reactivity of the diene.[5]

decarboxylation and it offers a level of functionalization which might be used effectively in further synthetic manipulations. The results of the Diels-Alder reactions of the diene **16** with dienone-ester **44** using different Lewis acid catalysts are summarized in Scheme V.

When the dienone-ester **44** was treated with diene **16** in the presence of stannic chloride at 0°C, the cycloaddition reaction proceeded slowly. After 65 h, it gave an inseparable mixture of two isomeric adducts in 23% yield and in a ratio of 4.5:1. The starting material **44** was recovered in 68%. The mixture showed a molecular ion peak at m/e 386.1496 in the mass spectrum indicating the molecular formula $C_{18}H_{27}PO_7$. The ir spectrum showed ester absorptions at 1746 and 1731 cm^{-1}, an α,β-unsaturated ketone band at 1675 cm^{-1} as well as phosphate group absorptions at 1275, 1054 and 1030 cm^{-1}. The ^1H nmr spectrum displayed two sets of signals in an integral ratio of 4.5:1. The major set showed two doublets (J = 10 Hz each) at δ6.60 and 5.90 due to the β- and the α-proton of an α,β-unsaturated ketone. Another vinylic proton appeared as a broad singlet at δ5.50. A sharp singlet at δ3.74 was due to a methyl ester. Two multiplets at δ4.15 and 1.35 were assigned to ethyl protons of the phosphate group. A methine proton appeared as a doublet of doublets (J = 7, J' = 3 Hz) at δ2.91 and two additional methyl singlets were observed at δ1.22 and 1.15. The minor set consisted of two doublets (J = 10 Hz each) at δ6.62 and 5.92 for the β- and the α-proton of a conjugated enone system, and three methyl singlets at δ3.76, 1.23 and 1.12. On the basis of these spectral data and the cis-principle governing the stereochemistry of the Diels-Alder reaction, the structures **45** and **46** could be tentatively assigned to the two adducts. Further identification of compound **45** as the major adduct and **46** as the minor one follows from the subsequent studies detailed below.

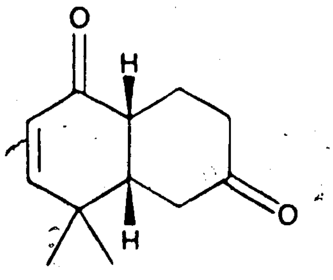


45

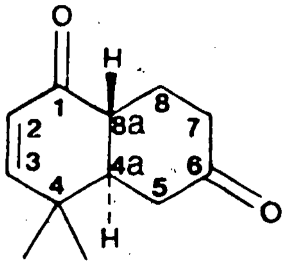


46

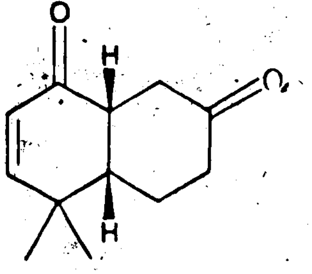
The Diels-Alder reaction of the enone-ester **44** and the diene **16** was found to be highly dependent on the Lewis acid used. When these two compounds were subjected to the cycloaddition in the presence of boron trifluoride etherate at room temperature, the reaction occurred more rapidly to give a single adduct in 48% yield. The spectral data of this compound indicated that it was identical with the major product obtained previously from the stannic chloride catalyzed reaction. The determination of the regiochemistry of this adduct might be achieved by the removal of the angular methyl ester and the hydrolysis of the phosphate. Such a derivatization could lead to the formation of a pair of the "para"-diketones **47** and **48** or a pair of the "ortho"-diketones **49** and **50**. Identification of these pairs of diketones might be possible by spectroscopic and/or chemical methods.



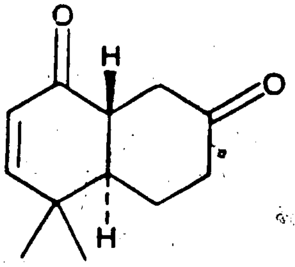
47



48



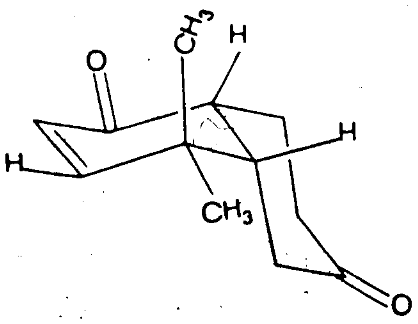
49



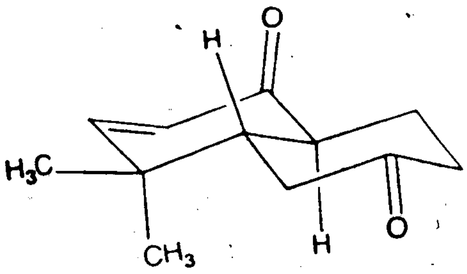
50

The single Diels-Alder adduct was treated with lithium iodide dihydrate[43] in refluxing 2,4,6-collidine to give a mixture of two epimeric diketones **47** and **48** (1:6) in 70% yield. These compounds were separated by careful flash chromatography on silica gel. The minor diketone **47** showed, in the mass spectrum, a molecular ion at m/e 192.1150 corresponding to the molecular formula $C_{12}H_{16}O_2$. The ir spectrum displayed two carbonyl absorption bands, one at 1714 cm^{-1} and the other at 1677 cm^{-1}. The ^1H nmr spectrum showed a β-enone proton as a doublet of doublets (J = 10, J' = 2 Hz) at δ6.56 and an α-enone proton as a doublet (J = 10 Hz) at δ6.00. Two methyl groups appeared as singlets at δ1.36 and 1.11. The major diketone **48** showed, in the mass spectrum, a molecular ion at m/e 192.1156 indicating the molecular formula $C_{12}H_{16}O_2$, and 12 lines in the ^{13}C nmr spectrum. The ir spectrum showed a ketone absorption at 1711 cm^{-1} and a band at 1678 cm^{-1} characteristic of an α,β-unsaturated ketone. The ^1H nmr spectrum showed a β-enone proton as a doublet (J = 10 Hz) at δ6.71 and an α-enone proton also as a doublet (J = 10 Hz) at δ5.91. Two methyl groups appeared as a singlet at δ1.12. A doublet of doublets of doublets (J = J' = 13, J" = 4 Hz) at δ2.09 was assigned to the methine proton adjacent to the gem-dimethyl group.

The cis ring junction of **47** was indicated by the ^1H nmr spectrum which showed a long range W-coupling of 2 Hz between the protons H-3 and H-4a. An examination of Dreiding model reveals that the protons can assume a W-arrangement only when the two rings are cis-fused as shown in formula **51**. When the rings are trans-fused as in **52**, the methine proton at C-4a is locked in an axial position relative to both rings and thus cannot achieve a W-configuration with the enone proton at C-3. In decalin systems, the trans-fused isomer is normally more stable than the cis-fused isomer and predominates under equilibrium conditions. In proof of the ring junction stereochemistry, treatment of compound **47** with aqueous sulfuric acid in refluxing ethanol affected its complete epimerization to give the trans isomer **48** in 87% yield.



51



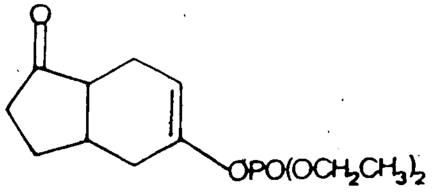
52

The regiochemistry of **48** was determined by an extensive study of the ^1H nmr spectrum including Nuclear Overhauser Enhancement (NOE) experiments. As expected, saturation of the gem-dimethyl singlet at $\delta 1.12$ caused substantial enhancement of the signals corresponding to H-4a (18%), H-5 axial (13%), H-5 equatorial and H-8a (a total of 22%). These experiments allowed the determination of the coupling patterns of both the axial and the equatorial protons attached to C-5. The former proton was found to be a doublet of doublets with two large couplings of 13 Hz each, while the latter was observed also as a doublet of doublets with a large geminal coupling constant of 13 Hz and a small vicinal coupling constant of 4 Hz. As indicated by these findings, the C-5 carbon must be linked directly to a carbonyl group as in structure **48** and not linked to a methylene group as in structure **50**.

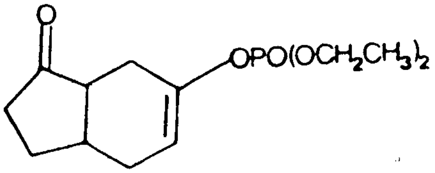
In order to further improve the Diels-Alder addition of the dienone-ester **44** to the diene **16**, the use of ferric chloride as a catalyst was also carried out. When the reaction was performed at room temperature, compound **45** was obtained as the sole product in 61% yield. An even better yield of 71% was obtained when the reaction temperature was reduced to 0°C. Clearly, ferric chloride is the catalyst of choice for this particular Diels-Alder reaction.

