

REACTIONS OF POLYMER-BOUND ANIONS OF PHOSPHINATES
WITH TYPICAL ALDEHYDES AND KETONES

By

ALTAF ELLAHI QURESHI

Bachelor of Science
University of the Punjab
Lahore, Pakistan
1977

Master of Science
Quaid-i-Azam University
Islamabad, Pakistan
1981

Submitted to the Faculty of the Graduate College
of the Oklahoma State University
in partial fulfillment of the requirements
for the Degree of
MASTER OF SCIENCE
May, 1984

Name: Altaf Ellahi Qureshi

Date of Degree: May, 1984

Institution: Oklahoma State University Location: Stillwater, Oklahoma

Title of Study: REACTIONS OF POLYMER-BOUND ANIONS OF PHOSPHINATES WITH
TYPICAL ALDEHYDES AND KETONES

Pages of Study: 45

Candidate for Degree of Master of Science

Major Field: Chemistry

Scope of Study: The Wittig reactions of triphenylphosphonium salts, alkyl diphenylphosphonium oxides and alkylphosphonates with aldehydes and ketones have been widely used for the synthesis of unsaturated compounds. The major objective of this study is to prepare a polymer-bound phosphinate for use in the Wittig reaction, where rapid separation of product from organophosphorus by-product is needed.

Finding and Conclusions: Wittig olefination of benzaldehyde (with 2%-cross-linked diethyl (4-polystyryl)phosphinoacetate at room temperature) gave ethyl trans-cinnamate (63%). The Wittig olefinations of cyclopentanone and cyclohexanone proceeded in yields of 11% and 33%, respectively. The desired α,β -unsaturated esters were separated from the by-product, sodium ethyl 4-polystyrylphosphonate, by simple filtration. They were purified by flash chromatography and were characterized by ^1H NMR, ^{13}C NMR and IR spectral analysis.

ADVISER'S APPROVAL

Warren T. Ford

Thesis
1984
Q901v
cop. 2



REACTIONS OF POLYMER-BOUND ANIONS OF PHOSPHINATES
WITH TYPICAL ALDEHYDES AND KETONES

Thesis Approved:

Walter T. Ford

Thesis Adviser

K. O. Berlin

Eldon Nelson

Norman N. Durbin

Dean of the Graduate College

ACKNOWLEDGMENTS

With deep sense of gratitude and appreciation, I would like to thank my learned teacher and guide, Dr. Warren T. Ford, Professor, Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma, for his enthusiastic encouragement, invaluable advice, inspiring guidance, and the valiant efforts during the research period. It is really due to his availability for long hours that his project came to a successful conclusion in a short period.

I wish to record here with immense pleasure, my sincere thanks to Dr. K. D. Berlin, Regents Professor, Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma, for his valuable suggestions and also for providing all possible facilities of ^{31}P NMR spectra.

I also thank gratefully the U. S. Army Research Office for providing a grant to this project.

Finally, I would like to thank my parents who helped me in achieving my goal and quenching my thirst for knowledge.

TABLE OF CONTENTS

Chapter	Page
I. INTRODUCTION	1
Polymer Bound Reagents	4
II. RESULTS AND DISCUSSION	7
Polystyrene (16) Gel Polymer Cross-Linked with 2% Divinylbenzene (DVB)	7
Bromination of Polystyrene <u>16</u>	8
Phosphination of Poly(4-bromostyrene) (<u>17</u>)	8
Phosphination of Poly(4-bromostyrene) (<u>17</u>) Using Diethyl Chlorophosphite [(EtO) ₂ PCl]	10
Reaction of Diethyl (4-Polystyryl)Phosphino- acetate (<u>23</u>) with Benzaldehyde Using NaOEt as Base	12
Reaction of Diethyl (4-Polystyryl)Phosphino- acetate (<u>23</u>) with Cyclopentanone Using NaOEt as Base	13
Reaction of Polymer <u>23</u> with Cyclohexanone Using THF as Solvent and NaOEt as Base	15
III. EXPERIMENTAL	18
General Procedure with Polymeric Reagents	18
Drying Methods for Solvents	18
Analysis and Spectra	20
General Procedure for the Suspension Polymeri- zation of Styrene Containing Divinylbenzene (DVB) as Cross-Linker Two Percent Cross- Linked Polystyrene (<u>16</u>)	20
General Procedure for the Bromination of 2% Cross-Linked Polystyrene (<u>16</u>)	21
Standardization of <u>n</u> -BuLi by the Diphenylacetic Acid Method	22
General Procedure for the Phosphination of Poly- (4-bromostyrene) (<u>17</u>) Using Dichlorophenyl- phosphine with <u>n</u> -BuLi	22
Phosphination of Poly(4-bromostyrene) (<u>17</u>) Using Diethyl Chlorophosphite [(EtO) ₂ PCl] with <u>n</u> -BuLi	23
General Procedure for the Wittig Olefination with Polymer-Bound Phosphinate Reagent <u>23</u>	25

Chapter	Page
Reaction of Diethyl (4-Polystyryl)phos- phinoacetate (23) with Benzaldehyde Using Dimethylformamide (DMF) as Solvent and Sodium Ethoxide as Base	25
GLC Conditions Common To All Samples	25
Flash Chromatography	26
Reaction of Diethyl (4-Polystyryl)phos- phinoacetate (23) with Benzaldehyde Using Tetrahydrofuran (THF) as Solvent and Sodium Ethoxide as Base	27
Reaction of Diethyl (4-Polystyryl)phos- phinoacetate (23) with Cyclopentanone Using THF as Solvent and NaOEt as Base	28
GLC Conditions Common to All Samples	28
Flash Chromatography	29
Reaction of Polymer 23 with Cyclopentanone Using DMF as Solvent and NaOEt as Base	30
Flash Chromatography	32
Reaction of 23 with Cyclohexanone Using THF as Solvent and NaOEt as Base (In Excess)	32
GLC Conditions	33
Flash Chromatography	33
Reaction of 23 (In Excess) with Cyclo- hexanone Using THF as Solvent and NaOEt as Base (In Excess)	34
REFERENCES	35
APPENDIX - SELECTED SPECTRA	37

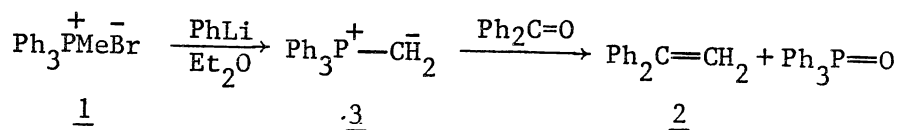
LIST OF SPECTRA

Spectrum	Page
1. ^{13}C NMR of Diethyl (4-Polystyryl)phosphinoacetate (<u>23</u>) . . .	38
2. ^{31}P NMR of Diethyl (4-Polystyryl)phosphinoacetate (<u>23</u>) . . .	39
3. ^{31}P NMR of Diethyl (4-Polystyryl)phosphonite (<u>24</u>)	40
4. ^1H NMR of Ethyl Cyclopentylideneacetate (<u>28</u>)	41
5. ^{13}C NMR of Ethyl Cyclopentylideneacetate (<u>28</u>)	42
6. ^1H NMR of 2-Cyclopentylidene-1-cyclopentanone (<u>29</u>)	43
7. ^1H NMR of Ethyl Cyclohexylideneacetate (<u>30</u>)	44
8. ^{13}C NMR of Ethyl Cyclohexylideneacetate (<u>30</u>)	45

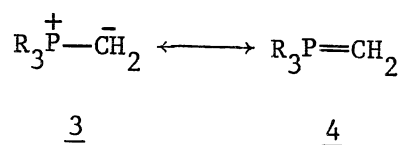
CHAPTER I

INTRODUCTION

In 1953 Wittig and Geissler¹ observed that when methyltriphenylphosphonium bromide (1) was treated with phenyllithium and then with benzophenone, a quantitative yield of triphenylphosphine oxide and 1,1-diphenylethylene (2) resulted. This discovery led to the development of a new method for the preparation of alkenes²⁻⁶ which has found widespread application in synthetic organic chemistry and is now universally known as the Wittig reaction.⁷⁻⁹



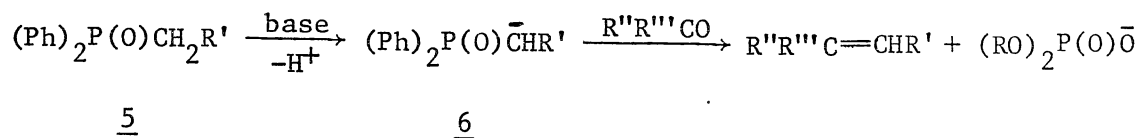
An ylide 3, also known as a phosphorane, was postulated as an intermediate. Phosphorus ylides are usually stable compounds and can be represented by two resonance structures, one known as ylide 3 and the other as ylene 4, as shown below:



This stabilization is attributed to valence shell expansion of the phosphorus atom with concomitant overlap of a vacant 3d orbital on phosphorus with a filled 2p orbital on carbon of the carbanion intermediate.

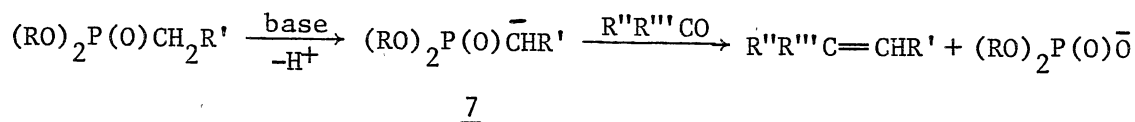
The successful synthesis of wide variety of unsaturated compounds

by treatment of phosphoranes with carbonyl compounds has stimulated the search for other synthetic methods that use organophosphorus reagents. One of the most fruitful results has been the discovery that phosphoryl stabilized carbanions have wide applicability in the preparation of unsaturated compounds and sometimes offer significant advantages over conventional Wittig procedures. Horner and Hoffmann¹⁰ utilized the carbanions of diphenylphosphine oxides (6) which were found to undergo reaction with aldehydes and ketones to form olefins.



R' = alkyl, aryl or alkoxycarbonyl.

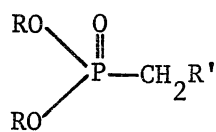
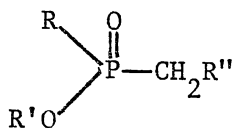
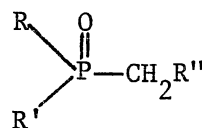
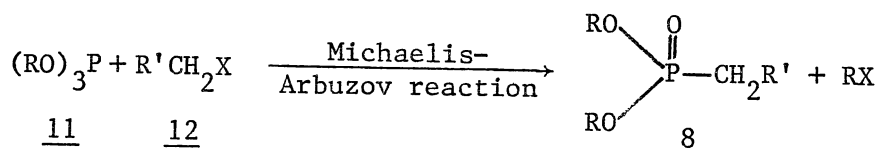
A further modification of the Wittig synthesis was developed by Horner and co-workers¹¹ and by Wadsworth and Emmons.¹² This reaction made use of resonance stabilized phosphonate carbanions (7), where R' is a group capable of stabilizing the adjacent anion. These carbanions were shown to undergo reaction with carbonyl compounds in a manner analogous to the phosphinoxy carbanions 6.



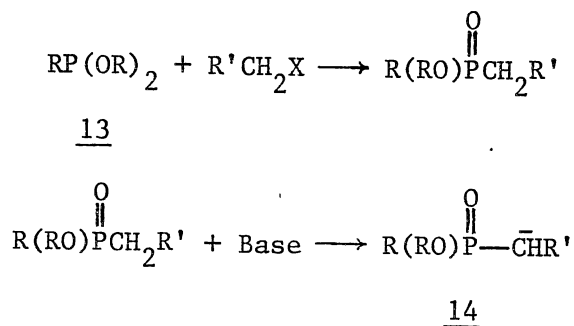
R' = CO₂R, CN, C(O)R.

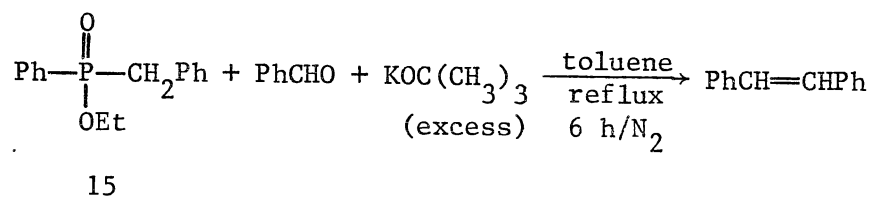
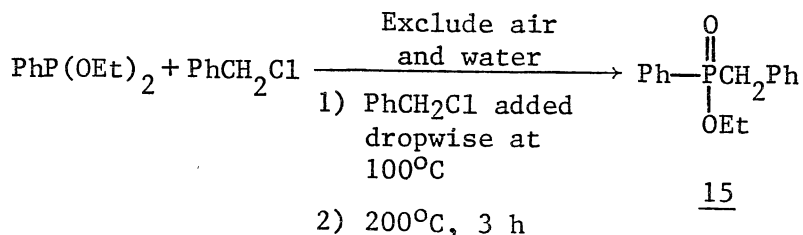
Anions that have their negative charge located on an atom adjacent to a P(O) group gain stability owing to delocalization of the charge through the phosphoryl group. However, the P(O) group is not as effective as the carbonyl group is stabilizing a negative charge. If other stabilizing groups are not present, formation of P(O) stabilized carbanions generally requires a strong base than does

the removal of a proton from a carbon atom alpha to a carbonyl group. The phosphonates 8 found great popularity because of their availability from reactions of trialkyl phosphites 11 and alkyl halides 14 and their ease of application.

