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PHOSPHORUS-STABILIZED, CARBANION-ACCELERATED CLAISEN REARRANGEMENTS: ASYMMETRIC INDUCTION VIA 1,3,2-OXAZAPHOSPHORINANES

John Emory Marlin II, Ph. D.
Department of Chemistry
University of Illinois at Urbana-Champaign, 1987
Professor Scott E. Denmark, Advisor

The carbanion-accelerated Claisen rearrangement has been extended to include phosphorus carbanion-stabilizing groups. The appropriately substituted allyl vinyl ethers are synthesized by the nucleophilic addition of allyloxides to phosphorus-substituted allenes, which are obtained in one step from simple starting materials. The phosphorus-stabilized, carbanion-accelerated Claisen rearrangements proceed rapidly at room temperature in high yield, and the rearrangements are regiospecific and highly stereoselective. Most importantly, the first examples of asymmetric induction in the Claisen rearrangement with chiral phosphorus anion-stabilizing groups are documented. The observed asymmetric induction, which is highly dependent on the metal counterion involved, is explained in terms of both internal and relative diastereoselectivity. The sense of asymmetric induction is established by degradation of the Claisen rearrangement products to (*R*)- and (*S*)-dimethyl methylsuccinates. Two limiting transition state models are proposed to rationalize the high levels of observed diastereoselectivity.

Methods of cleaving the phosphorus-carbon bond are examined. Phosphorus-carbon bond cleavage is observed only under harshly acidic conditions.

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PHOSPHORUS-STABILIZED, CARBANION-ACCELERATED CLAISEN REARRANGEMENTS: ASYMMETRIC INDUCTION VIA 1,3,2-OXAZAPHOSPHORINANES

BY

JOHN EMORY MARLIN II

B.S., United States Air Force Academy, 1981

THESIS

Submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy in Chemistry
in the Graduate College of the
University of Illinois at Urbana-Champaign, 1987

Urbana, Illinois

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

THE GRADUATE COLLEGE

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BE ACCEPTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

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Methods of cleaving the phosphorus-carbon bond are examined. Phosphorus-carbon bond cleavage is observed only under harshly acidic conditions.

This thesis is dedicated to

my mother,

Stephanie,

and the memory of my father

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During the course of my graduate career, I have been fortunate enough to interact with many (and a wide variety of) people, several of whom deserve special recognition.

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Others who have made my stay here much more enjoyable include Kathleen S. White, Reds fan Brad R. Henke, Ultimate players Dr. Jeffrey A. Sterberg and Christopher J. Cramer, Dr. Robert T. Jacobs, James P. Edwards, and Dr. Russell Klix.

I also thank John Casper for proving that the first yeast reaction was not an accident.

I am especially thankful for the love and support of my mother and sisters during my years here as a graduate student.

Finally, a special ackowledgement is due my wife, Stephanie. Her friendship, love, and encouragement were essential during both good and bad times. I express to her my deepest gratitude.

TABLE OF CONTENTS

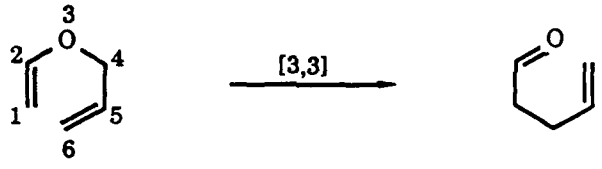
CHAPTER 1

INTRODUCTION

1.1. General Background.

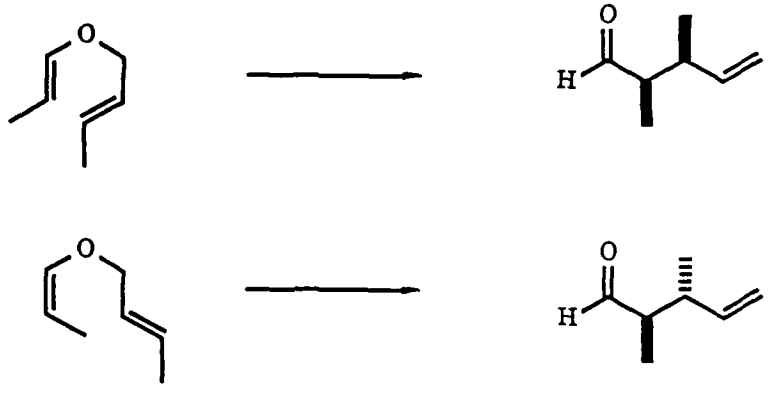
The Claisen rearrangement (Scheme 1), originally developed as the transformation of allyl aryl ethers to ortho allyl phenols,[1] has become not only an increasingly powerful transformation for synthetic chemists, but also an extremely challenging reaction for mechanistic study by physical organic chemists as well.[2]

Scheme 1



The value of this [3,3] sigmatropic rearrangement is due primarily to the formation of a new carbon-carbon bond in a highly stereoselective and predictable manner. Schmid and coworkers[3] were the first to provide insight into the nature of the transition state of the Claisen rearrangement by demonstrating that rearrangement of (*E*,*E*)-crotyl propenyl ether leads to *l*-2,3-dimethylpentenal[4] with 95.9% diastereoselectivity (Scheme 2). Likewise, rearrangement of (*E*,*Z*)-crotyl propenyl ether leads to *u*-2,3-dimethylpentenal with 95.5% diastereoselectivity. The

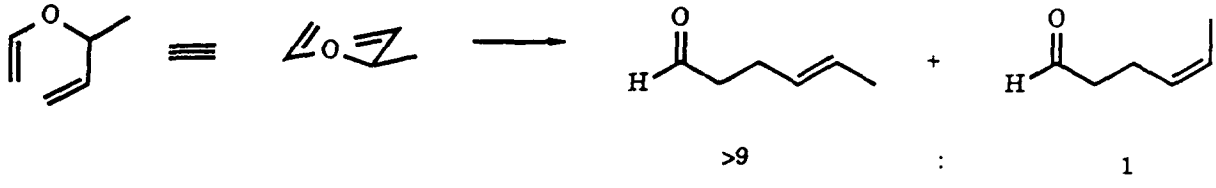
Scheme 2



high degree of observed stereoselectivity is most consistant with a highly ordered, chair-like transition state with substituents in pseudo-equatorial orientations.

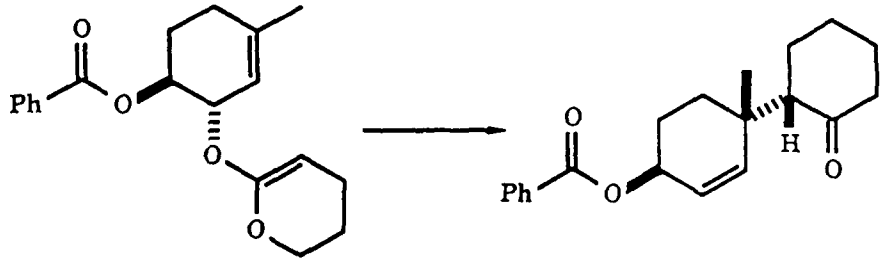
Burgstahler[5] provided further evidence for a chair-like transition state in the Claisen rearrangement by demonstrating that allyl vinyl ethers with methyl substitution at C(4) afford (E)-hexenals in greater than 90% stereoselectivity (Scheme 3). Faulkner[6] has also demonstrated that increasing the steric bulk at C(4) further increased the stereoselectivity of the rearrangement.

Scheme 3



However, Claisen rearrangement through boat-like transition states is preferred when severe steric interactions disfavor a chair-like conformation- usually when the allyl or vinyl double bond is contained in a ring. For example, Claisen rearrangement of the cyclic orthoester **I** proceeds through a boat-like transition state to yield **II** as a single diastereomer[7] (Scheme 4).

Scheme 4



I **II**

Through the stereochemical information gained from these studies, the Claisen rearrangement has become a powerful synthetic tool. Indeed, the Claisen rearrangement, through both chair- and boat-like transition state conformations, has been crucial in the stereoselective syntheses of several complex natural products.[2a]

1.2. Theoretical Analyses.

The Claisen rearrangement has also become a highly interesting subject for physical organic chemists, their goals being to determine the structure of the transition state and to formulate a predictive model for substituent effects.

The latter goal was first addressed by Carpenter[8], who used simple Huckel molecular orbital calculations to evaluate the effects of π-electron donating and π-electron withdrawing substituents of various mono-substituted aliphatic allyl vinyl ethers. The model ground state structure is an allyl anion and an isolated ethylene. The model for the chair-like transition state is a phenyl anion, while the model for the half-chair transition state is a heptatrienyl anion. A π-donor is represented by a carbanion and a π-acceptor by a carbocation. HMO calculations are performed for each substituted allyl vinyl ether model to determine the relative π-energies of the reactant and transition state. These values are then compared to the parent, unsubstituted case. The energy difference represents the change in the activation enthalpy of the reaction due to the substituent and is represented by $\Delta\Delta E_\pi$. The results are shown in Table I. A negative $\Delta\Delta E_\pi$ corresponds to a net rate acceleration and a positive $\Delta\Delta E_\pi$ corresponds to a net rate deccleration.

Table I. Substituent Effects on the Claisen Rearrangement

	$\Delta\Delta E$	
Substituted Carbon	Donor	Acceptor
1	-	+
2	-	-
4	-	-
5	+	±
6	+	+

These predictions are in agreement with most experimental observations, the most serious disagreement being a methoxy substituent at C(6) which rearranges 10 times faster than the unsubstituted allyl vinyl ether.[9a,b] However, this observation has been explained by a "vinylogous anomeric effect," a vinylogous hyperconjugative interaction between the lone pair on the C(6) oxygen and the oxygen-C(4) antibonding orbital. This interaction should facilitate cleavage of the oxygen C(4) bond,[9a,c] thereby accelerating the [3,3] sigmatropic rearrangement. An effect such as this is not accounted for in Carpenter's analysis. Furthermore, while a diethyl phosphonate group at C(1) decelerates the Claisen rearrangement as predicted, it also decelerates the rate when positioned at C(4), in contrast to Carpenter's predictions.[10]

In an attempt to determine the transition state structure for the Claisen rearrangement, Gajewski[11] has studied the secondary deuterium kinetic isotope effects in C(4) and C(6) dideuterated allyl vinyl ethers. The magnitude of the secondary kinetic isotope effect (KIE) at C(4), when compared to the maximum possible isotope effect (i.e. the equilibrium isotope effect (EIE)), reveals the extent of bond breaking in the transition state, while the magnitude at C(6) reveals the extent of bond making. Comparison of these ratios to the two limiting non-concerted alternatives, an oxaallyl radical-allyl radical pair and a 2-oxacyclohexane-1,4-diyl, provides a structural interpretation of the transition state in terms of the changing bond order between C(4)-O and C(1)-C(6). The relationship can be illustrated on a More O'Ferrall-Jenks diagram[12] (Figure 1).

The extrapolation of this method to predicting the effect of substituents on the rate of the Claisen rearrangement depends on: 1) the radical stabilization potential of the substituent and 2) its position on the allyl vinyl ether. Experimental data for the three allyl vinyl ethers depicted show higher values for the KIE/EIE ratio at the bond breaking site than at the bond making site, indicating an early transition state. Thus, Gajewski's model suggests that the transition state will be stabilized to a greater extent with radical stabilizing substituents at C(1), C(4), and C(6) than at C(2) and C(5). Furthermore, in the case of Ireland's ester enolate Claisen

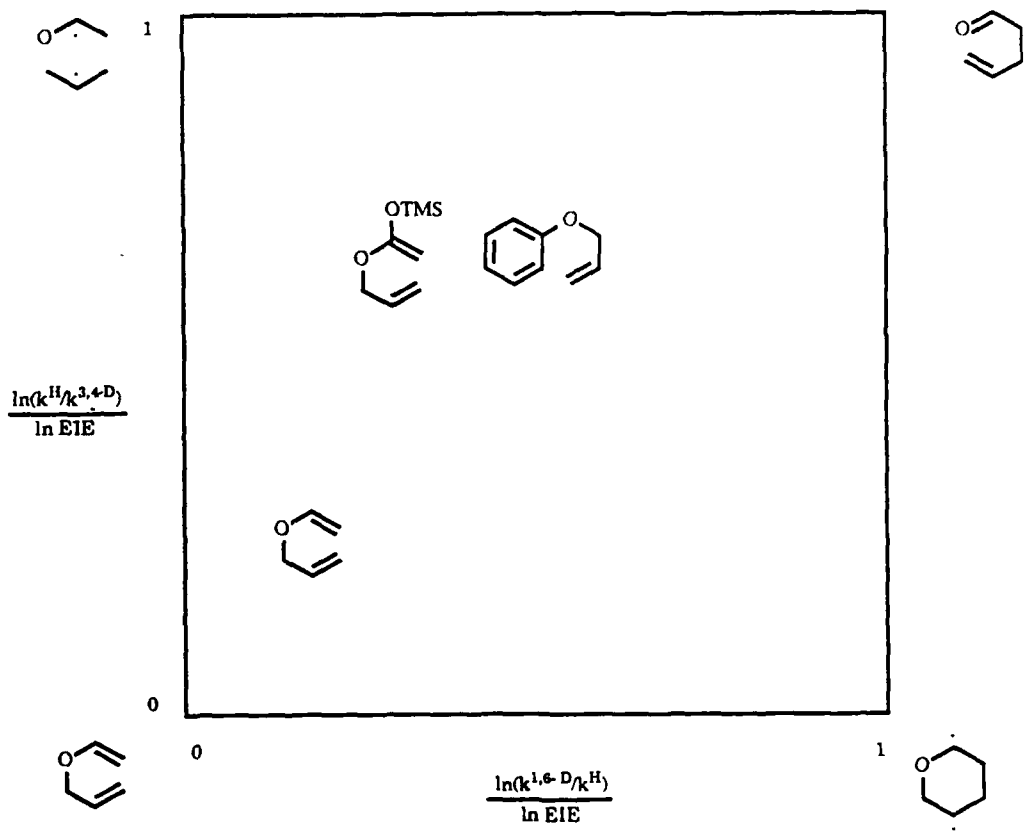


Figure 1. More O'Ferrall-Jenks diagram.

rearrangement[13], Gajewski implies that the stabilization is not associated with that of the free electron but of the π-bond associated with the unsymmetrical oxaallyl radical. Thus, strongly conjugating substituents at C(2) will also enhance the rate of Claisen rearrangement by stabilization of the transition state.

A theoretical treatment of the Claisen rearrangement has also been presented by Dewar[14], who performed MNDO calculations on the parent allyl vinyl ether and various methoxy and cyano derivatives. The calculations favor a chair-like 2-oxacyclohexane transition state (Figure 2). This model also predicts an early transition state, as the calculated C(4)-O and C(1)-C(6) bond lengths indicate more bond breaking than bond making taking place.

Furthermore, Dewar suggests that the transition state is biradical and becomes polarized as facile electron transfer takes place without any change in bonding (Scheme 5). Dewar's model predicts that electron donating substituents should facilitate Claisen rearrangement to a greater

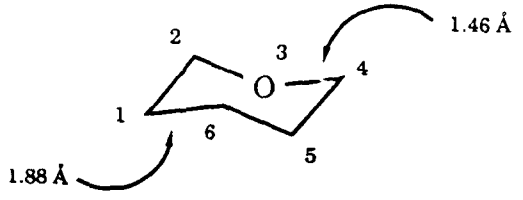
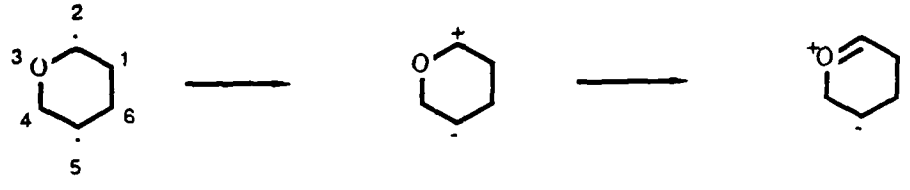


Figure 2. 2-Oxacyclohexane transition state.

extent at C(2) than at C(5) and electron withdrawing groups will increase the rate to a greater extent at C(5). Acceleration by groups at C(4) is rationalized by the double bond moving into conjugation. Dewar's model also accurately predicts rate variations observed experimentally for many substituted allyl vinyl ethers. This approach, however, fails to accurately predict a rate deceleration for a methoxy substituent at C(5)[9b,15] and a rate acceleration for a methoxy substituent at C(6).[9a,b]

Scheme 5



Although none of the theoretical models presented are in complete agreement concerning substituent effects at various positions on the allyl vinyl ether, they all suggest that π-donors at C(2) strongly accelerate the Claisen rearrangement. Empirically, this has been observed in a number of variants of the Claisen rearrangement that have been developed which allow direct routes to esters[16], amides[17], and acids[13, 18]. The trend is illustrated in Scheme 6. Note that these variants show dramatic rate enhancements as the strength of the π-electron donor increases. In fact, the temperature required for the Claisen rearrangement of ketene acetals (135°C) may well be misleading. In work involving amide acetals, Welch[17e] showed that if the appropriately substituted allyl vinyl ethers can be prepared at lower temperatures, Claisen rearrangement will occur at or slightly above room temperature. Thus, it is likely that the elevated temperatures

reported for the orthoester variant are necessary for allyl vinyl ether formation and not Claisen rearrangement.

Scheme 6

X	T°C
H,alkyl	160-200
OR	135
NR_2	25-50
OLi, OTMS	25-67
ZCH-	-20-50

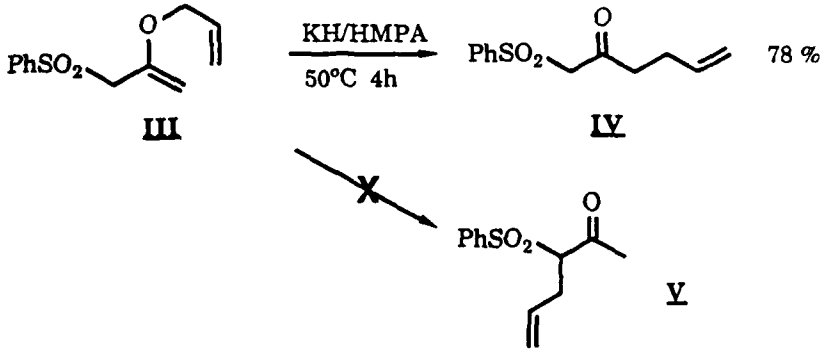
1.3. Sulfonyl-stabilized, Carbanion-accelerated Claisen Rearrangements.

Work performed in these laboratories demonstrated that the most powerful π- donor, a carbanion, would even further accelerate the Claisen rearrangement.[19] After various anion-stabilizing groups, such as -CN and $-CO_2Et$, proved unsuccessful, attention was focused on α-sulfonyl carbanions.

The carbanion is generated by deprotonation of an aryl sulfone, III, with potassium hydride which, following Claisen rearrangement, forms the β-ketosulfone IV (Scheme 7). Control experiments (no KH) resulted in 97% recovery of III unchanged, demonstrating the remarkable rate-accelerating effect of a sulfonyl-stabilized carbanion.

The kinetics of the carbanion-accelerated Claisen rearrangement have been studied quantitatively.[20] Under thermal and anionic conditions, the Claisen rearrangement of allyl vinyl ether III obeys first order kinetics. The thermal rearrangement (90°C) is twice as fast in

Scheme 7



DMSO than in HMPA. This is attributed to an entropy effect: although increased solvation of the polarized transition state in HMPA lowers $\Delta H^{\neq}$, the decrease in $\Delta S^{\neq}$ due to solvent ordering overrides $\Delta H^{\neq}$ stabilization. Both $\Delta H^{\neq}$ and $\Delta S^{\neq}$ contribute to lower $\Delta G^{\neq}$ for the anionic Claisen rearrangement of III in DMSO, accounting for a 300-fold rate increase over the thermal rearrangement.

Qualitatively, changes in counterion (Li^+, Na^+, K^+) and solvent (HMPA, DMSO, THF) showed only marginally different rates of rearrangement.[21]

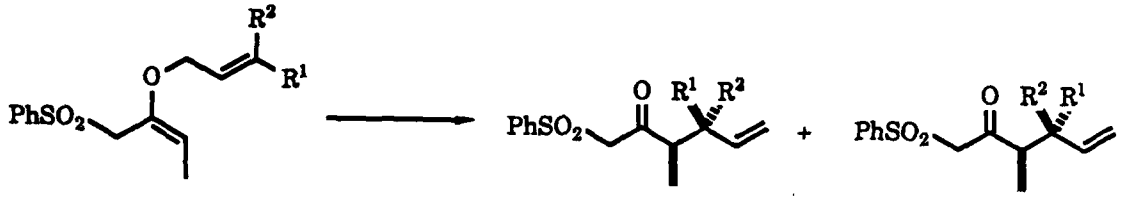
The effects of alkyl substitution were also studied.[19a] Methyl substitution at C(1) strongly accelerated the rate of rearrrangement while substitution at C(5) and C(6) decelerated the rate. Yields were high (71-85%) in all cases. These results are in agreement with predictions made by Carpenter and Gajewski.

This variant of the Claisen rearrangement has regiochemical implications as well. Interestingly, since an allyl anion is generated, carbon-carbon bond formation is possible at either terminus of the allyl anion. The anionic rearangements are regiospecific, producing only IV. This is attributed to the fact that the primary product of the rearrangement is a β-ketosulfone anion, while the product of the regioisomeric rearrangement is a simple ketone enolate[19a] (*vide infra*). Regioisomer V is observed with certain substituents at C(4) (most notably phenyl groups),[20]

but these products were found to be attributable to extremely facile thermal rearrangements of the isomeric α,β-unsaturated sulfones.[22]

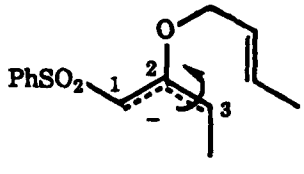
The sulfonyl-stabilized, carbanion-accelerated Claisen rearrangement is highly stereoselective[19b] (Scheme 8). Anionic rearrangement in DMSO of **VI** produced a 98:2 ratio of **VIII** to **IX** while anionic rearrangement of **VII** produced a 4:96 ratio of **VIII** to **IX**. Ratios of the thermal rearrangements of **VI** and **VII** are 96:4 and 4:96 respectively. These results are in agreement with a chair-like transition state with substituents arranged in pseudo-equatorial positions. The high

Scheme 8

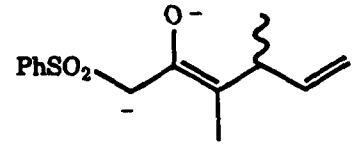


IV	$R^1 = CH_3$, $R^2 = H$	**VII** 98	**VIII** 2
V	$R^1 = H$, $R^2 = CH_3$	4	96

selectivities observed in these cases are particularly noteworthy in the face of two possible problems unique to the carbanion variant: rotation about the C(2)-C(3) bond of the allyl anion (**X**) and dianion formation after rearrangement (**XI**).



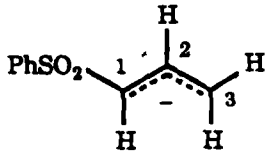
X



XI

By comparison of the diastereomeric ratios of the thermal and anionic Claisen rearrangements of **VI** and **VII**, it is clear that **XI** is not produced in DMSO even in the presence of excess base. However, the anionic rearrangement of **VI** in HMPA, which produces only a 2:1 ratio of **VIII** to **IX**, suggests that **XI** may well exist in HMPA.[21]

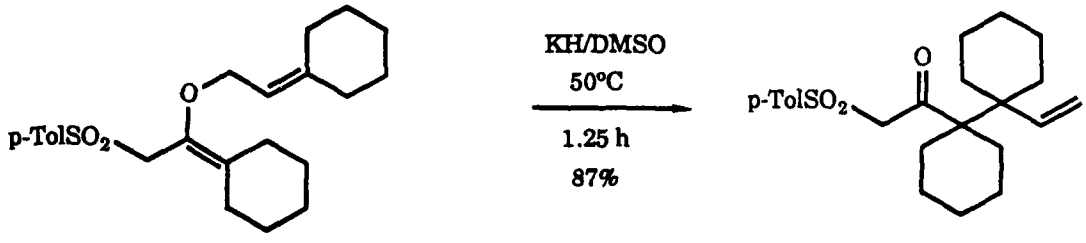
The issue of bond rotation in an allyl anion has been addressed by Gais,[23] who obtained ^1H NMR data on the sulfonyl-stabilized allyl anion **XII**. The absence of line broadening of the terminal olefin signals up to temperatures of 130°C reveals that the rotational barrier about the C(2)- C(3) bond in **XII** must be greater than 19.5 Kcal/mole (130°C), indicative of negligible bond rotation.



XII

Finally, the sulfonyl-stabilized, carbanion-accelerated Claisen rearrangment is also capable of producing vicinal quaternary centers.[19c,d] This is achieved with disubstitution at C(1) and C(6). Even with pentamethylene substitution at both centers, rearrangement is clean, facile, and regioselective (Scheme 9).

Scheme 9

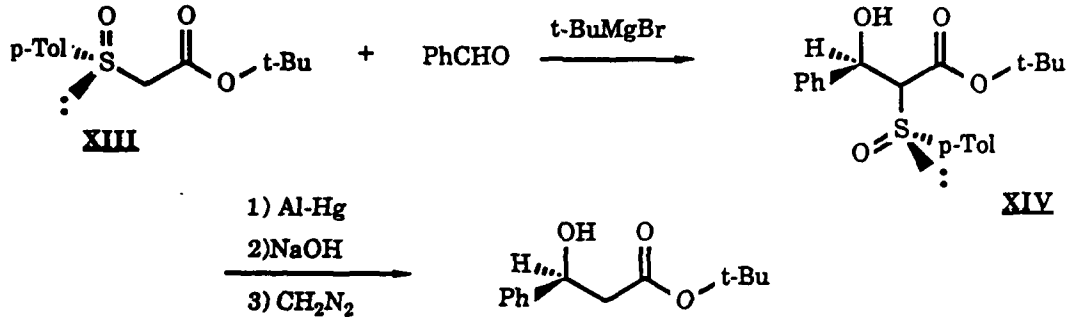


1.4. Heteroatom-based Asymmetric Induction.

The mild reaction conditions, high yields, regio- and stereoselectivities of the sulfonyl-stabilized, carbanion-accelerated Claisen rearrangement prompted an investigation into the possibility of asymmetric induction in the Claisen rearrangement using chiral, sulfur-based, anion-stabilizing groups.

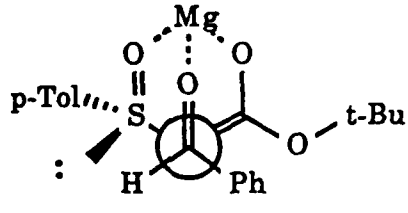
The general concept of asymmetric induction using anions stabilized by a chiral sulfur group (sulfoxide) is shown in Scheme 10 . Condensation[24] of (*R*)-(+)-*t*-butyl-*p*-tolylsulfinylacetate (**XIII**) with benzaldehyde in the presence of *t*-butyl magnesium bromide produces predominately

Scheme 10



XIII **XIV** **XV**

diastereomer **XIV**. The diastereoselectivity in this case was found to arise from a preferred, chelated transition state (**XVI**). The key features influencing the diastereoselectivity are: 1) approach of the electrophile (PhCHO) to the less hindered side of the anion (*syn* to the lone pair and *anti* to the aryl group) and 2) magnesium chelation to the sulfinyl oxygen, the ester, and the electrophile so that steric and electronic interactions between the carbonyl and sulfoxide group are minimized. Removal of the sulfoxide with aluminum amalgam[25] and saponification-



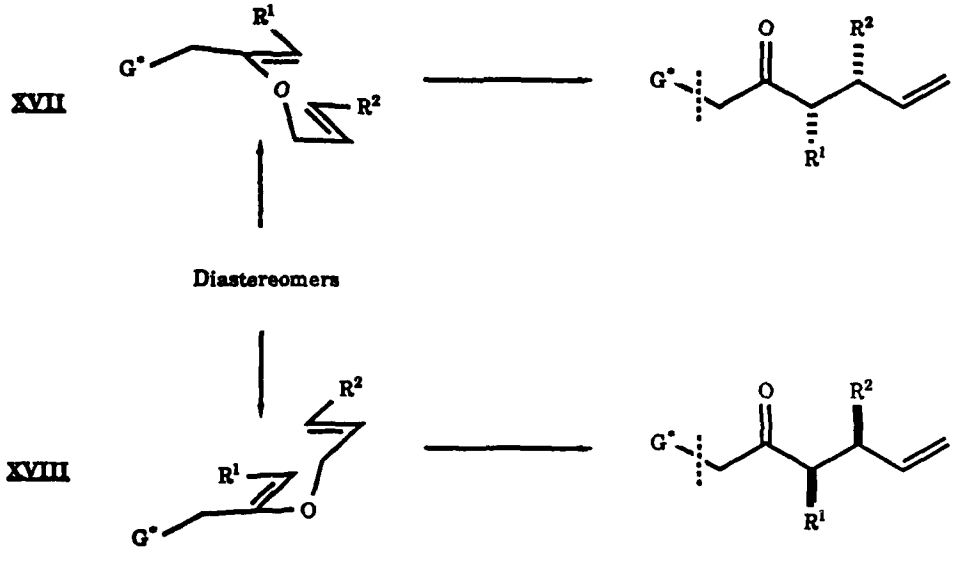
XVI

esterification gave hydroxyester **XV** with an enantiomeric excess of 91%. This condensation-degradation sequence has been shown to work well with a variety of aldehydes and ketones[24] and has also been employed in natural product syntheses.[26]

In the context of the carbanion-accelerated Claisen rearrangement, heteroatom-based asymmetric induction also requires a preferred diastereomeric transition state for the

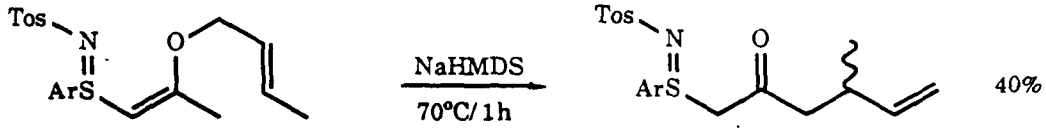
intramolecular approach of an electrophile. The concept is shown in Scheme 11. By virtue of the chirality of G*, the transition states **XVII** and **XVIII** are diastereomeric. Assuming R^1 and R^2 have priority over hydrogen but not over the vinyl ether carbon, Claisen rearrangement through transition state **XVII** corresponds to *si-si* carbon-carbon bond formation while Claisen rearrangement through transition state **XVIII** corresponds to *re-re* carbon-carbon bond formation. Therefore, any chiral group (G*) which preferentially stabilizes one transition state will result in a mixture of Claisen rearrangement products enriched in one diastereomer. Removal of G* then produces as enantiomerically enriched mixture of γ,δ-unsaturated carbonyl compounds.

Scheme 11



The investigation into sulfur-based asymmetric induction in the Claisen rearrangement proved to be disappointing.[21] Preliminary work on sulfoxides was abandonded due to poor yields in the rearrangements and all attempts at synthesizing α,β- or β,γ-unsaturated sulfoximine derivatives failed. The α,β-unsaturated sulfilimines (Scheme 12) could be prepared, but rearrangement lead to a 50:50 mixture of diastereomers in modest yield, reflecting no preferential stabilization of a diastereomeric transition state. The β,γ-unsaturated sulfilimines could not be prepared due to an irreversible sulfilimine-sulfenamide [2,3] sigmatropic rearrangement.[27]

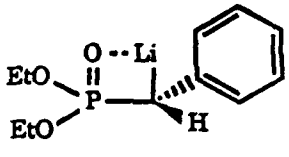
Scheme 12



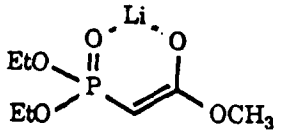
1.5. Phosphorus-based Anion-stabilizing Groups.

The successes and limitations of the sulfonyl-stabilized, carbanion-accelerated Claisen rearrangement led to the present investigation of phosphorus-based, anion-stabilizing groups.

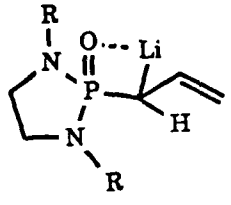
Relatively little information on the structure of phosphorus-stabilized allylic anions is available. However, ^{1}H , ^{13}C, and ^{31}P NMR studies on diethyl benzyl phosphonate and the corresponding lithio derivative **XIX** indicate a planar geometry at the anionic site.[28] This was determined by measuring $\Delta^{1}J_{PC}$, $\Delta^{1}J_{CH}$, and sign of $^{2}J_{PH}$ between the charged and uncharged species. The trends that are observed with these coupling constant changes have been correlated to the rehybridization at carbon in phosphonium salts and ylides with the aid of X-ray crystallography.[29] Furthermore, it is suggested that the lithium counterion coordinates with both the carbanionic carbon[30] and the phosphonate oxygen,[28a] which requires the π-system of the anion to adopt a conformation parallel to the P=O bond.



XIX



XX



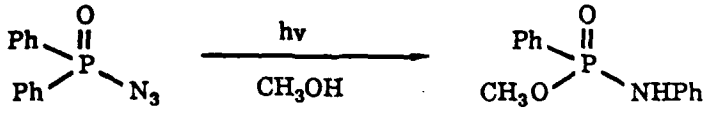
XXI

Similar spectroscopic studies on the lithio derivative of diethyl[(carbomethoxy)methyl]-phosphonate **XX** demonstrate the existence of a lithium-chelated structure. Note that the π-system of the anion is now perpendicular to the P=O bond. With potassium as a counterion, both chelates and free ions are reported to exist.[28b]

NMR spectroscopic studies on diazaphosphoryl allyl anions **XXI** are currently in progress in these laboratories.[31] The changes in $^1J_{PC}$ and $^1J_{CH}$ also indicate a planar carbanion in THF solution. Interestingly, these anions were found to be less planar in DMSO than in THF. Efforts are underway to examine the roles of various solvents and counterions on the structure and conformation of these anions.

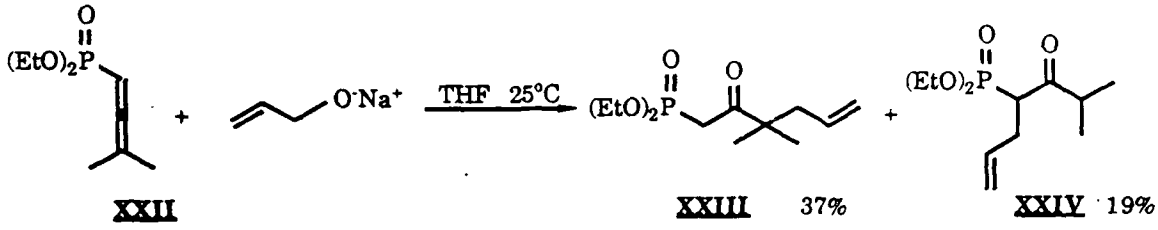
The advantages of phosphorus-based anion-stabilizing groups are many. A wide range of potential ligands exist which can be bound to phosphorus. By judicious choice of ligands, it is possible to control both the steric and electronic environments around the phosphorus atom. In this way, we planned to study the potential for absolute asymmetric induction *via* chiral, phosphorus-based, anion-stabilizing groups. Ideally, the chirality of the phosphorus group may be auxiliary-derived through the use of chiral, recoverable ligands. Finally, the possibility exists for stereospecific phosphorus-carbon bond cleavage. While there are no general methods for phosphorus-carbon bond cleavage at present, several examples of C-P to C-O and C-N transformations have been documented.[32] The most relevant to the work described here is the phosphoryl Curtius rearrangement (Scheme 13) developed by Harger.[32c] The reaction presumably proceeds *via* a [1,2] sigmatropic rearrangement. Work in these laboratories is currently aimed at determining the stereochemistry of the migrating carbon center.[33]

Scheme 13



Our interest in phosphorus was further stimulated by work published by Trippett and Cooper.[10] They reported an apparent carbanion-accelerated Claisen rearrangement illustrated in Scheme 14.

Scheme 14



XXII XXIII 37% XXIV 19%

Treatment of allene XXII with sodium allyloxide in THF at room temperature gave a mixture of regioisomeric Claisen products XXIII and XXIV as the major products. Formation of a mixture of regioisomers is in direct contrast to our experience with the related sulfones. If formation of XXIV were truly a result of a carbanion-accelerated Claisen rearrangement, then it would be necessary to identify those steric and/or electronic factors that are present with phosphorus-stabilized anions and clearly absent with sulfur-stabilized anions. Alternatively, XXIV may have been formed by a mechanism other than a carbanion-accelerated Claisen rearrangement.

In summary, our objectives were to: 1) survey various phosphorus-anion stabilizing groups with respect to regiochemistry, rate, and yield in the Claisen rearrangement, 2) establish the internal stereoselectivity of the phosphorus-stabilized, carbanion-accelerated Claisen rearrangement, 3) explore the possibility of relative asymmetric induction using recoverable chiral auxiliaries, and 4) investigate phosphorus-carbon bond cleavage reactions.

CHAPTER 2

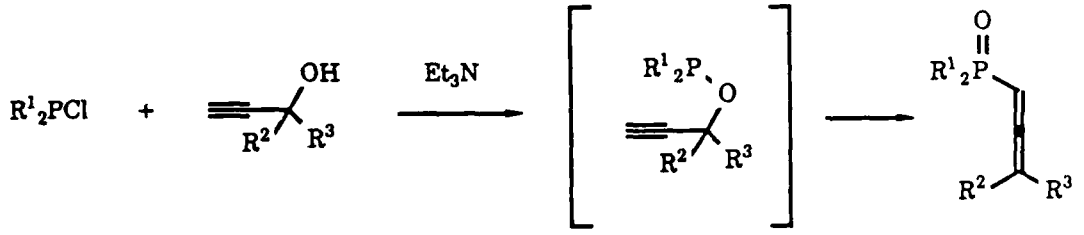
RESULTS AND DISCUSSION

2.1 Achiral Phosphorus Derivatives.

2.1.1. Synthesis of Allenes.

An obvious route to the allyl vinyl ethers required as precursors in the carbanion-accelerated Claisen rearrangement would involve allyloxide additions to the corresponding allenes, as in the sulfone series[21]. We therefore began this investigation by preparing allenic phosphorus compounds **1-5**. We chose phosphorus ligands such as diphenylphosphine oxides (pKa~ 24)[34a], phosphonates (pKa~ 28)[34b] and phosphonamides (pKa> 28)[35] which would allow us to survey a broad range of pKa values.

Table II. Synthesis of allenes.



Entry	R^1	R^2	R^3	Allene	Yield(%)[a]
1	Et_2N	CH_3	CH_3	**1**	81.3
2	Ph	CH_3	H	**2**	75.5
3	Ph	CH_3	CH_3	**3**	71.5
4	*t*-BuO	CH_3	H	**4**	78.3
5	*t*-BuO	CH_3	CH_3	**5**	77.3
6	*t*-BuO	-$(CH_2)_5$-		**6**	88.3[b]

(a) Unless otherwise specified, yield refers to isolated product following chromatography, distillation, or recrystallization. (b) Crude recovery; product used without further purification.

The necessary allenes were synthesized by the addition of a propargylic alcohol to the appropriately disubstituted chlorophosphine in the presence of triethylamine followed by a facile [2,3] sigmatropic shift of the phosphite ester.[36] The results are summarized in Table II.

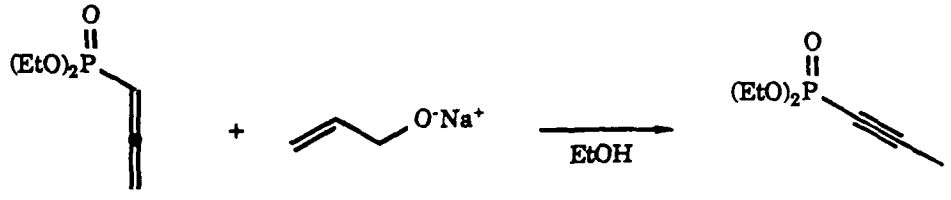
The required chlorophosphines were either purchased (R^1= Et_2N, Ph) or prepared *in situ* from PCl_3 and the appropriate alcohol in the presence of triethylamine.[37] Following the addition of the propargyl alcohol at 5°C, the reaction mixture was warmed to room temperature and stirred overnight. Workup and purification gave the desired allenes in high yield. The cyclohexylidene phosphonate **6** however, decomposed on attempted large-scale vacuum distillation and was used without further purification.