G. Addition to 2-Cyclopenten-1-one (Entry 7)

In the presence of stannic chloride the diene **16** was treated with 2-cyclopenten-1-one at room temperature for 54 h. After flash chromatography, a mixture of products was obtained as indicated by the ^{13}C nmr. The mass spectrum showed a small peak at 288.1130 corresponding to the molecular formula $C_{13}H_{21}PO_5$ of the Diels-Alder adduct(s) **53** (and/or **54**). However, a stronger peak appeared at 276.1131 in the mass spectrum corresponding to $C_{12}H_{21}PO_5$ which could not be explained as a fragment from the molecular ion $C_{13}H_{21}PO_5$. The ir spectrum of the mixture showed an absorption at 1740 cm^{-1} due to a 5-membered ring ketone. In addition, a stronger band appeared at 1710 cm^{-1} characteristic of a saturated ketone carbonyl. The presence of the molecular ion peak at 288.1130 and the ir absorption band at 1740 cm^{-1} strongly



53



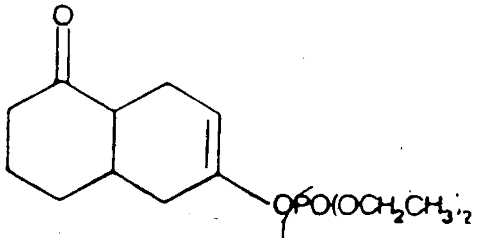
54

suggested that the desired adduct was formed. An inspection of the ^{1}H and ^{13}C nmr spectra of the mixture showed, however, that the major signals were identical with those of compound **28** previously obtained from the addition of methyl vinyl ketone to the diene **16**. It was subsequently observed that the major fragmentation pattern of the mass spectrum was also consistent with that of **28**. These observations suggested that the major component of the mixture was ketone-phosphate **28** representing 75% of the mixture as indicated by ^{1}H nmr integration. Therefore, compounds **53** and/or **54** were present in ca. 25%. Based on 75% of **28** and 25% of **53** and/or **54**, the carbon and hydrogen contents of the mixture should be 52.67% and 7.59% respectively. The microanalysis results were consistent with this calculation, showing 52.42% for carbon and 7.58% for hydrogen. Further proof of the structure of compound **28** was obtained by the aromatization reaction. When the mixture was treated with N-bromosuccinimide in refluxing carbon tetrachloride in the presence of a catalytic amount of benzoyl peroxide, the reaction proceeded rapidly to give an aromatic compound in 57% yield (based on the amount of **28** in the mixture). The spectral data of this product were found to be identical with those of aryl-ketone **38**.

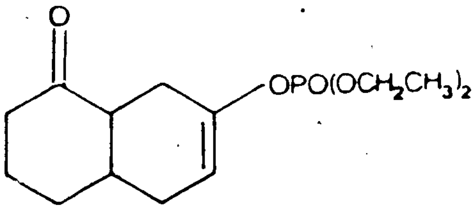
Compound **28** could have been derived from the Diels-Alder reaction between the diene phosphate **16** and methyl vinyl ketone, which, in turn, could have been generated by the cleavage of the diene phosphate **16** under the acidic conditions over a relatively long period of time. In order to verify this rationale, the diene phosphate **16** was treated with stannic chloride in ether at room temperature for 44 h. The compound **28** was indeed formed but only in a comparatively small quantity. Presumably, methyl vinyl ketone was generated more readily in the presence of 2-cyclopentenone which facilitated the cleavage of the diene phosphate **16**.

H. Addition to 2-Cyclohexen-1-one (Entry 8)

In the presence of stannic chloride, treatment of 2-cyclohexen-1-one with the diene **16** at room temperature for 34 h gave of a mixture of the desired adduct and the by-product **28** in a ^{1}H nmr integral ratio of 1.44:1. The latter compound could be removed by extensive column chromatography of the mixture on silica gel. The ^{13}C nmr spectrum of the pure adduct thus obtained indicated that it was a single compound. The mass spectrum showed a molecular ion at m/e 302.1273 indicating the molecular formula $C_{14}H_{23}PO_5$. The ir spectrum exhibited a ketone band at 1710 cm^{-1}. The ^{1}H nmr showed the presence of a vinylic proton with a broad singlet at δ5.50. Two multiplets at δ4.18 and 1.36 were due to ethyl protons of the phosphate group. These spectral data indicated that the adduct could be either ketone phosphate **55** or its regioisomer **56**.



55



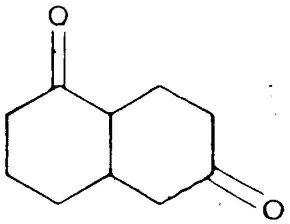
56

In order to determine the ring junction stereochemistry, the adduct was treated with sodium carbonate in aqueous methanol at room temperature for 20 h and also with aqueous sodium hydroxide in methanol at room temperature for 23 h. In both cases, the starting material was recovered intact. Since the compound was not affected under conditions which are expected to induce epimerization, it was highly likely that the original adduct with the expected cis stereochemistry had undergone epimerization to give the more stable trans-isomer during the reaction or during the purification.

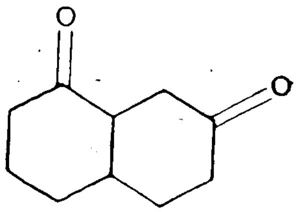
The regiochemistry of the compound might be determined by hydrolyzing the phosphate group. Such a transformation could lead to either the diketone **57** or the regioisomeric diketone **58**. The former must be derived from **55** while the latter from **56**. Differentiation of the two diketones could be achieved by direct comparison with the authentic samples.

Diketones **59** and **60** were easily prepared from 1,6-dihydroxynaphthalene (**61**) via the intermediary of cis-1,6-dihydroxydecalin (**62**). Using 5% rhodium on alumina as a catalyst, compound **61** was hydrogenated in acetic acid and ethanol at room temperature for 25 h to give the diol **62**. It showed a molecular ion at m/e 170.1307 ($C_{10}H_{18}O_2$) in the mass spectrum, and two hydroxy absorption bands at 3490 (hydrogen-bonded) and 3635 cm^{-1} (free) in the ir spectrum. The ^1H nmr showed a singlet at δ 4.61 due to the hydroxyl protons (exchangeable with D_2O). Two multiplets at δ 4.08 and 3.75 were assigned to the protons adjacent to the hydroxyl groups.

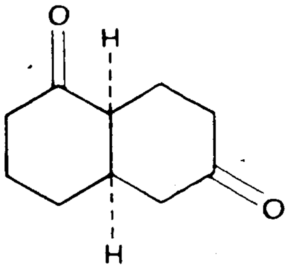
The transformation of the diol **62** to the cis-diketone **59** was achieved in 77% yield by treatment with pyridinium chlorochromate[45] in methylene chloride at room temperature for 3.5 h. The mass spectrum of **59** showed a molecular ion as the base peak at m/e 166.0994 ($C_{10}H_{14}O_2$). The ir spectrum showed a typical ketone absorption band at 1710



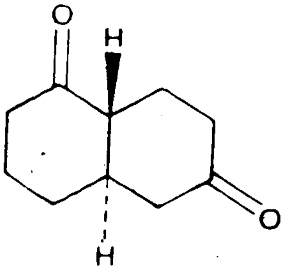
57



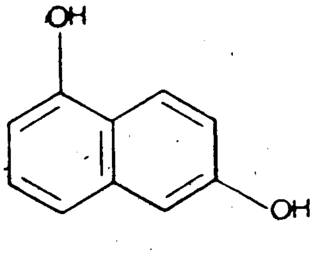
58



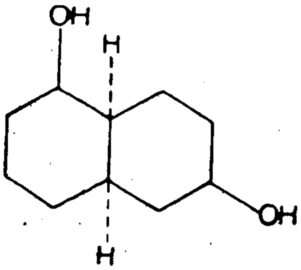
59



60



61



62

cm^{-1}. In the ^1H nmr spectrum, the signals were not well separated and appeared approximately between δ1 to 3. The ^{13}C nmr spectrum displayed ten signals which are listed in Table III.

Upon treatment with sodium hydroxide in aqueous methanol at room temperature for 10 h, cis-diketone **59** was isomerized to trans-diketone **60** in 97% yield. The ^{13}C nmr spectrum of **60** also showed 10 lines (Table III) which were found to be completely different from those of **59**. The mass spectrum of **60** showed a molecular ion as the base peak at m/e 166.0994 ($C_{10}H_{14}O_2$). The ir showed a strong ketone absorption band at 1710 cm^{-1}. All the signals in the ^1H nmr spectrum were observed in the region δ1.1-2.6.

In order to determine its regiochemistry, the Diels-Alder adduct was subjected to treatment with sodium hydroxide in refluxing aqueous methanol. After 3.5 h, two separable products were formed in a ratio of 11:1 in 61% yield. Thin layer chromatographic and spectroscopic analyses showed that the major and the minor products were identical with the diketones **60** and **59** respectively. As a result, the regiochemistry of the Diels-Alder adduct, must be defined by structure 55

In attempts to improve the Diels-Alder reaction, other Lewis acids, such as ferric chloride, aluminum chloride, zinc chloride and boron trifluoride etherate,

Table III. ^{13}C nmr Data of *cis*-Diketone **59** and *trans*-Diketone **60**

59 (δ)	211.76	211.11	48.81	44.19	41.18	40.86	38.27	29.09	25.10	23.03
60 (δ)	210.14	209.48	53.04	48.22	44.58	41.59	40.29	33.06	26.11	25.13

were also examined. Unfortunately, all these catalysts were found to be inferior to stannic chloride. With $FeCl_3$, $AlCl_3$ and $ZnCl_2$ no detectable amount of product was formed even over a long period of reaction time. With boron trifluoride etherate, the reaction did occur but the yield of the adduct was found to be considerably poorer.