8910

Carbanions prepared from phosphinates 9 have no known advantage over those prepared from phosphonates 8 or phosphine oxides 10. Horner and co-workers¹¹ utilized phosphinic esters 15 to prepare phosphinate carbanions 14. The phosphinate carbanions 14 were more difficult to prepare than the latter two because the phosphonite 13 (starting materials) are much less readily available¹³ than the trialkyl phosphite 11 precursors of the phosphonates 8. Moreover, they required high temperature and an excess of base as shown below:





Thus, little attention has been paid to the use of phosphinate carbanions 14.

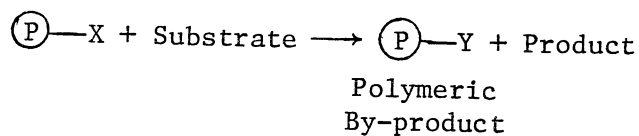
Polymer Bound Reagents

Polymeric reagents are polymers which carry functional groups. Polymers are being used as polymeric supports in organic synthesis because the functional groups on insoluble solvent swollen polymers undergo chemical reactions in much the same way as solutions of low molecular weight compounds. The benzene ring of polystyrene, for example, gives the common aromatic substitution reactions such as halogenation, acylation and sulfonation. In this study halogenation has been used as the first step for preparing a functionalized, insoluble polymer-bound phosphinate reagent.

There are three major advantages of insoluble polymeric reagents over conventional low molecular weight reagents. (1) Ease of processing: The reaction workup is very simple in case of polymer-supported reactions because the insoluble by-products attached to the polymer can be separated easily from the soluble product in the solution by simple filtration. In Wittig olefin synthesis, the by-

product phosphine oxide offers separation problems in certain solution reactions, whereas in polymer supported Wittig reaction, the polymer-bound, by-product phosphine oxide can be removed easily by simple filtration. Because the polymers can be removed quite easily from a reaction mixture after reaction of their functional groups, polymer reagents may also be used in excess to drive the reaction to completion. The polymer supported reactions are one-pot syntheses, which makes handling easy. The unstable species attached to the insoluble polymer support can be worked up quickly without exposure to the atmosphere. The synthesis of phosphinate reagents may involve many unstable intermediates from which other side products produced can easily be removed by simple filtration without affecting the unstable species. (2) Furthermore, odorless polymers of reduced toxicity can be made containing functionalities which, in low molecular weight compounds, would be associated with significant toxicity or noxious odors. So toxic and malodorous materials can be rendered environmentally more acceptable. Polymeric phosphinates present an example of being non-toxic and odorless when compared with monomeric phosphinates. (3) In some cases, improved yield and selectivity of the final product: Side reactions associated with the solution reactions can be minimized by the use of polymeric reagents, thereby improving the yields.

In general, the term polymeric reagent is used in a one step process in which the functional polymer itself reacts to transfer a low molecular weight substrate to product as shown below:



Ⓟ = Polymer support.

The most widely used insoluble polymers in organic synthesis are styrene-based with divinylbenzene as the cross-linker.¹⁴ Such polymers are produced by heterogeneous suspension polymerization techniques either in the presence or absence of an organic solvent, depending on the type of resin needed. The polymer comes out in the form of tough, insoluble, spherical, cross-linked beads whose size depends on the extent of dispersion in solution, the amount of agitation, the temperature, and the interfacial tension.

Styrene-based polymers have many advantages over other resins. Aromatic ring functionalization is achieved easily to give reactive, yet selective styrene-based reagents. The type and degree of cross-linking can easily be controlled. The degree of cross-linking of the polymer governs its ability to swell in the solvent. Polystyrene is not degraded by most chemical reagents under ordinary conditions and can withstand the chemical treatments and physical handling required in sequential synthesis.

This research was focused on the above mentioned problems in the modified Wittig reaction, the preparation and use of polymer-bound phosphinates to which little attention⁷ has been paid due to difficulties in the preparation.

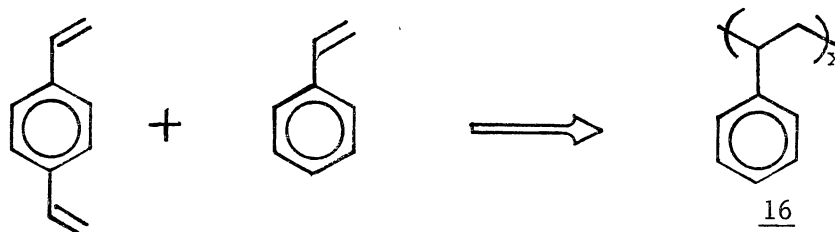
CHAPTER II

RESULTS AND DISCUSSION

Polymer supports have been tried in Wittig olefinations using polymeric phosphoranes,¹⁵⁻¹⁹ but polymer-bound phosphinates have never been attempted. Moreover, in solution chemistry, phosphinates have been used little, because the phosphonite (13) starting materials are much less readily available¹³ than phosphites. A search of the literature also revealed that the carbanions prepared from phosphinates have no known advantage over those prepared from phosphonates and phosphine oxides.⁷ However, phosphinate carbanions were used in this research because the P-C covalent bond linking the phosphinate to the polymer insures that the organophosphorus reagent cannot be cleaved from the polymer. Using 2% cross-linked polystyrene as a polymer support, the polymer-bound phosphinate ester 23 has been successfully prepared at room temperature and applied with benzaldehyde, cyclopentanone, and cyclohexanone for Wittig olefination.

Polystyrene (16) Gel Polymer Cross-Linked with 2% Divinylbenzene (DVB)

The 2% cross-linked polystyrene (16) was prepared by the suspension technique. For Wittig olefination, 60/100 and 100/200 mesh beads were used.



Bromination of Polystyrene 16

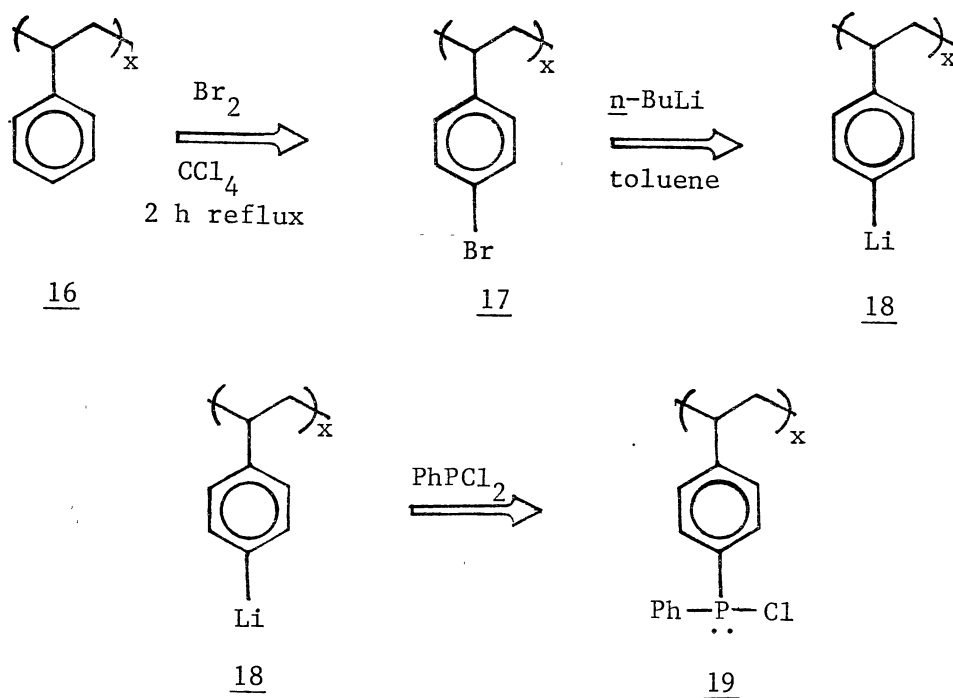
The ortho position of the polystyrene ring is highly hindered, and so electrophilic substitution proceeds mainly at the para position. Thus bromination by bromine in CCl_4 with catalytic amounts of thallium acetate sesquihydrate $[\text{Tl}(\text{OAc})_3]^{20}$ resulted in a yield of 90-100%, in all experiments, the only limiting factor being the amount of bromine added. The mmoles of bromine calculated by weight gained in the brominated sample were confirmed by the elemental analysis. Poly(4-bromostyrene) (17) is a yellow colored polymer.

Phosphination of Poly(4-bromostyrene) (17)

Polymer-bound phosphinate carbanions have never been prepared. Horner and co-workers¹¹ utilized phosphonites to prepare phosphinates. The preparation was not difficult, but the starting materials were not available. Following Scheme I, the synthesis of chloro(phenyl)(4-polystyryl)phosphine (19) was tried through the lithiation of the poly(4-bromostyrene) (17) using $n\text{-BuLi}$. Reaction of the lithiopolystyrene (18) with an equimolar amount of dichlorophenylphosphine (PhPCl_2) gave chloro(phenyl)(4-polystyryl)phosphine (19) (yield, 34% calculated on the basis of bromine elemental analysis in 17). A second attempt using a ten fold excess of dichlorophenylphosphine gave a 59% conversion of 17 into 19. This low conversion revealed that the reagent dichlorophenylphosphine was not able to reach to all of

the active sites in the polymer due to cross-linking.

Chloride contents of chloro(phenyl)(4-polystyryl)phosphine (19) were determined by the ion-exchange titrimetric method using THF and DMF as solvents to swell the polymer and sodium methoxide as a base. Using THF, 0.3 mmoles/g of chlorine, and DMF, 0.37 mmoles/g chlorine contents were obtained. The very low amount of chloride showed that perhaps the base is not able to reach all the chlorinated sites to displace chlorine. The ^{31}P NMR spectrum of the sample of 19 obtained (34%) showed a broad peak at 84.0 ppm from 85% H_3PO_4 , and the other sample of 19 obtained (59%) revealed two peaks in the ^{31}P NMR spectrum at 86.0 and 25.7 ppm from 85% H_3PO_4 . The literature value²¹ for chlorodiphenylphosphine $[(\text{Ph})_2\text{PCl}]$ is 81.5 ppm.



Scheme I.

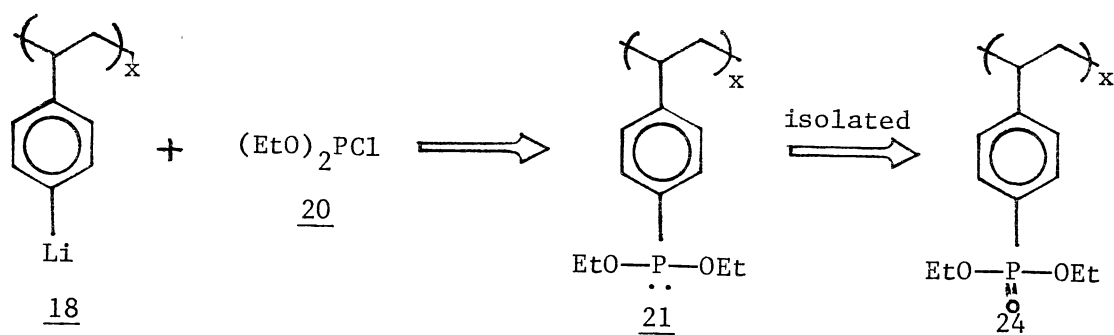
Phosphination of Poly(4-bromostyrene) (17) Using
Diethyl Chlorophosphite [(EtO)₂PCl]

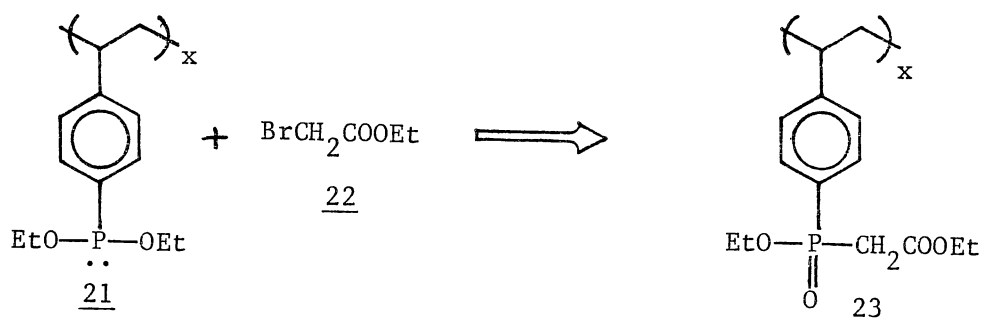
In Scheme II, as in Scheme I, the poly(4-bromostyrene) (17) in toluene was treated with excess *n*-BuLi to give the lithiated polymer 18, which in turn was treated with diethyl chlorophosphite in THF to give diethyl (4-polystyryl)phosphonite (21) which is the key intermediate. This intermediate phosphonite 21 was converted into diethyl (4-polystyryl)phosphinoacetate (23) using ethyl bromoacetate (22) in a Michaelis-Arbuzov reaction. The conversion of poly(4-bromostyrene) (17) to polymer-bound phosphinate ester 23 was carried out on 5.0 g and 20.0 g scales. In the case of 5.0 g scale, a weight increase was observed yielding 5.57 g of the product 23. Elemental analysis revealed 0.84% (0.11 mmol/g) of residual bromine and 4.31% phosphorus (1.39 mmol/g). Conversion of 58% was estimated on the basis of the bromine analysis of the starting material. The ³¹P NMR spectrum of 23 showed two peaks, a major peak at 34.7 ppm and a small peak at 20.0 ppm from 85% H₃PO₄. In the literature,²² the chemical shift for ethyl methyl phenylphosphinoacetate [CH₃OP(Ph)(O)CH₂COOC₂H₅] is at 38.1 ppm. The ¹³C NMR spectrum of 23 revealed peaks for an ester group at 61.0 (-O-CH₂-), 40.6 (-CH- backbone polymer) and at 14.0 ppm (-O-CH₂-CH₃). The IR spectrum also confirms the structure with bands for P-O-C₂H₅ at 1455, 1395, 1120 and 1035 cm⁻¹, for P=O at 1250 cm⁻¹, and the ester carbonyl band at 1740 cm⁻¹.