2.1.2. Synthesis of Allyl Vinyl Ethers.

2.1.2.1. Phosphonamides and Phosphine Oxides.

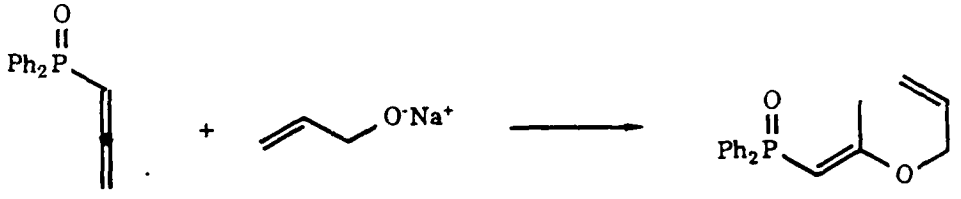
Nucleophilic additions to allenic phosphorus compounds are well known.[38] However, in contrast to allenic sulfones,[39] base-catalyzed equilibration of unsubstituted allenic phosphorus compounds results in exclusive formation of the conjugated acetylenes (Scheme 15).[40a] Therefore, we anticipated that tautomerization prior to addition or isomerization subsequent to addition

Scheme 15



might compete with the formation of the desired β,γ-unsaturated isomers. Indeed, Harmata found that sodium allyloxide addition to allenic diphenylphosphine oxide **XXV** resulted in exclusive formation of the α,β-unsaturated phosphine oxide **XXVI** (Scheme 16).[21] Subsequent treatment of this adduct with KH/HMPA resulted in only a 15% yield of the corresponding Claisen rearrangement product indicating that γ-deprotonation is too sluggish for a useful anionic rearrangement.

Scheme 16



Fortunately, γ-substituted allenes are less prone to undergo this isomerization due to the increased stability of the substituted olefin,[40b,c] and as expected, increased methyl substitution on the allene allowed isolation of the desired β,γ-unsaturated isomers. The results of allyloxide addition to allenes **1**-**5** are shown in Table III.

The optimal conditions for the isolation of desired products varied as a function of temperature, reaction time, stoichiometry of reagents, and the nature of the ligands bound to phosphorus. Addition of stoichiometric amounts of potassium allyloxide at 0°C to allene **1** (entry 1) produced the desired β,γ-allyl vinyl ether **7** in 56.3% yield along with the Claisen rearrangement product **22** and the α,β-unsaturated isomer in 24.2% combined yield. The secondary products most likely resulted from the longer reaction time.[41]

The β,γ-unsaturated phosphine oxides were obtained with catalytic amounts of base. Allyloxide addition to the monomethyl-substituted phosphine oxide **2** (entry 2) using 0.5 equivalents of base resulted in the formation of **8** in only 29.8% yield while similar addition to **2** using a full equivalent of base (entry 3) resulted in formation of the α,β-unsaturated phosphine oxide **9**. Allyl and crotyloxide additions to the dimethyl-substituted allene **3** (entries 4 and 5) produced compounds **10** and **11** in yields of 78.2% and 58.6%, respectively.

The additions to the monomethyl-substituted allene **2** required the most optimization (Table IV). Entries 1 and 2 show the optimal conditions for the synthesis of allyl vinyl ethers **8** and **9**. Note that the only parameter changed was the stoichiometry of the base. Lower temperatures resulted in exclusive formation of acetylenic derivatives (entry 3) while higher temperatures resulted in exclusive formation of **9** (entry 4). Using even less base for a longer reaction time

Table III. Synthesis of Allyl Vinyl Ethers.

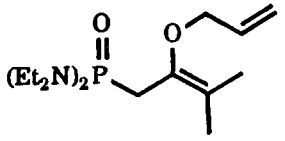
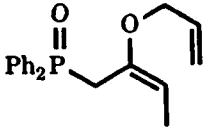
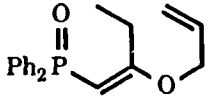
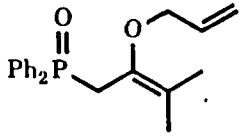
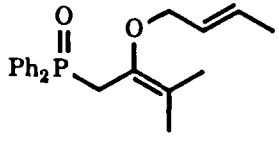
Entry	Allene(conc.)	Equiv. Alc.	Equiv. Base	Time(h)	Temp(°C)	Product		Yield(%)[a]
1	**1**(0.20)	1.1	0.95	8.0	0		**7**	56.3[b]
2	**2**(0.07)	2.0	0.50	0.5	-30		**8**	29.8
3	**2**(0.21)	2.0	1.0	0.5	-30		**9**	47.9
4	**3**(0.19)	1.5	0.22	3.5	0		**10**	78.2
5	**3**(0.10)	2.0	0.26	2.0	0		**11**	58.6

Table III. (continued)

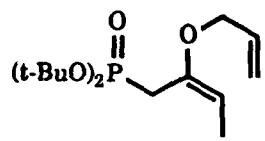
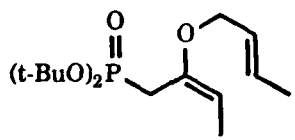
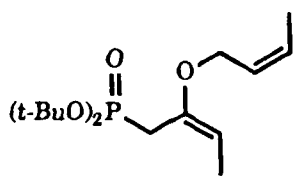
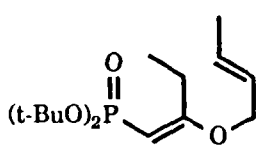
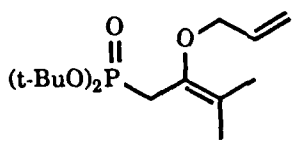
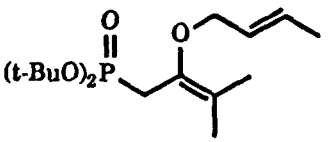
Entry	Allene(conc.)	Eq. Alc.	Eq Base	Time(h)	Temp(°C)	Product		Yield(%)[a]
6	4(0.11)	1.1	1.0	0.25	0		12	69.5
7	4(0.16)	1.1	1.0	0.25	0		13	64.8[c]
8	4(0.11)	1.1	1.0	0.25	0		14	50.9[c]
9	4(0.10)	1.1	1.0	0.25	20		15	56.4
10	5(0.10)	1.1	1.0	2.5	0		16	60.7

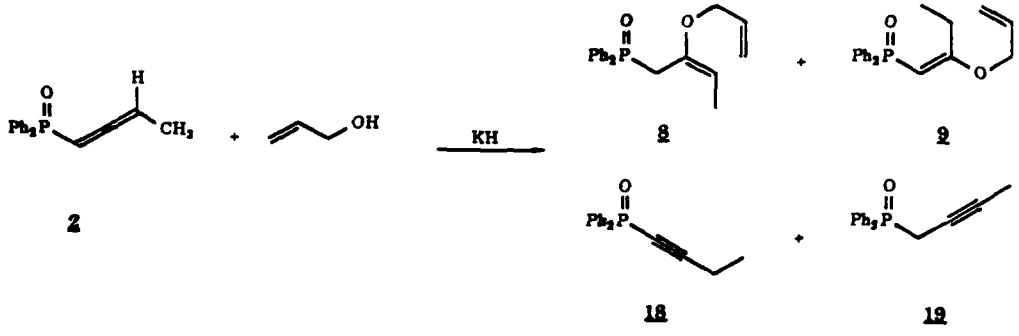
Table III. (continued)

Entry	Allene(conc.)	Eq. Alc.	Eq. Base	Time(h)	Temp(°C)	Product	Yield(%)[a]
11	5(0.10)	1.1	1.0	2.5	0	 17	58.7

(a) All reactions run in THF. Yield refers to isolated product following chromatography. (b) 21 and the α,β-unsaturated allyl vinyl ether was isolated in 24.2% yield. (c) The α,β-unsaturated allyl vinyl ether was isolated in < 5% yield. (d) 29 isolated in 6.5% yield. (e) 30 isolated in 17.0% yield.

(entry 5) resulted in formation of a complex product mixture. It is apparant that the course of the reaction depends on the relative nucleophilicity and the basicity of the allyloxide. Acetylenes are formed at lower temperatures (less nucleophilic, more basic conditions) and the α,β-unsaturated isomer predominates at higher reaction temperatures or longer reaction times (more nucleophilic, less basic conditions). The β,γ-unsaturated derivatives are formed under reaction conditions between these extremes. Unfortunately, it was not always possible to find conditions in which only the β,γ-unsaturated isomer was produced.

Table IV. Allyloxide additions to allenic phosphine oxides.



2 8 9 18 19

Entry	Alcohol(equiv)	KH(equiv)	Time(h)	Temp(°C)	Result
1	2.0	0.5	0.5	-30	8 (29.8%)
2	2.0	1.0	0.5	-30	9 (58.1%)
3	2.0	1.0	0.5	-78	18 only
4	1.0	1.0	0.33	20	9 only
5	2.0	0.34	1.0	-20	18:8:9 (3:3:1)

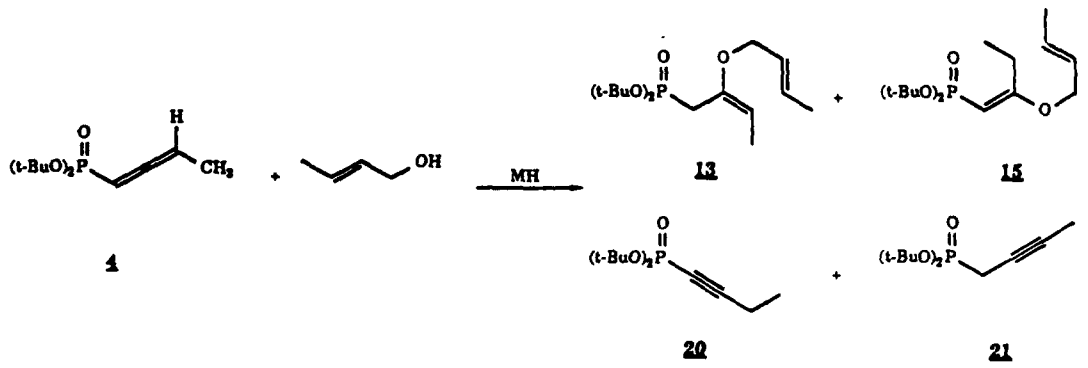
2.1.2.2. Phosphonates.

The results of allyl and crotyloxide additions to allenic phosphonates are also shown in Table III. The di-*t*-butyl phosphonate was employed to lessen the possibility of nucleophilic attack at phosphorus during the addition step.[10] Indeed, in this series, the desired β,γ-unsaturated products could be obtained in good yields with a minimum of secondary product contamination.

Allyl, *trans*-, and *cis*-crotyloxides (entries 6, 7, and 8) were added to the monomethyl-substituted allene **4** at 0°C employing a full equivalent of potassium hydride. The additions occurred rapidly (15 minutes) and gave the desired products in the yields indicated. The α,β-unsaturated isomer **15** (entry 9) was readily prepared by variation of only the reaction temperature (20°C). Allyl and crotyloxide additions to the dimethyl-substituted allene **5** (entries 10 and 11) at 0°C for 2.5 hours gave good yields of the β,γ-unsaturated isomers **16** and **17**.

The conditions described for allyloxide additions to allenic phosphonates were discovered only after extensive optimization. A representative study is shown in Table V. The optimal conditions for the β,γ- and α,β-unsaturated phosphonates **13** and **15** are given in entries 1 and 2. Crotyloxide addition in the presence of 0.23 equivalents of base (entry 3) failed to go to completion.

Table V. Allyloxide additions to allenic phosphonates.



4 **13** **15** **20** **21**

Entry	MH(equiv)	Time(h)	Temp(°C)	Result
1	KH(1.0)	0.25	20	**15** (56.4%)
2	KH(1.0)	0.25	0	**13** (64.8%) **15** (<5%)
3	KH(0.23)	1.0	0	incomplete reaction
4	KH(0.40)	0.75	-20	**13**:**20**:**21**(1:1:1)
5	NaH(0.50)	0.33	0	**21** only

Addition at -20°C with 0.40 equivalents of potassium hydride (entry 4) gave predominantly a mixture of acetylenes **20** and **21**. The use of sodium hydride (entry 5) gave only the unconjugated acetylene **21**.

It should be noted that in contrast to the report of Trippett and Cooper[10] (page 15), no Claisen rearrangement products were detected in any allyloxide addition to an allenic phosphonate.

We have shown that the addition of allyloxides to allenic phosphorus derivatives is a general reaction. The allyl vinyl ethers are obtained in only one step from the allenes, which are synthesized in good yields. Most importantly, stereochemical control of olefin geometry of the vinyl ether moiety in this reaction is assured. This observation may be understood by examination of the molecular orbital picture for nucleophilic addition to an allene (Figure 3). The nucleophilic addition of an alkoxide to a phosphorus-substituted allene may be viewed as a conjugate addition (the orbitals of the allenic carbons involved are those in conjugation with the phosphoryl group). Therefore, the nucleophile can approach from only two available pathways.

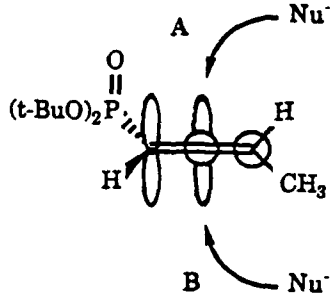


Figure 3. Nucleophilic addition to an allene.

The steric demands of the methyl group (path B) result in allyl vinyl ether formation exclusively through path A (the ^{1}H NMR spectra show only single stereoisomers). This type of stereocontrol has been documented with organocuprate additions to sulfonyl, sulfinyl, and phosphinyl allenes[42] and alkoxide additions to sulfinyl allenes.[43] Homogeneous olefin geometry is critical for internal and relative stereochemical selectivity in the carbanion-accelerated Claisen rearrangement (*vide infra*).

2.1.3. Carbanion Accelerated Claisen Rearrangements.

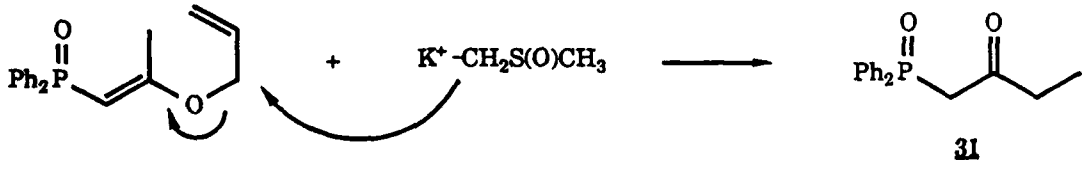
2.1.3.1. Phosphonamides and Phosphine Oxides.

Allyl vinyl ethers **7**-**11** were treated with excess base in a polar aprotic solvent. The results are compiled in Table VI.

Carbanionic rearrangement of phosphondiamide **7** (entry 1) was both slow and messy. The sluggishness is most likely due to the relatively large diethylamino ligands on phosphorus, which slow deprotonation and allow secondary reactions to predominate. Smaller, N-substituted diazaphospholidines rearrange more rapidly and in higher yield.[44]

Deprotonation of β,γ-unsaturated phosphine oxides **8**, **10**, and **11** (entries 2, 4, and 5) at room temperature resulted in rapid Claisen rearrangement (15- 45 minutes) to give products **23**, **24**, and **25**, respectively, in high yield. Carbanionic Claisen rearrangement resulting from γ-deprotonation of the α,β-unsaturated phosphine oxide **9** (entry 3) gave **23** in only 31.5% yield along with the phosphoryl butanone product **31**. In the sulfone series, phenylsulfonylbutanone formation was only observed with crotyl vinyl ethers.[19b] A mechanism involving intramolecular hydrogen abstraction and elimination of butadiene was proposed.[19b,21] Clearly, this is not possible in the rearrangement of phosphine oxide **9**. A plausible pathway may be simply nucleophilic attack of potassium dimsylate at C(4), resulting in direct generation of the stabilized β-ketophosphine oxide anion which is protonated during workup (Scheme 17).

Scheme 17



31

Although encouraged by the results of the carbanion-accelerated Claisen rearrangements of phosphine oxide derivatives, the unacceptably poor yield for the allyloxide addition to

Table VI. Carbanion Accelerated Claisen Rearrangements.

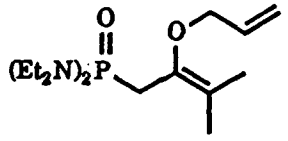
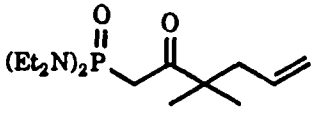
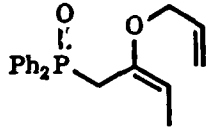
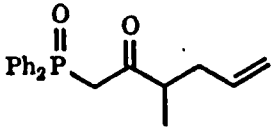
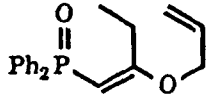
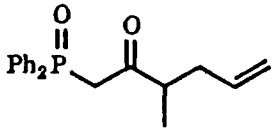
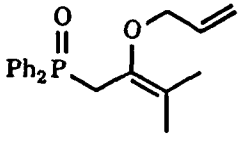
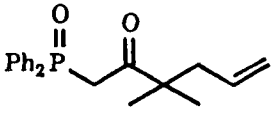
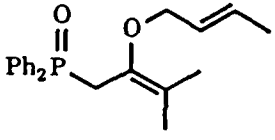
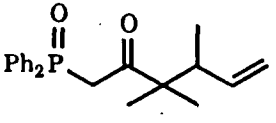
Entry	Substrate[a]		Temp(°C)	Time(h)	Base(equiv)	Solvent	Product		Yield(%)[b]
1		**7**	20	3.0	KH(1.9)	HMPA		**22**	9.9
2		**8**	20	0.75	KH(2.1)	DMSO		**23**	73.7
3		**9**	20	0.75	KH(2.0)	DMSO		**23**	31.5[c]
4		**10**	20	0.25	KH(2.0)	HMPA		**24**	70.5
5		**11**	20	0.25	KH(1.9)	DMSO		**25**	90.5

Table VI. (continued)

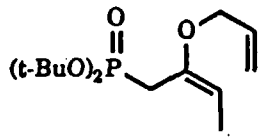
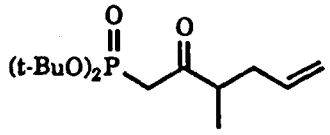
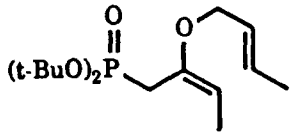
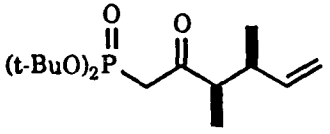
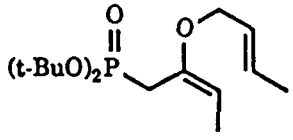
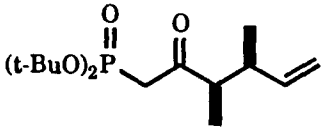
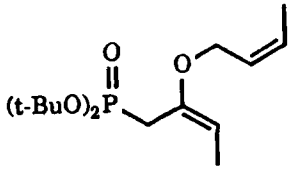
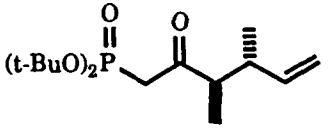
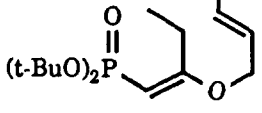
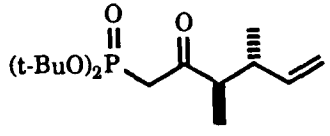
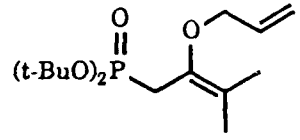
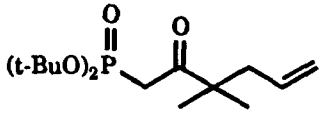
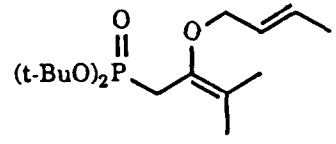
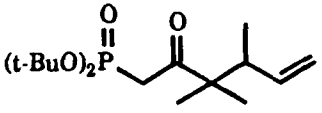
Entry	Substrate[a]		Temp(°C)	Time(h)	Base(eq)	Solvent	Product		Yield(%)[b]
6		**12**	20	0.25	KH(1.9)	DMSO		**26**	84.2
7		**13**	20	0.50	KH(2.1)	DMSO		**27**	92.7
8		**13**	100	10.0	none	THF		**27**	89.8
9		**14**	125	8.0	none	THF		**28**	19.0
10		**15**	20	1.5	KH(2.2)	DMSO		**28**	78.5[d]

Table VI. (continued)

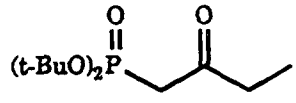
Entry	Substrate[a]		Temp(°C)	Time(h)	Base(eq)	Solvent	Product		Yield(%)[b]
11		**16**	20	0.25	KH(1.7)	DMSO		**29**	85.0
12		**17**	20	0.25	KH(1.8)	DMSO		**30**	91.7

(a) Reactions were run with substrate concentration of ca. 0.1M. (b) Yield refers to isolated yield following chromatography or distillation. (c) Butanone **31** was isolated in 5.4% yield. (d) Butanone **32** was isolated in 4.8% yield.

monomethyl-substituted allene **2** (Table III, entry 2) coupled with the expectation of still poorer yields upon the addition of more sterically encumbered allylic alcohols to allene **2**, led us to concentrate our efforts on the di-*t*-butylphosphonate series.

2.1.3.2. Phosphonates.

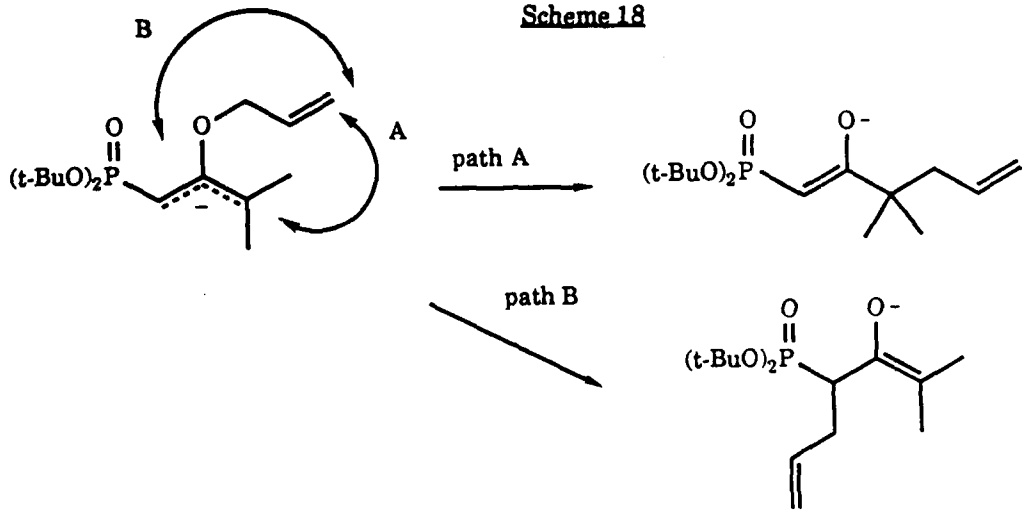
Table VI contains also the results of the carbanion-accelerated Claisen rearrangements of phosphonates **12**- **17** (entries 6, 7, and 10- 12). The rearrangements proceeded rapidly at room temperature and in high yield in the presence of excess potassium dimsylate and LiCl. By comparison, the thermal Claisen rearrangement of **13** (entry 8) in THF requires 10 hours at 100°C for complete reaction. Carbanion-accelerated Claisen rearrangement by γ-deprotonation of α,β-unsaturated phosphonate **15** (entry 10) also proceeded smoothly, although the phosphoryl butanone **32** was also isolated (5%).



32

Importantly, all anionic rearrangements lead to the single regioisomer shown. This observation may be explained by the large pKa difference between the two regioisomeric rearrrangement products[19a] (Scheme 18). Rearrangement through path A leads to a β-keto-

Scheme 18



phosphonate while rearrangement through path B leads to a simple ketone enolate. Based on pKa values, the β-keto phosphonate anion enjoys at least an 11 kcal/mole thermodynamic advantage over a simple ketone enolate.[45] This is such a large difference that only a small amount of product stability (~25%)[46] needs to be manifested in the transition state to account for the observed regioselectivity.

When the results of the carbanion-accelerated Claisen rearrangements of the di-*t*-butyl phosphonates are compared with the results reported by Trippett and Cooper[10], it is clear that the Claisen rearrangement products they isolated (XXIII and XXIV, Scheme 14) are not the result of carbanion-acceleration. Rather, formation of XXIII and XXIV must be the result of a thermal Claisen rearrangement process.[47]

The only limitation we encountered with the phosphorus-stabilized, carbanion-accelerated Claisen rearrangement was with *Z*-substitution at C(6) (compound **14**, entry 9). The chair-like transition state for **14** places the C(6) methyl and the large di-*t*-butyl phosphonate in a 1,3-diaxial position (Figure 4). The conjugate base of **14** could not be induced to rearrange. Thermal rearrangement of **14** afforded **28** in only 19% yield.

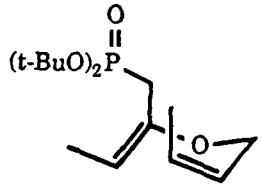


Figure 4. Chair-like transition state for the Claisen rearrangement of **14**.

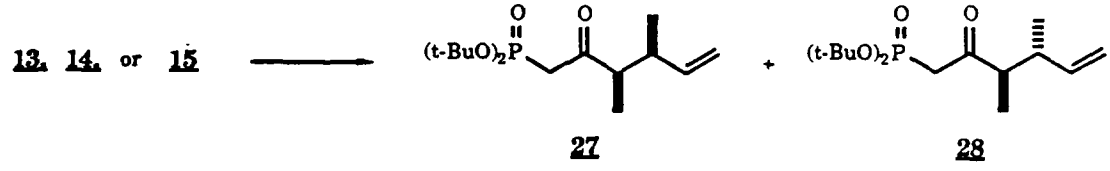
2.1.3.3. Internal Diastereoselectivity.

As in the sulfone series, compounds **27** and **28** were studied in order to determine the internal diastereoselectivity of the phosphorus-based carbanion-stabilizing groups (Table VII).

The ratios in Table VII were determined by integration of the corresponding singlets in the ^{1}H decoupled ^{31}P NMR spectrum. Anionic rearrangement of **13** proceeds with comparable selectivity to the thermal rearrangement and results in a higher yield (entry 2 vs. entry 1).

The problems associated with the rearrangement of **14** already described also account for the lower product diastereomeric ratio, as a severe 1,3-diaxial interaction will permit more rearrangement through a boat transition state. Interestingly, rearrangement of the α,β-

Table VII. Internal Stereoselectivity of Phosphonate Series



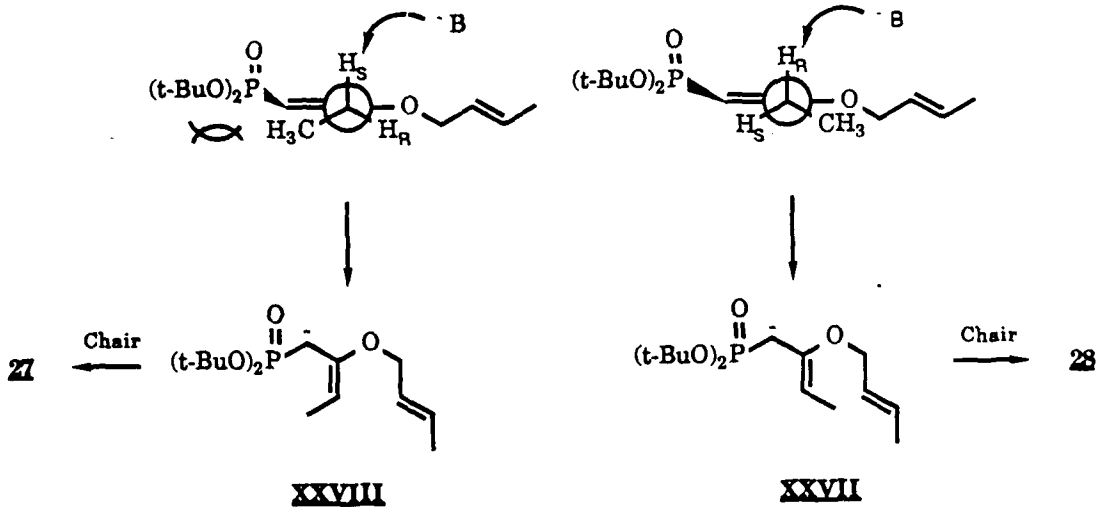
27 28

Entry	substrate	base	solvent	temp(°C)	time(h)	27:28 ratio[a]	yield(%)[b]
1	13	none	THF	100	10.0	93:7	89.9
2	13	KH/LiCl	DMSO	20	0.25	96:4	92.7
3	14	none	THF	125	8.0	14:86	19.0
4	15	KH/LiCl	DMSO	20	0.25	14:86	78.5

(a) Ratios obtained from ^{1}H decoupled ^{31}P NMR (101 MHz) specta. (b) Yield refers to isolated yield following chromatography or distillation.

unsaturated isomer **15** also leads to a 14:86 mixture of **27**:**28** in a 78.5% yield. Assuming an *E* configuration of the vinyl ether double bond and deprotonation occuring from the β-face in Scheme 19, the selectivity is a result of a kinetic preference for the pro-*R* proton. Removal of the pro-*R* proton leads to intermediate **XXVII**, while removal of the pro-*S* proton leads to intermediate **XXVIII**, higher in energy due to greater A-1,3 strain.[48]

Scheme 19

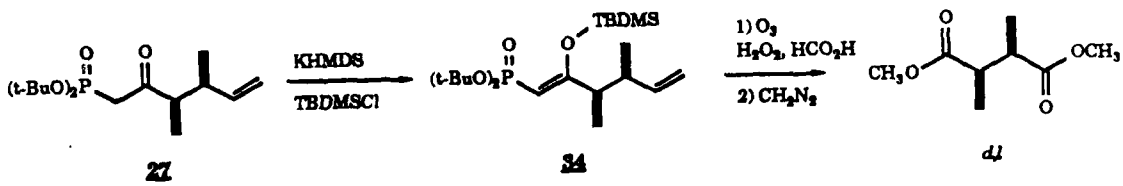


XXVIII XXVII

2.1.3.4. Correlation to Succinic Esters.

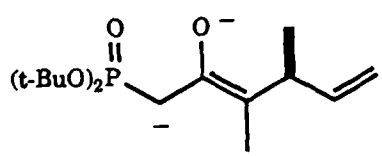
These diasteroemeric ratios were correlated to ratios of *meso* and *d,l*-dimethyl dimethylsuccinates[49] by the chemical transformations shown in Scheme 20. Deprotonation of the Claisen rearrangement product **27** with potassium hexamethyldisilazide (KHMDS) and trapping with *t*-butyldimethylsilyl chloride gave enol ether **34**. Ozonolysis with an oxidative workup[13] (HCO_2H, H_2O_2) gave the *d,l*-succinic acids which were esterified with diazomethane.

Scheme 20



27 **34** *d,l*

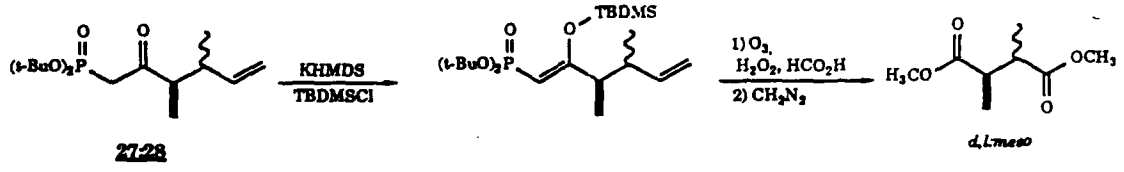
Dianion formation (**XXIX**) is a concern in this sequence since unselective reprotonation of the dianion will alter the diastereomeric ratio of the starting phosphonate mixture. The results of



XXIX

optimization studies are shown in Table VIII. Deprotonation with sodium hydride for 1 hour at room temperature (entries 1 and 2) led to partial epimerization. Deprotonation with KHMDS (entry 3) for 1 minute at room temperature also resulted in partial epimerization. However, treatment of **27**:**28** with KHMDS at low temperature led to deprotonation and subsequent silyation without epimerization.

Table VIII. Formation of silyl enol ethers.



27:**28**

Entry	**27**:**28** ratio	Base	R	Time(min)	Temp(°C)	Result
1	14:86	NaH	$(CH_3)_3C$	60	20	25:75 *meso*:*d,l*
2	92: 8	NaH	$(CH_3)_3C$	60	20	66:34 *meso*:*d,l*
3	92: 8	KHMDS	CH_3	1.0	20	85:15 *meso*:*d,l*
4	92: 8	KHMDS	CH_3	2.0	-78	98: 2 *meso*:*d,l*
5	92: 8	KHMDS	$(CH_3)_3C$	2.0	-78	98: 2 *meso*:*d,l*

The choice of silylating agent is also important. Both TMSCl and TBDMSCl can be used. However, the TMS-enol ether is considerably more labile. Hydrolysis to the starting ketophosphonate is often observed. Neither the TMS- nor the TBDMS-enol ethers survive silica gel chromatographic techniques.

2.1.3.5. Solvent and Counterion Effects.

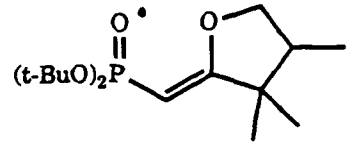
The effects of solvent and counterion were also studied with respect to yield and rate in the phosphorus-stabilized, carbanion-accelerated Claisen rearrangements. The results are shown in Table IX. Carbanionic rearrangement of phosphonate **16** proceeded rapidly and in good yields in

Table IX. Effect of Base and Solvent on Carbanion-Accelerated Claisen Rearrangements

Entry	Substrate[a]	Base[b]	Solvent	Temp(°C)	Time(h)	Product	Yield(%)	By products
1	16	KH/LiCl	DMSO	20	0.25	29	85.0	
2	16	KDA	THF	-70- 0	0.75	29	63.2	Allene 5 (7.6%)
3	16	LDA	THF	-70- RT	0.50	29	67.2	Allene 5 (22.3%)
4	16	KH	HMPA	20	2.0	29	25.0	Furan 33 (11.5%)
5	12	KH/LiCl	DMSO	20	0.25	26	84.2	
6	12	KH	DMSO	20	0.25	26	46.0	
7	13	KH/LiCl	DMSO	20	0.25	27	92.7	
8	13	KH	DMSO	20	0.25	27	62.5	Butanone 32 (1.0%)
9	17	KH/LiCl	DMSO	20	0.25	30	91.7	
10	17	KH	DMSO	20	0.25	30	62.2	

(a) Reactions run at ca. 0.1 M concentration. (b) Equivalents of base ranged from 1.7 to 2.1.

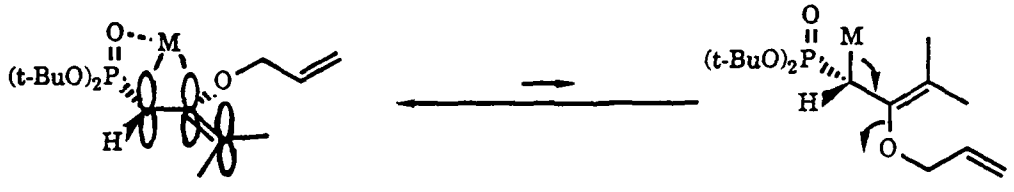
DMSO and THF (entries 1- 3). However, Claisen rearrangement of **16** in KH/HMPA (entry 4) resulted in secondary product formation of furan **33**. A possible mechanism for formation of **33** is an intramolecular nucleophilic attack of the allyl anion on the isolated olefin, although this would result in a primary unstabilized carbanion. A radical mechanism may also be involved.



33

Furthermore, rearrangement of **16** in THF with KDA (entry 2) resulted in β-elimination to give allene **5**. This may be explained by a more covalent metal-anion bond in THF resulting in a decreased contribution from the allyl anion A (Scheme 21). Elimination can then occur from conformation B. Indeed, with phosphonate **16** and LDA (entry 3), an even greater percentage of allene **5** was isolated.

Scheme 21



A B

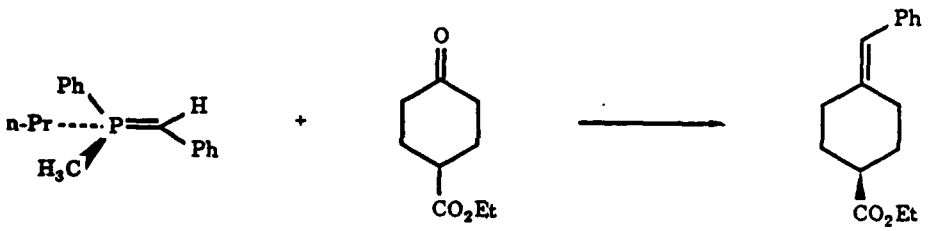
Formation of all undesired products could be suppressed by the use of KH/LiCl/DMSO (compare entries 5, 7, and 9 with 6, 8, and 10). The yields of ketophosphonates **26**, **27**, and **28** were increased 30-40% by the addition of LiCl. The reason for this dramatic jump in yields is not clear, but may involve the suppression of condensation reactions between the dimsylate anion with the allyl vinyl ether or Claisen rearrangement product.

2.2. Chiral Phosphorus Derivatives.

2.2.1. Survey of Ligands.

The success encountered in the di-*t*-butyl phosphonate series encouraged us to proceed onto the next challenge, chiral phosphorus derivatives. The asymmetric induction from phosphorus to carbon has already been documented with olefination reactions. Bestmann[50] showed that olefination of ethyl 4-oxocyclohexane carboxylate with (*R*)-(+)-benzylidine(methyl) phenyl(propyl)phosphorane (**XXX**, Scheme 22) results in the formation of optically active ethyl (+)-4-benzylidinecyclohexane carboxylate (**XXXI**). The observed asymmetric induction is explained by the approach of the electrophile to the less hindered diastereotopic face of the nucleophile.

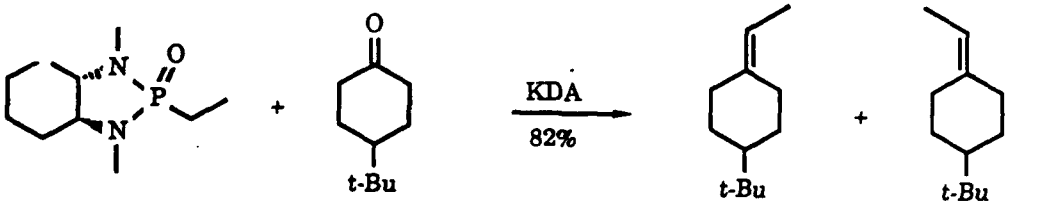
Scheme 22



XXX (+) **XXXI**

Hanessian[51] also demonstrated phosphorus-based asymmetric induction with the diazaphospholidine derivative **XXXII** (Scheme 23). Treatment of the (*S,S*) phosphonamide **XXXII** with KDA and 4-*t*-butylcyclohexanone gave a 95: 5 ratio of **XXXIII** to **XXXIV**. Alternatively, the

Scheme 23

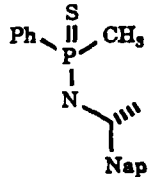


XXXII **XXXIII** **XXXIV**

95 : 5

(*R*,*R*) phosphonamide gave a 5:95 ratio of XXXIII to XXXIV. These anions were also alkylated to give diastereomeric excesses of 80%.

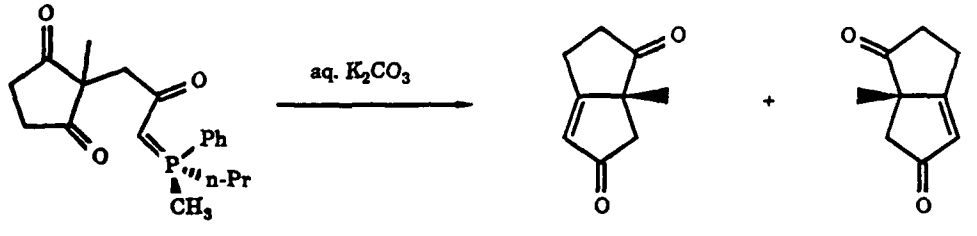
Johnson[52] reported the use of a chiral, nonracemic phosphinothioic amide (XXXV) as a methylenating agent to couple with racemic ketones. The resulting diastereomeric β-hydroxy-phosphinothioic amides were separated and fragmented to give optically pure olefins.



XXXV

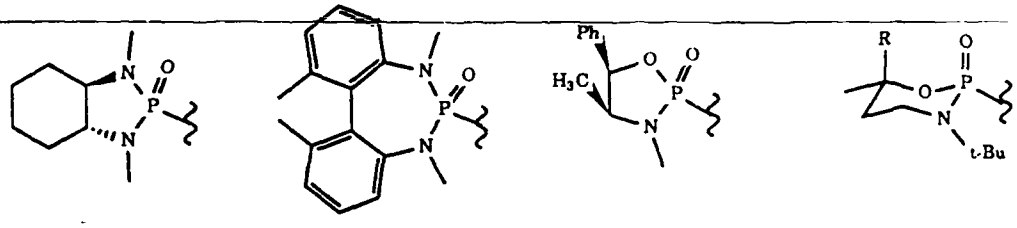
Finally, Trost and Curran[53] reported the intramolecular transfer of chirality from phosphorus to carbon with a Wittig olefination (Scheme 24). Treatment of the phosphonium salt (XXXVI) with aqueous potassium carbonate gave a 65:35 ratio of enediones (XXXVII) and (XXXVIII). In this case, the observed asymmetric induction is attributed to the relative stabilities of the oxaphosphetane intermediates.