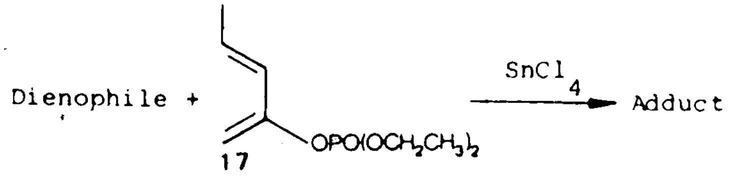
2. Diels-Alder Reactions of trans-2-Diethylphosphoryloxy-1,3-Pentadiene (**17**)

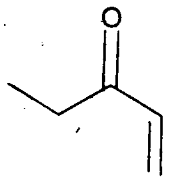
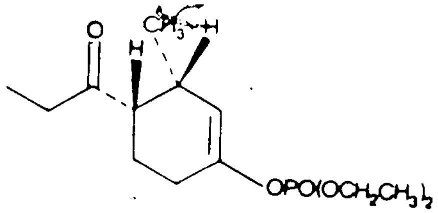
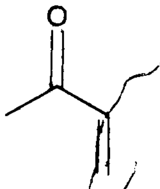
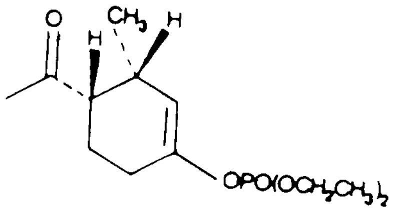
The diene phosphate **17** was subjected to the Diels-Alder reaction with several α,β-unsaturated ketones. The results are summarized in Table IV. Stannic chloride was used as the catalyst. The reactions were carried out in ether or methylene chloride over a temperature range of 0°C to -30°C.

A. Addition to Ethyl Vinyl Ketone (Entry 1)

In the presence of 1 equivalent of stannic chloride, ethyl vinyl ketone reacted rapidly (15 min) with the diene phosphate **17** in methylene chloride at 0°C to give an adduct in 61% yield. The ^{13}C nmr spectrum indicated that it was a single compound. The mass spectrum showed a molecular ion at m/e 304.1432 suggesting the molecular formula $C_{14}H_{25}PO_5$. The ir spectrum showed diagnostic

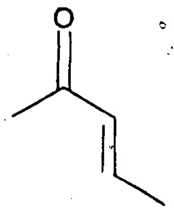
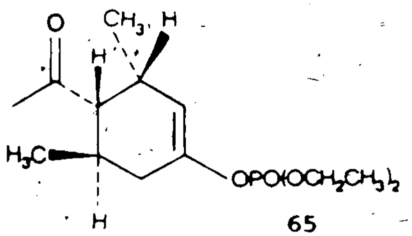
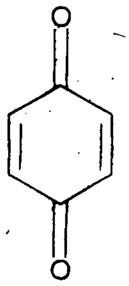
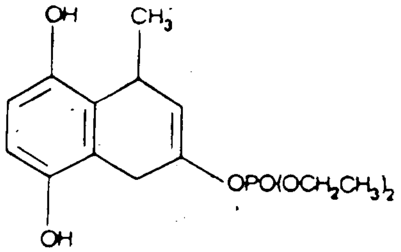
Table IV. Stannic Chloride Catalyzed Diels-Alder Reactions of Diene Phosphate **17**



Entry[a]	Dienophile	SnCl$_4$ (equiv.)	Solvent	Time (h)[b]	Temp. (°C)	Yield	Adduct
1		1	CH_2Cl_2	0.25	0	61%	 **63**
		0.5	Et_2O	24	-30	81%	
2		1	Et_2O	0.09	-30	72%	 **64**
		0.5	Et_2O	14	-30	79%	

(Continued)

Table IV. (Continued)

Entry[a]	Dienophile	$SnCl_4$ (equiv.)	Solvent	Time (h)[b]	Temp. (°C)	Yield	Adduct
3		1	Et_2O	11	0	72%	 65
4		1	CH_2Cl_2	0.5	0	52%	 67
		1	CH_2Cl_2	6.5	-20	60%	

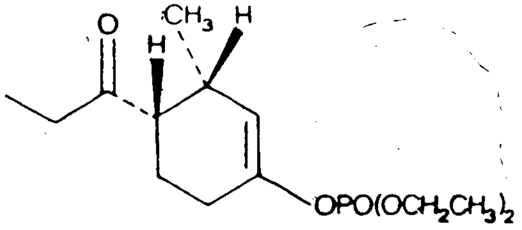
---

[a] All the reactions were carried out under a nitrogen or argon atmosphere.

[b] The cited times reflect only the periods used to ensure the completeness of the reactions.

[c] The yields were calculated based on the amounts of the dienophiles used.

absorption bands at 1710 (ketone), 1680 (enol-phosphate), 1273 and 1033 cm^{-1} (phosphate). The ^1H nmr spectrum showed a vinylic proton as a multiplet at δ5.53 and a methyl group as a triplet (J = 7 Hz) at δ1.02. Another methyl appeared as a doublet (J = 6.5 Hz) at δ0.81. Two multiplets at δ4.16 and 1.33 were assigned to the ethyl protons of the phosphate group. If the Diels-Alder reaction followed the normal rules, then these spectral data were in agreement with the structure **63**.



63

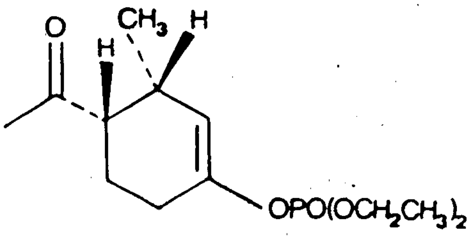
Evidence in support of the regiochemical and stereochemical assignments was obtained from ^1H nmr decoupling experiments. A one-proton signal appeared in the ^1H nmr spectrum as a doublet of doublets of doublets (J = 13, J' = 7, J" = 4 Hz) at δ2.72. This signal, which was assigned to the methine proton adjacent to the ketone carbonyl, was coupled with a one-proton multiplet at δ2.83

due to the allylic methine proton. Irradiation of the signal at δ 2.83 caused a change of the signal at δ 2.72 to a doublet of doublets (J = 13, J' = 7 Hz). The irradiation also led to a change of the vinylic proton at δ 5.53 from a multiplet to a broad singlet. As well, the methyl doublet collapsed to a singlet. These results indicated clearly the regiochemistry of the adduct as depicted in structure **63**. The cis stereochemistry was also deduced from the ^{1}H nmr analysis. A coupling constant of 13 Hz was observed for the methine proton adjacent to the ketone. As required by the large coupling, this proton must possess an axial orientation. This proton was further shown (vide supra) to couple with the allylic methine proton with a small coupling constant of 4 Hz indicating an equatorial orientation for the latter proton. Thus, a cis relationship of these two protons was concluded.

The Diels-Alder reaction was also found to proceed at -30°C in ether using 0.5 equivalent of stannic chloride. Although the reaction was much slower (24 h) under these conditions, a substantially improved yield of 81% was obtained for the adduct **63**.

B. Addition to Methyl Vinyl Ketone (Entry 2)

Under stannic chloride catalysis (1 equiv.) diene phosphate **17** reacted very rapidly with methyl vinyl ketone in ether at -30°C to give, in 72% yield, a 1:1 adduct which showed a single set of signals in the ^{13}C nmr spectrum. The mass spectrum showed a molecular ion at m/e 290.1283 characteristic of the molecular formula $C_{13}H_{23}PO_5$. The ir spectrum showed a band at 1709 cm^{-1} due to a ketone carbonyl and an absorption at 1678 cm^{-1} indicating an enol-phosphate. In addition, the absorptions of the phosphate group were displayed at 1273 and 1027 cm^{-1}. The ^1H nmr spectrum showed a vinylic proton as a multiplet at δ5.56 and a methyl ketone group as a sharp singlet at δ2.17. Another methyl group appeared as a doublet (J = 7 Hz) at δ0.87. A triplet (J = 7 Hz) at δ1.35 and a multiplet at δ4.18 were assigned to the ethyl groups of the phosphate moiety. If the Diels-Alder reaction followed the normal course, these spectral data were in agreement with the structure **64**.



64

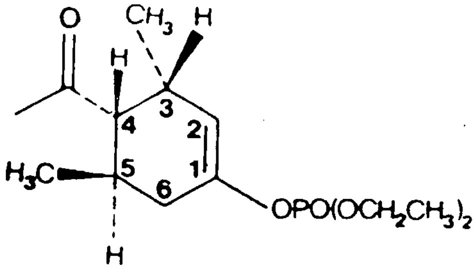
Evidence in support of the regiochemical and stereochemical assignments was obtained from ^{1}H nmr studies. A one-proton signal appeared as a doublet of doublets of doublets (J = 10, J' = J" = 5 Hz) at δ2.71. It was assigned to the methine proton adjacent to the ketone carbonyl group. By decoupling experiments, this proton was shown to be coupled with a proton at δ2.86 with a small coupling constant of 5 Hz. The latter was further coupled with the methyl protons at δ0.87 and the vinyl proton at δ5.56. On the basis of these results, the stereochemistry and regiochemistry were deduced. And the structure **64** was finally assigned to the Diels-Alder adduct.