Following Scheme II, a 20.0 g sample of poly(4-bromostyrene) (17) was converted into diethyl (4-polystyryl)phosphinoacetate (23)

(18.78 g). Elemental analysis of the sample showed 2.58% (0.83 mmols/g) of phosphorus. The ^{31}P NMR spectrum revealed two peaks as in the spectrum of the previous sample at 34.8 and 19.9 ppm from 85% H_3PO_4 . The IR spectrum was also similar to that of the previous sample. The very low ring substitution (10%, calculated on the base of phosphorus analysis) may be due to the non-accessability of the diethyl chlorophosphite (20) to the active sites of the 2% cross-linked polymer. On the 20 g scale, longer reaction times might have afforded higher yields.

With another sample of 20.0 g poly(4-bromostyrene) (17), isolation of the key intermediate diethyl (4-polystyryl)phosphonite (21) was attempted. The ^{31}P NMR spectrum revealed two peaks at 7.9 and at 25.53 ppm. Neither of these peaks corresponded to the required intermediate, because the literature value²³ for $[\text{PhP}(\text{OEt})_2]$ is at 158.5 ppm from 85% H_3PO_4 . The desired phosphonite 21 might have been oxidized to diethyl (4-polystyryl)phosphonate (24) during the workup procedure because the reported ^{31}P NMR shift²⁴ for diethyl phenylphosphonate $[(\text{EtO})_2\text{P}(\text{O})(\text{Ph})]$ is at 16.9 ppm. The phosphorus contents were observed to be almost identical in conversion of 21 to 23. The phosphorus analysis of the key intermediate 24 showed 4.15% phosphorus (17% ring substitution) while in the 23 analytically found phosphorus was 3.86% (17% ring substitution).

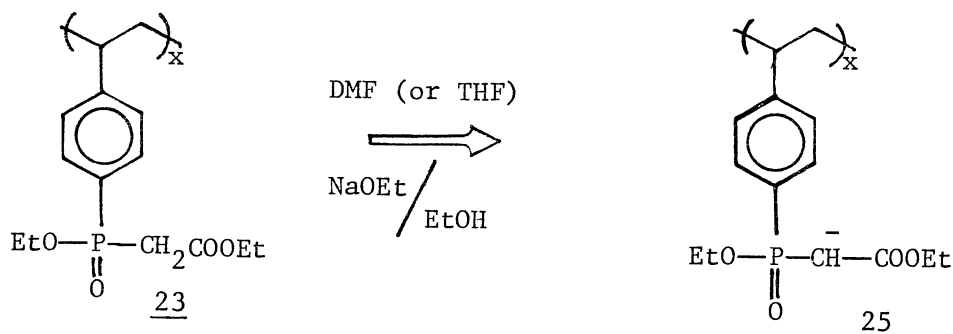


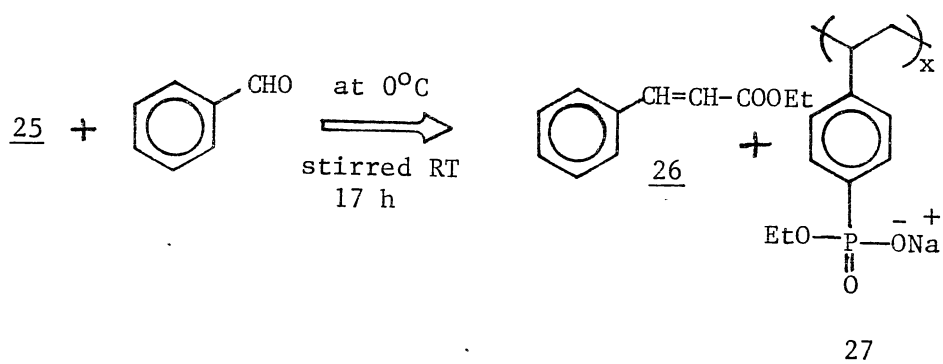


Scheme II

Reaction of Diethyl (4-Polystyryl)Phosphino-
acetate (23) with Benzaldehyde Using
NaOEt as Base

Following the Scheme III, polymer 23, swollen in DMF was treated with sodium ethoxide to generate carbanion 25. Treatment of 25 with benzaldehyde gave ethyl cinnamate (26) (63%). The sodium ethoxide and DMF was the best base-solvent system found to swell the polymer and to generate the carbanion 20. The reaction of diethyl (4-polystyryl)phosphinoacetate (23) with benzaldehyde was also tried using THF and ethanol as solvents and sodium ethoxide as base. The crude yields were 37% in THF and 9% in ethanol by GLC analysis. The poor yields with THF and ethanol as solvents confirmed that a much more polar solvent was needed to swell the polymer completely making the reactive sites accessible to the reagent.



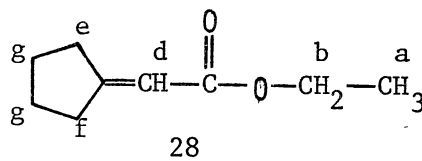


Scheme III

Reaction of Diethyl (4-Polystyryl)Phosphino-
acetate (23) with Cyclopentanone Using
NaOEt as Base

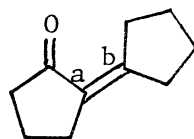
Following Scheme III, two solvents were tried, namely THF and DMF. Using THF as solvent the polymer-bound phosphinate ester 23 and sodium ethoxide were employed in equimolar amounts. After generating carbanion 25 the polymer was washed to remove any unreacted base. After addition of cyclopentanone, the reaction mixture was stirred at room temperature for 20 h and was worked up to yield crude product (31%). The GLC analysis of the crude product showed six major peaks with 4% (peak area %) of unreacted cyclopentanone. The product was flash chromatographed to yield ethyl cyclopentylideneacetate (28).

(11% yields were determined on the basis of phosphorus analysis of 23.) The IR spectrum of ester 28 showed the typical bands for an α,β -unsaturated ester at 1705 cm^{-1} for C=O , 1205 cm^{-1} and 1125 cm^{-1} for $\begin{pmatrix} \text{O} \\ \parallel \\ \text{C-O-C} \end{pmatrix}$ ester group and a band at 1650 cm^{-1} for C=C .



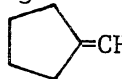
The ^1H NMR spectrum of 28 revealed a triplet at δ 1.28 for a- protons, a multiplet at δ 1.7 for g-protons, a triplet at δ 2.46 and a triplet at δ 2.8 for e- and f-protons, a quartet at δ 4.19 for b- protons and a singlet at δ 5.84 for the d-proton. Similarly, the ^{13}C NMR spectrum confirmed the above structure (values given in the experimental portion). The other fractions collected from flash chromatography did not show clean spectra.

When the above mentioned reaction was tried using DMF as solvent, the results were similar, but with excess of base and excess of cyclopentanone, a major amount of aldol condensation product 29 resulted. The low yields of olefin and high yield of aldol product in the cyclopentanone reactions indicated that even the carbanion 25 generated from diethyl (4-polystyryl)phosphinoacetate (23) abstracted an α -proton from cyclopentanone to form the enolate which gave aldol product 29.



The ^{13}C NMR spectrum of 29 revealed the carbonyl peak at 206.3

ppm, while for two doubly bonded carbons a and b, the peaks were at 127.4 and 157.8 ppm, respectively. The IR spectrum of 2-cyclopentylidene-1-cyclopentanone (29) showed a typical peak for an α,β -unsaturated carbonyl system at 1712 cm^{-1} and a peak at 1645 cm^{-1} for a double bond. The ^1H NMR spectrum also confirmed the aldol product 29 and signal values are given in the experimental portion.

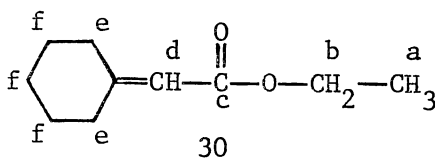
Previously,²⁵ the ethyl cyclopentylideneacetate (28) was prepared using phosphonate carbanion $[(\text{C}_2\text{H}_5\text{O})_2\text{P}(\text{O})-\text{CHCOOC}_2\text{H}_5]$ which was more reactive than the analogous triaryl phosphoranes ($\text{Ar}_3\text{P}^+-\text{CHR}^-$). Shulte²⁵ first prepared the alkyl cyclopentylideneacetate [, by treating ClCH_2COOR with $\text{P}(\text{OCH}_3)_3$ to give $(\text{CH}_3\text{O})_2\text{P}(\text{O})\text{CH}_2\text{COOCH}_3$ (75%), which was treated with cyclopentanone to give methyl cyclopentylideneacetate (92%). Transesterification gave ethyl cyclopentylideneacetate (28). A comparison of the Shulte²⁵ synthesis with our results showed that phosphonates in solution were much better than the polymer-bound phosphinate ester 23. Our study demonstrated that carbanion 25 was more basic than nucleophilic and formed the enolate, which gave aldol product 29 (80%).

Reaction of Polymer 23 with Cyclohexanone

Using THF as Solvent and NaOEt as Base

The reaction of cyclohexanone was tried with equimolar amounts of diethyl (4-polystyryl)phosphinoacetate (23) and cyclohexanone. It was also repeated with excess 23 following Scheme III. The first attempt (using equimolar amounts) yielded a product whose GLC analysis revealed (peak area %) starting cyclohexanone (49%) and ethyl cyclohexylideneacetate (30) (48%). The crude sample was flash chro-

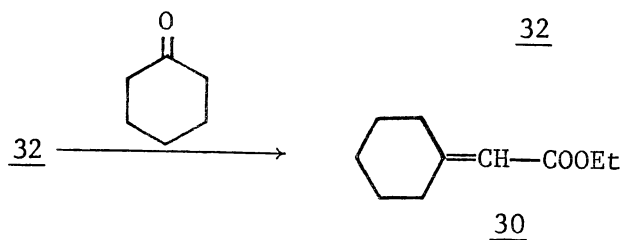
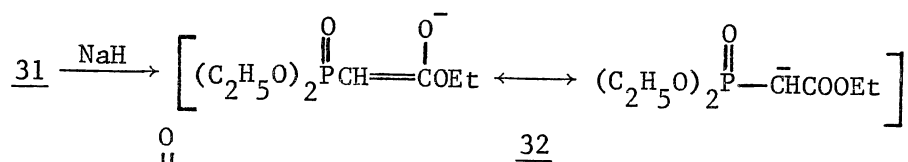
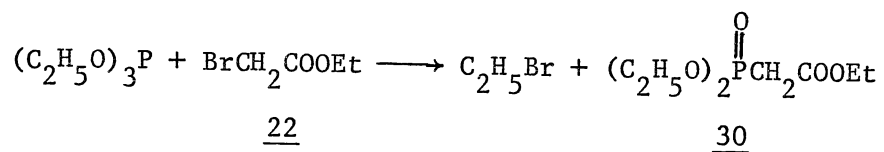
matographed to yield (33%) pure ethyl cyclohexylideneacetate (30). The yield was calculated on the basis of the phosphorus analysis of 23.



The IR spectrum of ester 30 showed a typical α,β -unsaturated ester with the C=O at 1725 cm^{-1} , the C=C at 1660 cm^{-1} , and the usual ester C-O bands at 1210 and 1160 cm^{-1} . The ^1H NMR spectrum revealed a triplet for a-protons at δ 1.28, a multiplet for f-protons at δ 1.64, two triplets for e-protons at δ 2.2 and δ 2.9, respectively, a quartet for b-protons at δ 4.16 and a singlet at 5.64 ppm for the d-proton. ^{13}C NMR spectrum also confirmed the above structure (values given in the experimental portion).

The above procedure was repeated using an excess (1.42 equivalents, 2.55 mmoles) of diethyl (4-polystyryl)phosphinoacetate (23) and 1.0 equivalent (1.8 mmoles) of cyclohexanone to yield a product whose GLC analysis showed recovered starting material, cyclohexanone (59% by peak area). No attempt was made to purify the product.

The preparation of ethyl cyclohexylideneacetate (30) in the literature¹² was also tried using phosphonate 31. Unlike the corresponding phosphoranes^{26,27} which would react with ketones only under forcing conditions, the anion 32, as shown below, was strongly nucleophilic and reacted with cyclohexanone at room temperature within a few minutes to give ethyl cyclohexylideneacetate (30) in a yield of 70%.



The low yield of ester 30 in our study revealed that it might be due to less diffusion of the cyclohexanone into the polymer beads, which was not a problem in the case of the phosphonates in the solution.

CHAPTER III

EXPERIMENTAL

General Procedure with Polymeric Reagents

All the volatile reagents used were vacuum distilled under nitrogen and argon before use and kept under argon. All polymer samples were washed and dried in a vacuum oven immediately before use. All reactions were conducted under a nitrogen or an argon atmosphere using three neck flasks (round bottom) with a fritted disc and stopcock at the bottom. Flasks were equipped with an overhead stirrer, a serum stopper, a nitrogen inlet and a condensor (whenever needed). Polymer samples were allowed to swell in the solvent without stirring before starting a reaction. The teflon blade of the stirrer was positioned high enough to avoid friction between the beads and the walls of the flask, and thus polymer was recovered with little or no breakage of beads. Reaction temperatures of -10°C to -20°C were achieved by use of an ice/salt bath, while -78°C was achieved using acetone/dry ice mixture.