Scheme 24



XXXVI XXXVII XXXVIII

From this work, it is clear that reactions of a simple phosphorus-stabilized carbanion can be influenced by the nature of a chiral ligand bound to phosphorus. Our goal was to design and synthesize chiral, anion-stabilizing phosphorus derivatives which would influence the reactions of phosphorus-substituted allyl anions in the context of the Claisen rearrangement. The phosphorus ligands which have thus far been examined in our laboratories are shown in Figure 5.

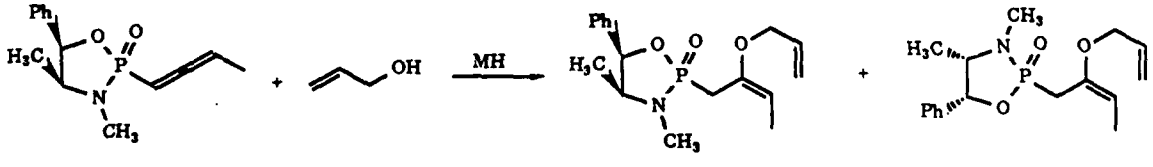


XXXIX XL XLI XLII

Figure 5. Potential anion-stabilizing phosphorus ligands.

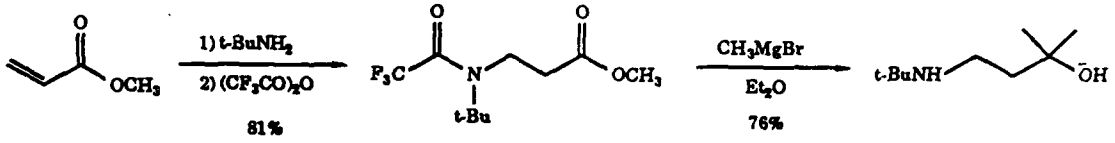
The C_2 chiral diazaphosphorus derivatives XXXIX and XL proved to be superior at the allyloxide addition stage by showing a decreased tendency toward isomerization to acetylenic and α,β-unsaturated addition products.[44] The crystalline allyl vinyl ethers obtained rearranged cleanly as their anions in high yields; the diastereoselectivity, however, was modest at best (69:31 for XXXIX and 75:25 for XL). Allenyl 1,3,2-oxazaphospholidine derivatives XLI were easily prepared in optically active form from *l*-ephedrine by the previously described procedure.[37] Unfortunately, the required allyl vinyl ethers could not be prepared in useful yields from allyloxide additions to allenes. Acetylenic compounds and products arising from oxazaphospholidine ring opening were the major contaminants. Furthermore, a mixture of phosphorus epimers was obtained under conditions which enabled the isolation of the β,γ-unsaturated isomer (Scheme 25). Due to the high reactivity at phosphorus of 1,3,2-oxazaphospholidine derivatives, we concentrated our efforts on the more stable 1,3,2-oxazaphosphorinanes XLII; with respect to diastereoselectivity, these derivatives proved to be the most rewarding.

Scheme 25



Preliminary work was carried out with these compounds using racemic mixtures of oxazaphosphorinanes derived from amino alcohol **36**, which was synthesized as shown in Scheme 26. Conjugate addition of *t*-butylamine to methyl acrylate[54] proceeds smoothly in 91% yield with no bis-addition product detected. Protection of the amine as the trifluoroacetamide **35** (89%) followed by addition of methylmagnesium bromide gave amino alcohol **36** in 76% yield.[55]

Scheme 26

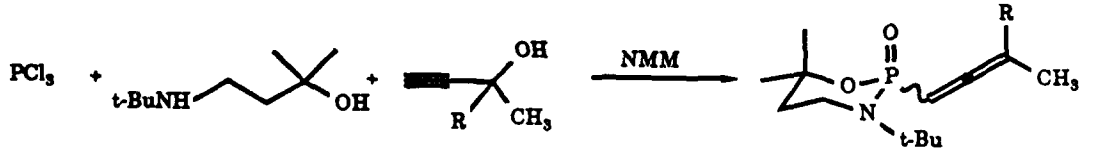


35 **36**

2.2.2. Synthesis of Allenes.

The chiral, phosphorus-substituted allenes were prepared by the addition of the appropriate propargylic alcohol to PCl_3 in the presence of N-methylmorpholine (NMM), followed by addition of the appropriate amino alcohol (Scheme 27).[56] Allene **37** is isolated in 58% yield as an inseparable pair of diastereomers, isomeric about the allene and distinguishable only by ^{13}C and ^{31}P NMR spectroscopy. However, it was not necessary to separate this mixture as both diastereomers lead to the same allyl vinyl ether following allyloxide addition. Allene **38** was isolated in 53% yield as a single diastereomer.

Scheme 27



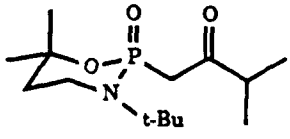
37 R= H 58%

38 R= CH_3 53%

2.2.3. Synthesis of Allyl Vinyl Ethers.

Allyloxide addition to allenyl 1,3,2-oxazaphosphorinanes required extensive optimization. As with the phosphine oxides and phosphonates, the β,γ-unsaturated addition products were at times accompanied by formation of secondary products: acetylenic and isomeric α,β-unsaturated addition products. The required allyl vinyl ethers were obtained in modest to good yields under carefully controlled conditions (Table X). Formation of the β,γ-unsaturated oxazaphosphorinanes **39** and **41** (entries 1 and 3) required the use of sodium allyloxide at room temperature in the presence of *t*-butanol. *t*-Butanol served as a proton source to trap the desired β,γ-unsaturated oxazaphosphorinanes prior to isomerization.

Formation of acetylenic and α,β-unsaturated addition products were not encountered with crotyloxide addition to dimethyl-substituted allene **38** . However, small amounts of butanone **46** and inseparable thermal Claisen rearrangement product **51** invariably accompanied isolation of the desired β,γ-unsaturated oxazaphosphorinane (entry 5).

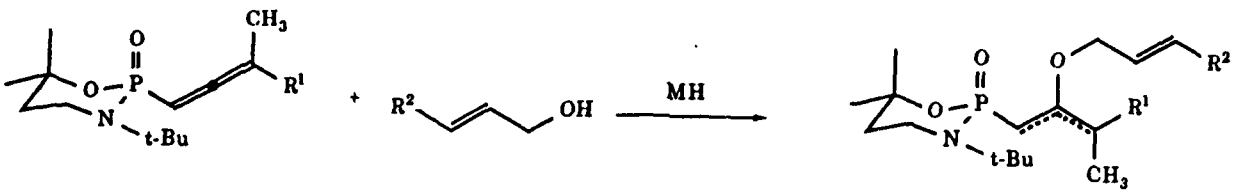


46

The α,β-unsaturated derivatives **40** and **42** (entries 2 and 4) were cleanly prepared at room temperature in the absence of *t*-butanol in high yields by the additions of potassium allyloxide and potassium crotyloxide, respectively.

The mechanism for the formation of the secondary products obtained during allyloxide additions deserves attention (Table XI). Entry 1 shows the optimum conditions for formation of the β,γ-unsaturated oxazaphosphorinane (sodium allyloxide in the presence of *t*-butanol). The α,β-unsaturated oxazaphosphorinane **40** is formed under the most nucleophilic conditions (potassium alkoxide in the absence of t-butanol). Interestingly, even in the presence of t-butanol (entry 3), potassium allyloxide addition resulted in formation of **40** exclusively. Less nucleophilic

Table X. Allyloxide Additions to Allenic Oxazaphosphorinanes.



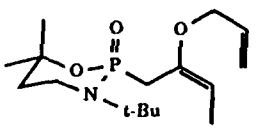
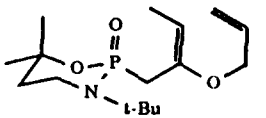
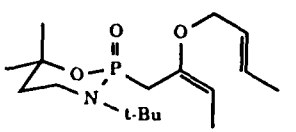
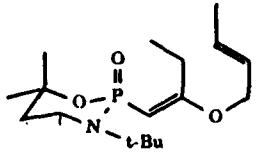
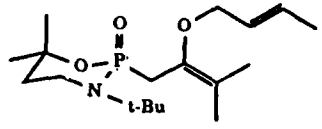
Entry	Allene	R^1	R^2	R^3	MH	t-BuOH(equiv)	Time(h)	Product		Yield(%)[a]
1	37	CH_3	H	H	Na	2.4	.33		39	63.7
2	37	CH_3	H	H	K	0	.50		40	71.4
3	37	CH_3	H	CH_3	Na	2.4	.33		41	46.1

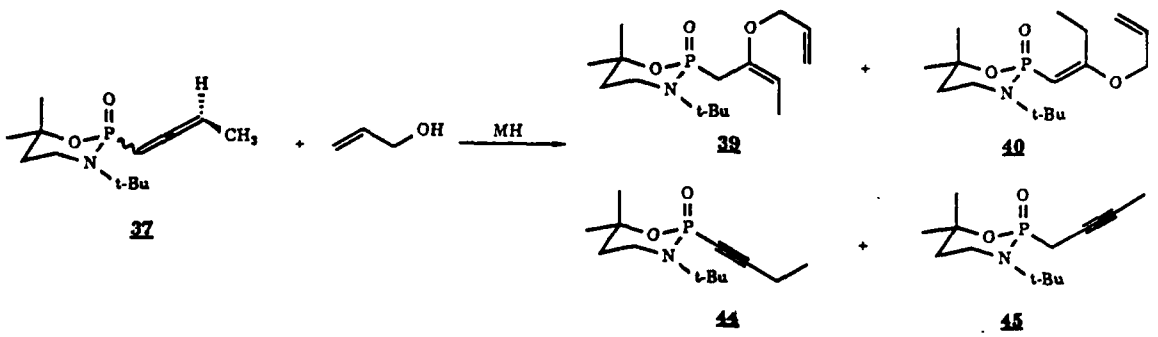
Table X. (continued)

Entry	Allene	R^1	R^2	R^3	MH	t-BuOH(equiv)	Time(h)	Product		Yield(%)[a]
4	37	CH_3	H	CH_3	K	0	.33		42	79.7
5	38	CH_3	CH_3	CH_3	K	0	3.0		43	51.0

(a) Reactions were run in THF (0.1 M). Yield refers to isolated yield following chromatography.

conditions such as colder temperatures (entries 4 and 5) or increased amounts of *t*-butanol (entry 6) increase the amount of base-induced acetylene formation. Formation of 40 may arise *via* one of two pathways (Scheme 28): 1) isomerization of the kinetically formed β,γ-unsaturated isomer or 2) alkoxide addition to the α,β-unsaturated acetylenic derivative. At present, it is not possible to distinguish between the two pathways. In all cases, only one olefin geometry is observed. Thus, generation of β,γ-unsaturated oxazaphosphorinanes depends on a delicate balance between the

Table XI. Optimization of allyloxide addition to allene 37.



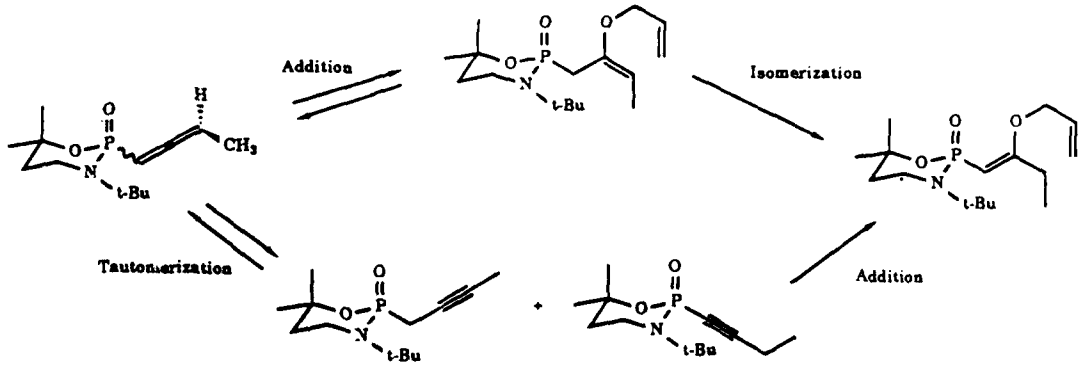
37 39 40 44 45

Entry	MH[a]	t-BuOH(equiv)	Temp(°C)	Time (h)	Result
1	NaH	2.4	20	0.50	39 (63.7%)
2	KH	0	20	0.50	40 (71.4%)
3	NaH	0	-20	3.5	44:45:39 (3:3:4)
4	KH	2.4	0	0.50	44:45:39 (1:1:1)
5	KH	1.8	20	0.25	40 only
6	KH	solvent	20	1.0	44 and 45 only

[a] All reactions were performed with a full equivalent of MH.

nucleophilicity and the basicity of the alkoxide anion. The proper conditions also vary depending on the ligands bound to phosphorus (compare Tables IV, V, and XI) thus making successful alkoxide additions a challenging task.

Scheme 28

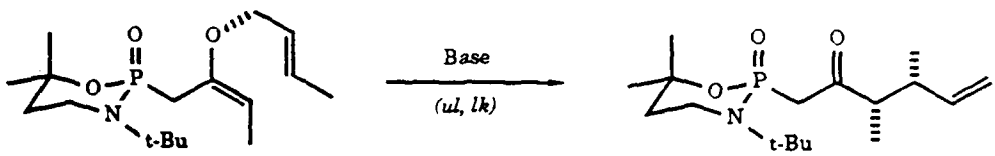


2.2.4. Claisen Rearrangements.

2.2.4.1. Relative Asymmetric Induction.

Two types of asymmetric induction will be discussed with regard to this work. Relative asymmetric induction refers to the allyl anion face selectivity. Internal asymmetric induction refers to the chair/boat transition state selectivity.[57] It is necessary to define two descriptors for use in discussing the transition states leading to the Claisen rearrangement products. For the sake of simplicity, discussion of the transition states of the Claisen rearrangements in the racemic 1,3,2-oxazaphosphorinane series will be limited to those compounds having the *S* configuration at phosphorus. The first descriptor defines the relationship between the configuration at phosphorus and the face of the allyl anion which interacts with the allyloxy chain. Using the terms introduced by Seebach and Prelog,[58] we define *lk* and *ul* as the (*S*, *si*) and (*S*, *re*) pairs, respectively. For example, given the *S* configuration at phosphorus, attack of the allyloxy side chain on the *re* face of the allyl anion (Scheme 29) is an *S*, *re* or *ul* combination. The second descriptor defines a *re-re* (*lk*) or *re-si* (*ul*) carbon-carbon bond forming event. Carbon-carbon bond formation which takes place between the *re*,*re* faces of the allyl anion and the allyloxy side chain as in Scheme 29 is a *lk* combination. Using both descriptors, the Claisen rearrangement depicted in Scheme 29 is described as proceeding with (*ul*, *lk*) topicity.

Scheme 29



The results of the anionic and thermal rearrangements of allyl vinyl ethers **39**-**43** are shown in Table XII. Note that all anionic rearrangements from β,γ-unsaturated oxazaphosphorinanes (entries 2, 3, 6, and 9) are complete in less than 15 minutes at room temperature. This compares to 4 hours at 100°C for complete thermal rearrangement (entries 1, 5, and 8). Entries 1 and 2 indicate that in the Claisen rearrangement of **39** in which a single stereogenic center is generated, the observed diastereoselectivity is poor (58:42 and 52:48, respectively) under both thermal and anionic (KDMSO) conditions. However, the addition of 6 equivalents of LiCl (entry 3) dramatically improved the relative diastereoselectivity to 91:9. Note that in this case, the ratios are a function of anion face selectivity only, i.e., any change in the chair/boat transition state selectivity will not affect the observed product ratio.

Anionic rearrangements of **41** and **43** also show vast improvements in diastereomeric product ratios over the corresponding thermal rearrangements (92:8 vs. 58:42 for **41** and 92:8 vs 68:32 for **43**). In these cases, the observed diastereoselectivity results from both a high anion face selectivity and a high chair/boat selectivity. The internal diastereoselectivity is 98:2 for the anionic rearrangement of **41** and 77:23 for the thermal rearrangement. In the rearrangement of **43**, it is not possible to factor out the internal diastereoselectivity.

2.2.4.2. Assignment of Claisen Rearrangement Products.

The diastereomer ratios of **47**- **50** were measured by integration of the ^{1}H decoupled singlets in the ^{31}P NMR spectra. Assignment of the relative configuration at carbon in the Claisen rearrangement products of racemic 1,3,2-oxazaphosphorinanes is based on work described in

Table XII. Carbanion-Accelerated Claisen Rearrangements

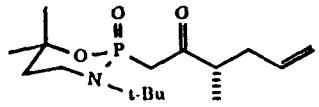
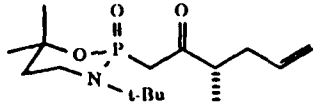
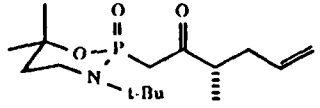
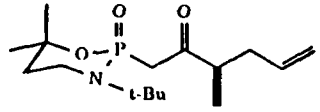
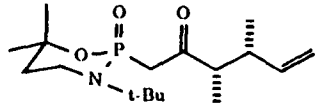
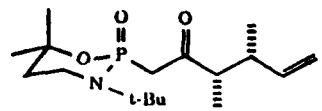
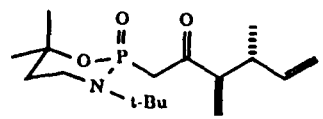
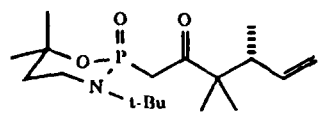
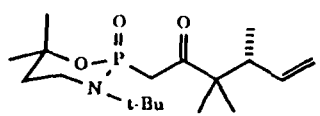
Entry	Substrate	Base	Temp(°C)	Time(h)	Product		Yield(%)[a]	Asymmetric Induction relative	internal
1	39	none	100	4		47	90	58:42	
2	39	KDMSO	20	.25		47	77	52:48	
3	39	KDMSO/LiCl	20	.25		47	81	91:9	
4	40	KDMSO/LiCl	20	1.5		48	21	see text	
5	41	none	100	4		49	84	58:42	77:23

Table XII. (continued)

Entry	Substrate	Base	Temp(°C)	Time(h)	Product		Yield(%)[a]	Asymmetric Induction relative	internal
6	**41**	KDMSO/LiCl	20	.25		**49**	80	92:8	98:2
7	**42**	KDMSO/LiCl	20	3.0		**50**	60	see text	
8	**43**	none	100	4.0		**51**	66	68:32	
9	**43**	KDMSO/LiCl	20	.25		**51**	94	92:8	

(a) *Reactions were run in THF (0.1 M). Yield refers to isolated yield following chromatography or distillation.*

Section 2.2.4.3. The ^{31}P NMR spectrum of **47**, obtained from the anionic rearrangement of the β,γ-unsaturated isomer **39**, is shown in Figure 6a. The major diastereomer results from a *ul* (*S, re*) transition state. The minor signal was identified as a Claisen rearrangement isomer as a result of the anionic rearrangement of the α,β-unsaturated oxazaphosphorinane **40** (entry 4, Table X). Rearrangement of **40** results in the formation of **48** as the major diastereomer (Figure 6b) *via* a *lk* (*S, si*) transition state of the allyl anion of opposite olefin geometry (see section 2.1.3.3). The two diastereomers were also distinguishable by ^{1}H NMR spectroscopy.

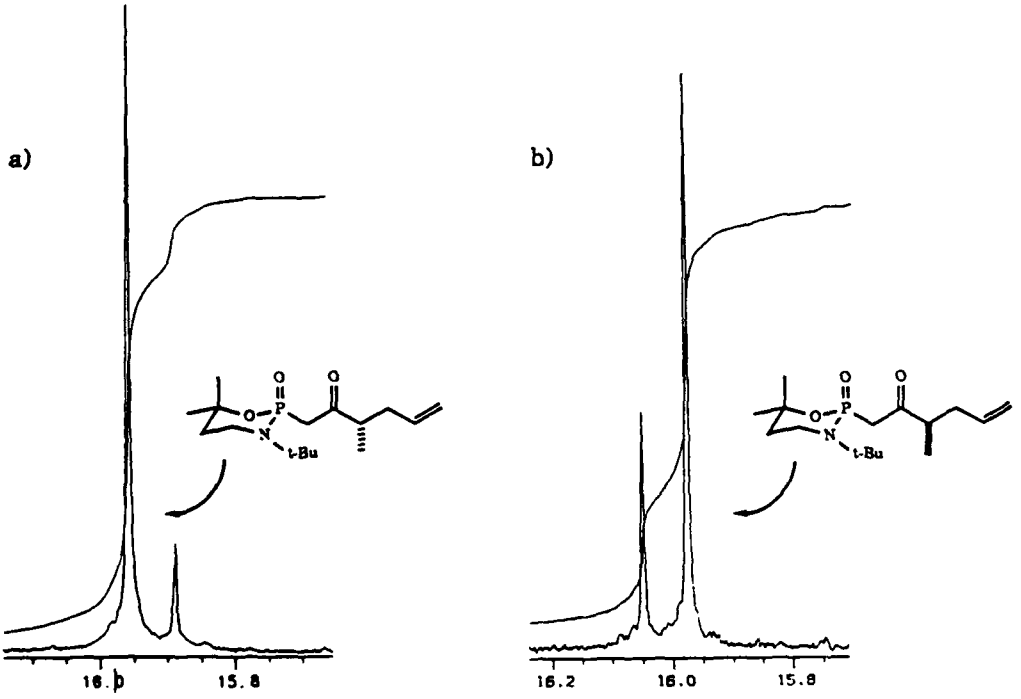
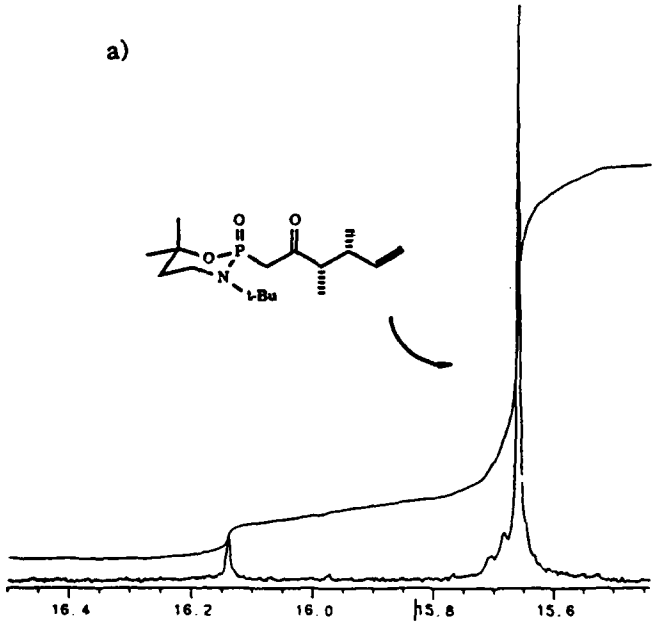


Figure 6. ^{31}P NMR spectrum of a) **47**, b) **48**.

Similarly, the ^{31}P spectrum of **49**, obtained from the anionic rearrangement of the β,γ-unsaturated isomer **41**, is shown in Figure 7a. Since two stereogenic centers are generated, there is a possibility of four distinguishable diastereomers. Integration of the ^{31}P signals in Figure 7a indicates a diastereomer ratio of 7:1:91:1. The major peak (∂= 15.7 ppm) was assigned as the product resulting from a (*ul, lk*) transition state.

Integration of the signals of the ^{31}P spectrum of the products from the anionic rearrangement of the α,β-unsaturated isomer **42** (Figure 7b) indicate a diastereomer ratio of 1:86:5:8. The major diastereomer in this case (**50**, ∂= 16.1 ppm) was assigned to the product resulting from a (*lk, ul*) transition state of the allyl anion of opposite olefin geometry.

The minor diastereomers were identified from the ^{31}P NMR spectrum of a thermal Claisen rearrangement of **41** (Figure 7c) based on the assumption that the two major diastereomers produced would be the *syn*-dimethyl isomers derived from the two possible chair-like transition states. These ratios are summarized in Scheme 30. The relative diastereoselectivities are the sums of the integrals of the products resulting from allyloxy attack on the favored (*re*) allyl anion face vs. allyloxy attack on the disfavored (*si*) allyl anion face, e.g., (*ul, lk*) + (*ul, ul*) vs. (*lk, lk*) + (*lk, ul*) from **41**. The internal diastereoselectivities are then the sums of the integrals of the products resulting from chair-like transition states vs. boat-like transition states, e.g., (*ul, lk*) + (*lk, lk*) vs. (*ul, ul*) + (*lk, ul*) from **41**.



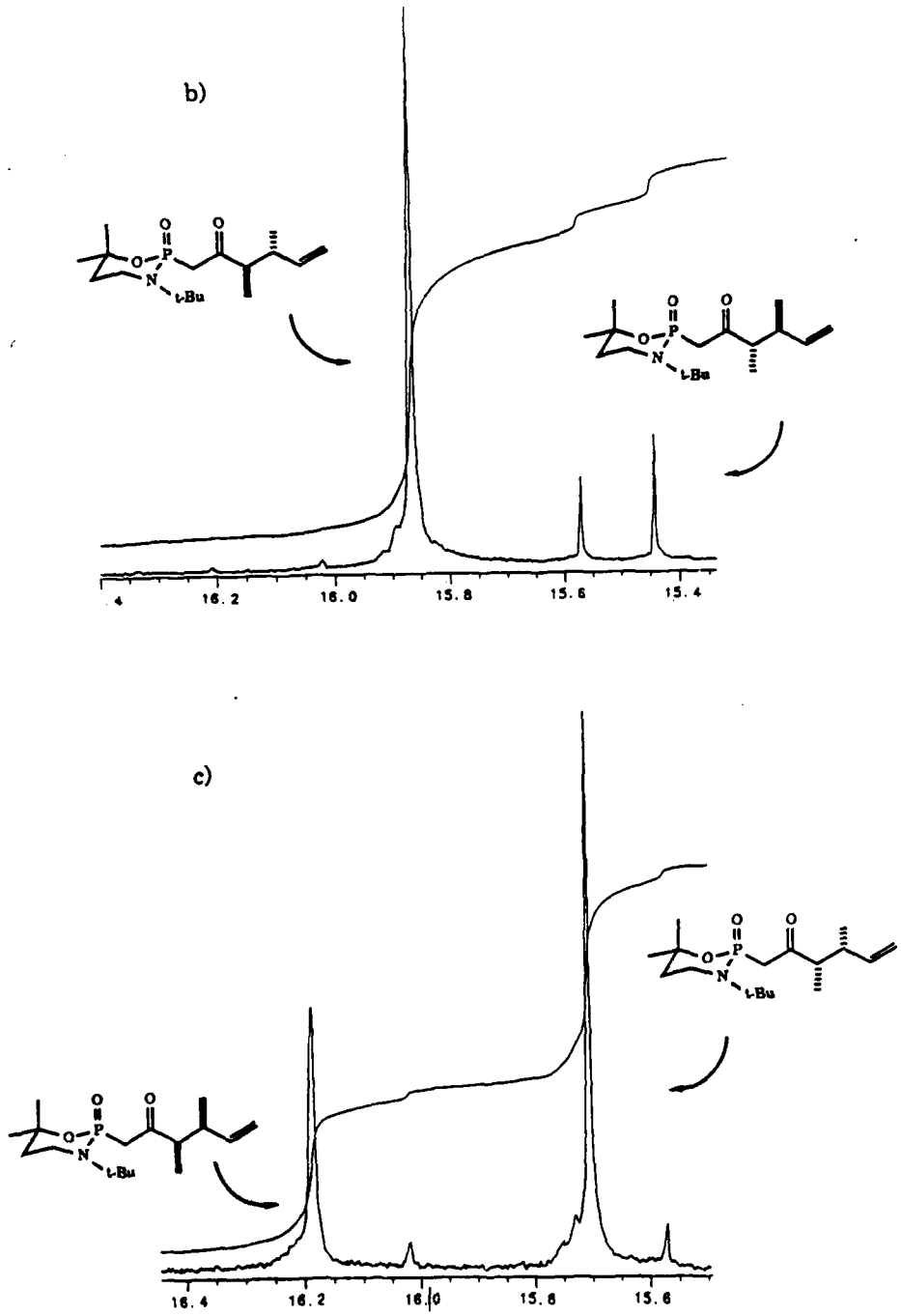
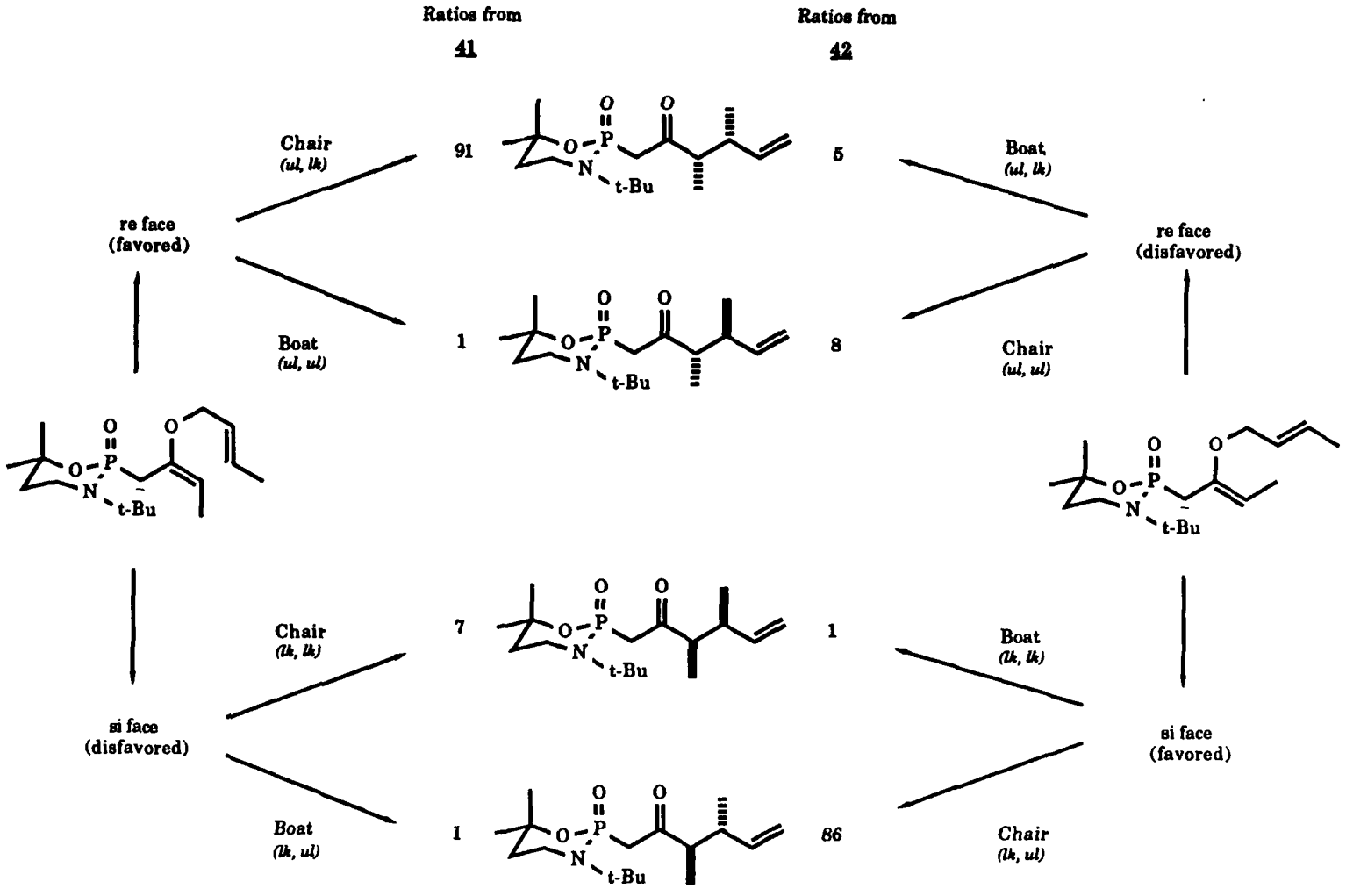


Figure 7. ^{31}P NMR spectrum of a) **49** from the anionic rearrangement of **41**, b) **50**, c) **49** from the thermal rearrangement of **41**.

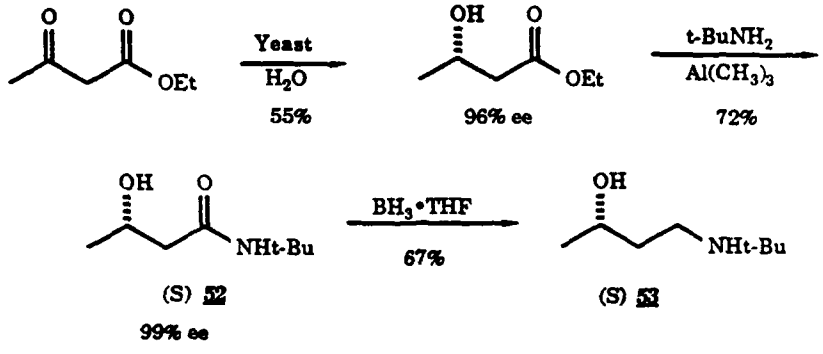
Scheme 30


Ratios from
41
Ratios from
42
Chair
(ul, lk)
91
5
Boat
(ul, lk)
re face
(favored)
re face
(disfavored)
Boat
(ul, ul)
1
8
Chair
(ul, ul)
t-Bu
Chair
(lk, lk)
7
1
Boat
(lk, lk)
si face
(disfavored)
si face
(favored)
Boat
(lk, ul)
1
86
Chair
(lk, ul)

2.2.4.3. Correlation to Succinic Esters.

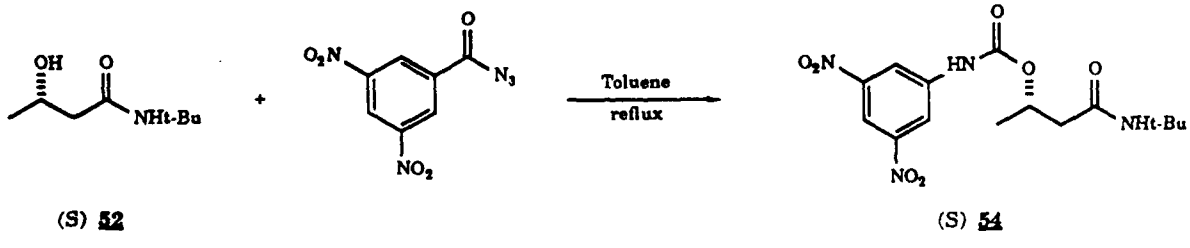
The use of racemic oxazaphosphorinanes would necessarily result in racemic Claisen rearrangement products. While diastereomeric ratios could be measured, it is not possible to determine the sense of relative asymmetric induction from racemic products. It was therefore necessary to synthesize chiral, non-racemic phosphorus derivatives. The amino alcohol **53** was chosen for its structural similarities to **36** and for its ease of preparation. This compound was prepared as shown in Scheme 31. Yeast reduction[59] of ethyl acetoacetate gave (*S*)-ethyl-3-hydroxybutanoate in 96% ee (55% yield). The optical purity was determined by optical rotation and

Scheme 31



G.C. analysis of the Mosher esters.[60] The observed enantiomeric excess is significantly higher than previously reported and can only be explained by the brand of yeast used.[61] Amidation[62] without protection of the hydroxyl moiety followed smoothly to produce hydroxyamide (*S*)-**52** in 72% yield. This reaction required a careful quenching protocol followed by acidification to pH~ 6. At lower pH, β-elimination to the butenamide occurred. The enantiomeric excess was determined by transformation of (*S*)-**52** to the 3,5-dinitrophenyl carbamate[63] derivative (*S*)-**54** as shown in

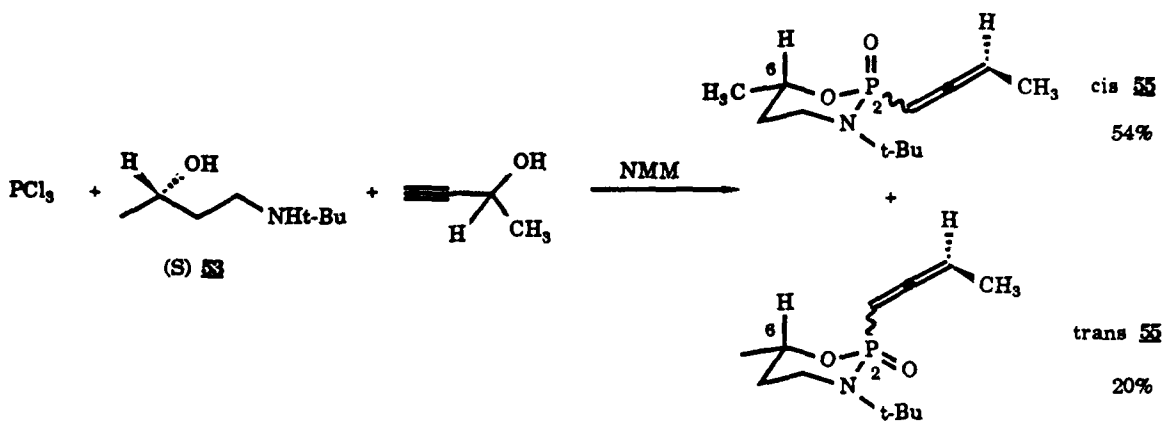
Scheme 32



Scheme 32. HPLC analysis on a Pirkle L-Naphthylalanine column revealed an enantiomeric excess of 98%. Diborane reduction[64] then gave amino alcohol (*S*)-53 in 67% yield.

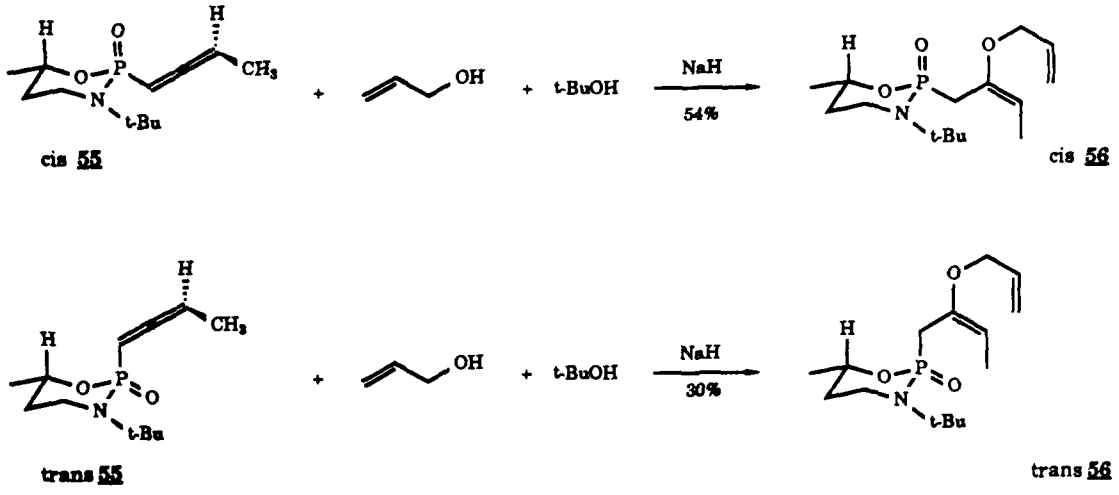
Allene formation from amino alcohol (*S*)-53 and 3-butyn-2-ol generated a mixture of four diastereomers (Scheme 33). From this mixture, diastereomeric allene pairs *cis*-55 (54%) and *trans*-55 (20%) could easily be separated by flash chromatography. Assignment of these phosphorus epimers was tenatively based on the downfield shifts of the C(6) proton in the ^{1}H NMR spectrum and phosphorus in the ^{31}P NMR spectrum of *cis*-55.[65]

Scheme 33



Allyl vinyl ethers *cis*-56 and *trans*-56 were prepared from the corresponding allenes by sodium allyloxide addition in the presence of *t*-butanol (Scheme 34). The formation of acetylenic tautomers was responsible for the low yield in the preparation of *trans*-56.