When a smaller amount of stannic chloride (0.5 equiv.) was used, the reaction was found to be much slower but the yield was slightly improved (79%).

C. Addition to trans-3-Penten-2-one (Entry 3)

When trans-3-penten-2-one was treated with the diene phosphate **17** under stannic chloride catalysis in ether at 0°C, the cycloaddition reaction proceeded smoothly to afford a 1:1 adduct in 72% yield. The ^{13}C nmr spectrum indicated that the adduct was a single compound.

The Diels-Alder adduct, if formed according to the usual rules, would have structure **65**. In agreement with



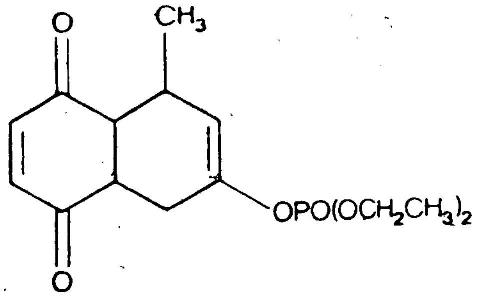
65

the expected structure, the ir spectrum displayed diagnostic absorption bands at 1710 (ketone), 1685 (enol-phosphate), 1270 and 1033 cm^{-1} (phosphate). In the mass spectrum, a molecular ion peak at m/e 304.1433 verified the required molecular formula of $C_{14}H_{25}PO_5$. The regiochemistry was indicated by the ^1H nmr spectrum. The signal due to the proton at C-4 (δ2.61) was a distinct doublet of doublets with coupling constants of 11 Hz and 5 Hz indicating that the proton had only two neighboring protons, as was the case in structure **65**. When the multiplet at δ2.75 (C-3 proton) was irradiated, the doublet of doublets collapsed to a doublet with a large coupling constant of 11 Hz. At the same time, the methyl doublet at δ0.86 changed to a singlet and the multiplet at δ5.55 due to the vinylic proton sharpened to give a broad singlet. These findings lent further support to the regiochemical assignment.

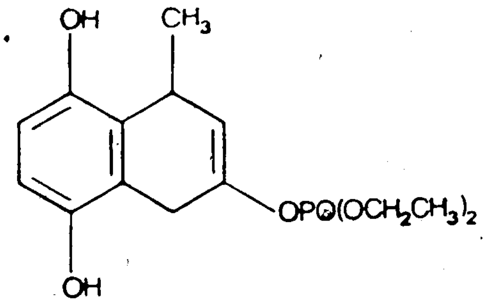
The stereochemistry of the adduct was also deduced from the splitting pattern of the doublet of doublets at δ2.61 due to the C-4 proton. The presence of a large coupling constant of 11 Hz and a small one of 5 Hz indicated that this proton was axial and further coupled to an axial proton (C-5 proton, J = 11 Hz) and an equatorial proton (C-3 proton, J = 5 Hz).

D. Addition to 1,4-Benzoquinone (Entry 4)

Under stannic chloride catalysis, diene phosphate **17** reacted rapidly with 1,4-benzoquinone in methylene chloride at 0°C to give an aromatic compound in 52% yield. The mass spectrum showed a molecular ion at 328.1075 characteristic of the chemical formula $C_{15}H_{21}PO_6$. The ir spectrum displayed bands at 3304 (-OH), 1700 (enol-phosphate), 1492 (aromatic ring), 1247 and 1035 cm^{-1} (phosphate group). The ^1H nmr spectrum (acetone-d_6) showed two phenolic hydroxyl protons (D_2O exchangeable) as a broad singlet at δ7.86. Two aromatic protons appeared as singlets at δ6.60 and 6.65. The appearance of these protons as singlets was apparently due to the closeness of their chemical shifts. The spectrum also indicated the presence of a vinyl proton with a multiplet at δ5.72. A doublet (J = 7 Hz) at δ1.27 was assigned to an allylic methyl group and two multiplets at δ 4.20 and 1.33 were attributed to the ethyl protons of the phosphate group. Other signals were found at δ 3.75, a broad singlet for a methine proton, and δ 3.43, a multiplet for two methylene protons. These spectral data suggested that the expected Diels-Alder adduct **66** had isomerized to the corresponding aromatic compound **67**. In agreement with this assignment, the ^{13}C nmr spectrum indicated the presence of eight sp^2 carbons.

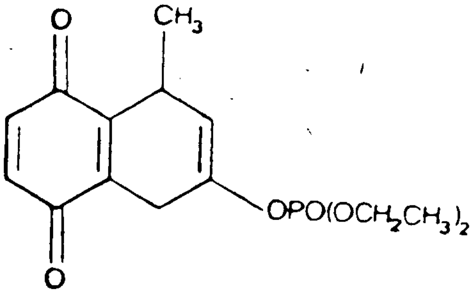


66



67

In an attempt to improve the yield of compound **67**, the Diels-Alder reaction was performed in ether at −30°C for 36 h and then at −5°C for 7 h. Interestingly, in addition to the desired product **67** (24% yield), an unexpected compound **68** was formed in 24% yield. A more successful result was obtained when the reaction was carried out in methylene chloride at −20°C using 3



68

equivalents of the diene **17**. Under these conditions, the yield of the product **67** was increased to 60%.

In conclusion, diene phosphates **16** and **17** have been shown to be useful substrates in Diels-Alder reactions under Lewis acid catalysis. These compounds were found to be unusually stable towards acids relative to other oxygen-substituted dienes such as silyloxy and alkoxy dienes. The applications of Lewis acids to the Diels-Alder reactions of diene phosphates are, therefore, more facile relative to other oxygen substituted dienes. Compounds **16** and **17** were found to react with a variety of α,β-unsaturated ketones (the more dienophilic ones in particular) with high regio- and stereoselectivity to give synthetically useful cyclohexene derivatives.

CHAPTER 3

EXPERIMENTAL

General

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Elemental analyses were performed by the microanalytical laboratory of this department. Infrared (ir) spectra were recorded on a Perkin-Elmer model 457 or Nicolet 7-199 FT-IR spectrophotometer and, except where otherwise stated, were obtained in solutions of chloroform. Proton nuclear magnetic resonance (^{1}H nmr) spectra were recorded on a Varian HA-100, HA-100/Digilab, Bruker WH-200, or WH-400 spectrometer and, except where otherwise stated, were obtained in solutions of deuterochloroform with tetramethylsilane as internal reference. Carbon-13 nuclear magnetic resonance (^{13}C nmr) spectra were recorded on a Bruker HFX-90/Nicolet 1085, Bruker WH-200, or WH-400 system and were obtained in solutions of deuterochloroform using tetramethylsilane as internal reference. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Mass spectra (ms) were recorded using an A.E.I. model MS9, MS12 or MS50 mass spectrometer. Anhydrous magnesium sulfate was used for drying organic solutions. Crystalline samples were recrystallized before submitting for elemental analysis.

Materials

Ether and benzene were freshly distilled over lithium aluminum hydride. Dichloromethane was freshly distilled over phosphorus pentoxide. Anhydrous stannic chloride was purchased from A.G. Fluka and used without further purification. Nitrogen and argon were passed through a purification train of Fieser's solution,[46] saturated aqueous lead acetate, concentrated sulfuric acid, and potassium hydroxide pellets. Flash chromatography developed by Still[47] was used routinely for purification and separation of product mixtures.

1-Diethylphosphoryloxy-4-(1-oxopropyl)-1-cyclohexene (**23**)

Diene **16** (773 mg, 3.75 mmol) was dissolved in dichloromethane (2 mL) under an atmosphere of nitrogen. The solution was cooled to 0°C. Anhydrous stannic chloride (753 mg, 2.89 mmol) was added dropwise to the stirred solution over a 2 min period, followed by the addition of ethyl vinyl ketone (243 mg, 2.89 mmol). After stirring at 0°C for 1 h, the reaction mixture was diluted with dichloromethane. Then 5% aqueous sodium bicarbonate was added and the resulting emulsion was filtered with suction. The filtrate was extracted with dichloromethane. The extracts were combined, dried, filtered and concentrated. The crude oily residue was subjected to flash chromatography on silica gel. Elution with a solution of 25% acetone in petroleum ether gave the diene **16** (144 mg, 19% recovery). Continued elution gave the pure enol-phosphate **23** (787 mg, 94% yield) as a light yellow oil. The adduct showed the following spectral data: ir 1710 (ketone C=O), 1680 (enol-phosphate C=C), 1277 and 1035 cm^{-1} (phosphate); ms M^+ 290.1278 (calcd. for $C_{13}H_{23}PO_5$: 290.1283); ^1H nmr δ 5.52 (broad s, 1H, -CH=C-), 4.17 (m, 4H, 2 × $-OC\underline{H_2}CH_3$), 2.53 (m, 2H, $CH_3C\underline{H_2}CO-$), 1.38 (m, 6H, 2 × $-OCH_2C\underline{H_3}$), and 1.08 (t, 3H, J = 7 Hz, $C\underline{H_3}CH_2CO-$); ^{13}C nmr δ 212.69, 147.05, 146.96, 108.78, 108.72, 63.99, 63.95, 45.17, 33.75, 26.96, 26.92, 25.38, 24.60, 15.92, 15.86, and 7.54. Anal. Calcd. for $C_{13}H_{23}PO_5$: C, 53.78; H, 8.00. Found: C, 53.87; H, 7.96.