Drying Methods for Solvents

Toluene and benzene were refluxed under nitrogen overnight over CaH_2 and were distilled at 108°C and 78°C , respectively, and stored over molecular sieves (Type 4A) under nitrogen. Tetrahydrofuran was

refluxed for at least three days with sodium metal under nitrogen to remove peroxides and moisture. Using benzophenone as an indicator, the THF gave a blue color upon drying. To check its dryness the THF was tested with lithium aluminum hydride (LAH). If bubbles evolved after drying over sodium metal, tetrahydrofuran was refluxed over lithium aluminum hydride for 24 hr under nitrogen. Triphenylmethane was used as an indicator and gave a dark red color indicating the 100% dryness of the THF. p-Xylene was used as such without distillation (from Fischer Chemical Co.). Thionyl chloride (SOCl_2)²⁷ 70.0 mL, was purified by refluxing with 10.0 mL of quinoline for three hours and then fractionated to remove the acid impurities. The distillate is refractionated as before from boiled linseed oil (40.0 mL). The collected thionyl chloride was transparent and colorless and it was kept under nitrogen atmosphere. Dimethylformamide (DMF) after refluxing over calcium hydride for two hours was distilled under nitrogen before use and was stored under nitrogen.

Dichlorophenylphosphine (PhPCl_2) and ethyl bromoacetate ($\text{BrCH}_2\text{COOC}_2\text{H}_5$) were distilled under an inert atmosphere using argon at reduced pressure. Diethyl chlorophosphite [$(\text{C}_2\text{H}_5\text{O})_2\text{PCl}$] (reagent grade, clear and colorless) was used without distillation. n-Butyl lithium (n-BuLi) was standardized using the diphenylacetic acid method.²⁸ Sodium methoxide (CH_3ONa) and sodium ethoxide ($\text{C}_2\text{H}_5\text{ONa}$) were prepared by dissolving a weighed amount of freshly cut sodium metal in a measured volume of the alcohol in a nitrogen atmosphere. For flash chromatography the petroleum ether was used (bp 37.7°C - 56.9°C ; from Fischer Chemical Co.). The silica gel used for flash chromatography had an average particle diameter of 40 μm with no

particles less than 25 μm (from J. T. Baker Chemical Co.).

Analysis and Spectra

Gas chromatographic analyses were performed on a Hewlett-Packard model 5840A instrument with a 6 ft x 0.125 in o.d. nickel column of 20% SE-30 on 80/100 mesh Chromosorb H and a thermal conductivity detector. ^1H NMR, ^{13}C NMR and ^{31}P NMR spectra were obtained in DCCl_3 solvent on a Varian model XL-300 instrument with tetramethylsilane $[(\text{CH}_3)_4\text{Si}]$ as internal standard for ^1H and ^{13}C , and 85% H_3PO_4 as external standard for ^{31}P . ^1H NMR spectra were recorded at 300 MHz, ^{13}C NMR at 75.5 MHz, and ^{31}P NMR at 121.5 MHz. IR spectra were recorded on a Perkin Elmer model 681 instrument. Elemental analyses were carried out by Mic. Anal. (Tucson, Arizona), by Galbraith Laboratories (Knoxville, TN), or by Huffman Laboratories, Inc. (Wheat Ridge, Colorado).

General Procedure for the Suspension Polymerization of Styrene Containing Divinylbenzene (DVB) as Cross-Linker²⁹ Two Percent Cross-Linked Polystyrene (16)

The general procedure²⁹ was followed with the monomer composition of 158.9 g styrene, 6.1 g divinylbenzene (DVB), using 0.0816 g of sodium dodecylbenzenesulfonate (from Polysciences, Inc.) and 0.825 g of AIBN as an initiator. The total weight of the polymer was 116.73 g with the following size distribution: 2.07 g on 40, 25.0 g on 60, 51.0 g on 100, 34.63 g on 200, 3.76 g on 325 and 0.27 g on 400 mesh. The starting materials styrene and divinylbenzene were distilled to

remove the inhibitor, and the polymer formed, if any on storage, under reduced pressure and an inert atmosphere before polymerization. The azobis(isobutyronitrile) (AIBN) was used as the free radical initiator and sodium dodecylbenzenesulfonate as the surfactant. The anionic surfactant sodium dodecylbenzenesulfonate gave some fibrous material along with the polymer. When polymerization was repeated using less amounts of monomers, styrene and divinylbenzene (123.0 g and 4.72 g, respectively), a sizeable amount of fibrous material was formed. The fibrous material was decanted off by suspending the polymer beads in water. The teflon blade stirrer was found more useful than the stainless steel one, with the optimum speed of 350 rpm to maximize the 60-100 mesh size. The position of the teflon blade was adjusted at the interface of organic and aqueous phase to effect better dispersion. The polymerization was completed at 70°C within 36 h.

General Procedure for the Bromination of

2% Cross-Linked Polystyrene²⁰ (16)

To 30.4 g (281.5 mmol) of 2% cross-linked polystyrene (16) (100-200 mesh size) in 335.0 mL of carbon tetrachloride (CCl_4) was added 2.37 g (5.81 mmol) of thallium acetate $[\text{Tl}(\text{OAc})_3]$ sesquihydrate. After 0.5 h of stirring bromine, [15.5 g (97.22 mmol)] in 30 mL of CCl_4 was added dropwise by means of a pressure equalizing addition funnel. The mixture was refluxed for 2 h (protected from light), cooled and filtered. After 2 h of refluxing, the color of bromine gradually disappeared, and HBr gas was evolved, initially quite vigorously, while as reaction proceeded towards completion, its evolution diminished. No evolution of HBr gas indicated the completion

of the reaction. The polymer was successively washed with 30 mL each of CCl_4 , acetone, 2 N methanolic HCl, water, acetone and finally with methanol and dried at 80°C under vacuum gave 37.24 g (98%) of poly-(4-bromostyrene) (17).

Anal. Found: Br 17.86% (2.23 mmol/g), (98%), 28% RS.

IR (KBr): 1235, 825 (br) cm^{-1} .

Standardization of n-BuLi by the Diphenylacetic Acid Method²⁸

Diphenylacetic acid has the advantage of being a solid, stable on storage and easily weighed. A sample of diphenylacetic acid, 0.300 g (1.415 mmol), was weighed and dissolved in 10 mL of tetrahydrofuran, and the n-butyllithium solution was run in from a syringe until the yellow end-point is reached. The yellow end-point indicates formation of α -lithiodiphenylacetate after all the carboxyl protons were consumed. The molarity of n-BuLi came out to be 1.41 M, while the reported value on the reagent bottle was 1.55 M.

General Procedure for the Phosphination of Poly(4-bromostyrene) (17) Using Dichloro- phenylphosphine with n-BuLi

To 5.0 g (11.15 mmol) of 2% cross-linked poly(4-bromostyrene) (17) was added 25.0 mL of toluene. After cooling to -20°C , 34 mL (48.0 mmol) of 1.41 M n-BuLi in hexane was added dropwise. The mixture was stirred at room temperature for 2 h and at 70°C for 14 h using an IR lamp for heat. It was then cooled and filtered through the frit under a slight nitrogen pressure. The polymer was washed

five times with toluene (5 x 20 mL). The flask was cooled to -20°C , 40 mL of THF was added, and then 2.2 mL (15.0 mmol) of dichlorophenylphosphine was added dropwise. The mixture was stirred at -20°C for 2 h and then for 3 h at room temperature, and filtered through the frit. This polymer was washed sequentially with acetone (3 x 25 mL), THF (3 x 25 mL), and finally with ether. The polymer was dried under vacuum at 60°C to give 5.33 g of chloro(phenyl)(4-polystyryl)-phosphine (19). The calculated yield was 47% on the basis of weight increase in the sample from poly(4-bromostyrene) (17).

^{31}P = 84.0 ppm.

IR (KBr): 1410, 1120, 1000, 950(br) cm^{-1} .

^{31}P of $\text{C}_6\text{H}_5\text{POCl}_2$, 36.3 ppm, Lit.²⁹ 34.5 ppm.

Phosphination of Poly(4-bromostyrene) (17) Using
Diethyl Chlorophosphite $[(\text{EtO})_2\text{PCl}]$ with
n-BuLi

To 5.0 g (12.5 mmol) of 2% cross-linked poly(4-bromostyrene) (17) in 25 mL of toluene at room temperature was added dropwise 10.6 mL of n-BuLi in hexane (15.0 mmol). The mixture was stirred at room temperature for 20 h and then filtered through the frit under slight pressure of nitrogen. The polymer was washed three times with toluene (3 x 15 mL) and four times with THF (4 x 15 mL). The flask was cooled to -78°C , and 1.8 mL (12.5 mmol) of diethyl chlorophosphite (20) was added dropwise. The mixture was brought to room temperature over 0.5 h with stirring and then was stirred at room temperature for 4 h. The mixture was filtered through the frit and the polymer was washed sequentially four times with THF (4 x 15 mL)

and p-xylene (4 x 15 mL). Ethyl bromoacetate (22), [1.4 mL (12.5 mmols)] was added dropwise at room temperature, and the mixture was stirred at room temperature overnight. The mixture was filtered and washed with THF four times (4 x 15 mL). The polymer was dried under vacuum at 60°C yielding 5.57 g (51%). [The conversion of poly(4-bromostyrene) (17) into diethyl (4-polystyryl)phosphinoacetate (23) was calculated on the basis of bromine elemental analysis in 17.] ³¹P NMR spectrum showed a major signal at 34.7 ppm and a small peak at 20.0 ppm from 85% H₃PO₄.

Anal. Found: Br, 0.84% (0.1 mmols/g), P, 4.31% (1.39 mmols/g, 19% RS, 58% yield).

IR (KBr): 1740, 1455, 1410, 1385(w), 1250(br), 1120(br), 1035(br), 960(br), 830(br) cm⁻¹.

¹³C NMR (DCCl₃): 145.0, 128.0, 61.0, 40.6, 22.4, 16.5, 14.0 ppm.

Following the above scheme on another sample of 20.0 g (50.0 mmols) poly(4-bromostyrene) (17), phosphination was again attempted. The bromine in that sample analytically found was 20.1% (2.51 mmols/g, 33% RS). After the completion of reaction a weight decrease was observed in the sample, yielding 18.78 g of diethyl (4-polystyryl)-phosphinoacetate (23). ³¹P NMR spectrum shows exactly the same peaks as in above sample at 34.8 and 19.9 ppm. IR analysis shows exactly the same spectrum as above.

Anal. Found: P, 2.58% (0.83 mmols/g, 10% RS, 30% yield).

General Procedure for the Wittig Olefination
with Polymer-Bound Phosphinate Reagent 23

Reaction of Diethyl (4-Polystyryl)phosphinoacetate (23) with Benzaldehyde Using Dimethylformamide (DMF) as Solvent and Sodium Ethoxide as Base

The polymer 23 [2.0 g (2.78 mmol)] was swollen in 10 mL DMF at room temperature. Sodium ethoxide [freshly prepared 1.5 mL (2.78 mmol)] was added at 0°C, and the mixture was warmed to room temperature and was stirred for 2 h. The flask was cooled to 0°C and 0.22 mL (2.14 mmol) of benzaldehyde was added and the mixture was stirred for 1.5 h at room temperature and an aliquot was taken out from the reaction mixture for GC analysis. A second aliquot, after 4.5 h of stirring at room temperature was taken out, and then after 17 h stirring at room temperature, mixture was filtered through the frit into ice acidified with HCl. The polymer beads were washed with ether and compound was extracted from water with ether. After drying over MgSO₄ the ether was evaporated on a rotary evaporator to yield 0.2857 g of ethyl cinnamate (crude yield 76%) after putting the sample on vacuum pump for 0.5 h. The crude product and the two aliquots were analyzed by GLC.

GLC Conditions Common To All Samples

Instrumental conditions were, attenuation 2⁶, injector temperature 225°C, TCD temperature 250°C, He flow rate 40 mL/min, sample injection size 0.2 µL-10 µL. From the first aliquot, 10 µL of reaction mixture

was injected, and analyzed by temperature programming with the initial temperature of 150°C for 3 min with a rate increase of 25°C/min, and the final temperature of 230°C for 20 min. The aliquot taken 1.5 h after the addition of benzaldehyde, contained 81.33% (peak area %) of ethyl cinnamate and 18.67% (peak area %) of benzaldehyde. Retention times (min) of dimethylformamide 0.77, benzaldehyde 1.26 and ethyl cinnamate 5.65 min. An injection of 10 μ L, after 4.5 h stirring of the reaction mixture revealed 84% (peak area %) of ethyl cinnamate with the same retention time of 5.65 min. Analysis of the reaction mixture after 17 h showed 95% of ethyl cinnamate. To remove the unreacted benzaldehyde, the sample was flash chromatographed.

Flash Chromatography

The crude reaction mixture was absorbed on 2.0 g of silica gel in an evaporatory dish after dissolving it in diethyl ether. Ether was evaporated and compound absorbed on silica gel was added to the column packed with 40.0 g of silica gel, and eluted sequentially with 1%, 2%, 3%, 4%, and 10% ethyl acetate in petroleum ether. The eluents were monitored with thin layer chromatography (TLC) using 1% ethyl acetate in petroleum ether to develop the TLC plates. The major fraction came out with 2% ethyl acetate in petroleum ether. The solvent was evaporated on rotary evaporator to yield 0.2372 g (63%) of ethyl cinnamate. The yield was calculated on the basis of phosphorus analysis of 23.