Scheme 34



Critical to the determination of the sense of the observed diastereoselectivity in the Claisen rearrangement is the assignment of the absolute stereochemistry of the starting allyl vinyl ethers. The tenative assignments made earlier on the basis of ^{1}H and ^{31}P NMR spectroscopic data were confirmed by a single crystal X-ray determination of allyl vinyl ether *cis*-**56** (Figure 8) which shows the *S*-configuration at phosphorus and a *cis* relationship between the C(6) methyl group and the allyl vinyl ether moiety. Also note that the oxazaphosphorinane ring is nearly flat with bond angles between the substituents on nitrogen of approximately 120°. The planarity at nitrogen, in

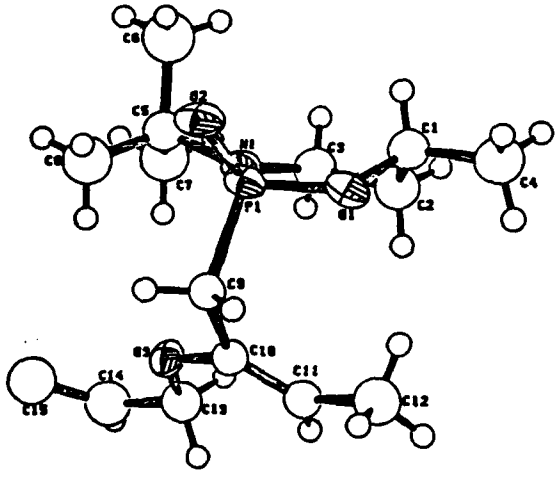
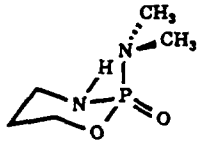
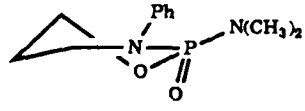


Figure 8. ORTEP drawing of *cis*-**56**.

accord with other reported 1,3,2-oxazaphosphorinanes,[66] stems from the longer P-O and P-N bond lengths which widen the angles between the atoms in the ring. The wider angles also contribute to the flattening of the ring. However, the most important interaction governing the ring conformation is the *geminal*-P(2)-N(3) substitution pattern. Bentrude[67] has shown that N-unsubstituted 1,3,2-oxazaphosphorinanes such as **XLIII** exist predominantly in a chair conformation. However, N-substituted 1,3,2-oxazaphosphorinanes (**XLIV**) exist exclusively in a twist-chair conformation. Clearly, the *geminal*-P(2)-N(3) interactions in *cis*-**56** strongly influence 1,3,2-oxazaphosphorinane ring conformations.



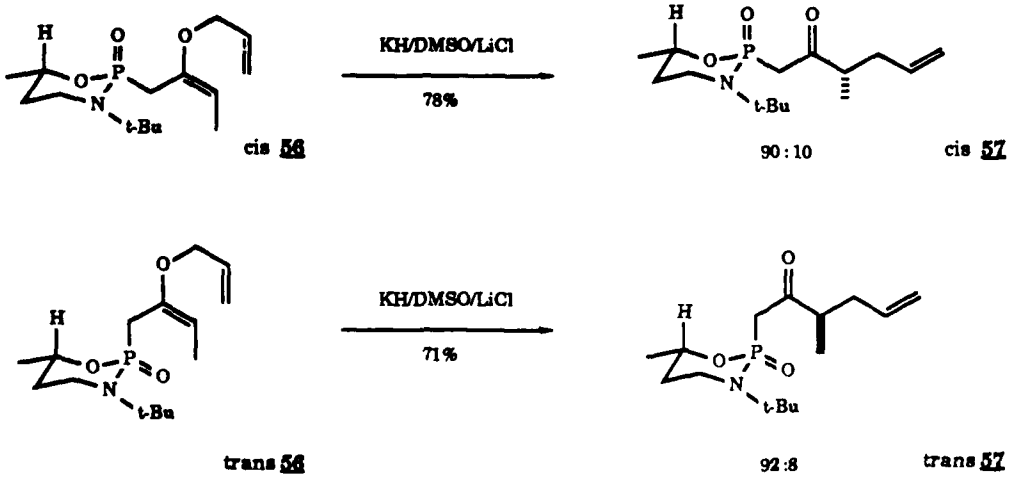
XLIII



XLIV

In order to determine the relative configuration at the newly created stereogenic centers with that of the existing phosphorus center, anionic rearrangements of chiral, non-racemic oxazaphosphorinanes *cis*-**56** and *trans*-**56** were performed (Scheme 35). Again, these anionic rearrangements (KH/DMSO/LiCl) were complete in less than 15 minutes at room temperature and showed comparable degrees of diastereoselectivity. These rearrangement products

Scheme 35

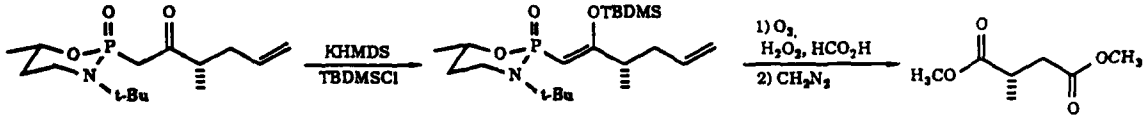


cis **56** cis **57**

trans **56** trans **57**

were degraded to optically active dimethyl methylsuccinates as shown in Scheme 36. Treatment of *cis*-**57** with KHMDS at -78°C and trapping with *t*-butyldimethylsilyl chloride gave the silyl enol ether **58**. Ozonolysis followed by an oxidative work-up gave an enantiomerically enriched ratio of methylsuccinic acids. The acids were esterified with diazomethane in an overall yield from *cis*-**57** of 59%. The same degradation procedure for *trans*-**57** gave a mixture of enantiomeric succinates in 24% overall yield.

Scheme 36



cis **57** cis **58**

We had hoped to determine the absolute configuration of the succinate esters by optical rotation. However, the absolute optical rotation of dimethyl methylsuccinate is quite small.[68] This, coupled with the limited amount of material we had in hand, made the use of optical rotation inappropriate.

Fortunately, the enantiomeric succinates could be distinguished by ^{1}H NMR in the presence of the chiral shift agent (CSA) (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[69] The methyl ester region of a mixture of racemic succinate and the CSA is shown in Figure 9a. Assignment of the observed peaks followed from the methyl ester region of the ^{1}H NMR spectrum of the racemic succinate enriched with authentic *R* succinate[70] and the CSA (Figure 9b). Thus, the ^{1}H NMR spectrum of the enantiomeric mixture of succinates from the degradation of *trans*-**57** and the CSA revealed that the major enantiomer has the *R* configuration (Figure 9c). Similar CSA studies with the enantiomeric mixture of succinates from the degradation of *cis*-**57** reveal that the major enantiomer has the *S* configuration.

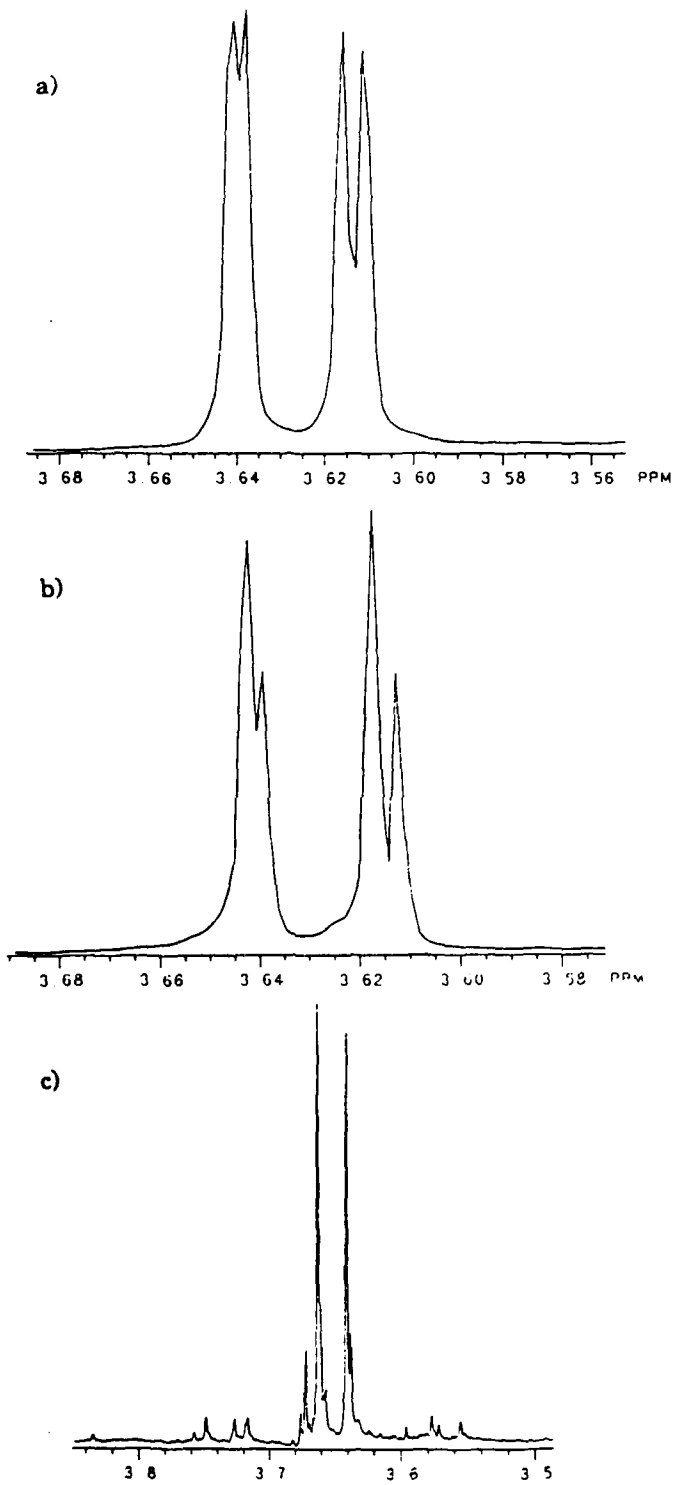
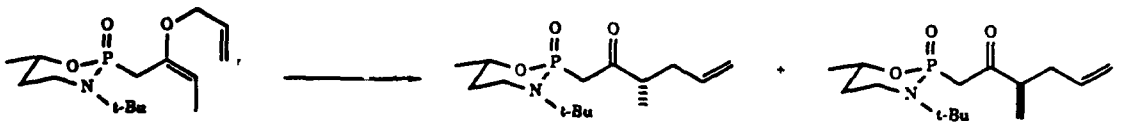


Figure 9. ^{1}H NMR Spectrum of chiral shift agent and a) racemic succinates, b) racemic succinate enriched in the *R* enantiomer, and c) succinates from the degradation of *trans*-**57**.

2.2.4.4. LiCl Effect.

The effect of LiCl on the anionic Claisen rearrangement on *cis*-**56** was also studied (Table XIII). In the absence of LiCl, there is no observed asymmetric induction in the anionic Claisen rearrangement of (entry 1). As the amount of LiCl is increased from 1-6 equivalents (entries 2-4), the diastereomeric ratios improved from 65:35 to 90:10. No further increase in selectivity is observed with additional equivalents of LiCl (entry 5). Note also that LiDMSO prepared from *n*-BuLi and DMSO in THF also results in high relative asymmetric induction Thermal rearrangements, in the presence or absence of LiCl show poor selectivities (entries 7 and 8).

Table XIII. LiCl Effects.



cis **56**

Entry	Base	LiCl(equiv)	Temp(°C)	Yield(%)	Relative Asymmetric Induction
1	KDMSO	0	20	62	50:50
2	KDMSO	1	20	77	65:35
3	KDMSO	2	20	69	80:20
4	KDMSO	6	20	78	90:10
5	KDMSO	12	20	65	89:11
6	LiDMSO	0	20	65	90:10
7	none	0	100	93	66:34
8	none	6	100	90	64:36

2.3. Proposed Transition States.

It is clear that ligand, anion structure, counterion effects, and conformational preferences are crucial to phosphorus-induced diastereoselectivity. We propose two limiting models to explain

relative stereocontrol in the carbanion-accelerated Claisen rearrangement, each possessing various steric and electronic properties which can be used to promote asymmetric induction. The first model, shown in Figure 10, includes the following characteristics: 1) a planar carbanion with the π-system aligned parallel to the P=O bond, 2) a strong O-Li interaction to minimize steric interaction between the allyl vinyl ether and the larger ligand bound to phosphorus, 3) anion delocalization to prevent rotation about the carbon-carbon bonds, 4) a steric preference of oxygen vs. methyl toward the phosphorus group, and 5) a stereoelectronic diastereofacial preference of attack by the allyloxy side chain on the allyl anion.

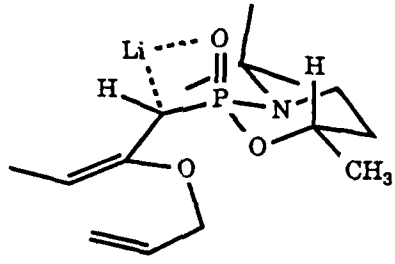


Figure 10. Parallel anion model.

With regard to this model, the strong preference for the *ul* transition state in the anionic rearrangement of 1,3,2-oxazaphosphorinanes in the presence of a Li^+ counterion demands that the new carbon-carbon bond is formed *anti* to the Li^+ counterion as portrayed in Figure 10.[71] The minor diastereomers (*lk* transition state) would then arise from carbon-carbon bond formation *syn* to the Li^+ counterion. Furthermore, inspection of Dreiding models clearly indicates that with a planar carbanion aligned parallel to the P=O bond, rotation about the P-C bond or the allyl anion carbon-carbon bond is disfavored due to severe steric congestion with the 1,3,2-

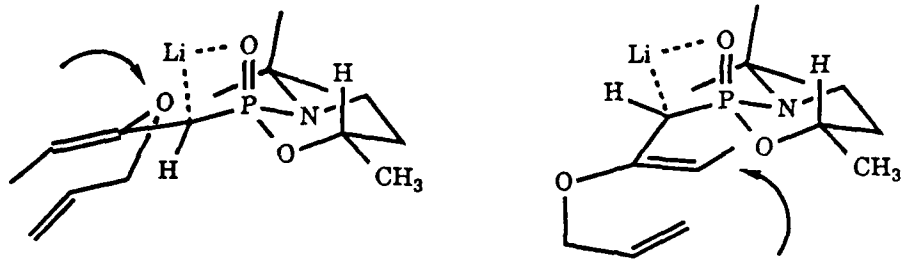


Figure 11. Alternate parallel anion conformations.

oxazaphosphorinane ring (Figure 11). Therefore, the primary factor which contributes to the observed diastereoselectivity in this model is the *stereoelectronic preference* for carbon-carbon bond formation *anti* to the Li^+ counterion.

The second model (Figure 12) possess the following characteristcs: 1) a planar carbanion with the π-system aligned perpendicular to the P=O bond, 2) Li^+ chelation to both the phosphoryl and vinyl ether oxygens, and 3) a *sterically directed, diastereofacial preference* of attack by the allyloxy side chain on the allyl anion.

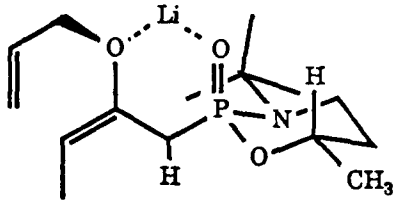
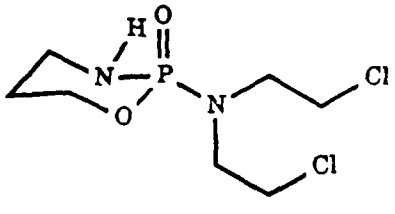


Figure 12. Perpendicular anion model.

With regard to this model, the strong preference for the *ul* transition state in the anionic Claisen rearrangements of 1,3,2-oxazaphosphorinanes is a result of approach of the allyloxy side chain to the sterically less hindered side, i.e., away fron the large *N*-*t*-butyl group.

Evidence for a perpendicular anion comes from X-ray structure determination data. Unfortunately, X-ray structures of phosphorus-stabilized allyl anions have yet to appear in the literature. However, for 1,3,2-oxazaphosphorinanes containing phosphorus-bound dialkylamino substituents in equatorial or pseudoequatorial positions (**XLV**), the dialkylamino group is invariably planar with the lone pair on nitrogen oriented perpendicular to the P=O bond.[67]



XLV

This geometry and the planarity at the exocyclic nitrogen have been explained by π-donation to an empty phosphorus d-orbital[72] or a π-interaction with an endocyclic P-O σ* orbital.[73]

However, evidence against a perpendicular anion includes the fact that LiCl had no effect in the diastereoselectivity in the thermal Claisen rearrangement of *cis*-56 (Table XIII, entries 6 and 7). One would expect that if any charge separation develops in the transition state of the thermal Claisen rearrangement, as has been proposed,[14, 9a] the added LiCl would chelate and the diastereomeric ratios would improve. Furthermore, the X-ray structure of 1,3,2-oxazaphosphorinane with an axial dialkylamino group (XLIII, page 55) shows that the exocyclic nitrogen is now pyramidal and the lone pair is parallel to the P=O bond. The perpendicular geometry is disfavored because of steric interactions of the N-alkyl groups and the axial ring protons.

Note that the carbanion-accelerated Claisen rearrangements of *cis*-56 and *trans*-56 show high levels of diastereoselectivity. The high diastereoselectivity observed with *trans*-56 is particularly noteworthy. In a chair-like ring conformation, the allyl vinyl ether would have an

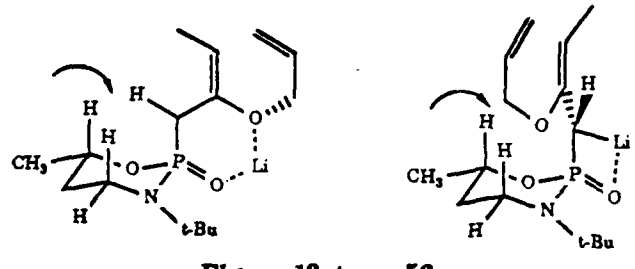
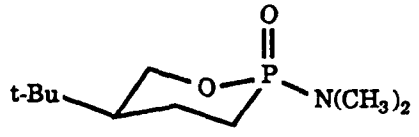


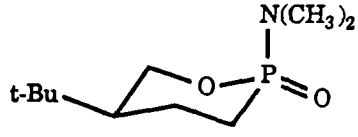
Figure 13. *trans*-56.

axial orientation. In this case, both models indicate strong steric interaction with the oxazaphosphorinane ring (Figure 13). Therefore, regardless of the allyl vinyl ether conformation, it is likely that *trans*-56 adopts a twist-boat conformation such that the allyl vinyl ether is oriented in a pseudoequatorial position.

Unfortunately, there is no simple way to distinguish between these two limiting proposals. An X-ray structure determination of a phosphorus-stabilized allyl anion would provide unambiguous structural information about the anion in the solid state. Information on the structural characteristics of phosphorus-stabilized allyl anions in solution could be gathered by ^{1}H, ^{7}Li, ^{13}C, and ^{31}P NMR studies of phosphorus-stabilized allyl anions. As mentioned earlier, a data base is currently being gathered in these laboratories.[31] These data could be compared to those for *trans*- and *cis*-1,2-oxaphosphorinanes **XLVI** and **XLVII**. Deprotonation should give phosphorus-stabilized anions in the parallel and perpendicular conformations, respectively.



XLVI



XLVII

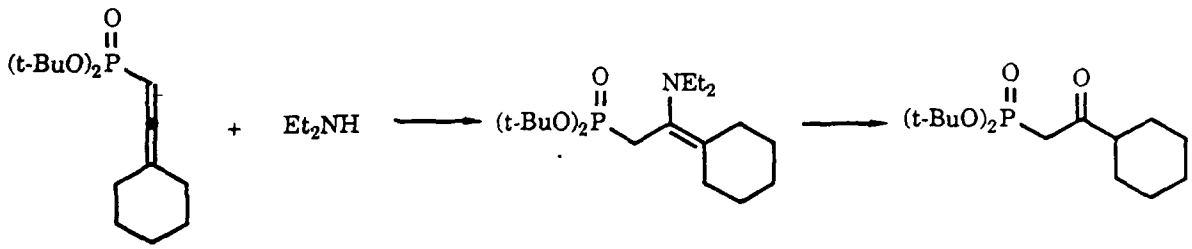
Trapping of the anions with electrophiles and noting the diastereoselectivity may provide evidence for the favored conformation of anions stabilized by 1,3,2-oxazaphosphorinanes.

2.4. Phosphorus-Carbon Bond Cleavage.

A more practical approach in the degradation of Claisen rearrangement products to compounds of known absolute and relative stereochemistry involves the direct cleavage of the phosphorus-carbon bond. Although sulfur-carbon bonds are easily cleaved by amalgams[74] and other methods,[75] phosphorus-carbon bond cleavage reactions of β-ketophosphono compounds have not been reported.[76]

Reductive cleavages were investigated using the model compound **60** which was prepared *via* enamine **59** (Scheme 37). The enamine was prepared by heating allene **6** in diethylamine at 120°C for 16 hours in a sealed tube.[38c] The crude enamine is hydroyzed during flash chromatography to afford ketophosphonate **60** in 51% yield.

Scheme 37



6 59 60

The results of attempted phosphorus-carbon bond cleavage reactions are shown in Table XIV. All attempts at Zn/HOAc[77] and dissolving metal reduction[75c, 78] resulted in either decomposition of 60 (entries 1- 3) or carbonyl reduction to the corresponding hydroxyphosphonate (entries 5,6).

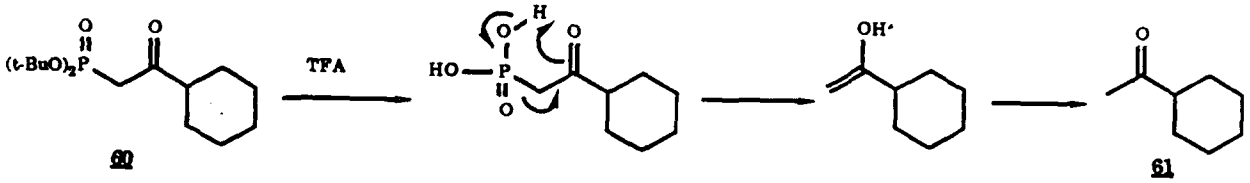
Table XIV. Phosphorus-Carbon Bond Cleavage Reactions.

60 61

Entry	reagents(eq)	temp(°C)	solvent	time(h)	comments
1	Zn(7.5)	reflux	AcOH	1.5	decomposed
2	Zn(6.0)	70	AcOH	2.0	decomposed
3	Li/Naphthalene	-70-RT	THF	2.0	4 products, TLC
4	TFA/LTA(1.0)	80	DMF	1.5	Decomposed
5	Li(10)	20	*n*-$PrNH_2$	20	C=O reduction, TLC
6	Li(11)	20	$(CH_2NH_2)_2$	0.5	60 + C=O reduction
7	TFA(6)	20	THF	0.5	61 formed upon distillation (78.3%)

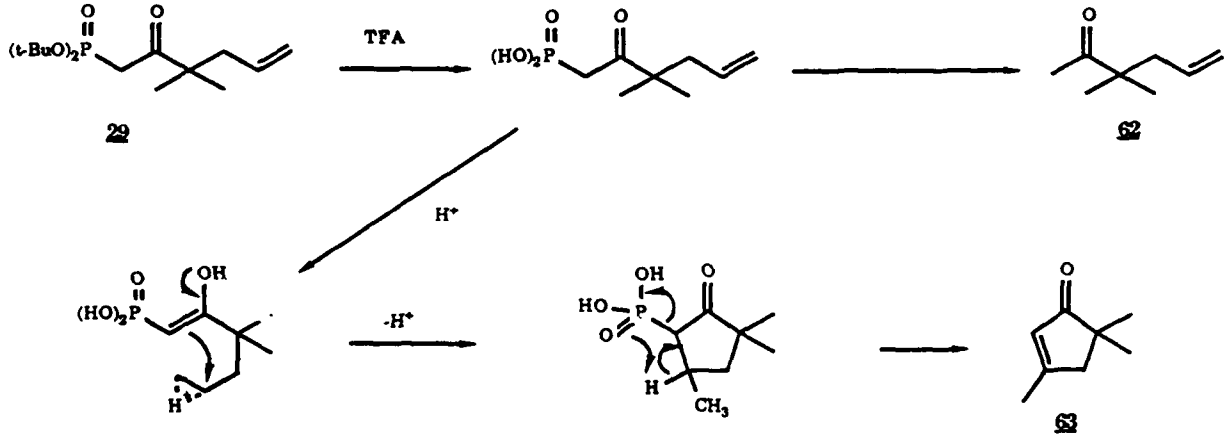
Hydrolysis of **60** with trifluoroacetic acid (TFA) and treatment with lead tetraacetate[76d] (LTA) also led to decomposition (entry 4). However, hydrolysis of **60** with excess TFA (entry 7) followed by distillation of the resulting β-keto phosphonic acid at atmospheric pressure did yield cyclohexyl methyl ketone, a phosphorus-carbon bond cleavage product (Scheme 38).

Scheme 38



However, treatment of ketophosphonate **29** with trifluoroacetic acid resulted in a 53.9% combined yield of ketones **62** and **63** in a 1:1 ratio (Scheme 39). Although the proposed mechanism

Scheme 39



was not rigorously proven, formation of **63** probably occurs via attack of the enol on the isolated olefin in acid medium followed by elimination of phosphorous acid. Furthermore, it is likely that stereogenic centers, such as in **27**, would epimerize under acidic conditions at elevated temperatures.

As mentioned previously, other avenues are currently being investigated in these laboratories which explore phosphorus-carbon bond cleavage reactions.[33]

CHAPTER 3

SUMMARY

The carbanion-accelerated Claisen rearrangement is efficiently promoted by several phosphorus anion-stabilizing groups. The required allyl vinyl ethers were synthesized by the nucleophilic addition of allyloxides to phosphorus-substituted allenes. Although secondary product formation can occur, this method establishes the geometry of the vinyl ether double bond.

Treatment of the allyl vinyl ethers with excess base in a dipolar aprotic solvent at room temperature resulted in rapid regio- and stereoselective rearrangements to β-ketophosphono derivatives. The internal diastereoselectivity was examined in the di-*t*-butyl phosphonate series. Rearrangement under anionic and thermal conditions were found to give comparable ratios of diastereomers.

The phosphorus-stabilized, carbanion-accelerated Claisen rearrangement was shown to proceed through a chair-like transition state by correlation of the Claisen rearrangement products to *meso* and *d,l* dimethyl dimethylsuccinates. A new method for this degradation was found which involves formation of silyl enol ethers from the Claisen rearrangement products followed by ozonolysis to the dimethylsuccinic acids.

Asymmetric induction using chiral phosphorus anion-stabilizing groups was demonstrated in the context of the Claisen rearrangement. We have observed high levels of diastereoselectivity in the carbanion-accelerated Claisen rearrangement of 1,3,2-oxazaphosphorinane derivatives. The observed asymmetric induction is a function of both internal and relative diastereoselectivity and is highly dependent on the counterion used. The sense of asymmetric induction was established by degradation of the chiral, non-racemic Claisen rearrangement products to (*R*) and (*S*) dimethyl methylsuccinates.

In general, attempted reactions aimed at cleaving the phosphorus-carbon bond were unsuccessful. Only at elevated temperatures in a highly acidic medium were phosphorus-carbon bond cleavages observed.

This work is highlighted by the asymmetric induction observed in the carbanion-accelerated Claisen rearrangement of chiral phosphorus anion-stabilizing groups. However, information on the nature of the phosphorus-stabilized allyl anions is still lacking. With the continued accumulation of knowledge in regard to these anions is sure to come additional advances in mechanistic and synthetic applications in organophosphorus chemistry.

CHAPTER 4

EXPERIMENTAL SECTION

4.1. General Information.

^{1}H NMR spectra were recorded on a Varian XL-200 (200 MHz), General Electric GE 300 (300 MHz), Nicolet NT-360 (360 MHz) or General Electric GN 500 (500 MHz) spectrometer with tetramethylsilane (0.0 ppm) or chloroform (7.26 ppm) as an internal reference in $CDCl_3$ solutions. Chemical shifts are given in ppm (∂) and multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) followed by a *J* (coupling constant) given in hertz. Data are presented in the form: chemical shift (multiplicity, integrated intensity, coupling constant, assignment). ^{13}C NMR spectra were recorded on a General Electric GE 300 (75.5 MHz) or General Electric GN 500 (125.8 MHz) spectrometer with $CDCl_3$ (77.0 ppm) as an internal reference in $CDCl_3$ solutions. ^{31}P NMR spectra were recorded on a Nicolet 250 (101.3 MHz) or General Electric GE 300 (121.4 MHz) spectrometer in acetone solutions with 85% phosphoric acid as an external reference. Infrared spectra were obtained on a Perkin Elmer 1320 or IBM IR-32 FT infrared spectrometer as a neat liquid, $CHCl_3$ solution or CCl_4 solution. Peaks are reported in cm^{-1} with s, m, and w corresponding to strong (66-100%), medium (33-66%) and weak (0-33%), respectively. Mass spectra (EI) were obtained on a Finnigan MAT CH-5 spectrometer with an ionization voltage of 10 or 70 eV. Data are reported in the form m/z (intensity relative to base=100). High resolution mass spectra (EI) were obtained on a Finnigan MAT 731 spectrometer. High resolution mass spectra (FAB) were obtained on a VG-ZAB-HF spectrometer. Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory. Melting points were obtained on a Thomas Hoover capillary melting point apparatus in evacuated capillary tubes and are corrected. Analytical TLC was performed by using 0.25 mm silica gel plates (Merck) with F-254 indicator. Visualization was accomplished by UV light, iodine, and/or ethanolic solutions of sulfuric acid and vanillin. Flash chromatography[79] was performed by using 30-60 μm silica gel (Woelm) with technical grade hexane (distilled from anhydrous $CaCl_2$) and ethyl acetate (distilled from anhydrous K_2CO_3). Reagent grade benzene and acetone were used as received

from commercial sources. Radial chromatography was performed on a Harrison Research Chromatotron using either 1, 2, or 4 mm SiO_2 rotors. Analytical HPLC was performed on a Hewlett Packard 1090 Liquid Chromatograph and a Perkin Elmer LC-75 Spectrophotometric Detector (variable UV). The column used was a Pirkle Covalent L-Naphthylalanine 5μ column. Retention times (R_t) and integrated ratios were obtained from a Hewlett Packard 3390A integrator. Solvents for HPLC were distilled in glass or UV grade and filtered immediately prior to use. Analytical gas chromatography was conducted on a Varian Model 3700 chromatograph fitted with a flame ionization detector (H_2 carrier gas, 1 mL/min, cOV-17 capillary column). Optical rotations were obtained on a Jasco DIP-360 Digital Polarimeter and are reported as follows: $[\alpha]_{wavelength}^{temperature}$, concentration (c= g/100mL), and solvent.

All solvents used in reactions were distilled from appropriate drying agents before use: THF (sodium benzophenone ketyl), hexane (CaH_2), HMPA (CaH_2), CH_2Cl_2 (CaH_2), benzene (CaH_2), DMF (CaH_2), and DMSO (CaH_2). Saturated aqueous sodium chloride is referred to as brine. House nitrogen was purified by passing through a tower of Drierite. *n*-Butyllithium was titrated by the double titration method.[80]

4.1.1. Reagents, Suppliers, and Purification.

Acetic acid	MCB
Acetone	Fisher, distilled
Allyl alcohol	Aldrich, distilled from CaH_2
Benzaldehyde	EK, distilled
Benzene	MCB, distilled from CaH_2
Benzophenone	Aldrich
Bis(diethylamino)chlorophosphine	Alfa
t-Butanol	Baker, distilled from CaH_2
n-Butyllithium	Aldrich
3-Butyn-2-ol	Farchan, distilled from CaH_2
Calcium hydride	Alfa
Carbon tetrachloride	MCB
Chlorodiphenylphosphine	Alfa
Chloroform	MCB
Deuteroacetone	Aldrich
Deuterochloroform	Aldrich
Dichloromethane	MCB, distilled from CaH_2

Diethylamine	Aldrich, distilled from CaH_2
Diethyl ether	Baker, distilled from Na/benzophenone
Diisopropylamine	Aldrich, distilled from CaH_2
Dimethylformamide	Baker, distilled from CaH_2
Meso-2,3-dimethylsuccinic acid	Aldrich
d,l-2,3-dimethylsuccinic acid	Aldrich
Dimethyl sulfoxide	Mallinckrodt, distilled from CaH_2
Ethanol	U.S. Industrial Chemicals
Ethyl acetate	Fisher, distilled from K_2CO_3
Ethylenediamine	Eastman Kodak, distilled from sodium
1-Ethynyl-1-cyclohexanol	Aldrich
Hexamethylphosphoramide (HMPA)	Aldrich, distilled from CaH_2
Hexane	Burdick and Jackson, distilled from CaH_2
Hydrochloric acid	MCB
Hydrogen peroxide	Mallinckrodt, 30%
Iodine	Baker
Lead tetraacetate	Aldrich, recrystallized from AcOH
Lithium	Mallinckrodt
Lithium aluminum hydride	Alfa
Lithium chloride	Aldrich
Magnesium, turnings	Alfa
Methanol	MCB,distilled from CaH_2
Methyl acetate	Aldrich
2-Methyl-3-butyn-2-ol	Aldrich, distilled from CaH_2
Methyl iodide	Aldrich, distilled
Methyllithium	Aldrich
N-Methyl morpholine	Aldrich, distilled from CaH_2
Napthalene	Aldrich
Phosphorous trichloride	Fisher, distilled
n-Propyl amine	Aldrich
Potassium carbonate	Mallinckrodt
Potassium Hydride	Aldrich, 35% in mineral oil
Potassium Hydroxide	Mallinckrodt
Pyridine	Aldrich, distilled from CaH_2
Sodium	Alfa
Sodium bicarbonate	Mallinckrodt
Sodium hydride	Alfa, 50% in mineral oil
Sodium hydroxide	Mallinckrodt
Sodium potassium tartrate tetrahydrate (Rochelle's Salt)	Fisher
Sucrose	Fisher
Tetrahydrofuran	Aldrich, distilled from sodium benzophenone
Triethylamine	Aldrich, distilled from CaH_2
Trifluoroacetic acid	Aldrich, distilled from P_2O_5
Triflouroacetic anhydride	Aldrich, distilled from P_2O_5
Trimethyl aluminum	Aldrich
Thionyl chloride	Aldrich, distilled
Zinc	Mallinckrodt

4.1.2.Literature Methods.

The following compounds were prepared by literature methods: *cis*-2-buten-1-ol[21], *trans*-2-buten-1-ol[21], diphenyl-3-methyl-1,2-propadienylphosphine oxide[37a], methyl-3-*t*-butylaminopropionate, [54] and (S)-ethyl-3-hydroxybutanoate.[59]

4.2. Experimental Procedures.

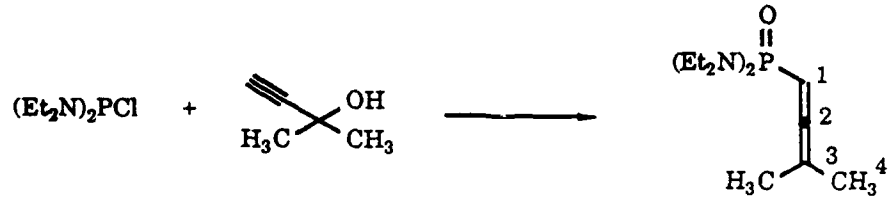
4.2.1. Achiral Phosphorus Derivatives.

4.2.1.1. Allenes.

General procedure for the synthesis of allenic phosphonamide and allenic diphenylphosphine oxides.

An oven-dried, 100-mL, 3-necked, round-bottomed flask equipped with a mechanical stirrer, dropping funnel, and thermometer was charged with 23.7 mmol of the appropriately substituted chlorophosphine and 45 mL of dry benzene. The solution was cooled to 5°C in an ice bath and 23.7 mmol of triethylamine was added over 2 minutes. After stirring for 10 minutes, 23.7 mmol of the appropriate butynol in 10 mL of benzene was added dropwise over 20 minutes. The ice bath was removed and the solution stirred overnight at room temperature. The mixture was diluted with 50 mL of water and extracted with ether (3 X 75 mL). The ether layers were washed with 2N HCl, 10% $NaHCO_3$, water, and brine (1 X 75 mL each). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed.

Preparation of Bis-(N,N-diethyl)-3-methyl-1,2-butadien-1-ylphosphondiamide 1



1

The crude product was purified by flash chromatography (hexane/acetone : 2.5/1) to afford 1 in 81.3% yield.

Analytical Data from 1

M.W. 258.35

bp: 100°C at 0.05 torr

^{1}H NMR: (200MHz, $CDCl_3$):

5.27-5.16 (m, 1H, HC(1)), 3.10-3.00 (m, 8H, $CH_3C\underline{H}_2N$), 1.72-1.68 (dxd, 6H, J= 9.4 Hz, 3.3 Hz, $(H_3C)_2C(3)$), 1.07 (t, 12H, J=7.1Hz, $C\underline{H}_3CH_2N$)

IR: (neat):

2980 s, 2940 s, 2880 s, 2710 w, 1967 s (C=C=C), 1462 s, 1380 s, 1360 s, 1295 s, 1224 s (P=O), 1205 s, 1102 m, 1061 m, 1020 s, 948 s, 796 s, 771 m (sh), 744 m, 700 m, 661 m

MS: (70 eV):

258 (M^+, 17.1), 191 (100), 187 (27), 186 (16), 140 (10), 120 (57), 118 (12), 72 (84), 67 (16), 58(12), 57 (12), 56 (13), 44 (23), 42 (19), 41 (27)

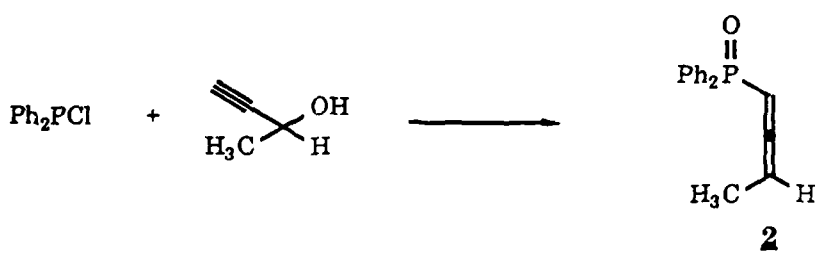
HRMS for $C_{13}H_{27}N_2OP$:

Calc: 258.1861

Found: 258.1851

TLC: hexane /acetone : 2/1 R_f= 0.35

Preparation of Diphenyl-1,2-butadien-1-ylphosphine oxide 2



2

The crude product was purified by recrystallization (hexane/ethyl acetate) to afford 2 in 75.7% yield.

Analytical data from 2

M.W. 254.27

mp: 88-89°C

^{1}H NMR: (200 MHz, $CDCl_3$):

7.84-7.68 (m, 4H, aromatic H ortho to P=O), 7.65-7.36 (m, 6H, aromatic), 5.82-5.73 (m, 1H, HC(1)), 5.30-5.17 (m, 1H, HC(3)), 1.62-1.53 (dxdxd, 3H, J= 7.3 Hz, 6.6 Hz, H_3C(4))

IR: (4% in $CHCl_3$):

3059 w, 2982 s, 2930 m (sh), 1951 s (C=C=C), 1591 w, 1485 w, 1439 s, 1367 s, 1310 w, 1170 s (P=O), 1120 s, 1101 m, 1067 w, 1025 w, 997 w, 857 m

MS: (70 eV):

254 (M^+, 40.4), 202 (14), 201 (100), 77 (29), 51 (17)

Analysis for $C_{16}H_{15}OP$:

Calc.: C 75.58%; H 5.95%; P 12.18%

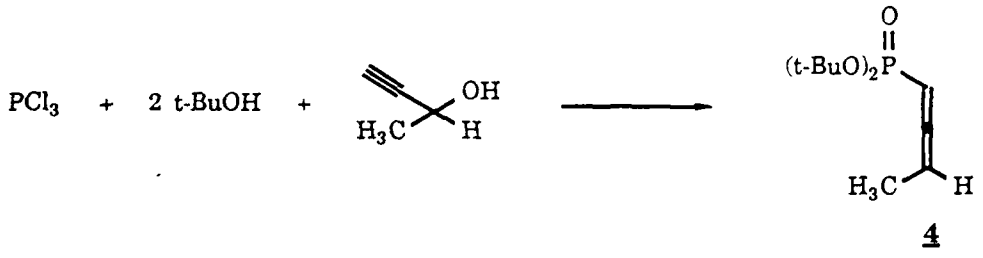
Found: C 75.46%; H 6.06%; P 12.42%

TLC: hexane/acetone : 1/1 R_f= 0.25

General procedure for the synthesis of allenic phosphonates

An oven-dried, 100-mL, 3-necked, round-bottomed flask equipped with a mechanical stirrer, dropping funnel, and thermometer charged with 23.7 mmol of PCl_3 and 35 mL of dry benzene. The solution was cooled to 5°C in an ice bath and 71.1 mmol of triethylamine was added over 2 minutes. After stirring for 20 minutes, a solution of 47.4 mmol of *t*-butanol in 10 mL of benzene was added over 90 minutes. After stirring for 90 minutes, 23.7 mmol of the appropriate butynol in 10 mL benzene was added dropwise over 10 minutes. The ice bath was removed and the solution stirred overnight at room temperature. The mixture was diluted with 50 mL of water and extracted with ether (3 X 75 mL). The ether layers were washed with 2N HCl, 10% $NaHCO_3$, water, and brine (1 X 75 mL each). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed.