4-[1-oxopropyl]-1-cyclohexanone (**25**) and 4-hydroxy-3-methylbicyclo[2,2,2]octan-2-one (**27**)

Enol phosphate **23** (251 mg, 0.87 mmol) was dissolved in methanol (14 mL) and a 0.5 N aqueous solution of sodium hydroxide (14 mL) was added with stirring. The reaction mixture was heated at reflux under an atmosphere of argon. After 5 h, the mixture was cooled to 0°C, poured into cold aqueous 10% hydrochloric acid, and extracted with methylene chloride and then ethyl acetate. The extracts were washed with water, dried, filtered and concentrated. The yellow oily residue was subjected to flash chromatography on silica gel. Elution with a solution of 10% acetone and 30% ether in petroleum ether gave diketone **25** (16 mg, 12% yield) as a yellow oil: ^1H nmr δ 2.82 (tt, 1H, J = 10, J' = 4 Hz, -COCH-), 2.58 (q, 2H, J = 7 Hz, $CH_3\underline{CH_2}CO-$), and 1.10 (t, 3H, J = 7 Hz, $\underline{CH_3}CH_2CO-$); ^{13}C nmr δ 212.24, 209.83, 47.64, 39.82, 34.04, 28.06, and 7.71; ir 1711 cm^{-1} (ketone C=O); ms M^+ 154.1000 (calcd. for $C_9H_{14}O_2$: 154.0994). Continued elution gave hydroxy ketone **27** as a white solid (59 mg, 44% yield): m.p. 123-127°C; ^1H nmr δ 2.58 (broad s, 1H, D_2O exchangeable, -OH), 2.25 (m, 2H, -CHCOCH-), 1.16 (d, 3H, J = 7 Hz, -CH_3); ^{13}C nmr δ 216.70, 71.72, 53.14, 41.33, 34.32, 27.38, 22.88, 21.76, and 9.36; ir 3420 (-OH) and

1710 cm^{-1} (ketone C=O); ms M^+ 154.1002 (calcd. for $C_9H_{14}O_2$: 154.0993).

4-Acetyl-1-diethylphosphoryloxy-1-cyclohexene (**28**)

Diene **16** (783 mg, 3.80 mmol) was dissolved in methylene chloride (2 mL). The solution was cooled to 0°C under an atmosphere of nitrogen. Anhydrous stannic chloride (753 mg, 2.89 mmol) was added dropwise to the stirred solution over a 2 min period, followed by the addition of methyl vinyl ketone (203 mg, 2.90 mmol). After stirring at 0°C for 1.5 h, the reaction mixture was diluted with methylene chloride. Then 5% aqueous sodium bicarbonate was added and the resulting emulsion was filtered with suction. The filtrate was extracted with methylene chloride and then ethyl acetate. The extracts were combined, dried, filtered, and concentrated. Flash chromatography of the yellow oily residue on silica gel, eluting with a solution of 10% acetone and 30% ether in petroleum ether, gave the diene **16** (119 mg, 15% recovery). Continued elution gave the pure Diels-Alder adduct **28** (797 mg, 100% yield) as a colorless oil. The adduct showed the following data: ir (film) 1710 (ketone C=O), 1685 (enol-phosphate C=C), 1276 and 1035 cm^{-1} (phosphate); ms M^+ 276.1125 (calcd. for $C_{12}H_{21}PO_5$:

276.1127); ^1H nmr δ 5.53 (broad s, 1H, -CH=C-), 4.18 (m, 4H, 2 × $-OC\underline{H}_2CH_3$), 2.20 (s, 3H, CH_3CO-), and 1.38 (m, 6H, 2 × $-OCH_2C\underline{H}_3$); ^{13}C nmr δ 209.85, 147.18, 147.10, 108.70, 108.65, 64.05, 64.00, 46.16, 27.81, 26.94, 26.90, 25.23, 24.47, 15.96, and 15.90. Anal. Calcd. for $C_{12}H_{21}PO_5$: C, 52.17; H, 7.66. Found: C, 52.42; H, 7.70.

4-Acetyl-1-cyclohexanone (**30**)

Adduct **28** (200 mg, 0.72 mmol) was dissolved in methanol (11 mL) and a 0.5 N aqueous sodium hydroxide solution (11.6 mL) was added with stirring. The reaction mixture was heated at reflux under an atmosphere of argon. After 3.5 h, the reaction mixture was cooled to 0°C. Cold aqueous 5% hydrochloric acid was added. The resulting mixture was extracted with methylene chloride and then ethyl acetate. The extracts were combined, dried, filtered, and concentrated. Flash chromatography of the yellow oily residue on silica gel, eluting with 10% acetone and 30% ether in petroleum ether, gave the diketone **30** (27 mg, 27% yield) which was a yellow oil: ^1H nmr δ 2.80 (tt, 1H, J = 10, J' = 4 Hz, -COCH-), 2.24 (s, 1H, CH_3CO-); ^{13}C nmr δ 48.46, 39.66, 27.99, and 27.76 (two carbonyl carbons did not appear); ir 1710 cm^{-1} (ketone C=O); ms M^+ 140.0844 (calcd. for $C_8H_{12}O_2$: 140.0837).

trans-4-Acetyl-1-diethylphosphoryloxy-5-methyl-1-cyclohexene (**32**)

To a solution of diene **16** (729 mg, 3.54 mmol) in dichloromethane (2 mL) at 0°C and under an atmosphere of nitrogen, was added anhydrous stannic chloride (709 mg, 2.72 mmol), followed by the addition of *trans*-3-penten-2-one (228 mg, 2.71 mmol). After stirring for 40 h, the reaction mixture was diluted with dichloromethane and 5% aqueous sodium bicarbonate solution was added. The resulting mixture was extracted with dichloromethane. The extracts were combined, dried, filtered, and evaporated to dryness. The light yellow oily residue was subjected to flash chromatography on silica gel. Elution with a solution of 20% acetone and 20% ether in petroleum ether gave diene **16** (150 mg, 21% recovery). Continued elution gave the pure enol-phosphate **32** (706 mg, 90% yield) as a pale yellow oil. Adduct **32** showed the following data: ^{1}H nmr δ5.48 (broad s, 1H, -CH=C-), 4.16 (m, 4H, 2 × $-OC\underline{H}_2CH_3$), 2.42 (dt, 1H, J = 10, J' = 5.5 Hz, -COCH-), 2.10 (s, 3H, CH_3CO-), 1.36 (m, 6H, 2 × $-OCH_2C\underline{H}_3$), and 0.98 (d, 3H, J = 6 Hz, $C\underline{H}_3-CH-$); ^{13}C nmr δ210.58, 146.42, 146.33, 108.01, 107.96, 63.89, 63.83, 53.00, 34.95, 34.92, 30.48, 29.10, 26.07, 19.16, 15.81, and 15.74; ir 1711 (ketone C=O), 1275 and 1036 cm^{-1} (phosphate); ms M$^+$

290.1284 (calcd. for $C_{13}H_{23}PO_5$: 290.1284). Anal. Calcd. for $C_{13}H_{23}PO_5$: C, 53.79; H, 7.98. Found: C, 54.05; H, 7.98.

4-Diethylphosphoryloxy-2-methylacetophenone (**34**)

To a solution of adduct **32** (101 mg, 0.35 mmol) in carbon tetrachloride (5 mL) was added N-bromosuccinimide (124 mg, 0.70 mmol) with stirring under an atmosphere of nitrogen. The reaction mixture was heated at reflux for 1 h. The mixture was then cooled to room temperature and filtered. The filtrate was concentrated. Flash chromatography of the residue on silica gel, eluting with 20% acetone in petroleum ether gave the impure aryl ketone **34**. Further purifications by Kuhrgelrohr distillation at 110°C under 1.0 mm Hg pressure, then preparative thin layer chromatography developed twice with 2% acetone in ether, gave the pure aryl ketone **34** (19 mg, 19% yield). Compound **34** was a light yellow oil and showed the following data: ^1H nmr δ 7.78 (d, 1H, J = 8.5 Hz, $=CH-\underline{CH}=C-C=O$), 7.18 (dd, 1H, J = 8.5, J' = 2.5 Hz, $=\underline{CH}-CH=C-C=O$), 7.14 (d, 1H, J = 2.5 Hz, $=\underline{CH}-C(CH_3)=C-C=O$), 4.27 (m, 4H, 2 × $-O\underline{CH_2}CH_3$), 2.59 (s, 3H, CH_3Ar), 2.56 (s, 3H, CH_3Ar) and 1.38 (m, 6H, 2 × $-OCH_2\underline{CH_3}$); ir (film) 3060 (aromatic C-H), 1684 (α,β-unsaturated ketone C=O), 1610 and 1580 (aromatic C=C), 1278 and 1031 cm^{-1} (phosphate); ms M$^+$ 286.0974 (calcd. for $C_{13}H_{19}PO_5$: 286.0970).