IR (Neat): 1712, 1641, 1203, 1177(br), 1038(br), 980, 750, 690 cm^{-1} .

^1H NMR (DCCl_3): δ 1.15 (t, 3 H), 4.15 (q, 2 H), 6.33 (d, 1 H).

^{13}C NMR (DCCl_3): 14.3, 60.3, 118.1, 127.8, 128.6, 130.0, 134.2, 144.3, 166.6 ppm.

Reaction of carbanion 25 with benzaldehyde at room temperature yielded pure ethyl cinnamate (63%) after flash chromatography. ^{13}C NMR analysis revealed a peak at 14.3 ($-\text{CH}_3$) and 60.35 ($-\text{O}-\text{CH}_2$) with peaks for ($-\text{CH}=\text{CH}-\overset{\text{O}}{\parallel}{\text{C}}$) double bonded carbons at 144.0 and 118.0 ppm, respectively. The $\text{C}=\text{O}$ appeared at 166.6 ppm, a high field position because of the unsaturation. IR analysis of the product also confirmed the structure.

Reaction of Diethyl (4-Polystyryl)phosphinoacetate (23) with Benzaldehyde Using Tetrahydrofuran (THF) as Solvent and Sodium Ethoxide as Base

To 3.0 g (2.5 mmoles on the basis of P-analysis) of 23, swollen in 15 mL of THF, at 0°C sodium ethoxide (2.5 mmoles in 1 mL of ethanol) was added and solution was stirred for 2 h at room temperature. The flask was cooled to 0°C , and 0.25 mL (2.5 mmoles) of benzaldehyde was added. The flask was gradually warmed to room temperature and was then stirred for 14 h. The mixture was filtered through the frit into ice and extracted with ether. The ether layer was separated and washed with 3 N HCl and with water. After drying over MgSO_4 , ether was evaporated on a rotary evaporator to yield 0.16 g of the yellow, oily ethyl cinnamate (37%). The yield was calculated on the basis of phosphorus analysis of 23. The IR spectrum was the same as that above, so other methods of analysis were not tried. The same experiment was repeated using ethanol as solvent and sodium ethoxide as base, but the

polymer beads did not swell very much in ethanol. The yield was only 0.04 g of ethyl cinnamate (9%) using exactly the same conditions as above.

Reaction of Diethyl (4-Polystyryl)phosphinoacetate (23) with Cyclopentanone Using THF as Solvent and NaOEt as Base

Diethyl (4-polystyryl)phosphinoacetate (23) [2.0 g (2.48 mmoles)] was swollen in 15 mL of THF at room temperature. Freshly prepared sodium ethoxide (2.48 mmoles in 1.0 mL of ethanol) was added, and the mixture was stirred for 2 h at room temperature. The mixture was filtered through the frit under slight pressure of argon to remove the unreacted sodium ethoxide, and the polymer beads were washed three times with THF (3 x 10 mL). Cyclopentanone [0.22 mL (2.48 mmoles)] was added at room temperature, and the reaction mixture was stirred for 20 h at room temperature and filtered through the frit. The polymer was washed three times with THF (3 x 10 mL), and the filtrate was analyzed by GLC.

GLC Conditions Common to All Samples

Instrumental conditions were, attenuation 2^6 , injector temperature 225°C , TCD temperature 250°C , flow rate 40 mL/min, and sample injection size 0.2 μL –5 μL . The filtrate (5 μL) from the reaction mixture was injected, and analyzed by temperature programming with the initial temperature of 150°C for 3 min, a rate of increase $25^{\circ}\text{C}/\text{min}$, and the final temperature of 230°C for 20 min. Retention times (min) cyclopentanone 0.6, ethyl cyclopentylideneacetate (28) 3.38, aldol product

29 5.15 was obtained. Solvent was evaporated on a rotary evaporator to yield 0.123 g of oily product. Again 0.6 μ L of oily product was injected onto the GC column using the conditions mentioned above. The major peaks had retention times of 0.61 and 3.38 min.

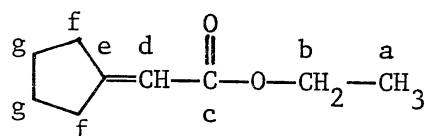
Flash Chromatography

The crude reaction mixture was dissolved in ether and the solution was absorbed on silica gel in an evaporating dish. The ether was evaporated and the compound absorbed on silica gel was added to the column packed with 40.0 g of silica gel. Sequential elution was effected with petroleum ether and 1%, 2%, 3%, 4%, 5% and 10% ethyl acetate in petroleum ether. The eluents were monitored with thin layer chromatography (TLC) using 1% ethyl acetate in petroleum ether to develop the TLC plates. Five fractions were collected with 2%-10% ethyl acetate in petroleum ether elutions. The solvent was evaporated on a rotary evaporator to yield 0.043 g, 0.018 g, 0.012 g, 0.009 g and 0.009 g, respectively. The five fractions were injected (3 μ L each in THF) onto a GLC column. Fraction number one showed a major peak with retention time 3.30 min for ethyl cyclopentylideneacetate (28) [0.043 g (yield 11%)], while total weight of all five fractions obtained from flash chromatography was 0.091 g. [All the yields are calculated on the basis of phosphorus analysis in 23.] Fraction number one was further characterized by IR, ^1H NMR and ^{13}C NMR.

IR (Neat): 1705, 1650, 1205(br), 1125 cm^{-1} .

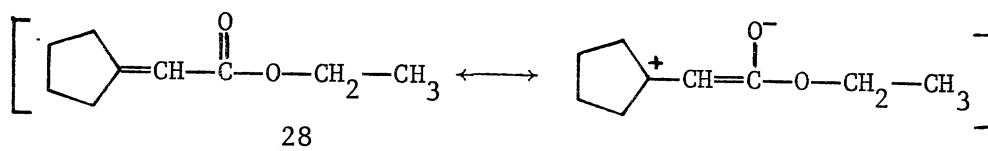
^1H NMR (DCCl_3): δ 1.28 (t, 3 H), 1.7 (m, 4 H), 2.46 (t, 2 H), 2.80 (t, 2 H), 4.19 (q, 2 H), 5.84 (s, 1 H).

^{13}C NMR (DCCl_3): 14.22, 25.33, 26.26, 32.45, 35.78, 59.25, 111.50, 166.77, 168.92 ppm.



28

^{13}C NMR analysis revealed a peak at 14.22 ppm ($-\text{CH}_3$), 25.33 ppm and 26.26 ppm for g-carbons, while the f-carbon, which is trans to the ester group, was at 32.45 ppm and the one which is cis is at 35.78 ppm due to shielding and deshielding, respectively. The peak at 59.25 ppm ($-\text{O}-\text{CH}_2-$) was for the methylene carbon which is attached to the oxygen of the ester group. The peaks for doubly bonded carbons ($>\text{C}=\text{CH}$) are at 166.77 and 111.50, respectively. The peak for the e-carbon of the ring is at very low field, due to deshielding in case of resonance and to the carbon atoms in the 5-membered ring as shown below:



28

The peak for $\text{C}=\text{O}$ of the ester is at 168.92 ppm, typical of α,β -unsaturated ester. IR and ^1H NMR also confirmed the above structure. Other fractions did not show clean spectra.

Reaction of Polymer 23 with Cyclopentanone

Using DMF as Solvent and NaOEt as Base

Diethyl (4-polystyryl)phosphinoacetate (23), [5.0 g (6.2 mmol)], was swollen in DMF. At room temperature, freshly prepared NaOEt

(6.76 mmol) was added, and the mixture was stirred for 2 h at room temperature. Cyclopentanone [1.6 mL (11.30 mmol)] was added at room temperature, and after stirring the mixture for 3 h at room temperature, an aliquot of the mixture was taken out. Another aliquot was taken out after 15 h of stirring. The mixture was refluxed and a third aliquot was taken out after 1 h. After 3.5 h refluxing the cooled reaction mixture was filtered through the frit into a beaker containing acidified ice. The polymer beads were washed with ether, and compounds were extracted from water with ether. After drying (MgSO_4), the ether was evaporated on a rotary evaporator, and the sample was held at 10 mm Hg with a vacuum pump for half an hour to yield 1.81 g crude product. The crude product and the three aliquots were analyzed by GLC under the same conditions as in previous experiment. The first aliquot was taken after 1 h of stirring at room temperature and 5 μL sample was injected on GLC to show a major peak with retention time of 5.14 min for the aldol product 29. The second aliquot (5 μL injection) revealed a major product with a retention time of 5.21 min for the aldol product 29 along with ethyl cyclopentylideneacetate (28) at 3.22 min. The third aliquot, after 1 h at reflux showed the same spectra like the second aliquot except for a new peak with a retention time of 11.69 min.

GLC analysis of the crude product revealed the following peaks with retention times in min, cyclopentanone 0.60, ethyl cyclopentylideneacetate (28) at 3.23, aldol product 29 at 5.27, and an unknown impurity 11.27 min.

Flash Chromatography

The crude reaction mixture dissolved in ether was absorbed onto silica gel in an evaporating dish. Ether was evaporated, and compound was added to a column packed with 60 g of silica gel, and eluted with 1% and 2% ethyl acetate in petroleum ether. The eluents were monitored by TLC using 1% and 2% ethyl acetate in petroleum ether. Moreover, the eluents were monitored by TLC, using 1% ethyl acetate in petroleum ether to develop the TLC plates. With 2% elution, two fractions came out after one another. The fraction which is an aldol product [2-cyclopentylidene-1-cyclopentanone (29)] came later in a yield of 1.695 g (80%). This aldol product was characterized by IR, ^1H NMR and ^{13}C NMR.

IR (Neat): 1710, 1645, 825 cm^{-1} .

^1H NMR (DCCl_3): δ 1.72 (m, 4 H), 1.94 (m, 2 H), 2.30 (t, 4 H),
2.57 (m, 2 H), 2.80 (m, 2 H).

^{13}C NMR (DCCl_3): 19.8, 24.9, 26.6, 29.2, 32.2, 33.9, 39.4, 127.4,
157.8, 206.3 ppm.

Reaction of 23 with Cyclohexanone Using THF as Solvent and NaOEt as Base (In Excess)

To polymer-bound phosphinate ester 23 [2.0 g (2.48 mmol)], swollen in 15 mL of THF, at room temperature was added freshly prepared sodium ethoxide (3.9 mmol in 1 mL of ethanol). The mixture was stirred at room temperature for 1.5 h. The mixture was filtered through the frit under slight pressure of argon to remove unreacted sodium ethoxide, and the polymer beads were washed three times with THF (3 x 10 mL). The filtrate was titrated against 5 N

HCl, indicating the recovery of 1.02 mmoles of sodium ethoxide. Cyclohexanone [0.26 mL (2.46 mmoles)] was added at room temperature, and reaction mixture was stirred overnight. The mixture was filtered through the frit, and the polymer was washed three times with THF (3 x 10 mL). The filtrate was analyzed by GLC.

GLC Conditions

The filtrate (5 μ L) was injected and analyzed by temperature programming with the initial temperature of 150°C for 3 min, a rate of increase 25°C/min, and a final temperature of 230°C for 20 min. Retention times (min), cyclohexanone (0.91 min), ethyl cyclohexylideneacetate (30) (4.19 min). The cyclohexanone peak was confirmed by spiking the filtrate with cyclohexanone. The solvent was evaporated on a rotary evaporator to yield 0.278 g of the crude product, and 1 μ L compound was injected onto GLC using the same conditions as above. Major peaks with retention times (min), cyclohexanone (0.99 min), and ethyl cyclohexylideneacetate (30) (4.41 min).

Flash Chromatography

The mixture absorbed on silica gel was added to a column packed with 40.0 g of silica gel. Sequential elution was effected with petroleum ether, 1%, 2%, 3%, 4%, 5% and 10% ethyl acetate in petroleum ether. The eluents were monitored with thin layer chromatography (TLC) using 1% ethyl acetate in petroleum ether to develop the plates. Solvent was evaporated on a rotary evaporator to yield 139.0 mg, 54.3 mg, 31.6 mg, 37.4 mg and 15.0 mg, respectively. Fraction number one (0.4 μ L) was injected on a GLC column. The major peak with retention

time (min) was ethyl cyclohexylideneacetate (30) (4.41 min, 33%). The total yield of all fractions obtained from flash chromatography was 66%. All the yields were calculated on the basis of phosphorus analysis on 23. Fraction number one was further characterized by IR, ^1H NMR and ^{13}C NMR.

IR (Neat): 1725, 1660, 1210, 1160(br), 860 cm^{-1} .

^1H NMR (DCCl_3): δ 1.28 (t, 3 H), 1.64 (m, 6 H), 2.2 (t, 2 H), 2.86 (t, 2 H), 4.16 (q, 2 H), 5.64 (s, 1 H).

^{13}C NMR (DCCl_3): 14.4, 26.0, 28.0, 30.0, 38.0, 59.0, 113.0, 163.0, 167.0 ppm.

Other fractions did not show clean spectra.