Synthesis of Di-*t*-butyl-1,2-butadien-1-ylphosphonate 4



4

The crude product was distilled (Kugelrohr) to afford 4 in 78.3% yield.

Analytical data from 4

M.W.: 246.29

bp: 90°C at 0.2 torr

^{1}H NMR (200 MHz, $CDCl_3$)

5.38-5.23 (m, 2H, HC(1), HC(3)), 1.81-1.67 (m, 3H, $H_3C(4)$), 1.49 (s, 18H, $(CH_3)_3C$)

IR: (4% in CCl_4)

2982 s, 2932 m, 1958 m (C=C=C), 1721 w, 1476 m, 1395 m (sh), 1370 s, 1264 s (P=O), 1173 s, 1038 s (sh), 994 s, 918 m, 857 m, 830 m, 818 s

MS: (70 eV):

135 (M^+-111, 14.1), 134 (65), 57 (100), 56 (11), 53 (10), 41 (38), 39 (11)

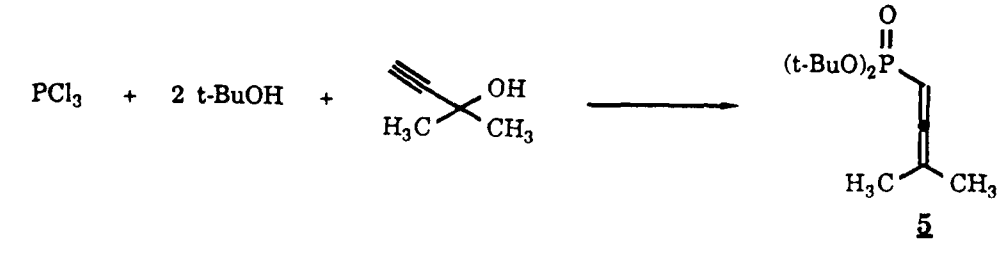
HRMS for $C_{12}H_{23}O_3P$ (FAB):

Calc.: 247.1463

Found: 247.1467

TLC: hexane/ acetone : 3/1 R_f= 0.29

Preparation of Di-*t*-butyl-3-methyl-1,2-butadien-1-yl phosphonate 5



5

The crude product was distilled (Kugelrohr) to afford **5** in 77.3% yield.

Analytical data from **5**

M.W.: 260.32

bp: 80°C at 0.05 torr

^{1}H NMR: (200 MHz, $CDCl_3$):

5.23-5.14 (m, 1H, HC(1)), 1.75-1.69 (dxd, 6H, J= 7.3 Hz, 3.5 Hz, $(CH_3)_2C$) 1.47 (s, 18H, $(CH_3)_3C$)

IR: (neat)

2985 s, 2940 s, 2880 m (sh), 2715 w, 1972 m (C=C=C), 1615 w, 1480 m, 1457 m, 1395 m, 1317 s, 1260 s (P=O), 1245 s (sh), 1171 s, 1040 s, 980 s (br), 922 s, 829 s, 798 s, 764 s, 696 s

MS: (70 eV)

189 (M^+-71, 10.4), 149 (15), 148 (100), 147 (11), 84 (12), 67 (23), 66 (37), 57 (78), 41 (47), 39 (14)

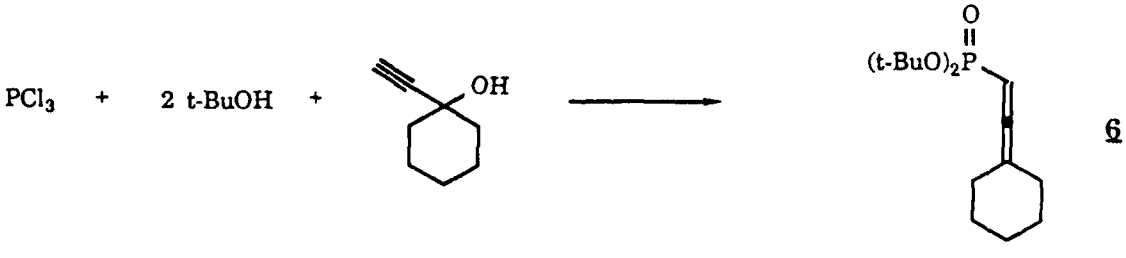
HRMS for $C_{13}H_{25}O_3P$:

Calc.: 260.1541

Found: 260.1547

TLC: hexane/acetone : 3/1 R_f= 0.26

Preparation of Di-*t*-butyl 3,3-pentamethylene-1,2-propadienyl phosphonate **6**



6

The crude product **6** was obtained in 88.3% yield and used without further purification.

Analytical data from **6**

M.W.: 300.19

bp: 130°C at .05 torr

^{1}H NMR: (300 MHz, $CDCl_3$):

5.21-5.17 (m, 1H, HC(1)), 2.20-2.11 (m, 4H, $H_2C(1')$, $H_2C(5')$), 1.65-1.37 (m, 6H, $H_2C(2')$-$H_2C(4')$), 1.49 (s, 18H, $(CH_3)_3C$)

^{13}C NMR: (75.5 MHz, $CDCl_3$):

206.0 (C(2)), 103.5 (C(3)), 83.5 (d, J= 204.5 Hz, C(1)), 82.0 (d, J= 8.3Hz, $(CH_3)_3\underline{C}$), 30.4 ($(\underline{C}H_3)_3C$), 29.7 (C(1'), C(5')), 26.8 (C(2'), C(4')), 25.8 (C(3'))

IR: (neat)

2979 s, 2932 s, 2857 m (sh), 1960 m (C=C=C), 1476 m (sh), 1447 m, 1393 s, 1370 s, 1340 m, 1316 m, 1262 s (P=O), 1219 m (sh), 1173 s, 1038 s (sh), 980 s, 918 m, 837 m

MS: (70 eV)

189 (M^+-111, 10.5), 188 (100), 198 (11), 107 (14), 106 (32), 91 (13), 57 (47), 43 (11), 41 (22)

HRMS for $C_{16}H_{29}O_3P$:

Calc.: 300.1854

Found: 300.1851

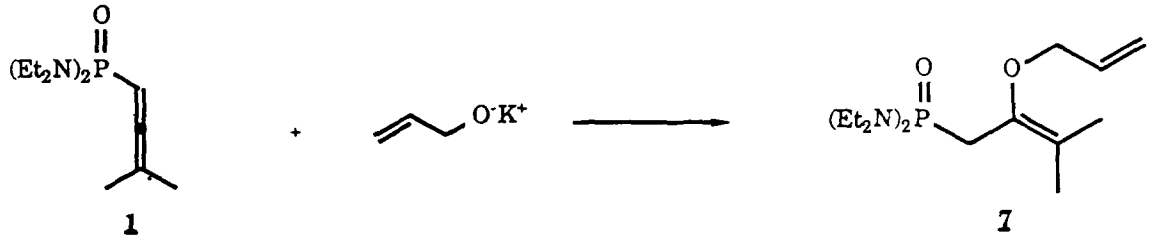
TLC: hexane/acetone : 3/1 R_f= 0.38

4.2.1.2. Allyl Vinyl Ethers.

General procedure for the synthesis of allyl vinyl ethers

An oven-dried, 15-mL, 3-necked, round-bottomed flask equipped with stirring bar, septum, N_2 inlet and thermometer was charged with KH dispersion. The KH dispersion was rinsed with hexane (3X) and suspended in 2.5 mL of THF. The suspension was cooled to 0°C and the allylic alcohol was added via syringe. After stirring for 5 minutes, a solution of the allene (0.30 mmol) in 0.5 mL THF was added via syringe. The reaction was monitiored by TLC. Upon completion, the reaction was quenched with water and extracted with ether (3 X 15mL). The organic layers were washed with water and brine (1 X 15 mL each), dried over $MgSO_4$, filtered, and the solvent removed.

Preparation of Bis(N,N-diethyl)(3-methyl-2'-propen-1'-yloxy)-2-buten-1-yl] phosphondiamide 7



1 7

The crude product was purified by flash chromatography (hexane/acetone : 2/1) to afford 7 in 56.3% yield as well as a 24.2% mixture of rearrangement product 22 and the α,β-unsaturated isomer.

Analytical data from 7

M.W.: 316.43

^{1}H NMR: (200 MHz, $CDCl_3$)

6.04-5.87 (m, 1H, HC(2')), 5.30 (d, 1H, J= 17.3 Hz, $H_tC(3')$), 5.15 (d, 1H, J= 10.3 Hz, $H_cC(3')$), 4.16 (d, 2H, J= 7.0 Hz, $H_3C(1')$), 3.16-2.96 (m, 8H, CH_3CH_2N), 2.75 (d, 2H, J=16.8 Hz, $H_2C(1)$), 1.69 (s, 3H, $CH_3C(3)$), 1.67 (s, 3H, $CH_3C(3)$), 1.13 (t, 12H, J= 4.8 Hz, CH_3CH_3N)

IR: (neat)

3080 w, 2980 s, 2940 s, 2880 s, 1700 w, 1680 w (C=C), 1608 w, 1462 m, 1408 m, 1381 s, 1295 m, 1267 m, 1220 s, 1208 s, 1187 s (P=O), 1094 m, 1060 m, 1018 s, 949 s, 833 w, 792 m, 695 m

MS: (70 eV)

316 (M^+, 0.14), 275 (21), 202 (24), 191 (38), 136 (11), 120 (13), 74 (32), 73 (11), 72 (100), 67 (16), 58 (22), 44 (20), 42 (11), 41 (36)

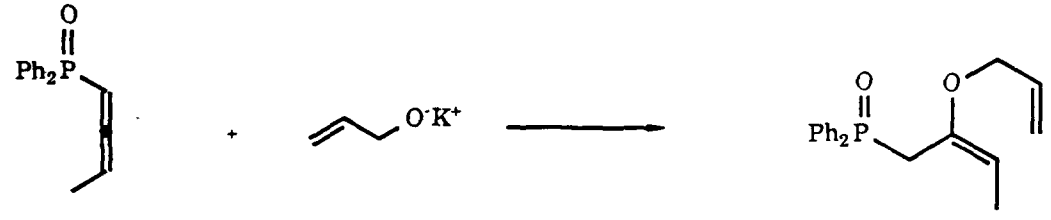
HRMS for $C_{16}H_{33}N_2O_2P$:

Calc: 316.2280

Found 316.2284

TLC: hexane/acetone : 2/1 R_f= 0.43

Preparation of (*E*)-Diphenyl [2-(2'-propen-1'-yloxy)-2-buten-1-yl]phosphine oxide 8



2 8

This addition was performed at -30°C. The crude product was purified by flash chromatography (hexane/acetone : 1/1)to afford 8 in 29.8% yield. An analytical sample was obtained by recrystallization from hexane/ethyl acetate.

Analytical data from 8

M.W.: 312.35

mp: 78-79°C

^{1}H NMR: (200 MHz, $CDCl_3$)

7.78-7.71 (m, 4H, aromatic ortho H to P=O), 7.57-7.35 (m, 6H, aromatic) 5.58-5.44 (m, 1H, HC(2')), 5.09-4.94 (m, 2H, $H_2C(3')$), 4.63-4.48 (m, 1H, HC(3)), 3.90 (d, 2H, *J*= 5.2 Hz, $H_2C(1')$), 3.28 (d, 2H, *J*= 14.0 Hz, $H_2C(1)$), 1.63-1.50 (m , 3H, $H_3C(4)$)

IR: (4% in CCl_4)

3063 w, 2921 w, 1669 m, 1592 w, 1439 s, 1400 w, 1343 w, 1235 s, 1198 s (P=O), 1119 s, 1103 s, 999 w, 926 w

MS: (70 eV)

312 (M^+, 2.50), 272 (11), 271 (61), 215 (20), 202 (31), 201 (88), 175 (10), 135 (15), 134 (65), 77 (22), 57 (100), 43 (22), 41 (51), 39 (17)

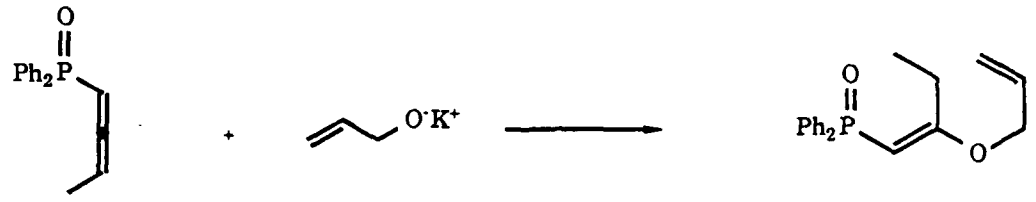
HRMS for $C_{19}H_{21}O_2P$:

Calc: 312.1279

Found: 312.1279

TLC: hexane/acetone : 1/1 R_f= 0.38

Preparation of (E)-Diphenyl 2-(2'-propen-1'-yloxy)-1-buten-1-ylphosphine oxide 9



2 9

This addition was performed at -30°C. The crude product was purified by flash chromatography (hexane/acetone : 1/1) to afford 9 in 47.9% yield. An analytical sample was obtained by recrystallization from acetone/ethyl acetate.

Analytical data from 9

M.W.: 312.35

mp: 118-120°C

^{1}H NMR: (360 MHz, $CDCl_3$)

7.78-7.72 (m, 4H, aromatic ortho H to P=O), 7.48-7.43 (m, 6H, aromatic) 6.03-5.92 (m, 1H, HC(2')), 5.37 (d, 1H, J= 17.2 Hz, $H_tC(3')$), 5.30 (d, 1H, J= 10.7 Hz, $H_cC(3')$), 4.86 (d, 1H, J= 4.9 Hz, HC(1)), 4.36 (d, 2H, J= 4.1 Hz, $H_2C(1')$), 2.54 (q, 2H, J= 7.3Hz, $H_2C(3)$), 0.99 (t, 3H, J= 7.3Hz, $H_3C(4)$)

IR: (4% in CCl_4)

3061 w, 2976 w, 2939 w, 1599 s (C=C), 1462 w, 1437m, 1377 w, 1343 m, 1304 w, 1188 s (P=O), 1116 s, 1093 s, 1069 w, 1028 w, 999 w, 928 m

MS: (70 eV)

312 (M^+, 23.4), 311 (10), 283 (20), 270 (18), 255 (22), 244 (12), 243 (84), 241 (12), 228 (12), 215 (11), 203 (16), 202 (81), 201 (100), 199 (12), 183 (22), 165 (32), 155 (16), 125 (15), 97 (41), 91 (24), 78 (13), 77 (69), 51 (22), 47 (28), 44 (41), 43 (13). 41 (73), 39 (22), 32 (13)

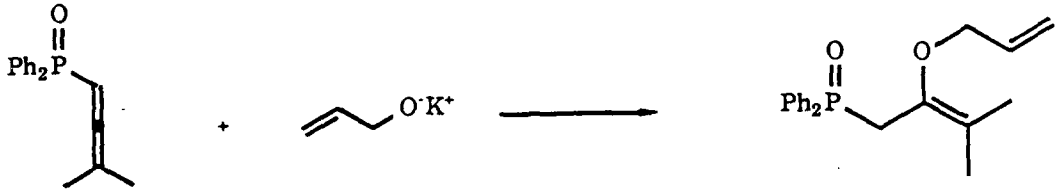
Analysis for $C_{19}H_{21}O_2P$:

Calc: C 73.06%; H 6.78%; P 9.92%

Found: C 72.77%; H 6.97%; P 9.81%

TLC: hexane/acetone : 1/1 R_f= 0.38

Preparation of Diphenyl 3-methyl-2-(2'-propen-1'-yloxy)-2-buten-1-yl phosphine oxide 10



3 10

Flash chromatography of the crude product (benzene/acetone : 2/1) afforded 10 in 78.2% yield.

Analytical data from 10

M.W.: 326.38

mp: 65-67°C

^{1}H NMR: (200 MHz, $CDCl_3$)

7.83-7.74 (m, 4H, aromatic H ortho to P=O), 7.58-7.41(m, 6H, aromatic), 5.84-5.70 (m, 1H, HC(2')), 5.20-5.06 (m, 2H, $H_2C(3')$), 4.05 (d, 2H, J= 5.0 Hz, $H_2C(1')$), 3.31 (d, 2H, J= 15.5 Hz, $H_2C(1)$), 1.61 (d, 3H, J= 5.1 Hz, $CH_3C(3)$), 1.35 (d, 3H, J=4.5 Hz, $CH_3C(3)$)

IR: (4% in $CHCl_3$)

3082 w, 3065 w, 2990 s, 2922 m, 2863 w, 1678 w, 1487 w, 1440 s, 1200 w, 1381 w, 1310 w, 1260 m, 1177 s (P=O), 1138 s, 1120 s, 1100 s, 1086 s (sh), 1070 m, 1028 w, 995 m, 931 m, 836 w, 822 w

MS: (70 eV)

326 (M^+, 3.7), 286 (13), 285 (70), 216 (17), 215 (23), 202 (22), 201 (100), 77 (23), 47 (10), 41 (17), 32 (15)

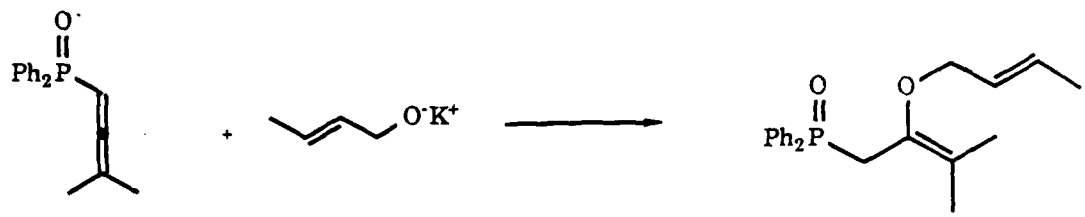
Analysis for $C_{20}H_{23}O_2P$:

Calc: C 73.60%; H 7.10%; P 9.49%

Found: C 73.79%; H 6.85%; P 9.71%

TLC: hexane/acetone : 1/1 R_f= 0.35

Preparation of Diphenyl 3-methyl-2-[(*E*)-2'-buten-1'-yloxyl-2-buten-1-ylphosphine oxide 11



3 11

Flash chromatography of the crude product (hexane/acetone : 1/1) afforded 11 in 58.6% yield.

Analytical data from 11

M.W.: 340.40

mp: 108-109°C

^{1}H NMR: (200 MHz, $CDCl_3$)

7.90 -7.75 (m, 4H, aromatic H ortho to P=O), 7.57-7.38 (m, 6H, aromatic), 5.64-5.30 (m, 2H, HC(2'), HC(3')), 3.96 (d, 2H, J= 6.2 Hz, $H_2C(1')$), 3.28 (d, 2H, J= 15.6 Hz, $H_2C(1)$), 1.66 (d, 3H, J= 6.2 Hz, $H_3C(4')$), 1.57 (d, 3H, J= 5.2 Hz, $CH_3C(3)$), 1.32 (d, 3H, J=4.2 Hz, $CH_3C(3)$)

IR: (4% in CCl_4)

3061 w, 2918 m, 2856 m, 1962 w, 1674 w, 1592 w, 1483 w, 1437 s, 1400 w, 1379 w, 1262 m, 1190 s (P=O), 1140 m, 1119 s, 1105 m, 1090 m, 1069 w, 1028 w, 999 m, 966 m, 904 w, 823 w

MS: (70 eV)

340 (M^+, 6.6), 286 (35), 285 (49), 243 (14), 216 (29), 215 (59), 203 (11), 202 (83), 201 (100), 91 (11), 77 (33), 55 (33), 47 (18), 41 (17)

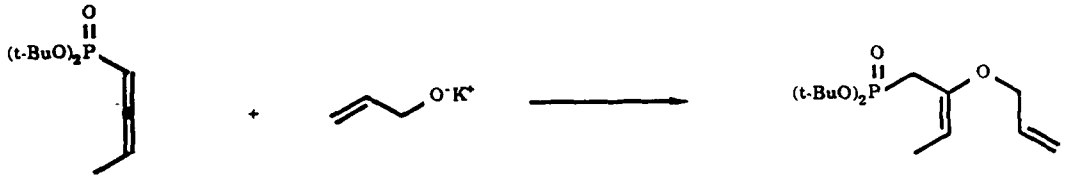
Analysis for $C_{21}H_{25}O_2P$:

Calc: C 74.10%; H 7.40%; P 9.10%

Found: C 74.15%; H 7.64%; P 9.03%

TLC: hexane/acetone : 1/1 R_f= 0.33

Preparation of (*E*)-Di-*t*-butyl 2-(2'-propen-1'-yloxy)-2-buten-1-ylphosphonate 12



4 12

The crude product was purified by flash chromatography (hexane/acetone : 5/1) to afford 12 in 69.5% yield.

Analytical data from 12

M.W.: 304.37

^{1}H NMR: (200 MHz, $CDCl_3$)

6.04-5.87 (m, 1H, HC(2')), 5.32 (d, 1H, J= 15.8 Hz, $H_tC(3')$), 5.18 (d, 1H, J= 10.4 Hz, $H_cC(3')$), 4.56-4.46 (m 1H, HC(3)), 4.18 (d, 2H, J= 5.4 Hz, $H_2C(1')$), 2.65 (d , 2H, J= 21.3 Hz, $H_2C(1)$), 1.80-1.53 (m, 3H, $H_3C(4)$), 1.49 (s, 18H, $(CH_3)_3C$)

IR: (neat)

3081 w, 2979 s, 2933 m, 1669 m, 1648 w, 1636 w, 1617 m, 1477 w, 1457 w, 1426 w, 1393 m, 1369 s, 1346 m, 1304 w, 1266 s (P=O), 1210 m, 1175 s, 1141 m, 1102 s, 1039 s, 979 s, 918 m, 854 w

MS: (70 eV)

304 (M^+, 1.1), 192 (35), 151 (82), 136 (22), 135 (15), 123 (25), 110 (36), 96 (16), 93 (18), 57 (60), 56 (12), 55 (13), 54 (11), 53 (11), 41 (100), 39 (23)

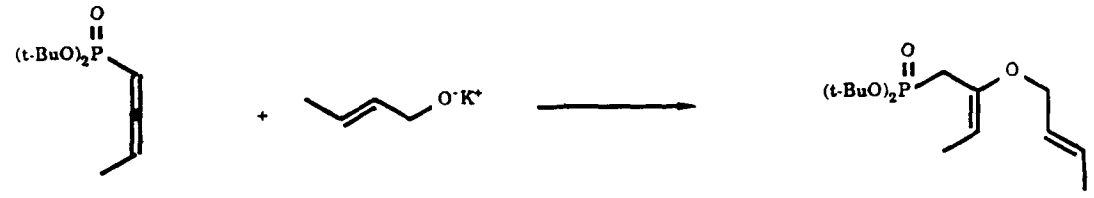
HRMS for $C_{15}H_{29}O_4P$:

Calc: 304.1825

Found: 304.1805

TLC: hexane/acetone : 3/1 R_f= 0.34

Preparation of (*E*)-Di-*t*-butyl 2-[(*E*)-2'-buten-1'-yloxyl-2-buten-1-ylphosphonate 13



4 13

Flash chromatography of the crude product (hexane/acetone : 5/1) to afford 13 in 64.8% yield and < 5% 15.

Analytical data from 13

M.W.: 318.40

^{1}H NMR: (200 MHz, $CDCl_3$)

5.73-5.62 (m, 2H, HC(2'), HC(3')), 4.54-4.48 (m, 1H, HC(3)), 4.09 (d, 2H, *J*= 4.8 Hz, $H_2C(1')$), 2.63 (d, 2H, *J*= 20.6 Hz, $H_2C(1)$), 1.74-1.55 (m, 6H, $H_3C(4)$, $H_3C(4')$), 1.48 (s, 18H, $(CH_3)_3C$)

IR: (neat)

2979 s, 2930 m, 1667 m, 1616 w, 1456 w, 1392 m, 1368 s, 1346 w, 1267 s (P=O), 1211 m, 1175 m, 1140 m, 1103 s, 1038 s (sh), 980 s, 918 m, 853 w, 826 w

MS: (70 eV)

152 (M^+-166, 100), 151 (32), 135 (27), 123 (25), 96 (28), 57 (44), 56 (11), 55 (43), 54 (14), 41 (40), 39 (17)

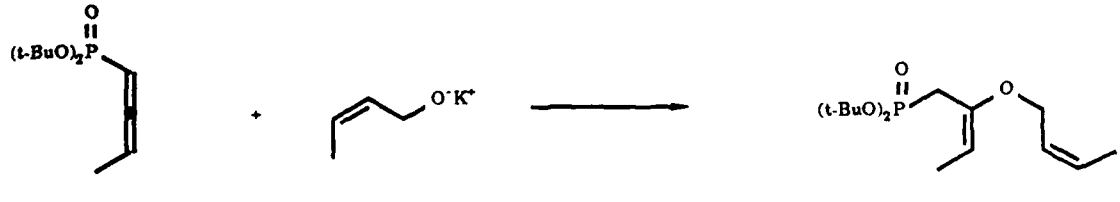
HRMS for $C_{16}H_{31}O_4P$:

Calc: 318.1960

Found: 318.1968

TLC: hexane/acetone : 3/1 R_f= 0.32

Preparation of (*E*)-Di-*t*-butyl 2-[(*Z*)-2'-buten-1'-yloxyl-2-buten-1-ylphosphonate 14



4 14

Flash chromatography of the crude product (hexane/acetone : 5/1) afforded 14 in 50.9% yield.

Analytical data from 14

M.W.: 318.40

^{1}H NMR: (200 MHz, $CDCl_3$)

5.65-5.58 (m, 2H, HC(2'), HC(3')), 4.56-4.50 (m, 1H, HC(2)), 4.25 (d, 2H, J= 4.1 Hz, $H_2C(1')$), 2.64 (d, 2H, J= 21.3 Hz, $H_2C(1)$), 1.68-1.57 (m, 6H, $H_3C(4)$, $H_3C(4')$), 1.49 (s, 18H, $(CH_3)_3C$)

IR: (neat)

2980 s, 2930 m, 1669 m, 1617 w, 1478 w, 1393 m, 1370 s, 1348 w, 1267 s (P=O), 1211 m (sh), 1175 s, 1140 m, 1102 s, 1038 s (sh), 980 s, 918 m, 852w, 826 w

MS: (70 eV)

152 (M^+-166, 100), 151 (40), 135 (29), 123 (20), 96 (25), 57 (58), 56 (12), 55 (41), 54 (15), 53 (13), 41 (45), 39 (19)

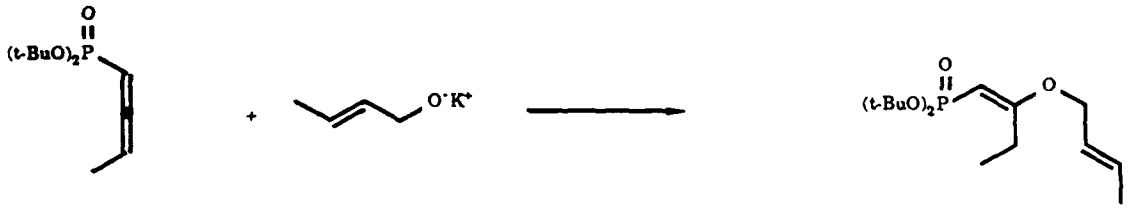
HRMS for $C_{16}H_{31}O_4P$:

Calc: 318.1951

Found: 318.1955

TLC: hexane/acetone : 3/1 R_f= 0.32

Preparation of Di-*t*-butyl 2-[(*E*)-2'-buten-1'-yloxyl-1-buten-1-yl phosphonate 15



4 15

Flash chromatography (hexane/acetone : 5/1) afforded 15 in 56.4% yield.

Analytical data from 15

M.W.: 318.40

bp: 115°C at .05 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

5.82-5.72 (m, 1H, HC(2')), 5.65-5.58 (m, 1H, HC(3')), 4.48 (d, 1H, *J*= 7.0 Hz, HC(1)), 4.16 (d, 2H, *J*=6.0 Hz, $H_2C(1')$), 2.57 (dxq, 2H, *J*= 7.5 Hz, 1.0 Hz, $H_2C(3)$), 1.73 (dxd, 3H, *J*=5.3 Hz, 1.2 Hz, $H_3C(4')$), 1.49 (s, 18H, $(CH_3)_3C$)), 1.11 (t, 3H, *J*= 2.5 Hz, $H_3C(4)$)

IR: (neat)

2977 s, 2936 m, 1717 w, 1617 s (C=C), 1462 m, 1393 m, 1370 s, 1347 m, 1242 s (P=O), 1186 s, 1096 s, 1069 s, 1038 s, 972 s, 916 s, 828 m

MS: (70 eV)

202 (M^+-116, 11.1), 201 (15), 177 (25), 152 (46), 149 (24), 135 (14), 133 (16), 131 (53), 123 (57), 107 (15), 105 (24), 104 (34), 103 (17), 91 (100), 78 (12), 77 (16), 65 (13), 57 (23), 55 (19), 51 (12), 41 (21), 40 (14), 32 (24)

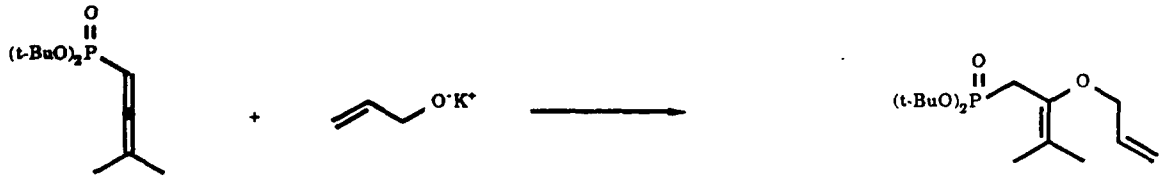
HRMS (FAB) for $C_{16}H_{31}O_4P$:

Calc: 319.2038

Found: 319.2028

TLC: hexane/acetone : 3/1 R_f= 0.32

Preparation of Di-*t*-butyl 3-methyl-2-(2'-propen-1'-yloxy)-2-buten-1-ylphosphonate 16



5 16

Flash chromatography (hexane/acetone :5/1) afforded 16 in 60.7% yield.

Analytical data from 16

M.W.: 318.40

^{1}H NMR: (200 MHz,$CDCl_3$)

6.07-5.88 (m ,1H, HC(2')), 5.33 (d,1H, J= 17.1 Hz, $H_tC(3')$), 5.16 (d, 1H, J= 10.5 Hz, $H_cC(3')$), 4.22 (d, 2H, J= 5.4 Hz, $H_2C(1')$), 2.66 (d, 2H, J= 21.3 Hz, $H_2C(1)$), 1.72(d, 3H, J= 4.2 Hz, $CH_3C(3)$), 1.66 (d, 3H, J= 3.0 Hz, $CH_3C(3)$), 1.50 (s, 18H, $(CH_3)_3C$)

IR: (neat)

3080 w, 2980 s, 2930 s, 2875 m, 2720 w, 1679 m (C=C), 1647 w, 1479 m, 1455 m, 1423 m, 1393 m, 1368 s, 1262 s (P=O), 1249 s (sh), 1195 s, 1172 s, 1143 m, 1090 s, 1036 s, 975 s, 920 s, 846 w, 824 m, 778 m, 690 m, 665 m

MS: (70 eV)

318 (M^+, 0.38), 206 (15), 165 (100), 107 (12), 96 (10), 83 (24), 41 (11)

HRMS for $C_{16}H_{31}O_4P$:

Calc: 318.1960

Found: 318.1960

TLC: hexane/acetone : 3/1 R_f=0.31

Preparation of Di-*t*-butyl 2-[(*E*)-2'-buten-1'-yloxyl-3-methyl-2-buten-1-ylphosphonate 17

5 17

Flash chromatography (hexane/acetone : 5/1) afforded 17 in 58.7% yield.

Analytical Data from 17

M.W.: 332.42

^{1}H NMR: (200 MHz, $CDCl_3$)

5.71-5.63 (m, 2H, HC(2'), HC(3')), 4.13 (d, 2H, J= 5.4 Hz, $H_2C(1')$), 2.64 (d, 2H, J= 21.6 Hz, $H_2C(1)$), 1.71-1.60 (m, 9H, $(CH_3)_2C(3)$, $H_3C(4')$), 1.49 (s, 18H, $(CH_3)_3C$)

IR: (neat)

2979 s, 2924 m, 1699 w, 1676 w, 1653 w, 1558 w, 1539 w, 1507 w, 1475 w, 1456 m, 1393 m, 1368 s, 1264 s (P=O), 1196 s, 1172 s, 1146 m (sh), 1096 s, 1038 s, 978 s, 918 m

MS: (70 eV)

166 (M^+-166, 100), 165 (27), 149 (23), 123 (14), 96 (18), 71 (15), 68 (18), 57 (32), 55 (25), 41 (31)

HRMS for $C_{17}H_{33}O_4P$:

Calc: 332.2116

Found: 332.2115

TLC: hexane/acetone : 3/1 R_f= 0.29

4.2.1.3. Claisen Rearrangements.

General procedure for the carbanion accelerated Claisen rearrangement in KH/HMPA/THF.

An oven-dried, 3-necked, 15-mL, round-bottomed flask equipped with a stirring bar, septa, and a vacuum/N_2 inlet was charged with KH dispersion. The dispersion was rinsed with hexane (3X) and suspended in HMPA (2.5 mL). A solution of allyl vinyl ether and THF (0.75 mL) was added via syringe. The reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with water (10 mL) and extracted with ether (3 X 15 mL). The organic layers were washed with water (3 X 15 mL) and brine (2 X 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed.

General procedure for the carbanion accelerated Claisen rearrangement in KH/DMSO/THF.

An oven-dried, 3-necked, 15-mL, round-bottomed flask equipped with a stirring bar, septa, and a vacuum/N_2 inlet was charged with KH dispersion. The dispersion was rinsed with hexane (3X) and DMSO (2.5 mL) was added. After stirring until H_2 evolution ceased (~10 minutes), LiCl was added all at once (if necessary), followed by stirring for 10 more minutes. Then a solution of allyl vinyl ether and THF (0.75 mL) was added via syringe. The reaction was monitored by TLC. Upon completion, the reaction mixture was quenched with water (10 mL) and extracted with ether

(3 X 15 mL). The organic layers were washed with water (3 X 15 mL) and brine (1 X15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed.

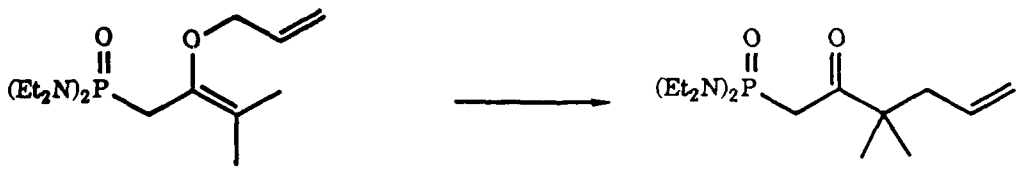
General procedure for the carbanion accelerated Claisen rearrangement in KDA/THF.

An oven-dried, 15-ml, 3-necked, round-bottomed flask equipped with a septum, stirring bar, thermometer, and N_2 inlet was charged with KH dispersion. The dispersion was washed with hexane (3X) and suspended in THF (2 mL). The reaction mixture cooled to 0°C and *t*-butyl alcohol added via syringe. The mixture was then cooled to -78°C and diisopropylamine added. After 10 minutes, *n*-BuLi was added via syringe. After stirring for 10 more minutes, a solution of allyl vinyl ether and 1 mL THF was added via syringe. The solution was warmed to 0°C and stirred until complete (by TLC). The reaction was quenched with water (10 mL) and extracted with ether (3 X 15 mL). The organic layers were washed with water and brine (1 X 15 mL each). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed.

General procedure for the thermal Claisen rearrangement.

The allyl vinyl ether (0.10 mmol in THF) was placed in a high pressure sealed vial and heated at the specified temperature until starting material was consumed (by TLC). The contents of the vial were transferred to a pear-shaped flask with ether and the solvent removed in vacuo.

Preparation of Bis-(N,N-diethyl)-(3,3-dimethyl-2-oxo-5-hexen-1-yl)phosphondiamide 22



7 22

KH/HMPA/THF: Flash chromatography (benzene/acetone : 2/1) afforded 22 in 9.9% yield.

Analytical data from 22

M.W.: 316.43

bp: 110°C at 0.05 torr

^{1}H NMR: (200 MHz, $CDCl_3$)

5.83-5.63 (m, 1H, HC(5)), 5.09-4.97 (m, 2H, $H_2C(6)$), 3.15-2.98 (m, 10H, CH_3CH_2N, $H_2C(1)$), 2.29 (d, 2H, J=7.3 Hz, $H_2C(4)$), 1.21 (s, 6H, $(CH_3)_2C(3)$), 1.12 (t, 12H, J=7.3 Hz, CH_3CH_3N))

IR: (neat)

3080 w, 2980 s, 2965 s, 2880 s, 1699 m (C=O), 1643 w, 1610 w, 1471 m, 1384 s, 1350 m, 1299 m, 1184 s (P=O), 1133 m, 1104 m, 1062 m, 1020 s, 967 s, 940 m, 925 m, 860 w, 836 w, 691 w, 661 w

MS: (70 eV)

316 (M^+, 0.54), 233 (19), 191 (16), 160 (21), 120 (17), 74 (23), 72 (100), 58 (13), 44 (11), 41 (12)

HRMS for $C_{16}H_{33}N_2O_2P$:

Calc: 316.2280

Found: 316.2287

TLC: hexane/acetone : 2/1 R_f= 0.46

Preparation of Diphenyl 3-methyl-2-oxo-5-hexen-1-ylphosphine oxide 23

8 23

From 8. KH/DMSO: Flash chromatography (hexane/acetone : 1/1) afforded 23 in 73.7% yield.

From 9. KH/DMSO: Flash chromatography (hexane/acetone : 1/1) afforded 23 in 31.5% and 5.4% diphenyl-2-oxo-1-butylphosphine oxide 31.

Analytical data from 23

M.W.: 312.35

mp: 68-69°C

^{1}H NMR: (200 MHz, $CDCl_3$)

7.83-7.72 (m, 4H, aromatic H ortho to P=O), 7.59-7.45 (m, 6H, aromatic), 5.73-5.53 (m 1H, HC(5)), 5.04-4.99 (m 2H, $H_2C(6)$), 3.66(d, 2H, J= 15.2 Hz, $H_2C(1)$), 2.98-2.85 (m, 1H, HC(3)),2.40-1.98 (m, 2H, $H_2C(4)$), 1.01 (d, 3H, J= 6.7 Hz, $CH_3C(3)$)

IR: (4% in CCl_4)

3081 w, 3063 w, 2979 w, 2911 w, 1709 s (C=O), 1456 w, 1439 m, 1208 s (P=O), 1121 m, 1107 w, 1028 w, 999 w, 918 w

MS: (70 eV)

312 (M^+, 11.7), 243 (14), 216 (17), 215 (50), 201 (49), 201 (100), 111 (20), 91 (15), 77 (36), 51 (17), 47 (15), 41 (33), 39 (11)

Analysis for $C_{19}H_{21}O_2P$:

Calc: C 73.06%; H 6.78%; P 9.92%

Found: C 73.07%; H 6.79%; P 9.98%

TLC: hexane/acetone : 1/1 R_f= 0.44

Preparation of Diphenyl 3,3-dimethyl-2-oxo-5-hexen-1-ylphosphine oxide 24

10 24

The crude product was purified by flash chromatography (benzene/acetone : 2/1).

KH/HMPA/THF: Yield: 70.5%.

KDA/THF: Yield: 67.9%.

KH/DMSO: Yield: 62.4%.