1-Acetyl-4-diethylphosphoryloxy-1,4-cyclohexadiene (36) and 1-Acetyl-5-diethylphosphoryloxy-1,4-cyclohexadiene (37)

To a solution of diene **16** (942 mg, 4.57 mmol) in methylene chloride (3 mL) at 0°C and under an atmosphere of nitrogen was added anhydrous stannic chloride (886 mg, 3.40 mmol), followed by the addition of 3-butyn-2-one (230 mg, 3.38 mmol). After stirring for 18 h, the reaction mixture was diluted with methylene chloride. 5% aqueous sodium bicarbonate was added. The resulting emulsion was filtered and the filtrate was extracted with methylene chloride. The extracts were combined, dried, filtered, and concentrated. The yellow oily residue was subjected to flash chromatography on silica gel. Elution with a solution of 20% acetone and 30% ether in petroleum ether gave the diene **16** (225 mg, 24% recovery). Continued elution afforded the pure enol phosphates **36** and **37** (747 mg, 81% yield) in a ratio of 8:1. The mixture was a pale yellow oil and showed the following data: ir 1705 (enol-phosphate), 1670 (α,β-unsaturated ketone C=O), 1277 and 1031 cm^{-1} (phosphate); ms M$^+$ 274.0968 (calcd. for $C_{12}H_{19}PO_5$: 274.0970). The ^1H nmr spectrum of the mixture of adducts showed two sets of signals in an integral ratio of 8:1. The major set, assignable to **36**, showed signals at δ6.82 (m, 1H, -CO-C=CH-), 5.58 (m, 1H, -CH=C-O-), 4.18 (m, 4H, 2 × $-OC\underline{H_2}CH_3$), 3.16 (m, 2H, $-CH_2-$), 3.03 (m, 2H, $-CH_2-$), 2.23 (s, 3H, CH_3CO-), and 1.36 (m, 6H, 2 × $-OCH_2C\underline{H_3}$); the other set, assignable to **37**, showed signals at δ6.86 (m, 1H, -CO-C=CH-), 5.52 (m, 1H, -CH=C-O-), 4.18 (m, 4H, 2 × $-OC\underline{H_2}CH_3$), 3.16 (m, 2H, $-CH_2-$), 3.03 (m, 2H, $-CH_2-$), 2.34 (s, 3H, CH_3-CO-), and 1.36 (m, 6H, 2 × $-OCH_2C\underline{H_3}$). The ^{13}C nmr spectrum also showed two sets of signals. The major set, belonging to **36**, showed signals at δ196.60, 142.62, 142.53, 135.41, 134.64, 107.15, 107.10, 63.48, 63.41, 28.79, 28.76, 24.28, 23.96, 15.23, and 15.16; the minor set, belonging to **37** showed signals at δ196.38, 145.05, 144.96, 135.66, 135.27, 104.83, 104.78, 63.48, 63.41, 26.92, 26.20, 26.15, 24.28, 15.23, and 15.16. Anal. Calcd. for $C_{12}H_{19}PO_5$: C, 52.55, H, 6.93. Found: C, 52.25; H, 6.91.

p-Diethylphosphoryloxyacetophenone (**38**) and *m*-Diethylphosphoryloxyacetophenone (**39**)

A 8:1 mixture of Diels-Alder adducts **36** and **37** (157 mg, 0.57 mmol) was dissolved in benzene (2 mL). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (145 mg, 0.64 mmol) was added. The reaction mixture was then heated at reflux under an atmosphere of nitrogen. After stirring for 2 h, the reaction mixture was cooled to room temperature and then filtered. The filtrate was concentrated. Flash chromatography of the brown-red oily residue on silica gel, eluting with 20% acetone and 30% ether in petroleum ether, gave the pure aryl ketones **38** and **39** in 79% yield (118 mg) in a ratio of 11:1. The mixture showed the following data: ir 3060 (aromatic C-H), 1686 (α,β-unsaturated ketone C=O), 1600 and 1505 (aromatic C=C), 1267 and 1035 cm^{-1} (phosphate); ms M^+ 272.0816 (calcd. for $C_{12}H_{17}PO_3$: 272.0813). The ^1H nmr spectrum of the aryl ketone mixture showed two sets of signals in an integral ratio of 11:1. The major set, assignable to **38**, showed signals at δ7.79 (d, 2H, J = 9 Hz, 2 × -CO-C=CH-), 7.32 (dd, 2H, J = 9, J' = 1 Hz, 2 × $-COC{=}CH{-}C\underline{H}{=}$), 4.24 (m, 4H, 2 × $-OC\underline{H_2}CH_3$), 2.58 (s, 3H, CH_3-CO-) and 1.36 (m, 6H, 2 × $-OCH_2C\underline{H_3}$); the other set, assignable to **39**, showed signals at δ7.78 (m, 2H, 2 × -CO-C=CH-), 7.47 (m, 2H, aromatic), 4.24 (m, 4H, 2 × $-OC\underline{H_2}CH_3$); 2.60 (s, 3H, CH_3-CO-), and 1.36 (m, 6H, 2 × $-OCH_2C\underline{H_3}$). Anal. Calcd. for $C_{12}H_{17}PO_5$: C, 52.93; H, 6.31. Found: C, 53.01; H, 6.20.

2-Diethylphosphoryloxy-5,8-dihydroxy-1,4-dihydronaphthalene (**41**)

Diene phosphate **16** (505 mg, 2.45 mmol) was dissolved in methylene chloride (2 mL) and the solution was cooled to 0°C. Then anhydrous stannic chloride (487 mg, 1.87 mmol) was added under an atmosphere of nitrogen, followed by the addition of p-benzoquinone (198 mg, 1.83 mmol). After stirring for 5 h, the viscous solution was diluted with methylene chloride. Water was added. The resulting emulsion was filtered by suction. The filtrate was extracted with methylene chloride. The extracts were combined, dried, filtered, and concentrated. The black oily residue was subjected to flash chromatography on silica gel. Elution with 10% acetone and 30% ether in petroleum ether gave very little diene **16**. Continued elution afforded the adduct **41** (532 mg, 93% yield). Adduct **41** was bright white and needle like after recrystallization from acetone and ether. It was soluble in methanol or hot acetone, but not in ether. Adduct **41** showed the following data: m.p. 124.5-126.5°C; ir (KBr) 3320 (-OH), 3010 (aromatic C-H), 1705 (enol-phosphate C=C), 1615 and 1491 (aromatic C=C), 1287 and 1038 cm^{-1} (phosphate); ms M^+ 314.0921 (calcd. for $C_{14}H_{19}PO_6$: 314.0919) ^1H nmr (in CD_3OD) δ 6.50 (s, 2H, aromatic), 5.64

(m, 1H, -CH=C-O-), 4.18 (m, 4H, 2 × $-OC\underline{H_2}CH_3$), 3.36 (slightly broad s, 4H, 2 × $-C=C-CH_2-$), 1.36 (m, 6H, 2 × $-OCH_2C\underline{H_3}$); ^{13}C nmr (in CD_3OD) δ 148.49, 146.62, 146.44, 122.04, 121.74, 133.1, 133.40, 109.16, 109.05, 64.98, 65.86, 28.23, 28.15, 25.87, 16.43, and 16.30. Anal. Calcd. for $C_{14}H_{19}PO_6$: C, 53.50; H, 6.11. Found C, 53.71; H, 6.15.

cis-1-Carbomethoxy-8-diethylphosphoryloxy-5,5-dimethylbicyclo[4,4,0]deca-3,8-dien-2-one (**45**)

To a solution of dienone ester **44** (306 mg, 1.69 mmol) and diene phosphate **16** (691 mg, 3.35 mmol) in ether (2.5 mL) at 0°C and under an atmosphere of nitrogen, was added anhydrous ferric chloride (270 mg, 1.66 mmol). After stirring for 72 h, water was added and the resulting mixture was extracted with dichloromethane. The extracts were washed with water, combined, dried, filtered, and concentrated. Flash chromatography of the red-brown oily residue on silica gel, eluting with a solution of 10% acetone and 30% ether in petroleum ether gave the diene **16** (326 mg, 47% recovery). Continued elution gave the pure enone phosphate **45** (462 mg, 71% yield) as a pale yellow oil. Adduct **45** showed the following data: ^1H nmr δ 6.60 (d, 1H, J = 10 Hz, $-CO-CH=C\underline{H}-$), 5.90 (d, 1H, J = 10 Hz,

-CO-C$\underline{H}$=CH-), 5.50 (broad s, 1H, -CH=C-O-), 4.15 (m, 4H, 2 × $-OC\underline{H}_2CH_3$), 3.74 (s, 3H, $-COOCH_3$), 1.35 (m, 6H, 2 × $-OCH_2C\underline{H}_3$), 1.22 and 1.15 (2×s, 6H, gem-dimethyl); ^{13}C nmr δ196.43, 172.02, 157.69, 145.78, 145.69, 123.72, 108.29, 108.24, 64.22, 64.17, 64.12, 56.09, 52.53, 41.80, 36.01, 30.07, 27.77, 26.52, 26.49, 23.08, 15.98, and 15.91; ir 1747 and 1731 (ester C=O), 1275 and 1029 cm^{-1} (phosphate); ms M^+ 386.1498 (calcd. for $C_{18}H_{27}PO_7$: 386.1494). Anal. Calcd. for $C_{18}H_{27}PO_7$: C, 55.94; H, 7.06. Found: C, 55.85; H, 7.11.

