SYNTHESIS AND APPLICATIONS OF FUNCTIONAL POLYMERS

By

M. Jean FARRALL

A thesis submitted to the School of Graduate Studies
of the University of Ottawa as partial fulfillment
for the requirements of the degree
of Doctor of Philosophy in
Chemistry

University of Ottawa
December 1978

Jean M. J. Fréchet
Research Supervisor

M. Jean Farrall
Ph. D. Candidate

©M. Jean Farrall, Ottawa, Canada, 1978
UMI Number: DC53560

INFORMATION TO USERS

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleed-through, substandard margins, and improper alignment can adversely affect reproduction. In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.
ACKNOWLEDGEMENTS

I would like to express my sincere thanks to my supervisor, Dr. J.M.J. Fréchet for continuing guidance and encouragement and the occasional prod when my enthusiasm for chemistry in the early morning waned. My thanks also to Dr. T. Durst for numerous profitable discussions and for permission to raid his chemical supplies.

I would also like to thank my co-workers Lucy Nuyens, James Warnock and Marc de Smet for their technical assistance, the National Science and Engineering Research Council for a scholarship and Ms. Jo-Ann Haynes for typing the manuscript.

A special thanks to my husband Kim for his help and encouragement and for keeping our small daughter out of my hair during the preparation of this thesis.
NOTE ON SYMBOLS USED IN THIS THESIS

-  represents a polystyrene resin \( \overbrace{\text{CH-CH}_2}^{\text{Ph}} \).

-  represents a polystyrene resin bearing substituent X on a fraction of the aromatic rings \( \overbrace{\text{CH-CH}_2-\text{CH-CH}_2}^{\text{Ph}} \).