Analytical data from 24

M.W.: 326.36

mp: 94-96°C

^{1}H NMR: (200 MHz, $CDCl_3$)

7.85-7.74 (m, 4H, aromatic H ortho to P=O), 7.58-7.44 (m, 6H, aromatic), 5.72-5.51 (m, 1H, HC(5)),, 5.04-4.96 (m, 2H, $H_2C(6)$), 3.69 (d, 2H, J= 15 Hz, $H_2C(1)$), 2.22 (d, 2H, J= 7.0 Hz, $H_2C(4)$), 1.08(s, 6H, $(CH_3)_2C(3)$)

IR: (neat)

3060 w, 2980 s, 1915 m (sh), 2875 m (sh), 2483 w, 1705 s (C=O), 1640 w, 1591 w, 1485 w (sh), 1468 m, 1438 s, 1418 w(sh), 1388 m, 1366 m, 1330 w, 1305 w, 1205 s (P=O), 1119 s, 1105 m (sh), 1070 m, 1029 m, 997 s, 925 s, 850 m, 835 m, 750 s (br), 665 s, 625 w

MS: (70 eV)

326 (M^+, 11.3), 243 (21), 216 (28), 215 (43), 202 (19), 201 (100), 77 (20), 55 (11). 47 (10), 41 (13)

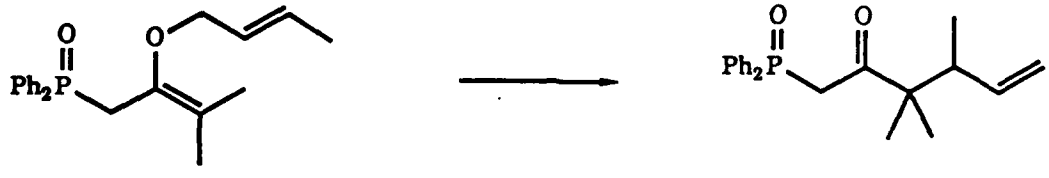
Analysis for $C_{20}H_{23}O_2P$:

Calc: C 73.60%; H 7.10%; P 9.49%

Found: C 73.51%; H 7.01%; P 9.53%

TLC: hexane/acetone : 1/1 R_f= 0.42

Preparation of Diphenyl 3,3,4-trimethyl-2-oxo-5-hexen-1-ylphosphine oxide 25



11 25

KH/DMSO: Flash chromatography (hexane/acetone : 1/1) afforded 25 in 90.5% yield.

Analytical data from 25

M.W.: 340.40

mp: 97.5-98.5°C

^{1}H NMR: (360 MHz, $CDCl_3$)

7.82-7.76 (m, 4H, aromatic H ortho to P=O), 7.54-7.45 (m, 6H, aromatic), 5.66-5.56 (m, 1H, HC(5)), 5.02-4.97 (m, 2H, $H_2C(6)$), 3.68 (d, 2H, J= 14.7 Hz, $H_2C(1)$), 2.51-2.42 (m, 1H, HC(3)), 1.02 (s, 3H, $CH_3C(3)$), 1.01 (s, 3H, $CH_3C(3)$), 0.86 (d, 3H, J= 6.9 Hz, $CH_3C(4)$)

IR: (4% in CCl_4)

3063 w, 2974 m, 1701 s (C=O), 1638 w, 1593 w, 1464 w, 1439 s, 1389 w, 1250 m, 1208 s (P=O), 1118 s, 1071 w, 1021 m, 997 m, 918 m, 847 w, 820 w, 816 s

MS: (70 eV)

340 (M^+, 6.9), 286 (17), 285 (14), 243 (19), 216 (31), 215 (50), 202 (30), 201 (100), 77 (23), 55 (23), 41 (14)

Analysis for $C_{21}H_{25}O_2P$:

Calc: C 74.10%; H 7.40%; P 9.10%

Found: C 74.05%; H 7.42%; P 9.20%

TLC: hexane/acetone : 1/1 R_f= 0.41

Preparation of Di-*t*-butyl3-methyl-2-oxo-5-hexen-1-ylphosphonate 26

12 26

KH/DMSO/LiCl: Kugelrohr distillation afforded 26 in 84.2% yield.

Analytical data from 26

M.W.: 304.37

bp: 125°C at 0.05 torr

^{1}H NMR: (200 MHz, $CDCl_3$)

5.74-5.66 (m, 1H, HC(5)), 5.10-4.99 (m, 2H, $H_2C(6)$), 3.02 (d, 2H, J= 22.9 Hz, $H_2C(1)$), 2.99-2.86 (m, 1H, HC(3)), 2.42-2.06 (m 2H, $H_2C(4)$), 1.50 (s, 18H, $(CH_3)_3$), 1.08 (d, 3H, J= 7.0 Hz, $CH_3C(3)$)

IR: (4% in CCl_4)

2982 s, 2936 m, 1713 s (C=O), 1641 w, 1620 w, 1478 w, 1458 w, 1395 m, 1372 s, 1267 s (P=O), 1171 s, 1038 s (sh), 990 s, 918 m, 830 w, 818 s

MS: (70 eV)

192 (M^+-112, 54), 179 (23), 175 (14), 123 (61), 110 (39), 96 (18), 95 (13), 93 (28), 69 (12), 57 (100), 56 (13), 43 (12), 41 (61), 39 (16)

Analysis for $C_{15}H_{29}O_4P$:

Calc.: C 59.19%; H 9.60%; P 10.18%

Found: C 58.89%; H 9.56%; P 10.44%

TLC: hexane/acetone : 1/1 R_f= 0.29

Preparation of *[R,S](3],4u)*Di-*t*-butyl 3,4-dimethyl-2-oxo-5-hexen-1-ylphosphonate 27

13 27

KH/DMSO/LiCl: Kugelrohr distillation afforded 27 in 92.7% yield.

KH/DMSO: Flash chromatography (hexane/acetone : 5/1) afforded 27 in 62.5% yield and di-*t*-butyl-2-oxo-1-butyl phosphonate 32 in 1.0% yield.

Thermal: Flash chromatography (hexane/acetone : 5/1) afforded 27 in 89.8% yield.

Analytical data for 27

M.W.: 318.40

bp: 140°C at 0.03 torr

^{1}H NMR: (200 MHz, $CDCl_3$)

5.81-5.67 (m, 1H, HC(5)), 5.02 (dxt, 1H, J= 5.4 Hz, 1.4 Hz, $H_tC(6)$), 4.95 (d, 1H, J= 1.3 Hz, $H_cC(6)$), 3.20-2.81 (m, 3H, $H_2C(1)$, HC(3)), 2.53-2.42 (m, 1H, HC(4)), 1.50 (s, 18H, $(CH_3)_3C$), 1.02 (d, 3H, J=6.7 Hz, $CH_3C(3)$), 0.95 (d, 3H, J= 6.7 Hz, $CH_3(4)$)

IR: (4% in CCl_4)

3079 w, 2980 s, 2936 m, 1711 s (C=O), 1639 w, 1617 w, 1456 w (sh), 1395 m, 1370 s, 1267 s (P=O), 1171 s, 1038 s (sh), 984 s, 918 m, 876 w, 826 w

MS: (70 eV)

206 (M^+-112, 16), 179 (14), 152 (19), 135 (26), 124 (60), 123 (50), 107 (12), 96 (16), 83 (11), 71 (11), 57 (100), 56 (17), 55 (36), 43 (10), 41 (59), 39 (20)

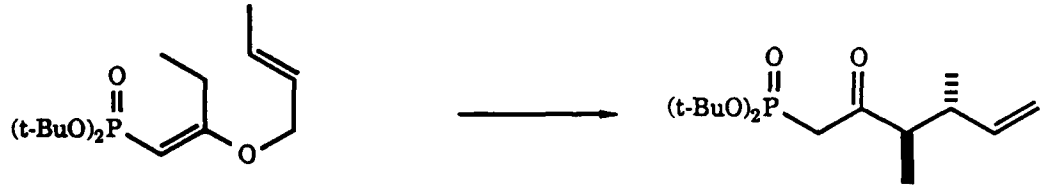
Analysis for $C_{16}H_{31}O_4P$:

Calc: C 60.36%; H 9.81%; P 9.73%

Found: C 60.37%; H 9.72%; P 9.81%

TLC: hexane/acetone : 3/1 R_f= 0.26

Preparation of [*R,S*](3,4))Di-*t*-butyl3,4-dimethyl-2-oxo-5-hexen-1-ylphosphonate 28



14 28

From 13 Thermal: The crude product was purified by flash chromatography to afford 28 in 19.0% yield.

From 14 KH/LiCl/DMSO: The crude product was purified by flash chromatography to afford 28 in 78.5% yield and 32 in 4.8% yield.

Analytical Data from 28

M.W.: 318.40

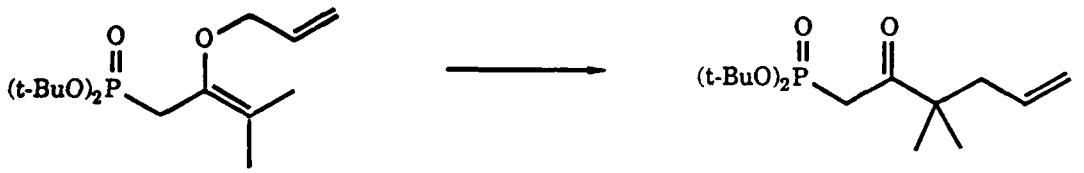
bp: 140°C at 0.03 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

5.70- 5.58 (m, 1H, HC(5)), 5.02- 4.96 (m,2H, $H_2C(6)$), 3.14- 2.87 (m, 2H, $H_2C(1)$), 2.82- 2.78 (m, 1H, HC(3)), 2.51- 2.46 (m, 1H, HC(4)), 1.51 (s, 18H, $(CH_3)_3C$), 1.03 (d, 3H, J= 2.6 IIz, $CH_3C(3)$), 1.00 (s, 3H, J= 2.4 Hz, $CH_3C(4)$)

TLC: hexane/acetone : 3/1 R_f= 0.26

Preparation of Di-*t*-butyl 3,3-dimethyl-2-oxo-5-hexen-1-ylphosphonate 29



16 29

KH/DMSO/LiCl: Kugelrohr distillation afforded 29 in 85.0% yield.

KH/HMPA/THF: Flash chromatography (benzene/acetone : 2/1) afforded 29 in 24.7% and furan 33 in 11.5%.

KDA/THF: Kugelrohr distillation afforded 29 in 60.9% and allene 5 in 12.2%.

LDA/THF: Kugelrohr distillation afforded 29 in 67.2% and allene 5 in 22.3%.

Analytical data from 29

M.W.: 318.40

bp: 130°C at 0.05 *torr*

^{1}H NMR: (200 MHz: $CDCl_3$)

5.81-5.60 (m, 1H, HC(5)), 5.08-4.97 (m, 2H, $H_2C(6)$), 3.05 (d, 2H, J= 23.0 Hz $H_2C(1)$), 2.26 (d, 2H, J= 7.0 Hz, $H_2C(4)$), 1.53 (s, 18H, $(CH_3)_3C$), 1.16 (s, 6H, $(CH_3)_2C$)

IR: (4% in $CHCl_3$)

2985 s, 2940 m, 2885 w (sh), 1707 s (C=O), 1640 m, 1459 m, 1394 s, 1370 s, 1260 s (P=O), 1167 s, 1037 s, 980 s, 920 s, 869 w, 832 w, 816 w, 658 w, 611 w

MS: (10 eV)

318 (M^+, 0.79), 207 (11), 206 (74), 189 (22), 179 (100), 152 (18), 124 (10), 123 (69), 107 (32), 96 (41), 83 (19), 57 (54), 41 (11)

HRMS for $C_{16}H_{31}O_4P$:

Calc: 318.1960

Found: 318.1967

TLC: hexane/acetone : 3/1 R_f= 0.26

Di-*t*-butyl (3',3',4'-trimethyl-2'-furanylidenemethyl)phosphonate 33

Analytical data for 33

M.W.: 318.40

^{1}H NMR: (200 MHz, $CDCl_3$)

4.41-4.33 (m, 2H, HC(1), HC(5')), 3.80 (t, 1H, *J*= 8.9 Hz, HC(5')), 2.11-2.00 (m, 1H, HC(4')), 1.48(s, 18H, $(CH_3)_3C$), 1.14 (s, 3H, $CH_3C(3')$), 0.99 (s, 3H, $CH_3C(3')$), 0.94 (d, 3H, *J*= 7.0 Hz, $CH_3C(4')$)

IR: (4% in CCl_4)

2975 s, 2932 m, 1640 s (C=C), 1460 m, 1391 s, 1368 s, 1337 m, 1277 m (sh), 1256 s (P=O), 1175 s, 1082 s, 1038 s, 997 s, 916 m, 866 m

MS: (70 eV)

318 (M^+, 2.11), 207 (100), 206 (39), 191 (24), 189 (19), 164 (52), 125 (13), 124 (13), 123 (29), 111 (26), 107 (27), 69 (17), 67 (14), 57 (35), 56 (22), 55 (26), 43 (20), 41 (93), 39 (27)

Preparation of Di-*t*-butyl3,3,4-trimethyl-2-oxo-5-hexen-1-ylphosphonate 30

17 30

KH/DMSO/LiCl: Kugelrohr distillation afforded 30 in 91.7% yield.

Analytical data for 30

M.W.: 332.43

bp: 145°C at 0.05 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

5.73-5.61 (m, 1H, HC(5)), 5.05-5.00 (m, 2H, $H_2C(6)$), 3.03 (d, 2H, J= 22.6 Hz, $H_2C(1)$), 2.50-2.45 (m, 1H, HC(4)), 1.52 (s, 18H, $(CH_3)_3C$), 1.10 (s, 3H, $CH_3C(3)$), 1.09 (s, 3H, $CH_3C(3)$), 0.92 (d, 3H, J= 4.9 Hz, $CH_3C(4)$)

IR: (4% in CCl_4)

2979 s, 2936 s, 1707 s (C=O), 1637 w (sh), 1462 s, 1393 s, 1370 s, 1267 s (P=O), 1170 s, 1005s, 918 s, 866 w, 834 m

MS: (70 eV)

220 (M^+-112, 15), 179 (63), 166 (33), 165 (21), 152 (16), 149 (45), 139 (34), 123 (67), 99 (81), 97 (20), 96 (53), 73 (15), 57 (100), 56 (12), 55 (40), 41 (49), 39 (13)

Analysis for $C_{17}H_{33}O_4P$:

Calc: C 61.42%; H 10.01%; P 9.32%

Found: C 61.46%; H 10.25%; P 9.11%

TLC: hexane/acetone : 3/1 R_f= 0.25

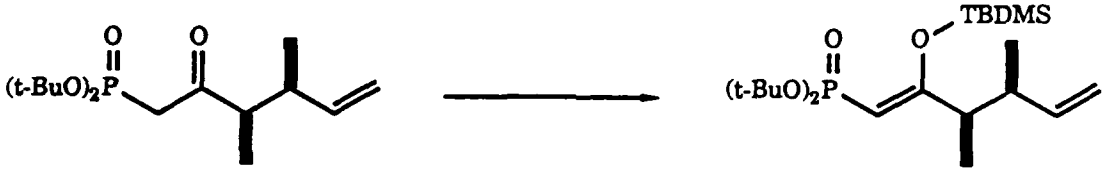
4.2.1.4. Degradation.

General procedure for the degradation of Claisen rearrangement products to succinic esters. Silyl enol ethers. An over-dried, 15-mL, 3-necked, round-bottomed flask equipped with septa, stirring bar, and N_2 inlet was charged with 0.183 mmol of Claisen rearrangement product and 3.0 mL THF. The mixture was cooled to -78°C and 0.615 mL (.403mmol) of 0.656M potassium hexamethyldisilazide was added dropwise via syringe. After stirring for 2 minutes, 0.508 mmol of *t*-butyldimethylsilyl chloride on 1.0 mL THF was added. The mixture was stirred at -78°C for 20 minutes and warmed to room temperature. The contents of the flask were transferred to a

centrifuge tube. Following centrifugation for 5 minutes at 5000 rpm, the supernatant was decanted and the solvents removed in vacuo. The silyl enol ethers were used without further purification.

Succinic esters. These reactions were performed according to a variation of the method of Ireland. The ozonolyses (0.183 mmol of silyl enol ether) were performed in methyl acetate at -10°C followed by the addition of 1.0 mL of 88% HCO_2H and 0.5 mL of 30% H_2O_2.

Preparation of [*R,S*](3l, 4u)-Di-*t*-butyl-3,4-dimethyl-2-*t*-butyldimethylsiloxy-1,5-hexadienyl phosphonate 34



27 34

Analytical data from 34

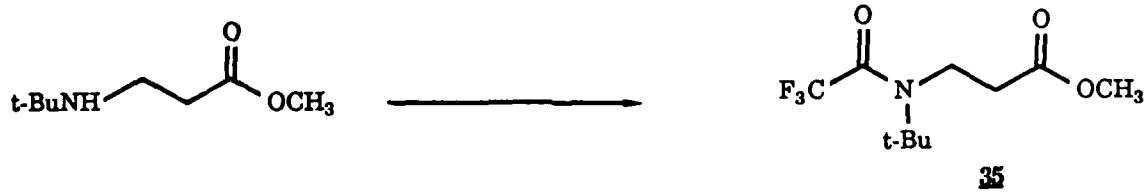
M.W.: 332.43

^{1}H NMR: (300 MHz, $CDCl_3$)

5.84-5.78 (m, 1H, HC(5)), 4.94-4.81 (m, 2H, $H_2C(6)$), 4.43 (d, 1H *J*= 8.6 Hz, HC(1)), 3.22- 3.15 (m, 1H, HC(3)), 2.25- 2.16 (m, 1H, HC(4)), 1.47 (s, 18H, $(CH_3)_3CO$), 1.20- 1.02 (m, 6H, $CH_3C(3)$, $CH_3C(4)$), 0.94 (s, 9H, $(CH_3)_3CSi$), 0.19 (s, 6H, $(CH_3)_3Si$)

4.2.2. Chiral Racemic Phosphorus Derivatives.

Preparation of Methyl-3-(N-*t*-butyl-N-trifluoroacetyl)aminopropionate 35



35

An oven-dried, 15-mL, 3-necked, round-bottomed flask equipped with a stirring bar, septum, and N_2 inlet was charged with 5.08g (25.2 mmol) of methyl-3-*t*-butylaminopropionate and 25 mL CH_2Cl_2. The mixture was placed in an ice bath and 5.35 ml (37.9 mmol) of trifluoroacetic anhydride was added via syringe over 5 minutes. The reaction mixture was warmed to room temperature and stirred for two hours. The solvent was removed in vacuo and the crude product purified by Kugelrohr distillation (90°C at 0.30 torr) to give 5.30g (84.3%) of amidoester 35.

Analytical data from 35

M.W.: 255.25

bp: 90°C at 0.3 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

3.71 (m, 2H, $H_2C(3)$), 3.66 (s, 3H, CH_3O), 2.60 (m, 2H, $H_2C(2)$), 1.44 (s, 9H, $(CH_3)_3C$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

170.5 (s,C(1)), 157.0 (q, J= 34.3 Hz, $CF_3\underline{C}$=O)), 116.4 (q, J=289.4 Hz, CF_3), 59.7 (s, $(CH_3)_3\underline{C}$), 51.8 (s, OCH_3), 39.9(q, J= 3.2 Hz, C(3)), 36.0(s, C(2)), 27.8 (s, $(\underline{C}H_3)_3C$)

IR: (neat)

2961 m, 1742 s(C=O), 1694 s (C=O), 1482 m, 1439 s, 1422 s, 1401 m, 1383 s, 1372 s 1327 s, 1294 m, 1266 s, 1198 s, 1123 s, 1048 s, 1026 m, 986 w, 899 w, 804 w

MS: (70 eV)

240 (M^+-15, 38), 208 (38), 199 (38), 168 (30), 167 (1), 166 (20), 139 (11), 57 (100), 56 (15), 55 (42)

Analysis for $C_{10}H_{16}F_3NO_3$:

Calc.: C 47.06%; H 6.32%; N 5.49%; F 22.33%

Found: C 47.04%; H 6.24%; N 5.56%; F 22.03%

Preparation of 4-*t*-butylamino-2-methyl-2-butanol 36

35 36

A flame-dried, 250-mL, 3-necked, round-bottomed flask equipped with a mechanical stirrer, addition funnel (with septum and N_2 inlet), and thermometer charged with 4.00 g (15.7 mmol) of amidoester **31** and 100 mL ether. The mixture was cooled to 5°C and the addition funnel charged with 36.2 mL (2.7M, 99.7 mmol) of methyl-magnesium bromide. The Grignard reagent was added dropwise over 30 minutes at 0-5°C. The ice bath was removed and the mixture stirred for 3 h. The mixture was then cooled to 0°C and 50 mL of a saturated K_2CO_3 solution was added. The mixture was diluted with 200 mL of a saturated solution of Rochelle's salt. The aqueous layer was extracted with ethyl acetate (3 X 250 mL) and the organic layers dried over $MgSO_4$, filtered, and the solvent removed. The crude product was purified by Kugelrohr distillation 80°C at 0.3 torr to yield 1.47 g (58.8%) of amino alcohol **36**.

Analytical data from **36**

M.W.: 159.28

bp: 80°C at 0.3 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

2.86 (t, 2H, J= 5.5 Hz, $H_2C(4)$), 1.57 (t, 2H, J= 5.5 Hz, $H_2C(3)$), 1.21 (s, 6H, $H_3C(1)$, $CH_3C(2)$), 1.10 (s, 9H, $(CH_3)_3C$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

71.0 (s, C(2)), 50.4 (s, $(CH_3)_3\underline{C}$), 40.8 (s, C(3)), 38.7(s, C(2)), 29.6 (s, C(1), $\underline{C}H_3C(2)$), 28.5 (s, $(\underline{C}H_3)_3C$)

IR: (neat)

3276 m (broadened, OH, NH), 2971 s, 2932 s, 2869 m, 1717 w, 1653 w, 1480 m, 1426 m, 1391 m (sh), 1362 s, 1267 w, 1233 m, 1215 m, 1154 m, 1086 w, 1017 w, 967 w, 938 w, 887 w

MS: (70 eV)

144 (M^+- 15, 100), 126 (90), 88 (14), 86 (30), 81 (11), 70 (75), 58 (43), 57 (11)

Analysis for $C_9H_{21}NO$:

Calc.: C 67.87%; H 13.29%; N 8.79%

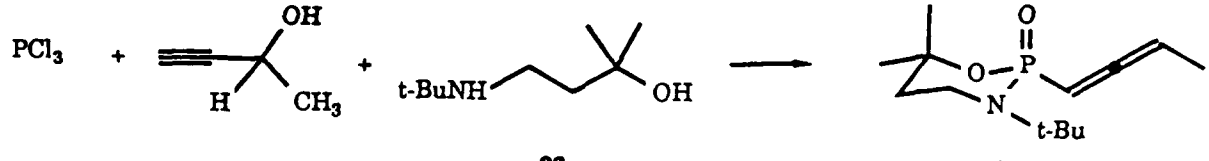
Found: C 67.52%; H 13.28%; N 8.84%

4.2.2.1 Allenes.

General procedure for the Synthesis of Allenic Oxazaphosphorinanes.

An oven-dried, 250-mL, 3-necked, round-bottomed flask equipped with a stirring bar, septum, thermometer, and N_2 inlet was charged with 100 mL of CH_2Cl_2 and cooled to 0°C. Phosphorus trichloride (13.7 mmol) and N-methylmorpholine (13.7 mmol) were added sequentially via syringe. After stirring for 5 minutes, the appropriate butynol (13.7 mmol) in 5 mL of CH_2Cl_2 was added via syringe (0-5°C). After stirring for 20 minutes, N-methylmorpholine (27.4 mmol) was added. After stirring for 5 minutes, the appropriate amino alcohol (13.7 mmol) in 5 mL of CH_2Cl_2 was added. The reaction mixture was warmed to room temperature and stirred for 16 hours. The mixture was diluted with 100 mL of water and extracted with CH_2Cl_2 (3 X 100 mL). The organic layers were washed with water and brine (1 X 50 mL each). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed.

Preparation of N-*t*-Butyl-2-(1',2'-butadienyl)-6,6-dimethyl-2-oxo-1,3,2-oxazaphosphorinane 37



36 37

The crude product was purified by flash chromatography (hexane/acetone : 1/1) to give 57.9% of allene 37.

Analytical Data from 37

M.W.: 257.31

bp: 175°C at 0.2 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

5.46- 5.42 (m, 1H, HC(3')), 5.30- 5.20 (m, 1H, HC(1')), 3.26- 3.07 (m, 2H, $H_2C(4)$), 1.94 -1.80 (m, 2H, $H_2C(5)$), 1.74- 1.66 (m, 3H, $H_3C(4')$), 1.44 (d, 3H, J= 2.5 Hz, $CH_3C(6)$), 1.38 (s, 12H, $(CH_3)_3C$, $CH_3C(6)$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

209.6 (s, C(2')), 209.2 (s, C(2')), 88.7 (d, J= 6.0 Hz, C(3')), 86.3 (d, J= 6.9 Hz, C(3')), 79.9 (d, J= 6.3 Hz, C(6)), 79.8 (d, J=7.2 Hz, C(6)), 54.5 (d, J=4.2 Hz, $(CH_3)_3$ C), 28.6 (s, $(CH_3)_3C$), 12.2 (d, J= 7.3 Hz C(4')), 11.7 (d, J= 7.0 Hz, C(4')). The following resonances could not be unambiguously assigned: 86.4, 86.3, 85.7, 85.5, 38.7, 38.5, 38.4, 38.3, 28.7, 28.5, 28.4

^{31}P NMR: (121.4 MHz, acetone)

9.26, 9.24

IR: (neat)

2977 s, 2874 m, 2357 w, 1952 m (C=C=C), 1639 w, 1466 m, 1370 s, 1291 w, 1254 s (P=O), 1208 s, 1152 s, 1102 m, 1061 s, 997 s, 936 m, 889 m, 855 m

MS: (70 eV)

257 (M^+, 6.9), 243 (13), 242 (100), 204 (11), 201 (47), 186 (94), 174 (40), 148 (91), 146 (59), 145 (58), 84 (16), 70 (61), 69 (48), 58 (37), 57 (78), 56 (13), 55 (19), 53 (28), 43 (15), 42 (20), 41 (82), 39 (13), 31 (19)

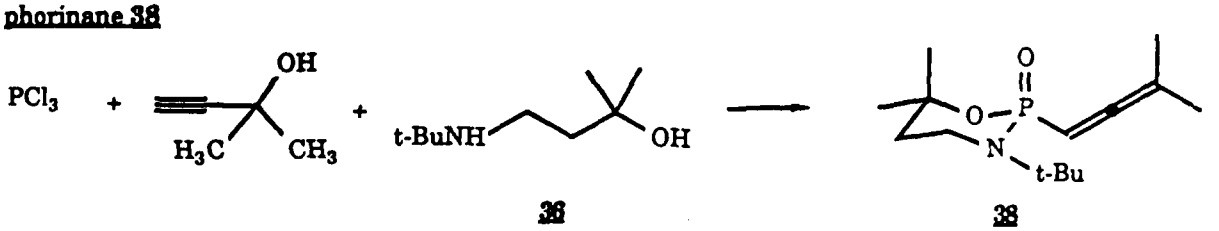
HRMS for $C_{13}H_{24}NO_2P$:

Calc.: 257.1542

Found: 257.1544

TLC: hexane/acetone : 1/1 R_f= 0.40

Preparation of N-*t*-Butyl-6,6-dimethyl-2-(3'-methyl-1',2'-butadienyl)-2-oxo-1,3,2-oxazaphosphorinane **38**



36 **38**

The crude product was purified by flash chromatography (hexane/acetone : 1/1) to give 53.1% of allene 38.

Analytical data from 38

M.W.: 271.34

bp: 205°C at 0.15 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

5.55-5.47 (m, 1H, HC(1')), 3.20- 3.08 (m, 2H, $H_2C(4)$), 2.04-1.94 (m, 2H,$H_2C(5)$), 1.89-1.82 (m, 6H, $(CH_3)_2C(3')$), 1.57(s, $CH_3C(6)$), 1.48 (s, 12H, $(CH_3)_3C$, $CH_3C(6)$)

^{13}C NMR: (75.5 MHz,$CDCl_3$)

207.3 (s, C(2')), 95.3 (d, J= 17.2 Hz, C(3')), 86.7 (d, J= 182.9 Hz, C(1')) 80.1 (d, J= 8.6 Hz, C(6)), 54.9 (d, J= 5.2 Hz, $(CH_3)_3\underline{C}$), 38.9 (d, J= 13.7 Hz, C(4)), 38.8(s, C(5)), 29.1 (s, $\underline{C}H_3C(6)$), 28.9 (s, $(\underline{C}H_3)_3C$), 28.8 (s, $\underline{C}H_3C(6)$), 19.2 (, J= 6.6 Hz C(4')), 18.7 (d, J= 7.7 Hz, $\underline{C}H_3C(3')$)

^{31}P NMR: (121.4 MHz, acetone)

9.6

IR: (4% in CCl_4)

2980 s, 2940 s, 2872 m (sh), 1964 m (C=C=C), 1632 w, 1559 w, 1466 m, 1445 m, 1395 m, 1385 m, 1362 s, 1291 s, 1252 s (P=O), 1235 s, 1204 s, 1152 s, 1103 m, 1061 m, 999 s, 932 m, 889 m

MS: (70 eV)

271 (M^+, 11.5), 257 (1), 256 (76), 215 (73), 201 (11), 200 (94), 198 (15), 188 (28), 160 (56), 159 (75), 148 (99), 132 (15), 126 (12), 84 (24), 70 (73), 69 (50), 67 (29), 58 (49), 57 (80), 56 (11), 55 (19), 43 (38), 42 (20), 41 (100), 39 (19), 31 (27)

HRMS for $C_{14}H_{26}NO_2P$:

Calc.: 271.1711

Found: 271.1706

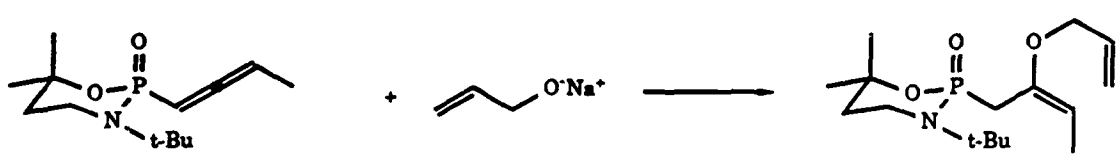
TLC: hexane/acetone : 1/1 R_f= 0.38

4.2.2.2. Allyl Vinyl Ethers.

General Procedure for the Synthesis of Oxazaphosphono Allyl Vinyl Ethers.

An oven-dried, 15-mL, 3-necked, round-bottomed flask equipped with stirring bar, septa, and N_2 inlet was charged with NaH dispersion (50%, 0.48 mmol). The NaH dispersion was rinsed with hexane (3X) and suspended in 3.0 mL THF. *t*-Butyl alcohol (0.96 mmol), if necessary, and the appropriate allyl alcohol (0.48 mmol) were added sequentially. After stirring for 10 minutes, a solution of the allene (0.40 mmol) in 1.0 mL THF was added via syringe, The reaction was monitored by TLC. Upon completion, the reacton was quenched with 5 mL water and extracted with ether (3 X 15 mL). The organic layers were washed with brine (1 X 15 mL), dried over $MgSO_4$, filtered, and the solvent removed.

Preparation of (*E*)-N-*t*-Butyl-6,6-dimethyl-2-oxo-[2'-(2-propenyloxy)-2'-butenyl]-1,3,2-oxaza-phosphorinane **39**



37 **39**

The crude product was purified by radial chromatography (hexane/acetone : 5/1) to give 63.7% of **39**.

Analytical Data from **39**

M. W.: 315.40

^{1}H NMR: (300 MHz, $CDCl_3$)

6.00- 5.88 (m, 1H, $HC{=}CH_2$), 5.31- 5.15 (m, 2H, $HC{=}CH_2$), 4.54- 4.46 (m, 1H, HC(3')), 4.20- 4.08 (m, 2H, OCH_2), 3.15- 2.93 (m, 3H, HC(1'), $H_2C(4)$), 2.61-2.50 (m, 1H, HC(1')), 1.89- 1.77 (m, 2H, $H_2C(5)$), 1.62- 1.51 (m, 3H, $CH_3C(4')$), 1.48 (s, 3H, $CH_3C(6)$), 1.37 (s, 9H, $(CH_3)_3C$)), 1.26 (s, 3H, $CH_3C(6)$)

^{13}C NMR (75.5 MHz, $CDCl_3$)

149.8 (d, J=12.2 Hz, C(2')), 133.8 (s, $\underline{C}H=CH_2$), 116.9 (s, $CH=\underline{C}H_2$), 93.9(d, J= 10.2 Hz, C(3')), 79.2 (d, J= 8.2Hz, C(6)), 67.8 (s, OCH_2), 55.1 (s, $(CH_3)_3\underline{C}$), 39.4 (s, C(4)), 39.3 (s, C(5)), 35.2 (d, J=134.6 Hz, C(1')), 29.7 (d, J= 8.0 Hz, $\underline{C}H_3C(6)$), 29.1 (s $(\underline{C}H_3)_3C$), 28.9(s, $\underline{C}H_3C(6)$), 12.3 (s, C(4'))

$^{31}\underline{P\ NMR:}$ (121.4 MHz, acetone)

20.5

IR: (neat)

2980 s, 2934 s, 2874 m (sh), 1665 s, 1466s, 1399m, 1387 m, 1372 s, 1362 m, 1348 m, 1293 s, 1256 s, 1231 s, 1202 s, 1152 s, 1102 s, 1063 m, 997 s, 926 s, 889 m

MS: (70 eV)

315 (M^+, 1.42), 300 (13), 274 (22), 242 (15), 218 (25), 186 (15), 174 (18), 162 (100), 150 (33), 148 (36), 146 (12), 126 (15), 84 (16), 80 (14), 70 (73), 69 (29), 58 (36), 57 (46), 56 (10), 55 (16), 53 (11) 42 (14), 41 (73), 39 (14), 32 (17)

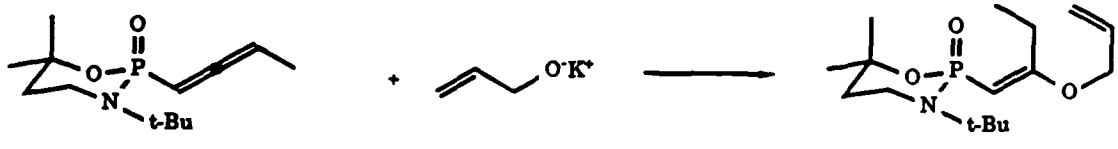
HRMS for $C_{16}H_{30}NO_3P$:

Calc.: 315.1975

Found: 315.1969

TLC: hexane/acetone : 1/1 R_f= 0.45

Preparation of (*E*)-N-*t*-Butyl-6,6-dimethyl-2-oxo-[(*E*)-2'-(2-propenyloxy)-1'-butenyl]-1,3,2-oxazaphosphorinane 40



37 40

The crude product was purified by flash chromatography (hexane/acetone : 1.5/1) to give 71.4% of 40.

Analytical data from40

M.W.: 315.40

mp: 60- 62°C

^{1}H NMR: (300 MHz,$CDCl_3$)

5.99-5.86 (m, 1H, $\underline{H}C=CH_2$), 5.34-5.20 (m, 2H, $CH=C\underline{H_2}$), 4.54 (d, 1H, J=7.5Hz, HC(1')), 4.23 (d, 2H, J= 5.1 Hz, OCH_2), 3.25- 3.05 (m, 2H, H_2C(4)), 2.66-2.45 (m, 2H, H_2C(3')), 2.09- 2.00 (m, 1H, HC(5')), 1.86-1.79 (m 1H, HC(5')), 1.51 (s, 3H, H_3CC(6)), 1.30 (s, 12H, $(CH_3)_3C$, H_3CC(6)), 1.09 (t, 3H, J= 7.5 Hz, H3C(4'))

^{13}C NMR: (75.5 MHz, $CDCl_3$)

171.7 (d, J= 19.7 Hz, C(2')). 132.5 (s, $\underline{C}H=CH_2$), 117.4 (s, $CH=\underline{C}H_2$), 92.5 (d, J= 195.4 Hz, C(1')), 78.9 (d, J= 7.5 Hz, C(6)), 67.9 (s, OCH_2), 54.7 (s, $(CH_3)_3\underline{C}$), 40.1 (d, J= 8.1 Hz, C(4)), 39.3 (s, C(5)), 29.9(s, $\underline{C}H_3C$(6)), 29.4 (d, J= 5.3 Hz, $\underline{C}H_3C$(6)), 29.0 (s,$(\underline{C}H_3)_3C$), 25.5,(s, C(3')), 11.4 (s, C(4'))

^{31}P NMR: (121.4 MHz, acetone)

15.8

IR: (4% in CCl_4)

2977 s, 2940 s, 2874 m, 1615 s (C=C), 1464 m, 1394 m, 1385 m, 1370 s, 1362 m, 1343 m, 1287 s, 1248 s, 1225 s (P=O), 1186 s, 1150 s, 1094 s, 1059 m, 1015 s, 968 s, 926 s, 887 s

MS: (70 eV)

315 (M^+, 19.2), 301 (15), 300 (89), 260 (11), 258 (11), 244 (32), 242 (19), 204 (46), 203 (16), 174 (11), 148 (15), 134 (12), 126 (76), 84 (13), 70 (100), 69 (11), 58 (31)

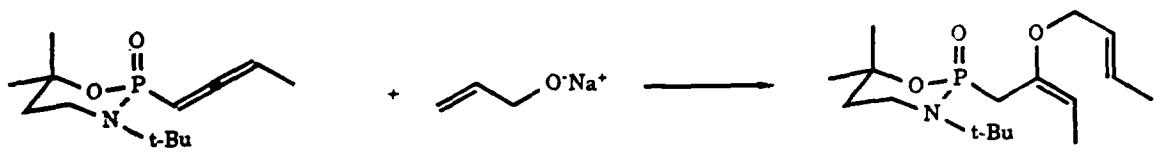
Analysis for $C_{16}H_{30}NO_3P$:

Calc.: C 60.93%; H 9.59%; N 4.44%; P 9.82%

Found: C 60.92%; H 9.65%; N 4.26%; P 9.73%

TLC: hexane/acetone : 1/1 R_f= 0.45

Preparation of (*E*)-N-*t*-Butyl-6,6-dimethyl-2-oxo-[2'-((*E*)-2-butenyloxy)-2'-butenyl]-1,3,2-oxazaphosphorinane 41



37 41

The crude product was purified by flash chromatography (hexane/acetone : 1/1) to give 46.1% of 41.

Analytical data from 41

M.W.: 329.42

^{1}H NMR: (300 MHz, $CDCl_3$)

5.77- 5.60 (m, 2H, CH=CH), 4.52-4.48 (m, 1H, HC(3')), 4.11-4.06 (m, 2H, OCH_2), 3.13- 2.94 (m, 3H, $H_2C(4)$, HC(1')), 2.57 (dxd, 1H, *J*= 18.1 Hz, 15.2 Hz, HC(1')), 1.87- 1.82 (m, 2H, $H_2C(5)$), 1.71 (d, 3H, *J*= 5.8 Hz, CH_3CH=CH) 1.62 (d, 3H, *J*= 6.7 Hz, 4.5 Hz, $H_3C(4')$), 1.50 (s, $CH_3C(6)$), 1.39 (s, 9H, $(CH_3)_3C$), 1.28 (d, 3H, *J*= 1.1 Hz, $CH_3(6)$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

149.8 (d, *J*= 15.5 Hz, C(2')), 129.4 (s, $\underline{C}H$=$CHCH_3$), 126.7 (s, CH=$\underline{C}HCH_3$), 93.7 (d, *J*= 9.9 Hz, C(3')), 79.2 (d, *J*= 9.6 Hz, C(6)), 67.5 (s, OCH_2), 55.1 (s, $(CH_3)_3\underline{C}$), 39.3 (d, *J*= 7.2 Hz, C(4)), 35.1 (d, *J*= 133.5 Hz, C(1')), 29.7 (s, $\underline{C}H_3C(6)$), 29.1 (s, $(\underline{C}H_3)_3C$), 28.8 (s, $\underline{C}H_3C(6)$), 17.7 (s, $\underline{C}H_3CH$=CH), 12.3 (s, C(4'))

^{31}P NMR: (121.4 MHz, acetone)

19.2

IR: (neat)

2977 s, 2587 w, 1719 w, 1665 s(C=C), 1464 m, 1397 m, 1372 m, 1293 s, 1256 s (P=O), 1231 s, 1200 s, 1152 s, 1102 s, 1065 m, 997 s, 926 m, 901 m, 847 m

MS: (70 eV)

329 (M^+, 10.2), 314 (16), 275 (14), 274 (74), 273 (15), 219 (39), 218 (39), 218 (62), 204 (24), 190 (13), 188 (11), 164 (27), 163 (70), 162 (100), 151 (66), 150 (36), 148 (15), 134 (16), 125 (11), 84 (14), 70 (21), 58 (11)

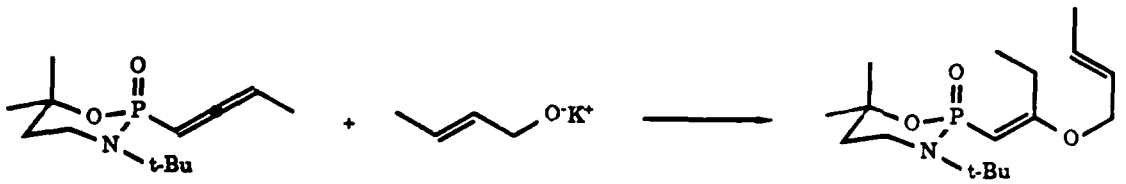
HRMS for $C_{17}H_{32}NO_3P$:

Calc.: 329.2120

Found: 329.2121

TLC: hexane/acetone : 1/1 R_f= 0.43

Preparation of (*E*)-N-*t*-Butyl-6,6-dimethyl-2-oxo-[2'-((*E*)-2-butenyloxy)-1'-butenyl]-1,3,2-oxazaphosphorinane 42



37 42

The crude product was purified by flash chromatography (hexane/acetone : 1/1) to give 79.7% of 42.