Lithium Iodide Dihydrate-Collidine Reagent

Finely divided anhydrous lithium iodide (514 mg, 3.84 mmol) was suspended in 2,4,6-collidine (3.05 mL) with vigorous stirring. Water (138 μL, 138 mg, 7.68 mmol) was added and the suspension dissolved. The resulting pale yellow solution had a calculated concentration of 1.20 N in lithium iodide dihydrate.

cis-(**47**) and trans-5,5-Dimethylbicyclo[4.4.0]dec-3-ene-2,8-dione (**48**)

A. From Enone Phosphate **45**

Enone phosphate **45** (355 mg, 0.92 mmol) was dissolved in lithium iodide dihydrate-collidine reagent (3.19 mL, 3.83 mmol) and heated at reflux with stirring. After 2.5 h, the mixture was cooled to room temperature, poured into cold 5% aqueous hydrochloric acid and extracted with methylene chloride. The extracts were washed with water, dried, filtered and concentrated. Flash chromatography of the yellow residue on silica gel, eluting with 10% ether in methylene chloride gave pure diketones **47** and **48** in 70% yield (124 mg) in a ratio of 1:6 (integral ratio in the ^1H nmr spectrum of the mixture). **47** was separated from **48** by further flash chromatography on silica gel. Elution with a solution of 10% acetone and 30% ether in petroleum ether gave diketone **47** as a white solid: ^1H nmr δ 6.56 (dd, 1H, J = 10, J' = 2 Hz, -CO-CH=C$\underline{H}$-), 6.00 (d, 1H, J = 10 Hz, -CO-C$\underline{H}$=CH-), 1.36 and 1.11 (2×s, 6H, *gem*-dimethyl); ir 1714 (ketone C=O) and 1677 cm^{-1} (α,β-unsaturated ketone C=O); ms M$^+$ 192.1150 (calcd. for $C_{12}H_{16}O_2$: 192.1150). Continued elution gave diketone **48** as a white solid: ^1H nmr δ 6.71 (d, 1H, J = 10 Hz, -CO-CH=C$\underline{H}$-), 5.91 (d, 1H, J = 10 Hz, -CO-C$\underline{H}$=CH-), 2.09 (td, 1H, J = 13, J' = 4 Hz, O=C-CH=CH-C-C$\underline{H}$-), 1.12 (s, 6H, *gem*-dimethyl); ir 1711 (ketone C=O) and 1678 cm^{-1} (α,β-unsaturated ketone C=O); ms M$^+$ 192.1156 (calcd. for $C_{12}H_{16}O_2$: 192.1151); ^{13}C nmr δ 210.00, 198.69, 160.00, 126.07, 48.00, 44.07, 41.79, 40.28, 35.98, 27.20, 26.17, and 20.36.

B. From Diketone **47**

Diketone **47** (5.68 mg) was dissolved in ethanol (0.5 mL) and 10% sulfuric acid (0.5 mL) was added with stirring. The reaction mixture was then heated at reflux. After stirring for 3 h, the mixture was cooled to room temperature, diluted with water and extracted with methylene chloride. The extracts were washed with water, dried, filtered, and concentrated. Flash chromatography of the residue on silica gel, eluting with 10% ether in methylene chloride, gave a diketone (4.92 mg, 87% yield) which was identical in ^{1}H nmr and ir spectra, as well as silica gel thin-layer chromatographic behavior to the *trans*-diketone **48**.

8-Diethylphosphoryloxybicyclo[4.4.0]dec-8-en-2-one (**55**)

To a solution of diene **16** (1.206 g, 5.85 mmol) in ether (1.5 mL) and methylene chloride (1.5 mL) at 0°C and under an atmosphere of nitrogen, was added anhydrous stannic chloride (399 mg, 1.53 mmol) followed by the addition of 2-cyclohexen-1-one (141 mg, 1.47 mmol). After stirring at room temperature for 34 h, the reaction mixture was diluted with methylene chloride. 5% aqueous sodium bicarbonate solution was added. The resulting emulsion was filtered by suction and the filtrate was extracted with methylene chloride. The extracts were combined, washed with water, dried, and concentrated. Flash chromatography of the yellow oily residue on silica gel, eluting with a solution of 20% acetone and 30% ether in petroleum ether, gave the diene phosphate **16** (779 mg, 65% recovery). Continued elution gave a mixture of adducts **55** and **28** (224 mg). The adduct **55** could be separated from **28** by extensive column chromatography on silica gel. **55** showed the following data: ^{1}H nmr δ 5.50 (broad s, 1H, $-CH=C-O-$), 4.18 (m, 4H, 2 × $-OC\underline{H_2}CH_3$) and 1.36 (m, 6H, 2 × $-OCH_2C\underline{H_3}$); ^{13}C nmr δ 210.69, 145.68, 145.51, 109.41, 109.30, 64.16, 64.04, 49.44, 41.76, 40.17, 35.28, 35.22, 32.21, 25.87, 23.03, 16.07, and 15.94; ir 1710 cm^{-1} (ketone C=O); ms M$^+$ 302.1273 (calcd. for $C_{14}H_{23}PO_5$: 302.1274). *Anal.* Calcd. for $C_{14}H_{23}PO_5$: C, 55.65; H, 7.67. Found: C, 55.72, H, 7.66. The spectral data of **28** were already reported (*vide supra*).

cis-1-Diethylphosphoryloxy-3-methyl-4-[1-oxopropyl]-1-cyclohexene (**63**)

To a solution of diene phosphate **17** (834 mg, 3.79 mmol) and ethyl vinyl ketone (240 mg, 2.85 mmol) in ether (2 mL) at -30°C and under an atmosphere of nitrogen, was added anhydrous stannic chloride (377 mg, 1.45 mmol).

After stirring for 24 h the reaction mixture was diluted with ether. 5% aqueous sodium bicarbonate was added. The resulting emulsion was filtered by suction. The filtrate was extracted with methylene chloride. The extracts were combined, washed with water, dried, filtered, and concentrated. Flash chromatography of the yellow oily residue on silica gel, eluting with a solution of 20% acetone and 30% ether in petroleum ether gave the diene **17** (157 mg, 19% recovery). Further elution afforded the pure enol-phosphate **63** (703 mg, 81% yield) which was a pale yellow oil. Adduct **63** showed the following data: ^1H nmr δ 5.53 (m, 1H, $-CH=C-O-$), 4.16 (m, 4H, 2 × $-OC\underline{H}_2CH_3$), 2.83 (m, 1H, $-C\underline{H}(Me)-CH=C-$), 2.72 (ddd, 1H, J = 13, J' = 7, J" = 4 Hz, $-CO-CH$), 1.33 (m, 6H, 2 × $-OCH_2C\underline{H}_3$), 1.02 (t, 3H, J = 7 Hz, $C\underline{H}_3-CH_2-CO-$) and 0.81 (d, 3H, J = 6.5 Hz, $-CH(\underline{Me})-CH=C-$); ^{13}C nmr δ 211.57, 146.92, 146.74, 114.67, 114.56, 63.64, 63.52, 48.62, 33.67, 29.63, 26.72, 26.65, 17.97, 15.78, 15.58, 15.45, and 7.00; ir 1710 (ketone C=O), 1680 (enol-phosphate C=C), 1273 and 1033 cm^{-1} (phosphate); ms M^+ 304.1432 (calcd. for $C_{14}H_{25}PO_5$: 394.1439). Anal. Calcd. for $C_{14}H_{25}PO_5$: C, 55.24; H, 8.30. Found: C, 55.27; H, 8.06.

cis-4-Acetyl-1-diethylphosphoryloxy-3-methyl-1-cyclohexene (**64**)

To a solution of diene phosphate **17** (801 mg, 3.64 mmol) and methyl vinyl ketone (196 mg, 2.80 mmol) in ether (2 mL) at -30°C and under an atmosphere of nitrogen, was added anhydrous stannic chloride (731 mg, 2.81 mmol). After stirring for 5 min the reaction mixture was diluted with ether. 5% aqueous sodium bicarbonate was added. The resulting emulsion was filtered by suction. The filtrate was extracted with dichloromethane. The extracts were washed with water, dried, filtered, and concentrated. The yellow oily residue was subjected to flash chromatography on silica gel. Elution with a solution of 20% acetone and 30% ether in petroleum ether gave the diene **17** (205 mg, 26% recovery). Continued elution gave the pure enol-phosphate **64** (586 mg, 72% yield) which was a pale yellow oil. Adduct **64** showed the following data: ^{1}H nmr δ 5.56 (m, 1H, $-CH=C-O-$), 4.18 (m, 4H, 2 × $-OC\underline{H}_2CH_3$), 2.86 (m, 1H, $-C\underline{H}(Me)-CH=C-$), 2.71 (ddd, 1H, J = 10, J' = J" = 5 Hz, $-CO-CH-$1, 2.17 (s, 3H, CH_3-CO-), 1.35 (t, 6H, J = 7 Hz, 2 × $-OCH_2C\underline{H}_3$) and 0.87 (d, 3H, J = 7 Hz, $-CH(\underline{Me})-CH=C-$); ^{13}C nmr δ 209.50, 147.33, 121.97, 114.97, 114.87, 64.04, 63.9[illegible] 50.15, 29.73, 28.34, 27.07, 27.00, 18.17, 15.96, and 15.81; ir (neat) 1709 (ketone C=O), 1678 (enol-phosphate

C=C), 1273 and 1027 cm^{-1} (phosphate); ms M$^+$ 290.1283 (calcd. for $C_{13}H_{23}PO_5$: 290.1283). Anal. Calcd. for $C_{13}H_{23}PO_5$: C, 53.77; H, 8.00. Found: C, 54.05; H, 7.94.