Reaction of 23 (In Excess) with Cyclohexanone

Using THF as Solvent and NaOEt as Base

(In Excess)

The procedure followed in the previous olefination reaction was repeated using 3.0 g (2.55 mmoles) of polymer-bound phosphinate ester 23, 5.25 mmoles of NaOEt and 0.19 mL (1.8 mmoles) of cyclohexanone, to yield 0.17 g crude product (56%). The yield was determined on the basis of the limiting reagent cyclohexanone. The filtrate (5 μL) from the reaction mixture was injected onto a GLC column under the same conditions as used in the previous experiment. The ethyl cyclohexylideneacetate (30) peak with a retention time of 4.21 min (peak area 29%) indicated a yield of 16%. This yield was calculated on the basis of peak area % in the GLC.

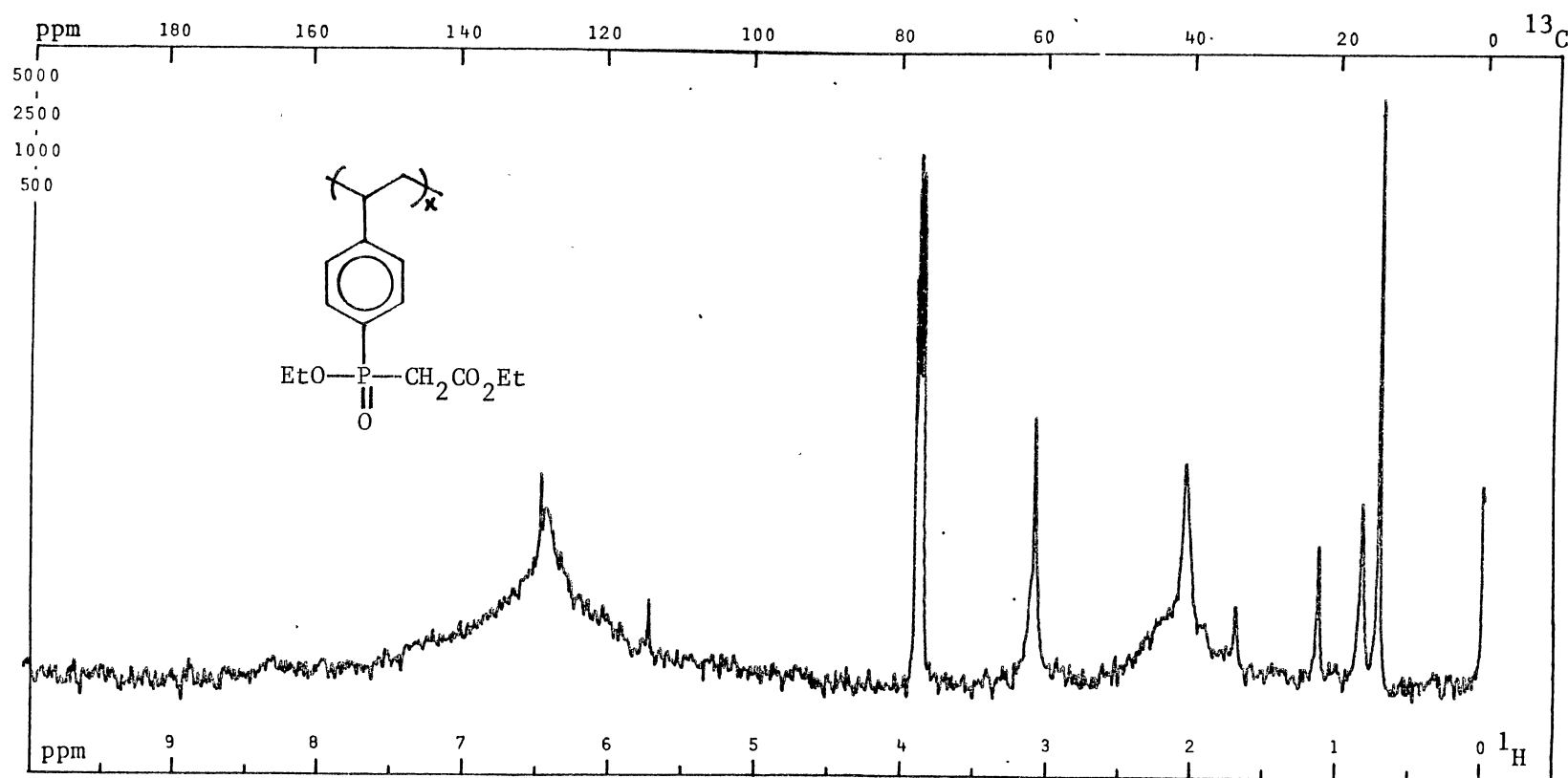
REFERENCES

1. Wittig, G.; Geissler, G. Ann. 1953, 580, 44.
2. Wittig, G.; Schollkopf, U. Chem. Ber. 1954, 87, 1318.
3. Wittig, G.; Hoag, W. Chem. Ber. 1955, 88, 1654.
4. Wittig, G. Angew. Chem. 1956, 68, 505.
5. Wittig, G. Experientia. 1956, 12, 41.
6. Horner, L.; Hoffmann, H.; Wippel, H. G.; Klahre, H. Chem. Ber. 1958, 91, 61.
7. Wadsworth, W. S., Jr. Organic Reactions. 1978, 25, 73-250.
8. Gosney, I.; Rowley, A. G. "Organophosphorus Reagents in Organic Synthesis", Cadogan, J. I. G., Ed. Academic Press, New York, 1979, Chapter 2, p. 17.
9. Bestmann, H. J. Pure Appl. Chem. 1980, 52, 771.
10. Horner, L.; Hoffmann, H.; Wippel, H. G.; Klahre, H. Chem. Ber. 1959, 92, 2499.
11. Horner, L.; Hoffmann, H.; Klink, W.; Ertel, H.; Toscano, V. G. Chem. Ber. 1962, 95, 581.
12. Wadsworth, W. S.; Emmons, W. D. J. Am. Chem. Soc. 1961, 83, 1733.
13. Walker, B. J. in "Organophosphorus Reagents in Organic Synthesis", J. I. G. Cadogan, Ed. Academic Press, New York, 1979, Chapter 3, p. 160.
14. For reviews see (a) Akelah, A.; Sherrington, D. C. Chem. Rev. 1981, 81, 557-587; (b) Frechet, J. M. J. Tetrahedron, 1981, 37, 663-683; (c) Akelah, A. Synthesis, 1981, 413-438; (d) Hodge, P. in "Polymer-Supported Reactions in Organic Synthesis", Hodge, P.; Sherrington, D. C. Eds. John Wiley and Sons, New York, 1980, pp. 83-155.
15. Camps, F.; Castells, L.; Font, J.; Vela, F. Tetrahedron Lett. 1971, 1715-1716.
16. Heitz, W.; Michels, R. Angew. Chem. Int. Ed. Engl. 1972, 11, 289-299.

17. McKinley, S. V.; Rakshys, J. W. J. Chem. Soc., Chem. Comm., 1972, 134-135.
18. Clarke, S. D.; Harrison, C. R.; Hodge, P. Tetrahedron Lett. 1980, 21, 1375-1378.
19. Akelah, A. Eur. Polym. J. 1982, 18, 559-561.
20. Farrell, M. J.; Frechet, J. M. J. J. Org. Chem. 1976, 41, 3877-3882.
21. Crutchfield, M. M.; Dungan, C. H.; Letcher, J. H.; Mark, V.; Van Wazer, J. R. "Topics in Phosphorous Chemistry", Vol. 5, ³¹P Nuclear Magnetic Resonance, Interscience Publishers, New York, 1967. p. 242.
22. Ref. No. 21, p. 293.
23. Ref. No. 21, p. 255.
24. Ref. No. 21, p. 296.
25. Shulte-Elte, H. K. Swiss. Pat., 616077, 1980; Chem. Abstr. 1980, 93, 79,890.
26. Foder, G., Tomoskogi, I. Tetrahedron Lett. 1961, 579.
27. Vogel, A. I. "Practical Organic Chemistry", 3rd Ed. Lowe and Brydone Printers, London, 1956. pp. 189.
28. Kofron, W. G.; Baclawski, L. M. J. Org. Chem. 1976, 41, 1879.
29. (a) Balakrishnan, T.; Ford, W. T. J. Appl. Polym. Sci. 1982, 27, 133-138; (b) Balakrishnan, T.; Lee, J.; Ford, W. T. Macromol. Syn., in press.
30. Ref. No. 21, p. 189.