Analytical data from 42

M.W.: 329.42

bp: 200°C at 0.5 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

5.83-5.56 (m, 2H, CH=CH), 4.55 (d, 1H, *J*= 7.6 Hz, HC(1')), 4.17 (d, 2H, *J*= 5.9 Hz, OCH_2), 3.27- 3.07 (m, 2H, $H_2C(4)$). 2.66- 2.47 (m, 2H, $H_2C(3')$). 2.11- 2.03 (m, 1H, HC(5)), 1.88- 1.81 (m, 1H, HC(5)), 1.72 (d, 3H, *J*= 5.7 Hz, CH_3CH=CH), 1.53 (s, 3H, $CH_3C(6)$), 1.33 (s, 12 H, $(CH_3)_3C$, $CH_3C(6)$), 1.10 (t, 3H, *J*= 7.5 Hz, $H_3C(4')$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

171.8 (d, *J*= 19.5 Hz, C(2')), 130.0 (s, CH=$CHCH_3$), 125.3 (s, CH=$CHCH_3$), 91.7 (d, *J*= 195.3 Hz, C(1')), 78.7 (d, *J*= 8.6 Hz, C(6)), 67.9 (s, OCH_2), 54.6 (d, *J*= 4.7 Hz, $(CH_3)_3C$), 40.0 (d, *J*= 7.5Hz, C(4)), 39.2 (s, C(5)), 29.8(s, $CH_3C(6)$), 29.3 (d, *J*= 5.6 Hz, $CH_3C(6)$), 28.9 (s, $(CH_3)_3C$), 25.5 (s, C(3')), 17.6 (s, CH_3CH=CH), 11.4 (s, C(4'))

^{31}P NMR: (121.4 MHz, acetone)

16.0

IR: (neat)

2975 s, 2876 m, 2361 w, 1709 w, 1613 s(C=C), 1464 m, 1370 m, 1347 m, 1289 m, 1250 s (P=O), 1223 s, 1186 s, 1152 s, 1094 s, 1063 m, 1017 m, 967 s, 932 m, 889 m

MS: (70 eV)

330 (M^++1, 11.4), 329 (M^+, 30.5), 314 (46), 273 (15), 272 (20), 260 (46), 258 (24), 256 (11), 246 (12), 219 (15), 218 (55), 217 (20), 216 (13), 206 (13), 205 (13), 204 (55), 202 (19), 192 (18), 190 (25), 188 (18), 164 (91), 163 (30), 162 (15), 160 (10), 152 (23), 151 (19), 148 (34), 135 (13), 134 (52), 127 (10), 126 (100), 84 (42), 83 (11), 70 (99), 58 (41), 55 (10)

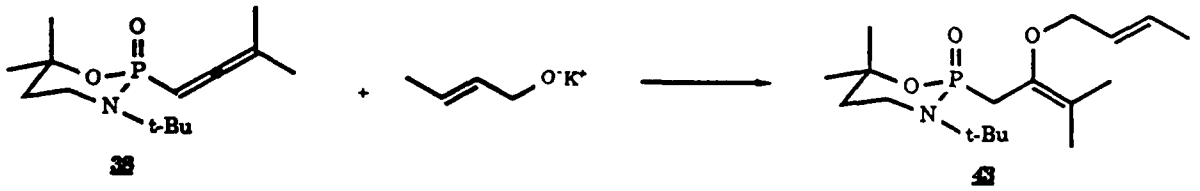
HRMS for $C_{17}H_{32}NO_3P$:

Calc: 329.2120

Found: 329.2124

TLC: hexane/acetone : 1/1 R_f= 0.43

Preparation of (*E*)-N-*t*-Butyl-6,6-dimethyl-2-oxo-[2'-((*E*)-2-butenyloxy)-3'-methyl-2'-butenyl]-1,3,2-oxazaphosphorinane 43



38 43

The crude product was purified by flash chromatography (hexane/isopropanol : 10/1) to give 51.0% of 43.

Analytical data from 43

M.W.: 343.45

^{1}H NMR: (300 MHz, $CDCl_3$)

5.72- 5.60 (m, 2H, CH=CH), 4.10-3.96 (m, 2H, OCH_2), 3.13- 3.04 (m, 2H, $H_2C(4)$), 2.89 (dxd, 1H, *J*= 18.9 Hz, 15.6 Hz, HC(1')), 2.62 (dxd, 1H, *J*= 15.9 Hz, 15.5 Hz, HC(1')), 1.83 (t, 2H, *J*= 6.3 Hz, $H_2C(5)$),

1.68 (d, 3H, J= 7.5 Hz, CH_3CH), 1.67- 1.62 (m, 6H, $(CH_3)_2C$=C), 1.48 (s, 3H, $CH_3C(6)$), 1.37(s, 9H, $(CH_3)_3C$), 1.25 (s, 3H, $CH_3C(6)$)

^{13}C NMR: (75.5MHz, $CDCl_3$)

142.6 (d, J= 12.5 Hz, C(2')), 127.7 (s, CH=CHCH$_3$), 123.8 (s, CH=CHCH$_3$), 117.5 (d, J= 11.0 Hz, C(3')), 78.8 (d, J= 8.7 Hz, C(6)), 69.2 (s, OCH_2), 54.7 (s, $(CH_3)_3C$), 38.7 (s, C(4)), 38.6 (s C(5)), 32.5 (d, J= 142.7 Hz, C(1')), 29.3 (s, $CH_3C(6)$), 29.0 (s, $(CH_3)_3C$), 28.9 (s, $CH_3C(6)$), 19.1 (s, CH=CHCH$_3$), 16.8 (s, $CH_3C(3')$), 16.7 (s, $CH_3C(3')$)

^{31}P NMR: (121.4 MHz, acetone)

20.5

IR: (neat)

2973 s, 2926 s, 2732 m (sh), 1676 w, 1609 w, 1464 m, 1387 m, 1370 m, 1293 s, 1254 s (P=O), 1196 s, 1152 s, 1094 s, 1065 m, 997 s, 928 m, 889 m, 843 w, 806 m

MS: (70 eV)

343 (M+, 3.38), 328 (26), 289 (11), 288 (28), 286 (12), 233 (28), 232 (29), 190 (18), 177 (46), 176 (42), 165 (56), 164 (19), 149 (11), 148 (100), 147 (12), 126 (26), 86 (17), 84 (15), 70 (28), 58 (14)

HRMS for $C_{18}H_{34}NO_3P$:

Calc: 343.2276

Found: 343.2278

TLC: hexane/acetone : 1/1 R_f= 0.45

4.2.2.3. Claisen Rearrangements.

Preparation of [*R,S*](P,3')-N-*t*-Butyl-6,6-dimethyl-2-(3'-methyl-2'-oxo-5'-hexenyl)-2-oxo-1,3,2-oxazaphosphorinane 47

46 47

KH/LiCl/DMSO: Radial chromatography (hexane/acetone : 3/1) afforded 81.3% of 47

Thermal: Radial chromatography (hexane/acetone : 3/1) afforded 92.6% of 47

M.W.: 315.40

^{1}H NMR: (500 MHz, $CDCl_3$)

Major diastereomer 47 5.76- 5.69 (m, 1H, HC(5')), 5.07- 5.02 (m, 2H, $H_2C(6')$), 3.39 (dxd, 1H, *J*= 21.5 Hz, 13.5 Hz,HC(1')), 3.18-3.05 (m, 2H, $H_2C(4)$), 2.93 (dxd, 1H, *J*= 21.5 Hz, 13.5 Hz, HC(1')), 2.92-2.87 (m, 1H, HC(3')), 2.43- 2.37 (m, 1H, $H_2C(5)$), 2.09- 2.03 (m, 1H, HC(4')), 2.00-1.95 (m, 1H HC(5)), 1.88- 1.84 (m, 1H, HC(5)), 1.51 (s, 3H, $CH_3C(6)$), 1.37 (s, 9H, $(CH_3)_3C$), 1.30 (s, 3H, $CH_3C(6)$), 1.09 (d, 3H, J= 7.2 Hz, $CH_3C(3')$). Minor diastereomer 48: 5.76- 5.69 (m, 1H, HC(5')), 5.07- 5.02 (m, 2H, $H_2C(6')$), 3.40 (dxd, 1H, *J*= 21.5 Hz, 13.5 Hz,HC(1')), 3.18-3.05 (m, 2H, $H_2C(4)$), 2.93 (dxd, 1H, *J*= 21.5 Hz, 13.5 Hz, HC(1')), 2.92-2.87 (m, 1H, HC(3')), 2.43- 2.37 (m, 1H, $H_2C(5)$), 2.09- 2.03 (m, 1H, HC(4')), 2.00-1.95 (m, 1H, HC(5)), 1.88- 1.84 (m, 1H, HC(5)), 1.51 (s, 3H, $CH_3C(6)$), 1.37 (s, 9H, $(CH_3)_3C$), 1.30 (s, 3H, $H_3C(6)$), 1.06 (d, 3H, *J*= 7.0 Hz, $CH_3C(3')$)

^{13}C NMR: (125.8 MHz, $CDCl_3$)

206.6 (d, *J*= 7.0 Hz, C(2')), 135 (s, C(5')), 116.7 (s, C(6')), 80.5 (d, *J*= 7.9 Hz, C(6)), 55.2 (s, $(CH_3)_3\underline{C}$), 46.7 (d, *J*= 118.3 Hz, C(1')), 45.7 (s, C(3')), 40.0(d, *J*= 7.1 Hz, C(4)), 39.3 (s, C(5)), 36.2 (s, C(4')), 29.9 (s, $\underline{C}H_3C(6)$), 29.2 (d, *J*=7.0- Hz, $\underline{C}H_3C(6)$), 28.8 (s,$(\underline{C}H_3)_3C$), 16.0 (s, $\underline{C}H_3C(3')$)

^{31}P NMR: (121.4 MHz, acetone)

47: 15.9. 48: 15.8

IR: (neat)

3077 w, 2975 s, 2934 s, 1705 s,(C=O), 1642 w, 1460 m, 1397 m, 1291 s, 1254 s (P=O), 1194 s, 1102 m, 1063m, 992 s, 920 s, 891 m, 868 m

MS: (70 eV)

315 (M^+, 5.52), 301 (15), 300 (100), 259 (12), 258 (30), 244 (23), 242 (11), 232 (20), 204 (27), 192 (24), 174 (12) 148 (15), 135 (13), 126 (28), 109 (12), 84 (17) 70 (98), 58 (44)

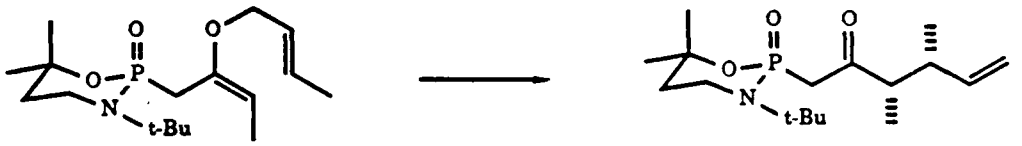
Analysis for $C_{16}H_{30}NO_3P$:

Calc.: C 60.93%; H 9.59%; N 4.44%; P 9.82%

Found: C 60.92%; H 9.34%; N 4.61%; P 10.09%

TLC: benzene/acetone : 2/1 R_f= 0.39

Preparation of [*R,S*](Pl,3'l,4'u)-N-*t*-Butyl-6,6-dimethyl-2-(3',4'dimethyl-2'-oxo-5'-hexenyl)-2-oxo-1,3,2-oxazaphosphorinane **49**



41 **49**

KH/LiCl/DMSO: Radial chromatography (hexane/acetone : 1/1) afforded 80.2% of **49**

Thermal: Radial chromatography (hexane/acetone : 1/1) afforded 84.2% of **49**

Analytical data from **49**

M.W.: 329.42

bp: 150°C at 0.05 torr

^{1}H NMR: (500 MHz, $CDCl_3$)

Major diastereomer **49**: 5.81-5.74 (m, 1H, HC(5')), 5.01- 4.96(m, 2H, HC(6')), 3.27 (dxd, 1H, *J*= 17.7 Hz, 13.7 Hz, HC(1')), 3.16- 3.11 (m, 2H, H_2C(4)), 2.98 (dxd, 1H, *J*= 16.9, 13.7 Hz, HC(1')), 2.81-2.77 (m, 1H, HC(3')), 2.55-2.51 (m, 1H, HC(4')), 1.99- 1.93 (m, 1H, HC(5)), 1.88- 1.84 (m, 1H, HC(5)), 1.50 (s, 3H, CH_3C(6)), 1.36 (s, 9H, $(CH_3)_3C$), 1.30(s, 3H, CH_3C(6)), 1.04 (d, 3H, *J*= 7.1 Hz, CH_3C(3')), 0.95 (d, 3H, *J*= 6.9 Hz, CH_3C(4')). Minor diastereomer: 5.81-5.74 (m, 1H, HC(5')), 5.01- 4.96(m, 2H, HC(6')), 3.46 (dxd, 1H, *J*= 18.7 Hz, 13.3 Hz, HC(1')), 3.16- 3.11 (m, 2H, H_2C(4)), 2.90 (dxd, 1H, *J*= 16.9, 13.7 Hz, HC(1')), 2.81-2.77 (m, 1H, HC(3')), 2.55-2.51 (m, 1H, HC(4')), 1.99- 1.93 (m, 1H, HC(5)), 1.88- 1.84 (m, 1H, HC(5), 1.50 (s, 3H, CH_3C(6)), 1.37 (s, 9H, $(CH_3)_3C$), 1.30 (s, 3H, CH_3C(6)), 0.99 (d, 3H, *J*= 6.9 Hz, CH_3C(3')), 0.93 (d, 3H, *J*= 6.8 Hz, CH_3C(4'))

^{13}C NMR: (125.8 MHz, $CDCl_3$)

206.6 (d, J= 4.9 Hz, C(2')), 142 (s, C(5')), 114 (s, C(6')), 80.5 (d, J= 66.1 Hz, C(6)), 55.3 (s, $(CH_3)_3\underline{C}$), 51.3 (s, C(3')), 47.0 (d, J= 120.2 Hz C(1')), 40.0 (s, C(4)), 39.3 (s, C(5)), 38.7 (s, C(4')), 30.0 (s, $\underline{C}H_3C(6)$), 29.1 (s, $(\underline{C}H_3)_3C$) 15.3(s, $\underline{C}H_3C(3')$), 12.3(s, $\underline{C}H_3C(4')$)

$^{31}\underline{P\ NMR:}$ (101.3 MHz, acetone)

15.2.

IR: (neat)

2977 s, 2878 m, 1705 s (C=O), 1638 w, 1456 m, 1456 m, 1397 m, 1372 s, 1291 s, 1254 s (P=O), 1196 s, 1150 s, 1100 m, 1063 m, 995 s, 918 m, 891 m, 868 m

MS: (70 eV)

329 (M^+, 16.5), 315 (26), 314 (100), 273 (25), 272 (43), 258 (20), 256 (10), 246 (16), 218 (18), 206 (27), 205 (10), 190 (16), 189 (13), 188 (11), 148 (12), 126 (33), 124 (12), 109 (10), 86 (22), 84 (21), 70 (65), 58 (25)

HRMS for $C_{17}H_{32}NO_3P$:

Calc.: 329.2120

Found: 329.2128

TLC: benzene/acetone : 2/1 R_f= 0.40

Preparation of [*R,S*](Pl,3'l,4'l)-N-*t*-Butyl-6,6-dimethyl-2-(3',4'dimethyl-2'-oxo-5'-hexenyl)-2-oxo-1,3,2-oxazaphosphorinane 50

42 50

KH/LiCl/DMSO: Radial chromatography (hexane/acetone : 3/1) afforded 60.2% of 50.

Analytical data from 50

M.W.: 329.42

bp: 150°C at 0.05 torr

^{1}H NMR: (500 MHz, $CDCl_3$)

5.67- 5.60 (m, 1H, HC(5')), 5.02- 4.96 (m, 2H, H2C(6')), 3.45 (dxd, 1H, *J*= 18.1 Hz, 13.5 Hz, HC(1')), 3.17- 3.04 (m, 2H, $H_2C(4)$), 2.87 (dxd, 1H, *J*= 16.7 Hz, 13.5 Hz, HC(1')), 2.91- 2.83 (m, 1H, HC(3')), 2.52- 2.48 (m, 1H, HC(4')), 2.01- 1.95 (m, HC(5)), 1.88- 1.84 (m, 1H, HC(5)), 1.52 (s, 3H, $CH_3C(6)$), 1.38 (s, 9H, $(CH_3)_3C$), 1.30 (s, 3H, $CH_3C(6)$), 1.04 (d, 3H, *J*= 8.6 Hz, $CH_3C(3')$), 1.01 (d, 3H, *J*= 8.6 Hz, $CH_3C(4')$)

^{13}C NMR: (125.8 MHz, $CDCl_3$)

206.9 (d, *J*= 7.4 Hz, C(2')), 140.3 (s, C(5')), 115.0 (s, C(6')), 80.5 (d, *J*= 7.8 Hz, C(6)), 55.3 (s, $(CH_3)_3\underline{C}$), 51.3 (s, C(3')), 48.5 (d, *J*= 118.4 Hz, C(1')), 40.1 (s, C(4')), 39.4 (s, C(4)), 39.4 (s, C(5)), 30.0 (s, $\underline{C}H_3C(6)$), 29.2 (s, $\underline{C}H_3C(6)$), 29.0 (s, $(\underline{C}H_3)_3C$), 18.0 (s, $\underline{C}H_3C(3')$), 12.6 (s, $\underline{C}H_3C(4')$)

^{31}P NMR: (121.4 MHz, acetone)

16.1

IR: (neat)

2975 s, 2878 m (sh), 1703 s (C=O), 1639 m, 1456 m, 1397 m, 1372 s, 1291 s, 1252 s (P=O), 1190 s, 1150 s, 1100 m, 1063 s, 995 s, 918 s, 891 s, 868 m

MS: (70 eV)

329 (M^+, 16.2), 315 (18), 314 (100), 273 (19), 272 (39), 258 (15), 246 (15), 218 (15), 206 (24.0), 190 (12), 126 (24), 84 (15), 70 (46), 58 (18)

HRMS for $C_{17}H_{32}NO_3P$:

Calc.: 329.2120

TLC: benzene/acetone : 2/1 R_f= 0.40

Preparation of [*R,S*](Pl,4'u)-N-*t*-Butyl-6,6-dimethyl-2-(3',3',4'trimethyl-2'-oxo-5'-hexenyl)-2-oxo-1,3,2-oxazaphosphorinane 51

43 51

KH/LiCl/DMSO: Radial chromatography (hexane/acetone : 1/1) afforded 94.2% of **51**.

Thermal: Radial chromatography (hexane/acetone : 1/1) afforded 65.8% of **51**.

Analytical data from **51**

M.W.: 343.46

bp: 160°C at 0.05 torr

^{1}H NMR: (500 MHz, $CDCl_3$)

Major diastereomer: 5.68- 5.60 (m, 1H, HC(5')), 5.09- 5.00 (m, 2H, $H_2C(6')$), 3.53 (dxd, 1H, J= 17.5 Hz, 15.7 Hz, HC(1')), 3.31- 3.26 (m, 1H, HC(4)), 3.16- 3.10 (m, 1H, HC(4)), 2.80 (dxd, 1H, J= 17.9, 15.7 Hz, HC(1')), 2.46- 2.43 (m, 1H, HC(4')), 1.97- 1.88 (m, 2H, $H_2C(5)$), 1.51 (s, 3H, $CH_3C(6)$), 1.38 (s, 9H, $(CH_3)_3C$), 1.27 (s, 3H, $CH_3C(6)$), 1.11 (s, 3H, $CH_3C(3')$), 1.04 (s, 3H, $CH_3C(3')$), 0.93 (d, 3H, J= 6.7 Hz, $CH_3C(4')$). Minor diastereomer: 5.68- 5.60 (m, 1H, HC(5')), 5.09- 5.00 (m, 2H, $H_2C(6')$), 3.54 (dxd, 1H, J= 17.5 Hz, 15.7 Hz, HC(1')), 3.31- 3.26 (m, 1H, HC(4)), 3.16- 3.10 (m, 1H, HC(4)), 2.79 (dxd, 1H, J= 17.9, 15.7 Hz, HC(1')), 2.46- 2.43 (m, 1H, HC(4')), 1.97- 1.88 (m, 2H, $H_2C(5)$), 1.51 (s, 3H, $CH_3C(6)$), 1.36 (s, 9H, $(CH_3)_3C$), 1.27 (s, 3H, $CH_3C(6)$), 1.11 (s, 3H, $CH_3C(3')$), 1.04 (s, 3H, $CH_3C(3')$), 0.89 (d, 3H, J= 6.8 Hz, $CH_3C(4')$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

208.4 (d, J= 8.2 Hz, C(2')), 140.6 (s, C(5')), 115.6 (s, C(6')), 80.3 (d, J= 9.3 Hz, C(6)), 55.0 (d, J= 4.8 Hz, $(CH_3)_3\underline{C}$), 51.2 (s, C(3')), 44.0, (s, C(4')), 42.7 (d, J= 127.5 Hz, C(1')), 40.1 (d, J= 7.0 Hz, C(4)), 39.1 (s, C(5)), 30.1 (s, $\underline{C}H_3C(6)$), 29.4 (d, J= 7.0 Hz, $\underline{C}H_3C(6)$), 29.0 (s, $(\underline{C}H_3)_3C$), 21.4 (s, $\underline{C}H_3C(3')$), 20.4 (s, $\underline{C}H_3C(3')$), 14.9 (s, $\underline{C}H_3C(4')$)

^{31}P NMR: (121.4 MHz, acetone)

16.1.

IR: (neat)

2975 s, 1701 s (C=O), 1636 w, 1466 m, 1389 m, 1372 m, 1291 s, 1254 s (P=O), 1233 s, 1200 s, 1103 w, 1065 m, 997 s, 920 s, 891 m, 853 w

MS: (70 eV)

343 (M^+, 7.91), 329 (13), 328 (68), 300 (11), 287 (10), 286 (46), 232 (10), 220 (13), 190 (22), 148 (16), 126 (22), 110 (49), 88 (10), 86 (65), 84 (100), 75 (14), 70 (22), 58 (13)

HRMS for $C_{18}H_{34}NO_3P$:

Calc.: 343.2276

Found: 343.2288

TLC: benzene/acetone : 2/1 R_f= 0.40

4.2.3. Chiral Non-racemic Phosphorus Derivatives

Preparation of (*S*)-N-*t*-Butyl-3-hydroxybutyramide 52

(S) 52

The enantiomeric excess of (*S*)-ethyl-3-hydroxybutanoate was measured by two methods. Optical rotation gave an enantiomeric excess of 97% ($[\alpha]_{589}^{28}$= +42.5° (c= 1.4; $CHCl_3$)).[59] Analytical gas chromatographic separation of the Mosher esters[60] gave an enantiomeric excess of 96% (cOV-17, 165°C, R_t= 14.5 (minor diastereomer), R_t= 14.9 (major diastereomer)). An oven-dried, 100-mL, 3-necked, round-bottomed flask equipped with septum, stirring bar, thermometer, and N_2 inlet was charged with 7.95 mL (75.7 mmol) of *t*-butylamine and cooled to 0°C. Trimethylaluminum (2M in toluene, 37.8 mL, 75.7 mmol) was added slowly via syringe (0°-10°C). The mixture was warmed to room temperature for 30 minutes. After cooling to 0°C, 5.00 g (37.8 mmol) of (*S*)-ethyl-3-hydroxybutanoate was added dropwise via syringe (0-10°C). The mixture was warmed to room temperature and stirred for 20 hours. The mixture was cooled to 0°C and water (50 mL) was added dropwise. CAUTION: Upon the initial addition of water (< 1 mL), there is an induction period of several minutes followed by rapid, exothermic evolution of methane. The mixture was acidified to pH~ 6, filtered through a Buchner funnel and continuously extracted with ether for 20 hours. The

organic layer was dried over K_2CO_3, filtered, and the solvent removed. The crude product was purified by flash chromatography to afford 4.33 g (71.9%) of **52**.

Analytical data from (*S*)-**52**

M.W.: 159.23

mp: 89-90°C

$[\alpha]_{589}^{28}$= +14.2° (c= 1.4; $CHCl_3$)

^{1}H NMR: (300 MHz, $CDCl_3$)

5.53- 5.37 (m, broadened, 1H, NH), 4.21- 4.10 (m, 1H, HC(3)), 3.92 (d, *J*= 2.9 Hz, 1H, OH), 2.28- 2.14 (m, 2H, $H_2C(2)$), 1.35 (s, 9H, $(CH_3)_3C$), 1.20 (d, 3H, *J*= 6.2 Hz, $H_3C(4)$).

^{13}C NMR: (75.5 MHz, $CDCl_3$)

171.9 (s C(1)), 64.7 (s, C(3)), 51.2 (s, $(CH_3)_3\underline{C}$), 44.4 (s, C(2)), 28.7 (s, $(\underline{C}H_3)_3C$), 22.6 (s, C(4))

IR: (4% in CCl_4)

3443 m (broadened, OH), 2971 s, 1744 w, 1698 m, 1671 s (C=O), 1511 m, 1455 m, 1420 m, 1393 w, 1366 m, 1250 w, 1198 s, 1167 s, 1142 s, 928 w

MS: (70 eV)

159 (M^+, 11.0), 144 (24), 86 (12), 59 (18), 58 (100), 57 (17)

Analysis for $C_8H_{17}NO_2$:

Calc: C 60.35%; H 10.76%; N 8.80%

Found: C 60.65%; H 10.99%; N 8.79%

Preparation of (*S*)-*N*-*t*-Butyl-4-animo-2-butanol (*S*)-**53**

(S) **52** (S) **53**

An oven-dried, 250-mL, 3-necked, round-bottomed flask equipped with addition funnel (and septum), thermometer, stirring bar, and N_2 inlet was charged with 90 mL (1.0M, 90 mLmol) of BH_3.THF and cooled to 0°C. (*S*)-N-*t*-butyl-3-hydroxybutyramide (4.00 g, 25.1 mmol) in 25 mL THF was added dropwise via addition funnel (0-10°C). The mixture was warmed to room temperature and stirred for 3.25 h. The mixture was cooled to 0°C and 22.5 mL of 6N HCl was cautiously added. The mixture was warmed to room temperature and KOH pellets were added until the aqueous layer was saturated. The aqueous layer was extracted with ether (3 X 100 mL), dried over K_2CO_3, filtered, and the solvents removed. The crude product was purified by Kugelrohr distillation followed by fractional distillation to afford 2.43 g (66.8%) of (*S*)-53.

Analytical data from (*S*)-53

M.W.: 145.25

bp: 55°C at 0.15 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

3.99- 3.92 (m, 1H, HC(2)), 2.99 (dxt, 1H, *J*= 11.7 Hz, 4.0 Hz, HC(4)), 2.67 (txd, 1H, *J*= 11.4 Hz, 2.8 Hz, HC(4)), 1. 67- 1.59 (m, 1H, HC(3)), 1.44- 1.30 (m, 1H, HC(3)). 1.15 (d, 3H, *J*= 7.3 Hz, H_3C(1)), 1.09 (s, 9H, $(CH_3)_3C$))

^{13}C NMR: (75.5 MHz, $CDCl_3$)

69.2 (s, C(2)), 50.1 (s, $(CH_3)_3\underline{C}$), 41.0 (s, C(4)), 37.4 (s, C(3)), 28.4 (s, $(\underline{C}H_3)_3C$), 23.3 (s, C(1))

IR: (neat)

3278 s (broadened, OH, NH), 2965 s, 2928 s, 2867 s, 1655 w, 1480 s, 1443 s, 1391 m, 1364 s, 1335 m, 1231 s, 1215 s, 1138 s, 1121 s, 1094 m, 1030 m, 976 m, 911 m

MS: ((70 eV)

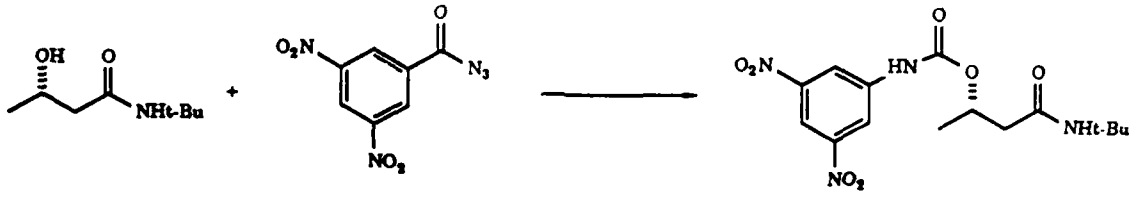
145 (M^+, 0.69), 130 (100), 112 (22), 72 (17), 70 (17), 58 (16)

Analysis for $C_8H_{19}NO$:

Calc: C 66.15%; H 13.18%; N 9.65%

Found: C 66.12%; H 13.23%; N 9.71%

Preparation of (*S*)-N-*t*-Butyl-3-hydroxybutryamido-3',5'-dinitrophenyl carbamate (*S*)-54



(S) 52 (S) 54

Compound (*S*)-54 was prepared by the method of Pirkle.[63]

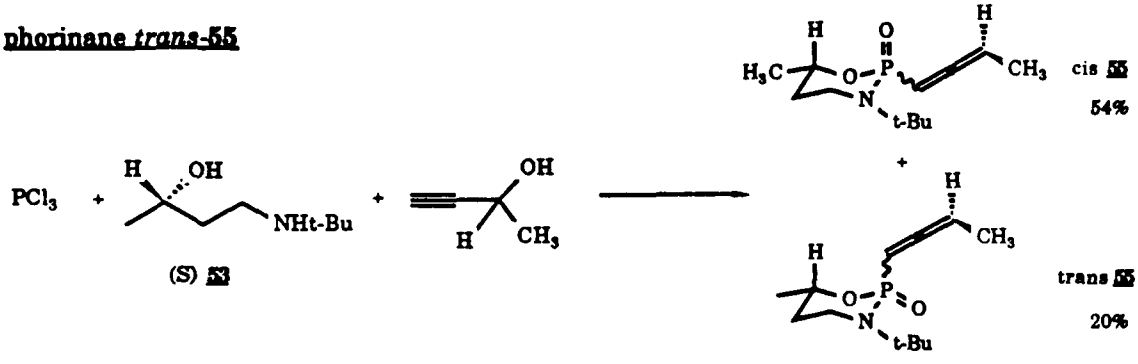
Analytical data from (*S*)-54

M.W.: 301.37

^{1}H NMR: (300 MHz, $CDCl_3$)

9.59-9.54 (m, broadened,1H, NH), 8.84- 8.81 (m, 2H, aromatic, ortho to carbamate) 8.56- 8.52 (m, 1H, aromatic para to carbamate) 6.84- 6.79 (m, broadened, 1H, NH) 5.36- 5.21 (m, 1H, CH_3CH) 2.53 (dxd, 1H, *J*= 7.2, 19.8, HC(2)), 2.38 (dxd, 1H, *J*= 7.2, 19.8, HC(2)),1.33 (d, 3H, *J*= 7.8 Hz, CH_3CH), 1.29 (s, 9H, $(CH_3)_3C$)

Preparation of [*S*](P 1,6 l)-N-*t*-Butyl-2-(1',2'-butadienyl)-6-methyl-2-oxo-1,3,2-oxazaphosphorinane *cis*-55 and [*R*](P 1,6 u)-N-*t*-Butyl-2-(1',2'-butadienyl)-6-methyl-2-oxo-1,3,2-oxazaphosphorinane *trans*-55



(S) 53 cis 55 54% trans 55 20%

The crude products were purified by flash chromatograpy (hexane/acetone : 3/1) to afford 54.3% of *cis*-55 and 19.5% of *trans*-55

Analytical data from *cis*-55

M.W.: 243.29

bp: 160°C at 0.03 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

5.47- 5.39 (m, 1H, HC(3')), 5.38- 5.23 (m, 1H, HC(1')), 4.62- 4.49 (m, 1H, HC(6)), 3.31- 3.03 (m, 2H, H_2C(4)), 2.09- 1.93 (m, 1H, HC(5)), 1.76- 1.61 (m, 4H, H_3C(4'), HC(5)), 1.35 (s, 9H, $(CH_3)_3C$), 1.32 (d, 3H, J= 6.3 Hz, CH_3C(6))

^{13}C NMR: (75.5 MHz, $CDCl_3$)

210.6 (s, C(2')), 210.3 (s, C2')), 54.7(s, $(CH_3)_3\underline{C}$), 40.3 (s, C(4)), 34.2 (s, C(5)), 29.1 (s, $(\underline{C}H_3)_3C$), 29.0 (s, $(\underline{C}H_3)_3C$), 12.5 (d, J= 6.9Hz, $\underline{C}H_3C$(6)), 12.1 (d, J= 7.0 Hz, $\underline{C}H_3C$(6)). The following resonances could not be unambiguously assigned: *87.6, 87.5, 86.3, 86.1, 85.9, 85.7, 85.2, 71.9, 71.8, 71.7, 22.0, 21.9.*

^{31}P NMR: (121.4 MHz, acetone)

13.1, 12.9

IR: (neat)

2975 s, 1952 s (C=C=C), 1653 w, 1445 m, 1366 s, 1279 s, 1254 s (P=O), 1204 s, 1129 s, 1044 s, 1013 s, 990 s, 949 s, 895 m, 828 m, 808 m

MS: (70 eV)

243 (M^+,3.20), 229 (12), 228 (100), 187 (49), 186 (26), 174 (16), 164 (11), 148 (10), 146 (14), 145 (14), 134 (12), 70 (20), 58 (29), 57 (12), 55 (10)

HRMS for $C_{12}H_{22}NO_2P$:

Calc: 243.1388

Found: 243.1385

TLC: hexane /acetone : 3/1 R_f= 0.30

Analytical data from *trans*-55

M.W.: 243.29

bp: 160°C at 0.03 torr

^{1}H NMR: (500 MHz, $CDCl_3$)

5.44- 5.39 (m, 1H, HC(3')), 5.33- 5.26 (m, 1H, HC(1')), 4.35- 4.30 (m, 1H, HC(6)), 3.32- 3.23 (m, 1H, HC(4)), 3.08- 3.00 (m, 1H, HC(4)), 1.80- 1.73 (m, 5H, $H_2C(5)$, $H_3C(4')$), 1.35 (s, $(CH_3)_3C$), 1.34- 1.32 (m, 3H, $CH_3C(6)$)

^{13}C NMR: (125.8 MHz, $CDCl_3$)

210.6 (s, C(2')), 210.3 (s, C(2')), 55.7 (s, $(CH_3)_3C$), 42.4 (s, C(4)), 34.9 (s, C(5)), 29.4 (s, $(CH_3)_3C$). The following resonances could not be unambiguously assigned: 85.9, 85.8, 85.7, 84.7, 84.5, 84.2, 83.1, 82.9, 75.1, 75.0, 74.9, 22.5, 22.4, 13.2, 13.1, 13.0.

^{31}P NMR: (121.4 MHz, acetone)

9.1, 8.9

IR: (neat)

2975 s, 2724 w (sh), 1949 s (C=C=C), 1638 m, 1557 w, 1474 w, 1366 s, 1321 m, 1281 s, 1256 s (P=O), 1204 s, 1152 s, 1111 s, 1046 s, 1016 s, 989 s, 893 s, 853 s, 810 s

MS: (70 eV)

243 (M^+, 4.59), 229 (13), 228 (100), 187 (41), 186 (14), 145 (13), 134 (13)

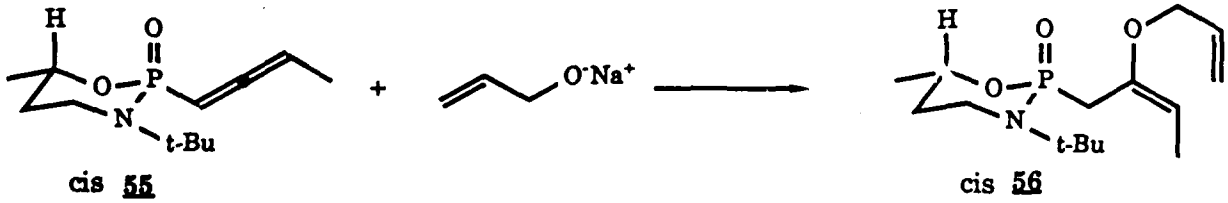
HRMS for $C_{12}H_{22}N_2P$:

Calc: 243.1388

Found: 243.1387

TLC: hexane /acetone : 3/1 R_f= 0.39

Preparation of [*S*](P 1, 6])(*E*)-N-*t*-Butyl-6-methyl-2-oxo-[2'-(2-propenyloxy)-2'-butenyl]-1,3,2-oxazaphosphorinane *cis*-56



cis 55 cis 56

The crude product was purified by flash chromatograpy (hexane/acetone : 2/1) to afford 54.0% of *cis*-**56**

Analytical data from *cis*-**56**

M.W.: 301.37

mp: 42- 44 °C

^{1}H NMR: (300 MHz, $CDCl_3$)

6.02- 5.89 (m, 1H, $CH{=}CH_2$), 5.33- 5.16 (m, 2H, $CH{=}CH_2$), 4,57- 4.45 (m, 2H, HC(6), HC(3')), 4.21- 4.09 (m, 2H, OCH_2), 3.15- 2.95(m, 3H, $H_2C(4)$, HC(1')), 2.63 (dxd, 1H, *J*= 17.1 Hz, 15.4 Hz, HC(1')), 2.01- 1.91 (m, 1H, HC(5)), 1.65- 1.51 (m, 4H, $H_3C(4')$, HC(5)), 1.37 (s, 9H, $(CH_3)_3C$), 1.27 (d, 3H, *J*= 6.4 Hz, $CH_3C(6)$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

149.2 (d, *J*= 6.4 Hz, C(2')), 133.7 (s, $\underline{C}H{=}CH_2$), 116.9 (s, $CH{=}\underline{C}H_2$), 94.3 (d, *J*= 10.6 Hz, C(3')), 70.3 (d, *J*= 7.9 Hz, C(6)), 67.8 (s, OCH_2), 55.1 (d, *J*= 4.9 Hz $(CH_3)_3\underline{C}$), 40.5 (s, C(4)), 34.4 (s, C(5)), 34.1 (d, *J*= 131.7 Hz, C(1')), 29.4 (s, $(\underline{C}H_3)_3C$), 22.3 (d, *J*= 9.0 Hz, $\underline{C}H_3C(6)$), 12.2 (s, C(4'))

^{31}P NMR: (121.4 MHz, acetone)

24.4

IR: (4% in CCl_4)

2977 m, 2932 m, 1667 m, 1458 w, 1401 w, 1364 w, 1347 w, 1277 m, 1258 s (P=O), 1233 s, 1202 s, 1146 m, 1127 m, 1102 m, 1044 m, 1009 m, 992 m, 947 m, 893 w

MS: (70 eV)

301 (M^+, 2.9), 286 (14), 260 (52), 204 (100), 162 (36), 110 (24), 70 (11)

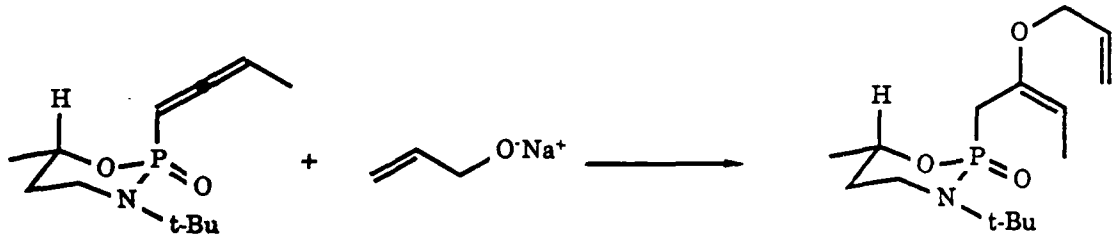
HRMS for $C_{15}H_{28}NO_3P$:

Calc: 301.1807

Found: 301.1799

TLC: hexane /acetone : 1/1 R_f= 0.35

Preparation of [*R*](P), 6u)(*E*)-N-*t*-Butyl-6-methyl-2-oxo-[2'-(2-propenyloxy)-2'-butenyl]-1,3,2-oxazaphosphorinane *trans*-56



trans 55 trans 56

The crude product was purified by flash chromatograpy (hexane/acetone : 2/1) to afford 30.0% of *trans*-56

Analytical data from *trans*-56

M.W.: 301.37

mp: 72-75°C

^{1}H NMR: (500 MHz, $CDCl_3$)

5.99- 5.93 (m, 1H, C<u>H</u>=CH_2), 5.32- 5.19 (m, 2H, CH=C<u>H</u>$_2$), 4.58- 4.55 (m, 1H, HC(3')), 4.44- 4.40 (m, 1H, HC(6)), 4.21- 4.15 (m, 2H, OCH_2), 3.28- 3.20 (m, 1H, HC(4)), 3.05- 2.95 (, 1H, HC(4)), 2.99 (dxd, 1H, *J*= 17.9 Hz, 15.1 Hz, HC(1')), 2.69 (dxd, 1H, *J*= 16.5 Hz, 15.7 Hz, HC(1')), 1.80- 1.68 (m, 5H, $H_2C(5)$, $H_3C(4')$), 1.35 (s, 9H, $(CH_3)_3C$), 1.31 (d, 3H, *J*= 6.2 Hz, $CH_3C(6)$)

^{13}C NMR: (125.8 MHz, $CDCl_3$)

163.0 (s, C(2')), 133.6 (s, <u>C</u>H=CH_2), 117.2 (s, CH=<u>C</u>H$_2$), 94.6 (d, *J*= 11.4 Hz, C(3')), 76.0 (d, *J*= 6.0 Hz, C(6)), 67.9 (s, OCH_2), 55.6 (s, $(CH_3)_3$<u>C</u>), 42.1 (s, C(4)), 35.1 (s, C(5)), 32.5 (d, *J*= 120.5 Hz, C(1')), 29.5 (s, (<u>C</u>H$_3$)$_3$C), 22.8 (d, *J*= 7.6 Hz, <u>C</u>H$_3$C(6)), 12.2(s, C(4'))

^{31}P NMR: (121.4 MHz, acetone)

19.9

IR: (4% in CCl_4)

2977 s, 2936 m, 2870 m (sh), 1711 w, 1667 m, 1553 m, 1458 m, 1399 m, 1385 m, 1366 m, 1346 w, 1281 s, 1260 s (P=O), 1202 s, 1102 s, 1048 s, 1017 s, 992 s, 930 m, 893 m

MS: (70 eV)

301 (M^+, 6.16), 286 (54), 260 (55), 245 (12), 204 (100), 176 (15), 174 (12), 162 (36), 148 (10), 135 (36), 134 (15), 112 (20), 70 (27)

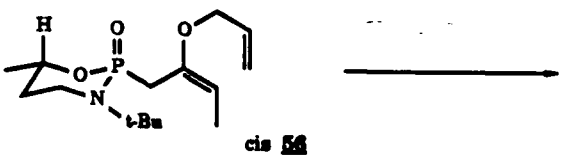
HRMS for $C_{15}H_{28}NO_3P$:

Calc: 301.1807

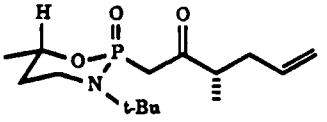
Found: 301.1816

TLC: hexane /acetone : 1/1 R_f= 0.44

Preparation of [S](Pl,6l,3'l)-N-*t*-Butyl-6-methyl-2-(3'-methyl-2'-oxo-5'-hexenyl)-2-oxo-1,3,2-oxazaphosphorinane *cis*-57



cis 56



cis 57

KH/LiCl/DMSO: Radial chromatography (hexane/acetone : 1/1) afforded 78.3% of *cis*-57.

n-BuLi/DMSO/THF: A flame-dried 15-mL, 3-necked, round-bottomed flask equipped with septa, stirring bar, and N_2 inlet was charged with 2.5 mL THF and 1.5 mL DMSO. *n*-BuLi (1.6 M, 0.46 mmol) was added dropwise via syringe. After 5 minutes, a solution of *cis*-56 (.186 mmol) in THF was added to the clear, colorless mixture. TLC indicated complete reaction after 15 minutes. The reaction was quenched with 5 mL of water and extracted with ether (3 X 15 mL). The organic layers were washed with water (3 X 5 mL) and brine (1 X 5 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed. The crude product was purified by rotary chromatography to afford 65.2% of *cis*-57.