4α-Acetyl-1-diethylphosphoryloxy-3α,5β-dimethyl-1-cyclohexene (65

To a solution of diene **17** (783 mg, 3.56 mmol) and trans-3-penten-2-one (204 mg, 2.43 mmol) in ether (2 mL) at 0°C and under an atmosphere of argon, was added anhydrous stannic chloride (620 mg, 2.38 mmol). After stirring for 11 h, the reaction mixture was diluted with ether. 5% aqueous sodium bicarbonate was added. The resulting emulsion was filtered by suction. The filtrate was extracted with dichloromethane. The extracts were combined, dried, filtered, and evaporated to dryness. Flash chromatography of the dark yellow oily residue on silica gel, eluting with a solution of 20% acetone and 30% ether in petroleum ether gave the pure adduct **65** (529 mg, 72% yield, no diene **17** recovery). Enol-phosphate **65** was a light yellow oil and showed the following data: ^1H nmr δ 5.55 (m, 1H, -CH=C-O-), 4.19 (m, 4H, 2 × -O$\underline{CH_2}$$CH_3$), 2.75 (m, 1H, -C$\underline{H}$(Me)-CH=C-), 2.61 (dd, 1H, J = 11, J' = 5 Hz, -CO-CH), 2.17 (s, 3H, CH_3-CO-), 1.36 (t, 6H, J = 7 Hz, 2 × -O$CH_2$$\underline{CH_3}$), 0.96 (d, 3H, J = 6 Hz, -CO-CH-CH($\underline{Me}$)-, equatorial) and 0.86 (d, 3H, J = 7 Hz, CH(Me)-CH=C, axial); ^{13}C nmr δ 209.22, 145.97, 145.88, 114.45, 114.40, 63.83, 63.79, 56.29, 35.13, 35.10, 30.31, 30.00, 24.64, 19.25, 16.71, 15.77, and 15.70; ir 1710 (ketone C=O), 1658 (enol-phosphate C=C), 1270 and 1033 cm^{-1} (phosphate); ms M^+ 304.1445 (calcd. for $C_{14}H_{25}PO_5$: 304.1440). Anal. Calcd. for $C_{14}H_{25}PO_5$: C, 55.24; H, 8.30. Found: C, 55.16; H, 8.18.

2-Diethylphosphoryloxy-5,8-dihydroxyl-4-methyl-1,4-dihydronaphthalene (**67**)

To a solution of diene **17** (598 mg, 2.72 mmol) and p-benzoquinone (195 mg, 1.80 mmol) in dichloromethane (2 mL) at 0°C and under an atmosphere of nitrogen, was added anhydrous stannic chloride (465 mg, 1.79 mmol). After stirring for 30 min, water was added and the resulting emulsion was filtered with suction. The filtrate was extracted with dichloromethane. The extracts were combined, dried, filtered, and evaporated to dryness. Flash chromatography of the black oily residue on silica gel, eluting with a solution of 20% acetone and 30% ether in petroleum ether, gave the aromatic enol-phosphate **67** (308 mg, 52% yield, no diene **17** recovery). **67** could be crystallized from acetone and petroleum ether to form a light yellow crystal. Adduct **67** showed the following data: m.p. 130.5–132.0°C; ^{1}H nmr (in acetone-D_6) δ7.86 (broad s, 2H, D_2O exchangeable, 2 × -OH), 6.60 and 6.59 (two single peaks, 2H, aromatic), 5.72 (m, 1H, $-C\underline{H}=C-O-$), 4.20 (m, 4H, 2 × $-OC\underline{H_2}CH_3$), 1.33 (m, 6H, 2 × $-OCH_2C\underline{H_3}$), and 1.27 (d, 3H, J = 7 Hz, $-CH(C\underline{H_3})-C=CO$); ^{13}C nmr (in acetone-d_6) δ148.15, 145.99, 145.90, 127.28, 121.53, 115.18, 115.13, 113.81, 113.16, 64.96, 64.92, 31.44, 28.16, 28.12, 22.62, 16.41, and 16.35; ir 3304 (-OH), 1700 (enol-phosphate C=C), 1492 (aromatic C=C), 1247 and 1035 cm^{-1} (phosphate); ms M$^+$ 328.1075 (calcd. for $C_{15}H_{21}PO_6$: 328.1075). <u>Anal.</u> Calcd. for $C_{15}H_{21}PO_6$: C, 54.86; H, 6.46. Found: C, 54.84; H, 6.46.

REFERENCES

1. A.S. Onishchenko, "Diene Synthesis", Israel Program for Scientific Translation, Jerusalem, 1964.
2. Yu A. Titon, Russ. Chem. Rev., 31, 267 (1962).
3. K. Alder and G. Stein, Angew. Chem., 50, 510 (1937).
4. J. Sauer, Angew. Chem. Int. Ed. Engl., 5, 211 (1966).
5. J. Sauer, Angew. Chem. Int. Ed. Engl., 6, 16 (1967).
6. J.G. Martin and R.K. Hill, Chem. Rev., 61, 537 (1961).
7. K. Alder, "Nobel Lectures in Chemistry 1942-1962", Elsevier, Amsterdam, London, New York, 1964.
8. H.O. Holmes, Organic Reactions, 4, 60 (1948).
9. J.A. Norton, Chem. Rev., 31, 319 (1942).
10. K. Alder in W. Foerst, "Neuere Methoden der Präparativen Organischen Chemie", Verlag Chemie, Berlin, Vol. 1, p. 251, 1943.
11. M.C. Kloelzel, Organic Reactions, 4, 1 (1948).
12. H. Wollweber in Houben-Weyl, "Methoden der Organischen Chemie", Georg Thieme Verlag, Stuttgart, Vol. 5, p. 977, 1970.
13. O. Diels and K. Alder, Ann., 460, 98 (1928).
14. K.N. Kouk, Acc. Chem. Res., 8, 361 (1975).
15. R.B. Woodward and R. Hoffmann, Angew. Chem. Int. Ed. Engl., 8, 781 (1969).
16. K.N. Houk, J. Am. Chem. Soc., 95, 4092 (1973).

17. K.N. Houk, J. Am. Chem. Soc. 95, 4094 (1973).

18. M.J.S. Dewar, A.C. Griffin and S. Kirschner, J. Am. Chem. Soc., 96, 6225 (1974).

19. R.B. Woodward and T.J. Katz, Tetrahedron, 5, 70 (1959).

20. W. Dilthey, W. Schommer and O. Trösken, Ber., 66, 1627 (1933).

21. W. Dilthey, I. Thewalt and O. Trösken, Ber., 67, 1959 (1934).

22. K. Alder, G. Stein, F. Von Bruddenbrock, W. Eckardt, W. Frercks and S. Schneider, Ann., 514, 1 (1934).

23. A.A. Petrov and N.P. Sopov, Zhurnal Obschchei Khimii, 22, 591 (1952).

24. I. Fleming, F.L. Gianni and T. Mah, Tetrahedron Letters, 881 (1976).

25. I. Fleming, "Frontier Orbitals and Organic Chemical Reactions", Wiley, London, p. 161, 1978.

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

27. G.I. Fray and R. Robinson, J. Am. Chem. Soc., 83, 249 (1961).

28. T. Inukai and M. Kasai, J. Org. Chem., 30, 3567 (1965).

29. T. Inukai and T. Kojima, J. Org. Chem., 31, 2032 (1966).

30. E.F. Lutz and G.M. Bailey, J. Am. Chem. Soc., <u>86</u>, 3899 (1964).

31. T. Inukai and T. Kojima, J. Org. Chem., <u>31</u>, 1121 (1966).

32. T. Inukai and T. Kojima, J. Org. Chem., <u>32</u>, 869 (1967).

33. I. Nagakura, H. Ogata, M. Ueno and Y. Kitahara, Bull. Chem. Soc., Japan, <u>48</u>, 2995 (1975).

34. F. Fringuelli, F. Pizzo, A. Taticchi and E. Wenkert, Syn. Comm., <u>9</u>, 391 (1979).

35. E.N.C. Browne, Ph.D. Dissertation, the University of Alberta, 1980.

36. J. Sauer and J. Kredel, Tetrahedron Letters, 731 (1966).

37. M. Petrzilka and J.I. Grayson, Synthesis, 753-784 (1981).

38. F. Kienzle and P. Rosen, Helv. Chim. Acta, <u>62</u>, 2 (1979) -Nr. 43, P442.

39. K.F. Burri, F. Kienzle, P. Rosen, U.S. Patent 4025584 (1977); 4077985, Hoffmann-La Roche Inc. (1978); C.A. <u>87</u>, 39015 (1977).

40. T.K. Ngooi, Ph.D. Dissertation, the University of Alberta, 1984.

41. H.J. Liu and E.N.C. Browne, Can. J. Chem., <u>59</u>, 601 (1981).

42. H.J. Liu and E.N.C. Browne, Tetrahedron Letters, 2919 (1977).

43. F. Elsinger, Org. Syn., 45, 7 (1965).

44. H.C. Odom and A.R. Pinder, Org. Syn., 51, 115-120 (1971).

45. E.J. Corey and J.W. Suggs, Tetrahedron Letters, 31, 2647 (1975).

46. L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley and Sons, Inc. New York, 1967.

47. C. Still, M. Kahn and A. Mitra, J. Org. Chem., 43, 2923 (1978).