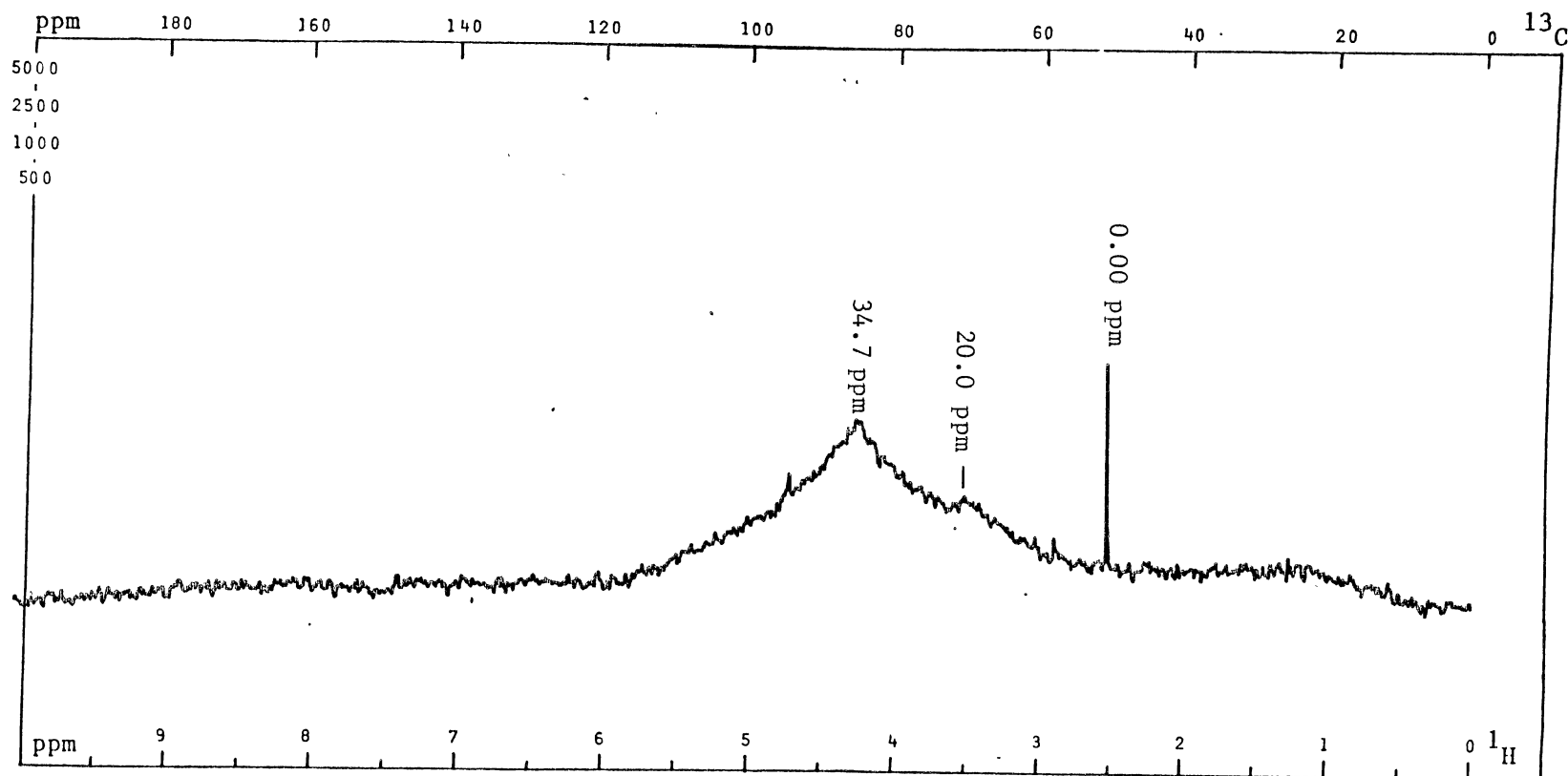
APPENDIX

SELECTED SPECTRA



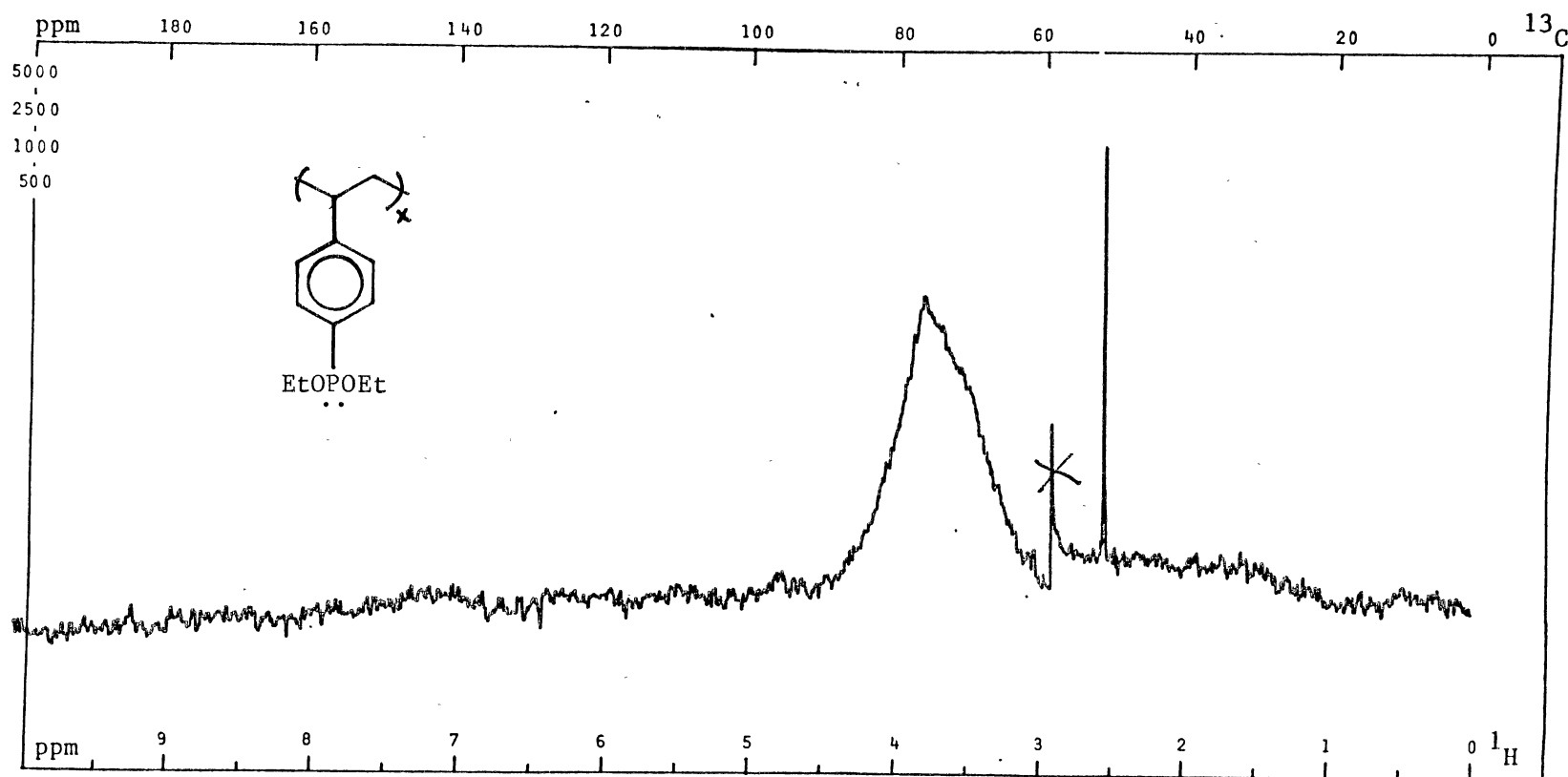
Spectrum 1. ^{13}C NMR of Diethyl (4-Polystyryl)phosphinoacetate (23)

PFT X CW _ ; Solvent: DCCl_3 ; SF: 75.429 MHz; WC: 500 Hz; T: 25°C; NT: 600 .
 Size: 20K; PW/RF: 12 $\mu\text{s/dB}$; SO: 1000 Hz; FB: NA Hz; Lock: D; Delay: 2.0 s .
 DC: ^1H ; Gated Off: no; Offset: 0 Hz; RF: 10 W/dB; NBW: NA Hz; LB: 5.0 .



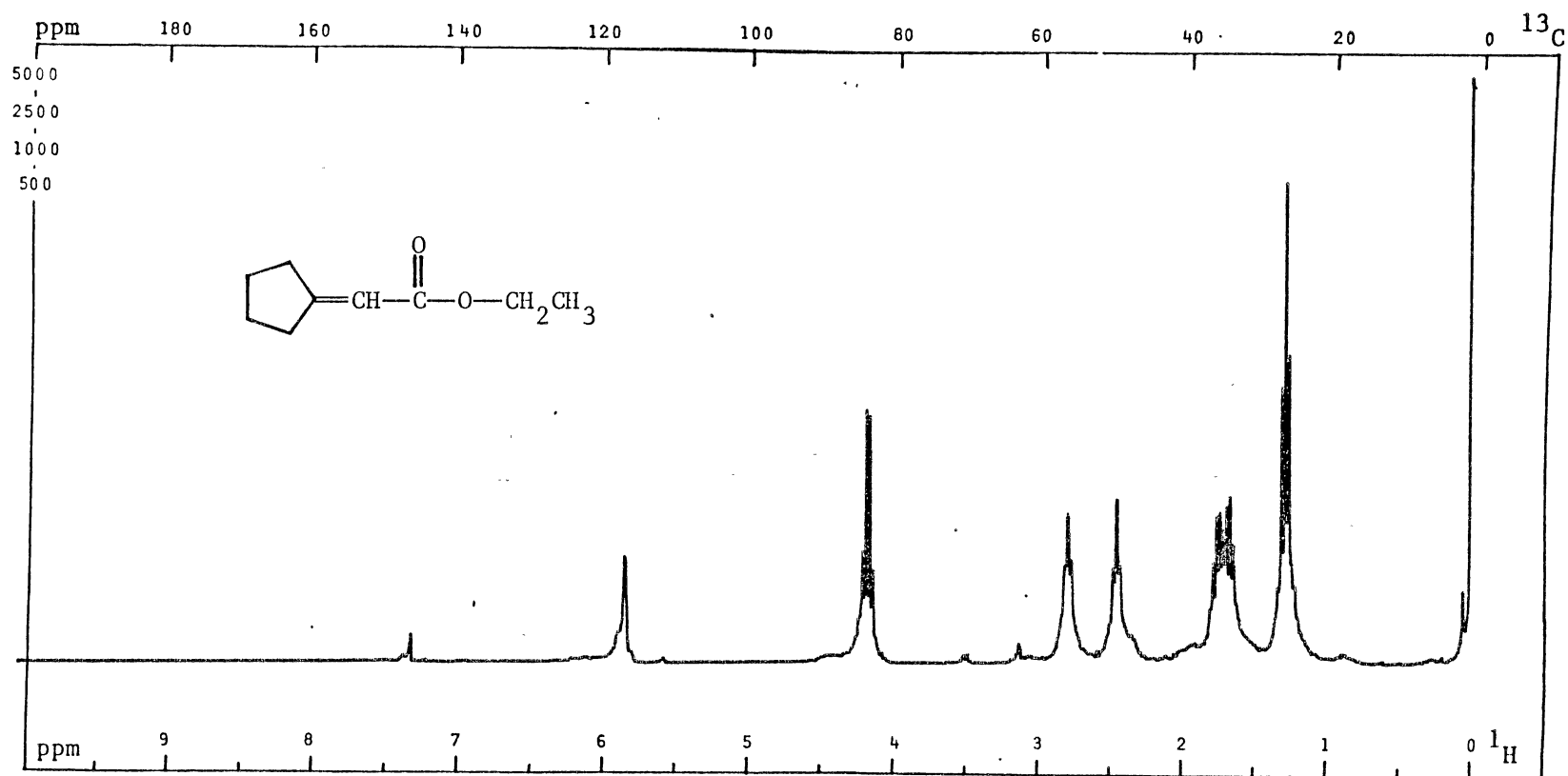
Spectrum 2. ^{31}P NMR of Diethyl (4-polystyryl)phosphinoacetate (23)

PFT X CW _ ; Solvent: DCCl_3 ; SF: 121.421 MHz; WC: 100 Hz; T: 23°C; NT: 300 .
 Size: 50K; PW/RF: 10 $\mu\text{s}/\text{dB}$; TO: 2000 Hz; FB: NA Hz; Lock: D; D1, ~~D5~~: 6.0 s.
 DC: Y, ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 0 W/dB; NBW: NA Hz; LB: 10 Hz.



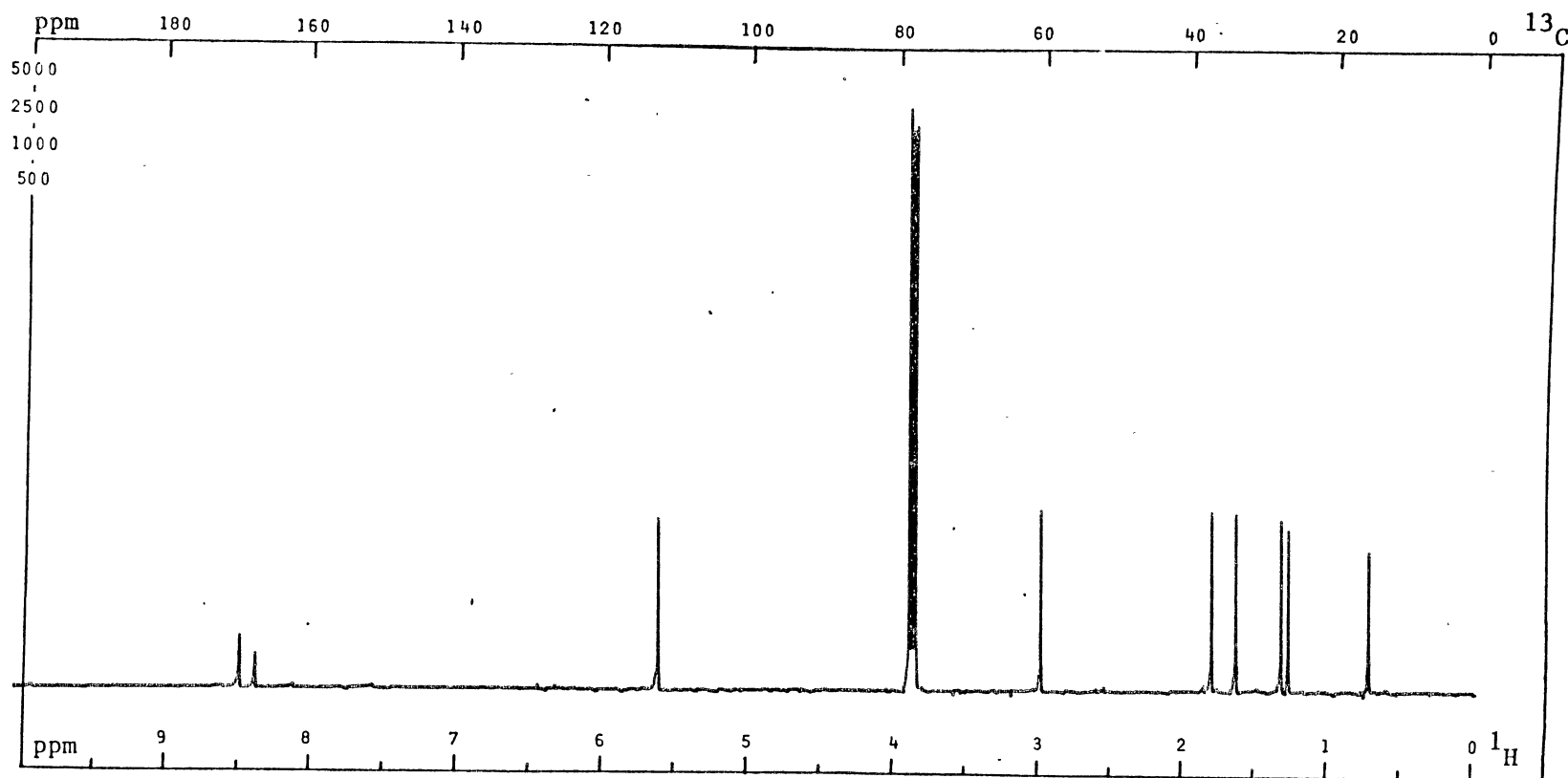
Spectrum 3. ^{31}P NMR of Diethyl (4-Polystyryl)phosphonite (24)

PFT X CW ; Solvent: DCCl_3 ; SF: 121.421 MHz; WC: 100 Hz; T: 23°C; NT: 300 .
 Size: 50K; PW/RF: 10.0 $\mu\text{s}/\text{dB}$; TO: 2000 Hz; FB: NA Hz; Lock: D ; D1 ~~DS~~: 6.0 s .
 DC: Y, ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 0 W/dB; NBW: NA Hz; LB: 10.0 Hz.