Analytical data from *cis*-57

M.W.: 301.37

bp: 160°C at 0.5 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

Major diastereomer: 5.80- 5.67 (m, 1H, HC(5')), 5.09- 5.00 (m, 2H, $H_2C(6')$), 4.60- 4.54 (m, 1H, HC(6)), 3.38 (dxd, 1H, *J*=17.8 Hz, 13.3 Hz, HC(1')) 3.21- 2.90 (m, 4H, $H_2C(4)$, HC(1'), HC(3')), 2.46- 2.35 (m, 1H, HC(4')), 2.16- 2.01 (m, 2H, HC(4'), HC(5)), 1.70- 1.59 (m, 1H, HC(5)), 1.38 (s, 9H, $(CH_3)_3C$), 1.30 (d, 3H, *J*= 6.0 Hz, $CH_3C(6)$), 1.10 (d, 3H, *J*= 6.8 Hz, $CH_3C(3')$). Minor diastereomer: 5.80- 5.67 (m, 1H, HC(5')), 5.09- 5.00 (m, 2H, $H_2C(6')$), 4.60- 4.54 (m, 1H, HC(6)), 3.39 (dxd, 1H, *J*=17.8 Hz, 13.3 Hz, HC(1')) 3.21- 2.90 (m, 4H, $H_2C(4)$, HC(1'), HC(3')), 2.46-2.35 (m, 1H, HC(4')), 2.16- 2.01 (m, 2H, HC(4'), HC(5)), 1.70- 1.59 (m, 1H, HC(5)), 1.38 (s, 9H, $(CH_3)_3C$), 1.30 (d, 3H, *J*= 6.0 Hz, $CH_3C(6)$), 1.08 (d, 3H, *J*= 6.6 Hz, $CH_3C(3')$)

^{13}C NMR: (75.5 MHz, $CDCl_3$)

206.5 (d, *J*=6.8 Hz, C(2')), 135.7 (s, $\underline{C}H=CH_2$), 116.7 (s, $CH=\underline{C}H_2$), 70.7 (d, *J*= 7.1 Hz, C(6)), 55.3 (d, *J*=3.2 Hz, $(CH_3)_3\underline{C}$), 46.3 (s, C(3')), 45.5 (d, *J*= 116.1 Hz, C(1')), 40.1 (s, C(4')), 36.4 (s, C(5)), 34.5 (d, *J*= 3.5 Hz, C(4)), 29.3 (s, $(\underline{C}H_3)_3C$), 22.2 (d, *J*=2.2 Hz, $\underline{C}H_3C(6)$), 16.0 (s, $\underline{C}H_3C(3')$)

^{31}P NMR: (121.4 MHz, acetone)

19.2

IR: (neat)

2975 s, 2934 m, 1707 s (C=O), 1642 w, 1458 m, 1399 m, 1366 m, 1277 s, 1254 s, (P=O), 1198 s, 1125 s, 1044 s, 990 s, 947 m, 893 m, 870 m, 810 m

MS: (70 eV)

301 (M^+, 5.1), 286 (76), 244 (33), 228 (12), 192 (39), 174 (19),148 (12), 124 (21), 112 (48), 93 (12), 70 (100), 55 (26), 41 (44)

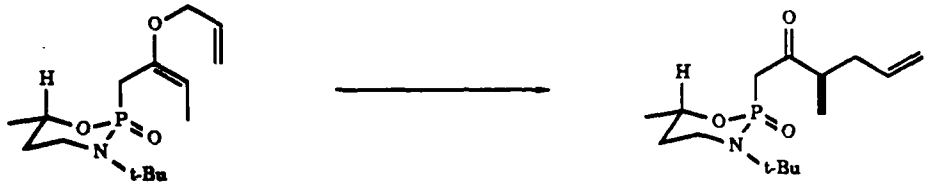
HRMS for $C_{15}H_{28}NO_3P$:

Calc: 301.1807

Found: 301.1810

TLC: benzene/acetone : 2/1 R_f= 0.28

Preparation of [*R*](Pl,6u,3'l)-*N*-*t*-Butyl-6-methyl-2-(3'-methyl-2'-oxo-5'-hexenyl)-2-oxo-1,3,2-oxazaphosphorinane *trans*-57



trans 56 trans 57

KH/LiCl/DMSO: Radial chromatography (hexane/acetone : 1/1) afforded 70.8% of *trans*-57

Analytical data from *trans*-57

M.W.: 301.37

bp: 160°C at 0.5 torr

^{1}H NMR: (500 MHz, $CDCl_3$)

Major diastereomer: 5.78- 5.70 (m, 1H, HC(5')), 5.07- 5.00 (m, 2H, $H_2C(6')$), 4.44- 4.37 (m, 1H, HC(6)), 3.35 3.25 (m, 1H, HC(4)), 3.30 (dxd, 1H, *J*= 17.0 Hz, 13.0 Hz, HC(1')), 3.11- 3.00 (m, 3H, HC(1'), HC(3'), HC(4)), 2.47-2.42 (m, 1H, HC(5)), 2.13- 2.07 (m, 1H, HC(5)), 1.86- 1.73 (m, 2H, HC(5)), 1.34 (s, 1H, $(CH_3)_3C$), 1.34- 1.31 (m, 3H, $CH_3C(6)$), 1.12 (d, 3H. *J*= 7.1 Hz, $CH_3C(3')$). Minor diastereomer: 5.78- 5.70 (m, 1H, HC(5')), 5.07- 5.00 (m, 2H, $H_2C(6')$), 4.44- 4.37 (m, 1H, HC(6)), 3.35 3.25 (m, 1H, HC(4)), 3.30 (dxd, 1H, *J*= 17.0 Hz, 13.0 Hz, HC(1')), 3.11- 3.00 (m, 3H, HC(1'), HC(3'), HC(4)), 2.47-2.42 (m, 1H, HC(5)), 2.13- 2.07 (m, 1H, HC(5)), 1.86- 1.73 (m, 2H, HC(5)), 1.34 (s, 1H, $(CH_3)_3C$), 1.34- 1.31 (m, 3H, $CH_3C(6)$), 1.11 (d, 3H, *J*= 7.1 Hz, $CH_3C(3')$)

^{13}C NMR: (125.8 MHz, $CDCl_3$)

207.2 (s, C(2')), 135.7 (s, C(5')), 116.8 (s, C(6')), 67.1 (d, *J*= 9.8 Hz, C(6)), 56.0 (s, $(CH_3)_3\underline{C}$), 43.7 (d, *J*= 105.4 Hz, C(1')), 36.5 (s, C(4')), 35.2 (s, C(5')), 29.4 (s, $(\underline{C}H_3)_3C$), 22.6 (d, *J*=7.3 Hz, $\underline{C}H_3C(6)$), 19.1(s, $\underline{C}H_3C(3')$)

^{31}P NMR: (121.4 MHz, acetone)

14.7

IR: (neat)

2977 s, 1703 s (C=O), 1642 w, 1458 w, 1368 m, 1283 s, 1256 s (P=O), 1196 m, 1152 w, 1109 m, 1043 s, 1017 s, 992 s, 972 m, 893 m, 862 w

MS: (70 eV)

301 (M^+, 5.25), 287 (16), 286 (100), 244(17), 192(16), 112 (24), 70 (34)

HRMS for $C_{15}H_{28}NO_3P$:

Calc: 301.1807

Found: 301.1811

TLC: benzene/acetone : 2/1 R_f= 0.35

Preparation of (*S*)[Pl, 6l, 3'l)-N-*t*-Butyl-6-methyl-2-(3'-methyl-2'-*t*-butyldimethylsiloxy-1,5-hexadienyl)-1,3,2-oxazaphosphorinane *cis*-58

cis 57 cis 58

Analytical data from *cis*-58

M.W.: 415.63

^{1}H NMR: (300 MHz, $CDCl_3$)

5.80-5.71 (m, 1H, HC(5')), 5.08- 5.01 (m, 2H, H_2C(6')), 4.61 (d, 1H, *J*= 15.4 Hz, HC(1')), 4.15- 4.10 (m, 1H, HC(6)), 3.29- 3.20 (m. 1H, HC(4)), 2.83- 2.91 (m, 1H, HC(4)), 2.42- 2.38 (m, 1H, HC(5)), 2.23- 2.18 (m, 1H, HC(5)), 2.15-2.07 (m, 1H, HC(3')), 1.34 (s, 9H, $(CH_3)_3$CN) 1.29 (d, 3H, *J*= 6.0 Hz, CH_3C(6)), 1.08 (d, 3H, *J*=8.1 Hz, CH_3C(3')), 097 (s, 9H, $(CH_3)_3$CSi), 0.30 (s, 3H, CH_3Si), 0.23 (s, 3H, CH_3Si)

Preparation of (*R*)[Pl, 6u, 3'l)-N-*t*-Butyl-6-methyl-2-(3'-methyl-2'-*t*-butyldimethylsiloxy-1,5-hexadienyl)-1,3,2-oxazaphosphorinane *trans*-58

trans 57 trans 58

Analytical data from *trans*-58

M.W.: 301.37

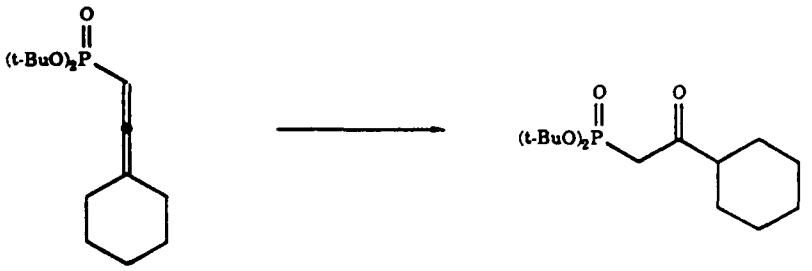
^{1}H NMR: (300 MHz, $CDCl_3$)

5.82-5.70 (m, 1H, HC(5')), 5.10- 5.01 (m, 2H, $H_2C(6')$), 4.66 (d, 1H, *J*= 15.4 Hz, HC(1')), 4.62- 4.53 (m, 1H, HC(6)), 3.19- 3.04 (m, 1H, HC(4)), 2.45- 2.35 (m, 1H, HC(4)), 2.42- 2.38 (m, 1H, HC(5)), 2.23- 2.18 (m, 1H, HC(5)), 2.15-2.07 (m, 1H, HC(3')), 1.34 (s, 9H, $(CH_3)_3CN$) 1.33 (d, 3H, *J*= 6.1 Hz, $CH_3C(6)$), 1.08 (d, 3H, *J*=6.1 Hz, $CH_3C(3')$), 0.99 (s, 9H, $(CH_3)_3CSi$), 0.27 (s, 6H, CH_3Si)

Chiral shift agent (CSA) study of (*R*)- and (*S*)-Dimethyl methylsuccinate. To a solution of the appropriate dimethyl methylsuccinate (0.25 M) in $CDCl_3$, was added (*R*)-2,2,2-trifluoro-1-(9-anthryl)ethanol in increments of 1.0 equivalents until separation was observed by 500 MHz ^{1}H NMR spectroscopy.

4.2.4. Phosphorus-Carbon Bond Cleavage.

Preparation of Di-*t*-butyl(2-cyclohexyl-2-oxo)ethylphosphonate 60



9 60

A 250-mL, high-pressure vial equipped with a stirring bar was charged with 3.26 g (10.8 mmol) af allene **6** and 25 mL diethylamine. The mixture was heated at 120°C for 16 h. The contents of the vial were transferred to a 100 mL pear-shaped flask with CH_2Cl_2. The solvents were removed in vacuo. The enamine was hydrolyzed by flash chromatography (hexane/acetone : 10/1) to yield 1.75 g (50.7%) of ketophosphonate **60**.

Analytical data from **60**

M.W.: 318.40

bp: 120°C at 0.05 torr

^{1}H NMR: (300 MHz, $CDCl_3$)

3.00 (d, 2H, J= 22.8 Hz, $H_2C(1)$), 2.70-2.62 (m, 1H, HC(1')), 1.85- 1.14 (m, 10H, $H_2C(2')$- $H_2C(6')$), 1.49 (s, 18H, $(CH_3)_3C$)

IR: (neat)

2978 s, 2930 s, 2855 m, 1705 s (C=O), 1478 w (sh), 1451 m, 1393 m, 1370 s, 1312 w, 1270 s (P=O), 1171, 1138 w, 1040 s (sh), 984 s, 920 m, 895w, 860 w, 826 w

MS: (70 eV)

207 (M^+- 111, 14.5), 206 (100), 124 (28), 123 (36), 110 (14), 107 (31), 96 (16), 83 (14), 57 (66), 56 (10), 55 (19), 41 (37)

Analysis for $C_{16}H_{31}O_4P$:

Calc: C 60.36%; H 9.81%; P 9.73%

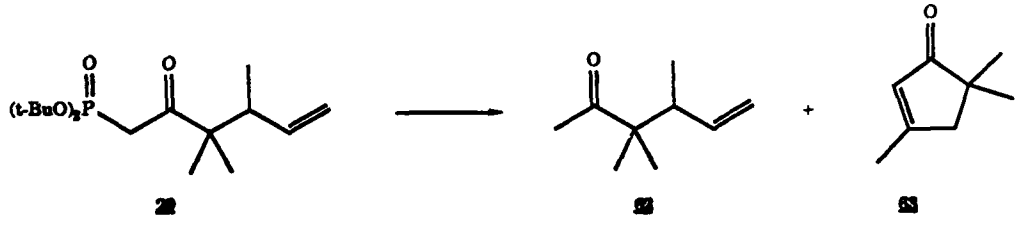
Found: C 60.23%; H 9.57%: P 9.54%

Dephosphorylation of phosphonate **60**

60 **61**

A flame-dried, 25-mL, 1-necked, round-bottomed flask equipped with a stirring bar and N_2 inlet charged with 245 mg (0.769 mmol) of phosphonate **60** and 3 ml CH_2Cl_2. Trifluoroacetic acid 35.5 μL (4.62 mmol) was added via syringe. After stirring for 30 minutes, the solvent was removed and the residue was distilled (bath temperature 200°C, 1 atm.) to afford 76.0 mg (78.3%) of methyl cyclohexyl ketone. This material was identical by ^1H NMR to methyl cyclohexyl ketone purchased from Aldrich.

Dephosphorylation of phosphonate **29**



29 **62** **63**

A flame-dried, 25-mL, 1-necked, round-bottomed flask equipped with a stirring bar and N_2 inlet charged with 188 mg (0.590 mmol) of phosphonate **29** and 5 ml CH_2Cl_2. Trifluoroacetic acid 275 μL (3.75 mmol) was added via syringe. After stirring for 30 minutes, the solvent was removed and the residue was distilled (bath temperature 200°C, 1 atm.) to afford 40.2 mg (53.9%) of a 1:1 mixture of **62** and **63**.

Analytical data from **62**

^{1}H NMR: (300 MHz, $CDCl_3$)

5.75- 5.56 (m, 1H, HC(5)), 5.10- 5.00 (m, 2H, $H_2C(6)$), 2.27 (d, 2H, J= 8.0 Hz, $H_2C(4)$), 2.17 (s, 3H, $H_3C(1)$), 1.17 (s, 6H, $(CH_3)_2C(3)$)

Analytical data from **63**

^{1}H NMR: (300 MHz, $CDCl_3$)

5.56 (q, 1H, J= 6.1 Hz, HC(2)), 2.18 (s, 2H, $H_2C(4)$), 1.72 (d, 3H, J= 6.1 Hz, $CH_3C(3)$), 1.21 (s, 6H, $(CH_3)_2C(5)$)

APPENDIX A

X-RAY CRYSTAL STRUCTURE DATA FOR 40

The following data were provided by Dr. Scott Wilson, X-Ray Crystallography Laboratory, Department of Chemistry, University of Illinois. An Enraf-Nonius CAD4 automated diffractometer with a molybdenum X-ray source was used for data gathering. The structure was solved by direct methods and refined by weighted and unweighted difference Fourier, and least squares methods.

Space group: P $2_1/c$ (C^5_{2h}) Monoclinic.

Cell parameters: a = 10.051(4) Angstroms; α = 90 degrees
b = 18.100(6); β = 116.95(2)
c = 11.527(2); γ = α
V = 1869(2) Angstoms^3

Density: ρ = 1.121

Positional Parameters

	Atom	X/A	Y/B	Z/C	Elevation	Radius
1	P	0.4624	0.2475	0.1426	1.74	1.33
2	O1	0.4963	0.1618	0.1510	1.67	0.71
3	O2	0.4816	0.2771	0.0333	2.65	0.71
4	O4	0.7886	0.3599	0.4409	1.80	0.71
5	N	0.2926	0.2520	0.1300	0.91	0.75
6	C1	0.4397	0.1011	0.2005	0.88	0.82
7	C2	0.2810	0.1198	0.1672	0.28	0.82
8	C3	0.2503	0.1933	0.1965	0.09	0.82
9	C4	0.4468	0.0353	0.1254	1.26	0.82
10	C5	0.5377	0.0918	0.3409	0.45	0.82
11	C6	0.2121	0.3232	0.1167	0.73	0.82
12	C7	0.2290	0.3506	0.2487	0.00	0.82
13	C8	0.2718	0.3832	0.0626	1.56	0.82
14	C9	0.0476	0.3129	0.0202	0.45	0.82
15	C10	0.5864	0.2850	0.2947	1.49	0.82
16	C11	0.7022	0.3280	0.3228	2.04	0.82
17	C12A	0.7901	0.3367	0.2406	3.10	0.82
18	C13A	0.7773	0.4178	0.2038	3.47	0.82
19	C14	0.7447	0.3484	0.5400	0.87	0.82
20	C15	0.8433	0.3928	0.6559	0.73	0.82
21	C16	0.9340	0.4397	0.6681	1.26	0.82

Bond Distances

P -O1	1.583(4)
P -O2	1.460(4)
P -N	1.648(5)

O1 -C1	1.466(8)
C1 -C2	1.50(1)
N -C3	1.480(9)
C2 -C3	1.44(1)
C1 -C4	1.493(9)
C1 -C5	1.474(9)
N -C6	1.492(9)
C6 -C7	1.535(10)
C6 -C8	1.51(1)
C6 -C9	1.529(10)
P -C10	1.763(6)
O3 -C11	1.368(8)
C10 -C11	1.313(9)
C11 -C12A	1.57(1)
C12A -C13A	1.52(1)
O3 -C14	1.414(8)
C14 -C15	1.49(1)
C15 -C16	1.21(1)

Bond Angles

O1 -P -O2	107.7(2)
O1 -P -N	103.8(3)
O1 -P -C10	106.3(2)
O2 -P -N	116.3(2)
O2 -P -C10	114.0(3)
N -P -C10	107.8(3)
P -O1 -C1	130.4(4)
C11 -O3 -C14	116.9(5)
P -N -C3	116.6(4)
P -N -C6	122.9(4)
C3 -N -C6	113.8(5)
O1 -C1 -C2	106.7(5)
O1 -C1 -C4	104.1(5)
O1 -C1 -C5	109.2(5)
C2 -C1 -C4	110.8(6)
N -C3 -C2	113.6(6)
N -C6 -C7	111.5(5)
N -C6 -C8	111.5(5)
N -C6 -C9	109.1(5)
C7 -C6 -C8	107.0(6)
C7 -C6 -C9	111.0(6)
C8 -C6 -C9	106.8(6)
P -C10 -C11	128.4(5)
O3 -C11 -C10	126.0(6)
O3 -C11 -C12A	106.4(6)
C10 -C11 -C12A	126.1(6)
C11 -C12A -C13A	105.4(8)

APPENDIX B

X-RAY CRYSTAL STRUCTURE DATA FOR *cis*-56

The following data were provided by Dr. Scott Wilson, X-Ray Crystallography Laboratory, Department of Chemistry, University of Illinois. An Enraf-Nonius CAD4 automated diffractometer with a molybdenum X-ray source was used for data gathering. The structure was solved by direct methods and refined by weighted and unweighted difference Fourier, and least squares methods.

Space group: $P\,2_1 2_1 2_1$ (D^4_2) Orthorhombic.

Cell parameters: a = 11.222(11) Angstroms; α = 90 degrees
b = 16.661(5); β = α
c = 18.764(10); γ = α
V = 3508(6) Angstoms^3

Density: ρ = 1.141

Positional Parameters

	Atom	X/A	Y/B	Z/C	Elevation	Radius
1	P1	0.0972	0.6694	0.0247	1.05	1.38
2	P21	-0.3564	0.3169	-0.0153	0.81	1.38
3	O1	0.1653	0.6639	0.0989	1.51	0.76
4	O2	0.0373	0.7451	0.0149	0.40	0.76
5	O3	0.0243	0.4840	-0.0430	1.07	0.76
6	O21	-0.4047	0.3183	0.0622	1.21	0.76
7	O22	-0.3024	0.2398	-0.0352	0.01	0.76
8	O23	-0.2981	0.5098	-0.0665	1.37	0.76
9	N1	0.1974	0.6452	-0.0345	1.89	0.80
10	N21	-0.4634	0.3486	-0.0663	1.69	0.80
11	C1	0.2848	0.6772	0.1054	2.35	0.87
12	H1	0.3114	0.7277	0.0882	2.41	0.47
13	C2	0.3431	0.6114	0.0616	2.99	0.87
14	H2a	0.3135	0.5610	0.0776	2.90	0.47
15	H2b	0.4268	0.6136	0.0690	3.59	0.47
16	C3	0.3129	0.6185	-0.0164	2.85	0.87
17	H3a	0.3317	0.5674	-0.0376	3.10	0.47
18	H3b	0.3740	0.6560	-0.0358	3.16	0.47
19	C4	0.3169	0.6780	0.1836	2.52	0.87
20	H4a	0.4000	0.6872	0.1886	3.11	0.47
21	H4b	0.2970	0.6276	0.2042	2.50	0.47
22	H4c	0.2741	0.7194	0.2071	2.08	0.47
23	C5	0.1772	0.6695	-0.1114	1.73	0.87
24	C6	0.2259	0.7547	-0.1234	1.86	0.87
25	H6a	0.3061	0.7574	-0.1075	2.43	0.47
26	H6b	0.1789	0.7921	-0.0974	1.39	0.47
27	H6c	0.2225	0.7672	-0.1728	1.84	0.47

28	C7	0.2515	0.6106	-0.1573	2.47	0.87
29	H7a	0.3329	0.6140	-0.1437	3.05	0.47
30	H7b	0.2438	0.6243	-0.2063	2.41	0.47
31	H7c	0.2238	0.5573	-0.1501	2.41	0.47
32	C8	0.0591	0.6614	-0.1341	0.90	0.87
33	H8a	0.0100	0.6966	-0.1072	0.42	0.47
34	H8b	0.0335	0.6077	-0.1271	0.86	0.47
35	H8c	0.0535	0.6747	-0.1832	0.86	0.47
36	C9	-0.0145	0.5894	0.0346	0.44	0.87
37	H9a	-0.0747	0.5978	-0.0002	0.00	0.47
38	H9b	-0.0481	0.5940	0.0809	0.15	0.47
39	C10	0.0322	0.5046	0.0263	1.03	0.87
40	C11	0.0834	0.4619	0.0770	1.48	0.87
41	H11	0.1198	0.4130	0.0626	1.90	0.47
42	C12	0.0911	0.4819	0.1533	1.43	0.87
43	H12a	0.1331	0.4407	0.1776	1.84	0.47
44	H12b	0.0129	0.4863	0.1724	0.83	0.47
45	H12c	0.1319	0.5314	0.1592	1.59	0.47
46	C13	0.0822	0.4122	-0.0648	1.71	0.87
47	H13a	0.1659	0.4181	-0.0592	2.31	0.47
48	H13b	0.0550	0.3691	-0.0359	1.61	0.47
49	C14	0.0547	0.3947	-0.1388	1.61	0.87
50	H14	0.1003	0.3542	-0.1616	2.08	0.47
51	C15	-0.0302	0.4322	-0.1779	0.91	0.87
52	C21	-0.5249	0.3220	0.0810	2.09	0.87
53	H21	-0.5629	0.2730	0.0686	2.10	0.47
54	C22	-0.5847	0.3907	0.0394	2.85	0.87
55	H22a	-0.5446	0.4392	0.0510	2.82	0.47
56	H22b	-0.6657	0.3945	0.0537	3.45	0.47
57	C23	-0.5803	0.3809	-0.0359	2.71	0.87
58	H23a	-0.6418	0.3443	-0.0485	2.94	0.47
59	H23b	-0.5953	0.4315	-0.0574	3.07	0.47
60	C24	-0.5393	0.3242	0.1598	2.26	0.87
61	H24a	-0.6219	0.3251	0.1706	2.86	0.47
62	H24b	-0.5028	0.3716	0.1775	2.26	0.47
63	H24c	-0.5035	0.2786	0.1815	1.79	0.47
64	C25	-0.4604	0.3272	-0.1445	1.51	0.87
65	C26	-0.5356	0.2462	-0.1533	1.61	0.87
66	H26a	-0.4945	0.2032	-0.1309	1.11	0.47
67	H26b	-0.5457	0.2345	-0.2025	1.58	0.47
68	H26c	-0.6115	0.2528	-0.1315	2.19	0.47
69	C27	-0.5415	0.3918	-0.1842	2.39	0.87
70	H27a	-0.5419	0.3806	-0.2338	2.30	0.47
71	H27b	-0.5100	0.4440	-0.1764	2.45	0.47
72	H27c	-0.6204	0.3891	-0.1662	2.94	0.47
73	C28	-0.3419	0.3250	-0.1769	0.64	0.87
74	H28a	-0.2939	0.2866	-0.1529	0.11	0.47
75	H28b	-0.3061	0.3765	-0.1729	0.66	0.47
76	H28c	-0.3486	0.3108	-0.2257	0.57	0.47
77	C29	-0.2411	0.3926	-0.0109	0.39	0.87
78	H29a	-0.1967	0.3891	-0.0539	0.03	0.47
79	H29b	-0.1912	0.3793	0.0283	0.00	0.47
80	C30	-0.2764	0.4770	-0.0021	1.09	0.87
81	C31	-0.3007	0.5142	0.0576	1.50	0.87

82	H31	-0.3367	0.5657	0.0549	2.02	0.47
83	C32	-0.2749	0.4806	0.1284	1.19	0.87
84	H32a	-0.2999	0.5175	0.1640	1.58	0.47
85	H32b	-0.1918	0.4712	0.1330	0.56	0.47
86	H32c	-0.3169	0.4315	0.1339	1.23	0.47
87	C33	-0.3461	0.5890	-0.0698	2.12	0.87
88	H33a	-0.4223	0.5888	-0.0477	2.67	0.47
89	H33b	-0.2946	0.6241	-0.0446	1.96	0.47
90	C34	-0.3601	0.6201	-0.1451	2.33	0.87
91	H34	-0.4094	0.6657	-0.1526	2.91	0.47
92	C35	-0.3110	0.5899	-0.1971	1.79	0.87

Bond Distances

P1 -O1	1.59(1)
P1 -O2	1.44(1)
P21 -O21	1.55(1)
P21 -O22	1.47(1)
P1 -N1	1.63(2)
P21 -N21	1.62(1)
O1 -C1	1.36(2)
C1 -H1	0.95(3)
C1 -C2	1.52(3)
C2 -H2a	0.95(3)
C2 -H2b	0.95(3)
N1 -C3	1.48(2)
C2 -C3	1.49(3)
C3 -H3a	0.95(3)
C3 -H3b	0.95(3)
C1 -C4	1.51(2)
C4 -H4a	0.95(3)
C4 -H4b	0.95(3)
C4 -H4c	0.95(3)
H1 -C5	1.52(3)
C5 -C6	1.54(3)
C6 -H6a	0.95(3)
C6 -H6b	0.95(3)
C6 -H6c	0.95(3)
C5 -C7	1.55(3)
C7 -H7a	0.95(3)
C7 -H7b	0.95(3)
C7 -H7c	0.95(3)
C5 -C8	1.40(3)
C8 -H8a	0.95(3)
C8 -H8b	0.95(3)
C8 -H8c	0.95(3)
P1 -C9	1.84(2)
C9 -H9a	0.95(2)
C9 -H9b	0.95(2)
O3 C10	1.35(2)
C9 -C10	1.52(2)
C10 -C11	1.32(3)
C11 -H11	0.95(2)

C11 -C12	1.47(3)
C12 -H12a	0.95(3)
C12 -H12b	0.95(3)
C12 -H12c	0.95(3)
O3 -C13	1.42(2)
C13 -H13a	0.95(3)
C13 -H13b	0.95(3)
C13 -C14	1.45(3)
C14 -H14	0.95(3)
C14 -C15	1.36(3)
O21 -C21	1.39(2)
C21 -H21	0.95(3)
C21 -C22	1.54(3)
C22 -H22a	0.95(3)
C22 -H22b	0.95(3)
N21 -C23	1.53(2)
C22 -C23	1.42(3)
C23 -H23a	0.95(3)
C23 -H23b	0.95(3)
C21 -C24	1.49(3)
C24 -H24a	0.95(3)
C24 -H24b	0.95(3)
C24 -H24c	0.95(3)
N21 -C25	1.51(3)
C25 -C26	1.60(3)
C26 -H26a	0.95(3)
C26 -H26b	0.95(3)
C26 -H26c	0.95(3)
C25 -C27	1.59(3)
C27 -H27a	0.95(3)
C27 -H27b	0.95(3)
C27 -H27c	0.95(3)
C25 -C28	1.46(3)
C28 -H28a	0.95(3)
C28 -H28b	0.95(4)
C28 -H28c	0.95(3)
P21 -C29	1.81(2)
C29 -H29a	0.95(2)
C29 -H29b	0.95(2)
O23 -C30	1.35(2)
C29 -C30	1.47(2)
C30 -C31	1.31(3)
C31 -H31	0.95(3)
C31 -C32	1.47(3)
C32 -H32a	0.95(3)
C32 -H32b	0.95(4)
C32 -H32b	0.95(3)
O23 -C33	1.43(2)
C33 -H33a	0.95(3)
C33 -H33b	0.95(3)
C33 -C34	1.51(3)
C34 -H34	0.95(4)
C34 -C35	1.23(4)

Bond Angles

O1 -P1 -O2	113.4(7)
O1 -P1 -N1	104.6(7)
O1 -P1 -C9	101.4(7)
O2 -P1 -N1	116.1(8)
O2 -P1 -C9	109.2(7)
N1 -P1 -C9	111.1(7)
O21 -P21 -O22	113.3(7)
O21 -P21 -N21	106.8(7)
O21 -P21 -C29	101.4(8)
O22 -P21 -N21	116.0(7)
O22 -P21 -C29	109.1(7)
N21 -P21 -C29	109.3(7)
P1 -O1 -C1	123(1)
C10 -O3 -C13	117(1)
P21 -O21 -C21	125(1)
C30 -O23 -C33	119(1)
P1 -N1 -C3	124(1)
P1 -N1 -C5	119(1)
C3 -N1 -C5	116(1)
P21 -N21 -C23	122(1)
P21 -N21 -C25	119(1)
C23 -N21 -C25	118(1)
O1 -C1 -H1	115(2)
O1 -C1 -C2	105(2)
O1 -C1 -C4	109(1)
H1 -C1 -C2	109(2)
H1 -C1 -C4	104(2)
C1 -C2 -C4	115(2)
C1 -C2 -H2a	108(2)
C1 -C2 -H2b	109(2)
C1 -C2 -C3	113(2)
H2a -C2 -H2b	109(3)
H2a -C2 -C3	108(2)
H2b -C2 -C3	109(2)
N1 -C3 -C2	115(2)
N1 -C3 -H3a	108(2)
N1 -C3 -H3b	108(2)
C2 -C3 -H3a	108(2)
C2 -C3 -H3b	108(2)
H3a -C3 -H3b	109(2)
C1 -C4 -H4a	109(2)
C1 -C4 -H4b	109(2)
C1 -C4 -H4c	110(2)
H4a -C4 -H4b	109(3)
H4a -C4 -H4c	109(2)
H4b -C4 -H4c	109(2)
N1 -C5 -C6	109(2)
N1 -C5 -C7	106(2)
N1 -C5 -C8	114(2)
C6 -C5 -C7	108(2)
C6 -C5 -C8	112(2)

C7 -C5 -C8	106(2)
C5 -C6 -H6a	110(2)
C5 -C6 -H6b	109(2)
C5 -C6 -H6c	109(2)
H6a -C6 -H6b	109(3)
H6a -C6 -H6c	109(3)
H6b -C6 -H6c	109(3)
C5 -C7 -H7a	109(2)
C5 -C7 -H7b	110(2)
C5 -C7 -H7c	110(2)
H7a -C7 -H7b	109(3)
H7a -C7 -H7c	109(3)
H7b -C7 -H7c	109(3)
C5 -C8 -H8a	109(2)
C5 -C8 -H8b	110(2)
C5 -C8 -H8c	110(2)
H8a -C8 -H8b	109(3)
H8a -C8 -H8c	109(3)
H8b -C8 -H8c	109(3)
P1 -C9 -H9a	108(1)
P1 -C9 -H9b	108(1)
P1 -C9 -C10	115(1)
H9a -C9 -H9b	109(2)
H9a -C9 -C10	108(2)
H9b -C9 -C10	108(2)
O3 -C10 -C9	108(1)
O3 -C10 -C11	126(2)
C9 -C10 -C11	125(2)
C10 -C11 -H11	116(2)
C10 -C11 -C12	127(2)
H11 -C11 -C12	116(2)
C11 -C12 -H12a	109(2)
C11 -C12 -H12b	109(2)
C11 -C12 -H12c	110(2)
H12a -C12 -H12b	109(3)
H12a -C12 -H12c	109(3)
H12b -C12 -H12c	109(2)
O3 -C13 -H13a	109(2)
O3 -C13 -H13b	109(2)
O3 -C13 -C14	110(2)
H13a -C13 -H13b	109(3)
H13a -C13 -C14	110(2)
H13b -C13 -C14	109(2)
C13 -C14 -H14	117(2)
C13 -C14 -C15	125(2)
H14 -C14 -C15	118(3)
O21 -C21 -H21	110(2)
O21 -C21 -C22	109(2)
O21 -C21 -C24	111(2)
H21 -C21 -C22	109(2)
H21 -C21 -C24	102(2)
C22 -C21 -C24	116(2)
C21 -C22 -H22a	108(2)
C21 -C22 -H22b	109(2)

C21 -C22 -C23	114(2)
H22a -C22 -H22b	109(2)
H22a -C22 -C23	108(2)
H22b -C22 -C23	109(2)
N21 -C23 -C22	116(2)
N21 -C23 -H23a	108(2)
N21 -C23 -H23b	108(2)
C22 -C23 -H23a	107(2)
C22 -C23 -H23b	108(2)
H23a -C23 -H23b	109(3)
C21 -C24 -H24a	109(2)
C21 -C24 -H24b	109(2)
C21 -C24 -H24c	111(2)
H24a -C24 -H24b	109(3)
H24a -C24 -H24c	109(3)
H24b -C24 -H24c	109(3)
N21 -C25 -C26	107(2)
N21 -C25 -C27	106(2)
N21 -C25 -C28	115(2)
C26 -C25 -C27	103(2)
C26 -C25 -C28	115(2)
C27 -C25 -C28	110(2)
C25 -C26 -H26a	110(3)
C25 -C26 -H26b	110(3)
C25 -C26 -H26c	109(2)
H26a -C26 -H26b	109(3)
H26a -C26 -H26c	109(3)
H26b -C26 -H26c	109(3)
C25 -C27 -H27a	109(3)
C25 -C27 -H27b	110(3)
C25 -C27 -H27c	110(3)
C27a -C27 -H27b	109(3)
C27a -C27 -H27c	109(3)
C27b -C27 -H27c	109(3)
C25 -C28 -H28a	110(3)
C25 -C28 -H28b	109(3)
C25 -C28 -H28c	110(3)
C28a -C28 -H28b	109(3)
C28a -C28 -H28c	109(3)
C28b -C28 -H28c	109(3)
P21 -C29 -H29a	107(2)
P21 -C29 -H29b	107(1)
P21 -C29 -C30	119(1)
C29a -C29 -H29b	109(2)
C29a -C29 -C30	107(2)
H29b -C29 -C30	107(2)
O23 -C30 -C29	110(1)
O23 -C30 -C31	122(2)
C29 -C30 -C31	127(2)
C30 -C31 -H31	118(2)
C30 -C31 -C32	124(2)
H31 -C31 -C32	118(2)
C31 -C32 -H32a	109(2)
C31 -C32 -H32b	110(2)

C31 -C32 -H32c	109(2)
H32a -C32 -H32b	109(3)
H32a -C32 -H32c	109(3)
H32b -C32 -H32c	109(3)
O23 -C33 -H33a	108(2)
O23 -C33 -H33b	108(2)
O23 -C33 -C34	113(2)
H33a -C33 -H33b	109(3)
H33a -C33 -C34	108(2)
H33b -C33 -C34	109(2)
C33 -C34 -H34	118(3)
C33 -C34 -C35	124(2)
H34-C34 -C35	118(3)

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