- The epoxides described in Part II of this thesis have been represented with condensed structural formulae such as \( \text{Ph(Et)-C} \overbrace{\text{CH}_2}^{\text{Et}} \) equivalent to \( \text{Et-C} \overbrace{\text{CH}_2}^{\text{Ph}} \).
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Acknowledgement</th>
<th>i</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note on Symbols Used in this Thesis</td>
<td>ia</td>
</tr>
<tr>
<td>List of Figures</td>
<td>xii</td>
</tr>
<tr>
<td>List of Tables</td>
<td>xiv</td>
</tr>
<tr>
<td>List of Schemes</td>
<td>xvi</td>
</tr>
<tr>
<td>Abstract</td>
<td>xviii</td>
</tr>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>Review of the Literature</td>
<td>1</td>
</tr>
<tr>
<td>1. Functionalization of Polystyrene</td>
<td>1</td>
</tr>
<tr>
<td>2. Polymers as Supports in Organic Synthesis</td>
<td>13</td>
</tr>
<tr>
<td>3. Polymers as Reagents in Organic Synthesis</td>
<td>23</td>
</tr>
<tr>
<td>4. Polymers as Catalysts and Catalyst Supports</td>
<td>34</td>
</tr>
<tr>
<td>5. Other Applications of Functionalized Polymers</td>
<td>37</td>
</tr>
<tr>
<td><strong>PART 1. Synthesis of Functional Polymers</strong></td>
<td>39</td>
</tr>
<tr>
<td>Results and Discussion</td>
<td>40</td>
</tr>
<tr>
<td>Chemical Modification of $\text{P}-\text{CH}_2\text{Cl}$ by Phase Transfer Catalysis</td>
<td>41</td>
</tr>
<tr>
<td>a. Preparation of $\text{P}-\text{CH}_2\text{OCOCCH}_3$</td>
<td>45</td>
</tr>
<tr>
<td>b. Preparation of $\text{P}-\text{CH}_2\text{OH}$</td>
<td>45</td>
</tr>
<tr>
<td>c. Reaction of $\text{P}-\text{CH}_2\text{Cl}$ with other O-nucleophiles</td>
<td>47</td>
</tr>
<tr>
<td>d. Reaction of $\text{P}-\text{CH}_2\text{Cl}$ with C-nucleophiles</td>
<td>48</td>
</tr>
<tr>
<td>e. Preparation of $\text{P}-\text{CH}_2\text{CN}$</td>
<td>51</td>
</tr>
<tr>
<td>f. Reaction of $\text{P}-\text{CH}_2\text{Cl}$ with an N-nucleophile</td>
<td>51</td>
</tr>
<tr>
<td>g. Reaction of $\text{P}-\text{CH}_2\text{Cl}$ with S-nucleophiles</td>
<td>52</td>
</tr>
<tr>
<td>h. Preparation of $\text{P}-\text{CH}_2\text{SH}$</td>
<td>59</td>
</tr>
</tbody>
</table>
Preparation and Reactions of Lithiated Polystyrene $\text{P-Li}$ 60  
  a. $\text{P-Li}$ by Direct Lithiation 60  
  b. $\text{P-Li}$ by Bromination-Lithiation 65  
  c. Reactions of $\text{P-Li}$ 78  
Preparation of Nucleophilic Polymers from $\text{P-Li}$ 84  
  a. Preparation of $\text{P-SH}$ 84  
  b. Preparation of $\text{P-OH}$ 88  
Reactions of Polymeric Nucleophiles using Phase Transfer Catalysis 89  
Nucleophilic Additions to $\text{P-CHO}$ under Phase Transfer Conditions 95  
Experimental 97  
Washing of Cross-Linked Polystyrene Resins 97  
Calculation of the degree of functionalization (D.F.) and of the Functional Yield 98  
Preparation of $\text{P-CH}_2\text{Cl}$ 99  
Preparation of $\text{P-CH}_2\text{OCOCH}_3$ 100  
  a. in dichloromethane solvent 100  
  b. in o-dichlorobenzene solvent 100  
Preparation of $\text{P-CH}_2\text{OH}$ 101  
  a. Conversion of $\text{P-CH}_2\text{OCOCH}_3$ to $\text{P-CH}_2\text{OH}$ in a three phase system 101  
  b. Phase transfer reaction with simultaneous addition of acetate and hydroxide ions 101  
  c. Phase transfer reaction with successive addition of acetate and hydroxide 103  
  d. Hydroxymethylation of soluble polystyrene 103  
Preparation of $\text{P-CH}_2\text{O-Ph-CHO}$ 103  
Preparation of $\text{P-CH}_2\text{O-Ph-NO}_2$ 105  
Preparation of $\text{P-CH}_2\text{CH(CN)}_2$ 105
Preparation of \( \text{P-CH}_2\text{CH(CH}_2\text{NH}_2)\text{}_2 \) 105
Preparation of \( \text{P-CH}_2\text{CH(CN)COOEt} \) 108
Preparation of \( \text{P-CH}_2\text{CH(COOEt)}\text{}_2 \) 108
Reaction of \( \text{P-CH}_2\text{Cl} \) with \( \text{CH}_2\text{(COCH}_3\text{)}\text{}_2 \)
  a. in 1,2-dichloroethane 108
  b. in o-dichlorobenzene 110
Preparation of \( \text{P-CH}_2\text{CN} \)
  a. in DMF solvent 110
  b. in a three phase system 111
Attempted reaction of \( \text{P-CH}_2\text{Cl} \) with under phase transfer conditions 111
Preparation of \( \text{P-CH}_2\text{N} \text{O}_2\text{H} \) in a two phase system 111
Preparation of \( \text{P-CH}_2\text{NH}_2 \) 112
Preparation of \( \text{P-CH}_2\text{S(CH}_2\text{)}\text{3CH}_3 \) 112
Reaction of \( \text{P-CH}_2\text{Cl} \) with 1,4-butanedithiol 113
  a. in DMF solvent 113
  b. in a three phase system 113
Preparation of \( \text{P-CH}_2\text{SH} \) 114
Preparation of \( \text{P-CH}_2\text{SS-CH}_2\text{-P} \) 115
Preparation of \( \text{P-Li} \) by Direct Lithiation 115
  a. with TMEDA 115
  b. with TEDA 116
Preparation of Soluble \( \text{P-CH}_3 \) from \( \text{P-Li} \): Determination of Position of Substitution in Direct Lithiation Reaction 117
  a. Methylation of polystyrene with n-BuLi-TMEDA and Methyl Iodide 117
b. Methylation of Polystyrene with t-BuLi-TMEDA and Methyl Iodide

Preparation of P-Br by Thallation-Bromination

Preparation of P-Br by Catalytic Bromination
  a. with FeCl₃
  b. with Tl(OAc)₃
  c. with TlCl₃

Preparation of P-I

Preparation of Soluble o, m, and p-polystyryl bromide

Bromination of Soluble Polystyrene with FeCl₃ Catalyst

Bromination of Soluble Polystyrene with Tl(OAc)₃ Catalyst

Iodination of Polystyrene with Tl(OCOCF₃)₃ and Iodine

Lithiation of 1% Crosslinked P-Br followed by Methanol Quenching

Lithiation of 1% Crosslinked P-Br followed by CO₂ Quenching
  a. in tetrahydrofuran
  b. in cyclohexane
  c. in benzene or toluene