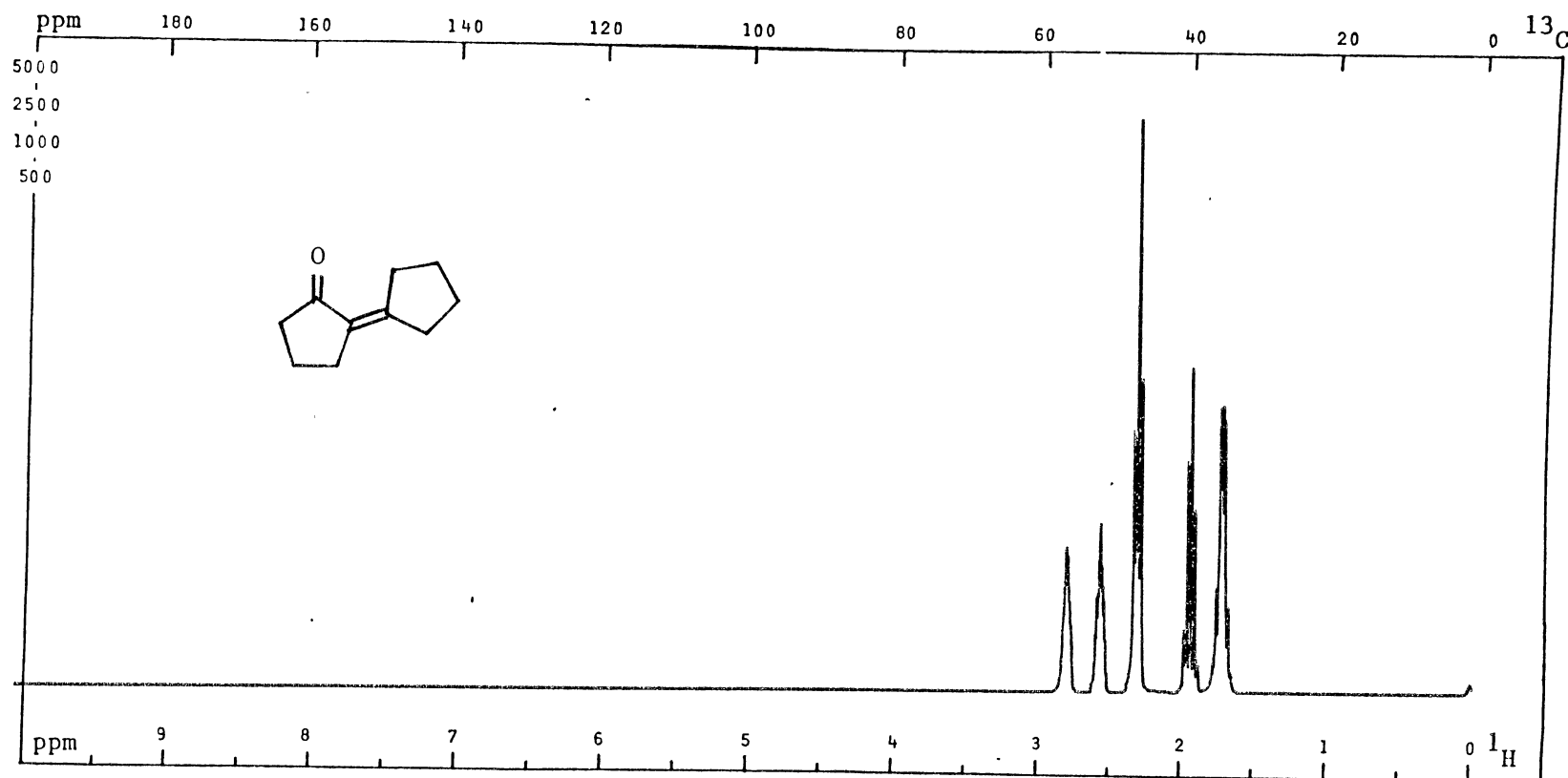
Spectrum 4. ¹H NMR of Ethyl Cyclopentylideneacetate (28)

PFT X CW ; Solvent: DCCl₃; SF: 299.944 MHz; WC: 200 Hz; T: 24 °C; NT: 40 .
 Size: 4K; PW/RF: 5.1 μs/dB; TO: 200 Hz; FB: NA Hz; Lock: D ; D1, ~~D5~~: 0.5 s .
 DC: , N ; Gated Off: A or D ; DO: -1173.0 Hz; RF(Power): 0 W/dB; NBW: NA Hz; LB: 1.0 Hz.



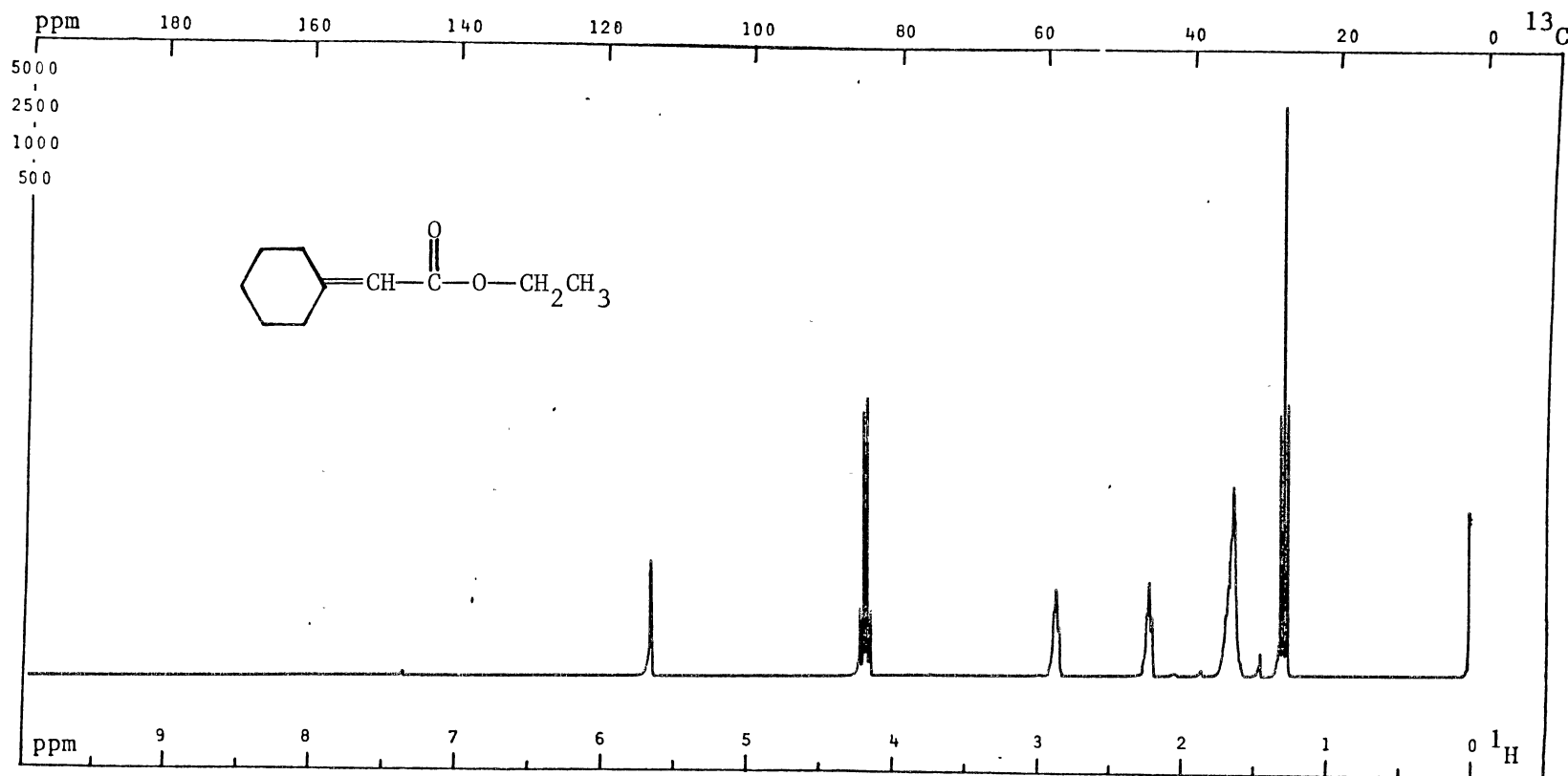
Spectrum 5. ^{13}C NMR of Ethyl Cyclopentylideneacetate (28)

PFT X CW ; Solvent: DCCl_3 ; SF: 75.429 MHz; WC: 500 Hz; T: 24°C; NT: 600 .
 Size: 20K; PW/RF: 12.1 $\mu\text{s}/\text{dB}$; TO: 1000 Hz; FB: NA Hz; Lock: D ; D1, ~~D5~~: 6.0 s .
 DC: Y, ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 0 W/dB; NBW: NA Hz; LB: 2.0 Hz.



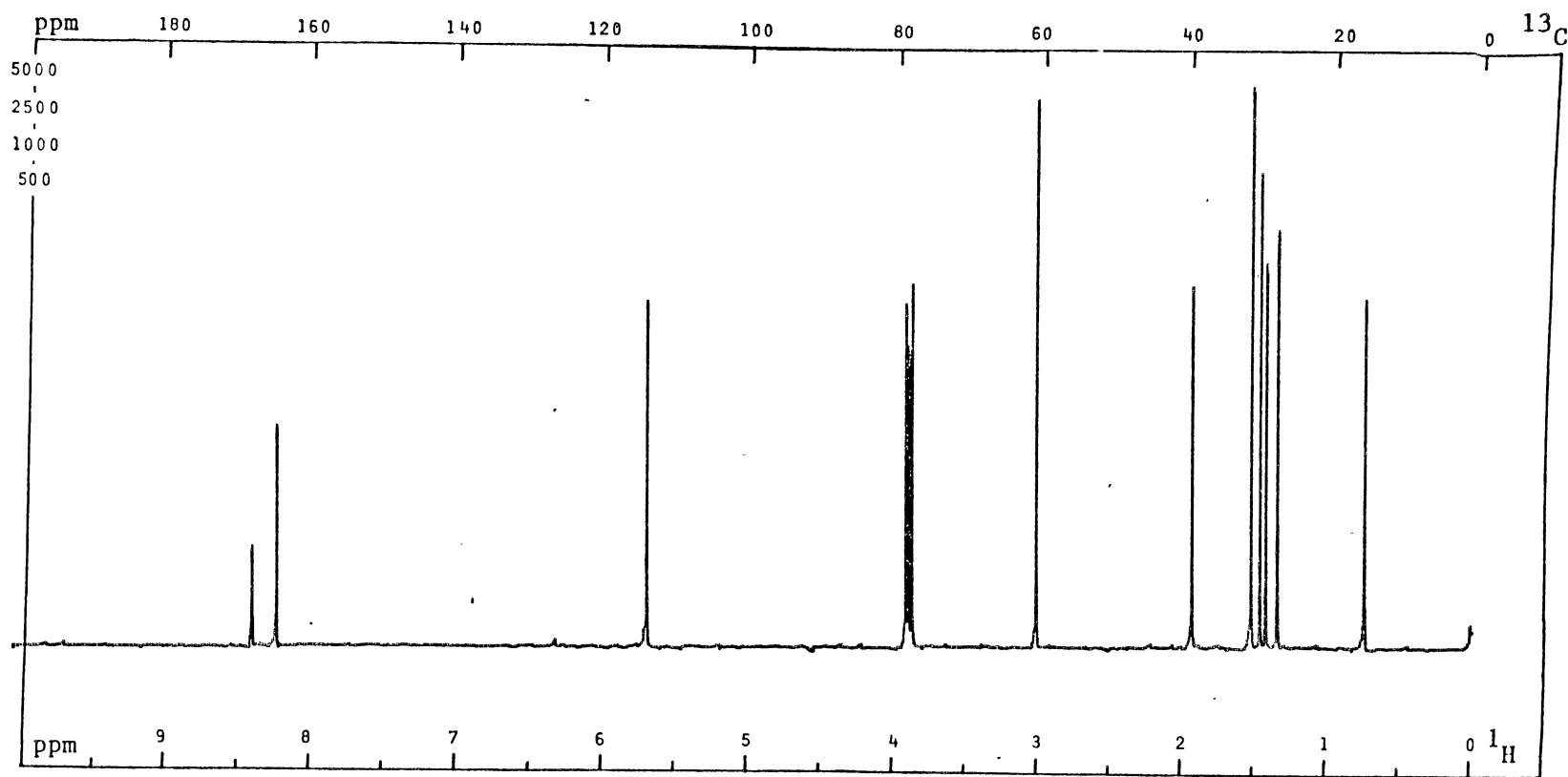
Spectrum 6. ^1H NMR of 2-Cyclopentylidene-1-cyclopentanone (29)

PFT X CW ; Solvent: DCCl_3 ; SF: 299.944 MHz; WC: 500 Hz; T: 24°C; NT: 4 .
 Size: 4K; PW/RF: 5.0 $\mu\text{s}/\text{dB}$; TO: 0 Hz; FB: NA Hz; Lock: D ; D1, ~~D5~~: 0.5 s .
 DC: Y, ; Gated Off: A or D ; DO: 350.3 Hz; RF(Power): 0 W/dB; NBW: NA Hz; LB: 1.0 Hz.



Spectrum 7. ¹H NMR of Ethyl Cyclohexylideneacetate (30)

PFT X CW ; Solvent: DCCl₃; SF: 299.944 MHz; WC: 500 Hz; T: 23°C; NT: 4 .
 Size: 4K; PW/RF: 5.0 μs/dB; TO: 0 Hz; FB: NA Hz; Lock: D ; D1, D5: 0.5 s .
 DC: Y, ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 0 W/dB; NBW: NA Hz; LB: 1.0 Hz.



Spectrum 8. ^{13}C NMR of Ethyl Cyclohexylideneacetate (30)

PFT X CW ; Solvent: DCCl_3 ; SF: 75.429 MHz; WC: 500 Hz; T: 23°C; NT: 300 .
 Size: 16K; PW/RF: 12.0 $\mu\text{s}/\text{dB}$; TO: 0 Hz; FB: NA Hz; Lock: D; D1, D5: 6.0 s.
 DC: Y, ; Gated Off: A or D ; DO: 0 Hz; RF(Power): 0 W/dB; NBW: NA Hz; LB: 1.0 Hz.

VITA 2

Altaf Ellahi Qureshi

Candidate for the Degree of

Master of Science

Thesis: REACTIONS OF POLYMER-BOUND ANIONS OF PHOSPHINATES WITH TYPICAL ALDEHYDES AND KETONES

Major Field: Chemistry

Biographical:

Personal Data: Born in Rawalpindi, Pakistan, December 17, 1956, son of Karam Ellahi Qureshi.

Education: Graduated from Christian High School, Rawalpindi, Pakistan, in 1972; received Bachelor of Science Degree in Pre-medical Science from University of the Punjab, Pakistan, in 1977; received Master of Science degree from Quaid-i-Azam University, Islamabad, Pakistan in February 1981; completed requirements for the Master of Science degree at Oklahoma State University, Stillwater, Oklahoma, U.S.A., in May, 1984.

Professional Experience: Teaching Assistant, Department of Chemistry, Oklahoma State University, August, 1983 to present.