Preparation of P-SCH₃ from P-Li

Preparation of P-B(OH)₂ from P-Li

Preparation of P-CONHPh from P-Li

Preparation of P-Si(CH₃)₂Cl

Use of P-Si(CH₃)₂Cl as an Alcohol Protecting Group

Preparation of P-P(Ph)₂ from P-Li

Preparation of P-CH₂CH₂Br from P-Li

Preparation of P-CHO from P-Li
Preparation of $\mathbf{P}-\text{CH}_2\text{CH}_2\text{OH}$ from $\mathbf{P}$-Li 128
Preparation of $\mathbf{P}$-C(Ph)$_2$OH from $\mathbf{P}$-Li 129
Preparation of $\mathbf{P}$-SH from $\mathbf{P}$-Li 130
  a. via bromination-lithiation 130
  b. via direct lithiation with TMEDA and n-BuLi or t-BuLi 131
Preparation of $\mathbf{P}$-OH from $\mathbf{P}$-Li 133
  a. via bromination-lithiation 133
  b. via direct lithiation with TMEDA and n-BuLi or t-BuLi 133
Reaction of $\mathbf{P}$-CH$_2$SH with p-nitrophenethyl bromide under phase transfer conditions 135
Preparation of $\mathbf{P}$-OCH$_2$CH$_2$Ph-NO$_2$ 135
Preparation of $\mathbf{P}$-OCH$_2$-CH=CH$_2$ 135
Preparation of $\mathbf{P}$-SCH$_2$CH$_2$PhNO$_2$ 137
Reaction of $\mathbf{P}$-SH with 1,4-dibromobutane 137
Reaction of $\mathbf{P}$-SH with 2-chloroethanol 137
Preparation of $\mathbf{P}$-CH(CN)CH$_2$CN 139
Preparation of $\mathbf{P}$-CH(CN)OCOCH$_3$ 139
Preparation of $\mathbf{P}$-CH(CN)OCH$_2$PhNO$_2$ 139

PART 2. Polymeric Reagents 141

Results and Discussion 142

Poly(vinylpyridinium hydrobromide perbromide): A Brominating Agent 142
  a. Preparation of PVPHP 143
  b. Reaction of PVPHP with Alkenes and Ketones 144
Poly(vinylpyridinium chlorochromate): An Oxidizing Agent 146
  a. Preparation of PVPCC 146
  b. Reaction of PVPCC with alcohols 148
c. Regeneration of PVPCC 155
d. Comparison of PVPCC with a similar oxidizing agent 157

Polymeric Sulfonium Salts: Alkylidene Transfer Agents 159
a. Preparation of Polymeric Sulfonium Salts 163
b. Reactions of Polymeric Methyl Sulfonium Salts 167
c. Reactions of Polymeric Ethyl Sulfonium Salts 171
d. Reactions of Polymeric Benzyl Sulfonium Salts 173
e. Reactions of Polymeric Allyl Sulfonium Salt 174

Experimental 176

Preparation of Polyvinylpyridine (PVP) 176
a. 4-Vinylpyridine-styrene-divinylbenzene copolymer 176
b. 4-Vinylpyridine-divinylbenzene copolymer 176

Preparation of Poly(vinylpyridinium hydrobromide perbromide)(PVPHP) 177

Bromination of Alkenes with PVPHP 177
a. Preparation of d,l-dibromostilbene from cis-stilbene 177
b. Preparation of 1,2-dibromocyclohexane from cyclohexene 177
c. Preparation of 1,2,7,8-tetrabromooctane from 1,7-octadiene 178
d. Preparation of 3-phenyl-2,3-dibromopropanol from cinnamyl alcohol 178
e. Preparation of 3-phenyl-2,3-dibromopropanoic acid from cinnamic acid 178

Bromination of Ketones with PVPHP 179
a. Preparation of 2-bromocyclohexanone 179
b. Preparation of $\alpha$-bromoacetophenone 179
c. Preparation of phenyl 1-bromoethyl ketone 179
d. Preparation of bromobenzyl methyl ketone 179
Regeneration of the Spent Reagent to PVPHP 180
  a. Direct regeneration 180
  b. Indirect regeneration 180

Preparation of PVPCC 180

Reaction of PVPCC with alcohols 181
  a. Small scale procedure 181
  b. Reactions with dried PVPCC resins 181
  c. Larger scale reaction 182
  d. Reaction with partially spent PVPCC 182

Regeneration of PVPCC 183
  a. Standard procedure 183
  b. Partial regeneration with HCl and CrO$_3$ 183

Comparison of PVPCC with Chromate Ion Exchange Resin 184

Preparation of Polymeric Sulfides 184
  a. P-SCH$_3$ 184
  b. P-SCH$_2$CH$_3$ 185
  c. P-SPh 185
  d. P-SCH$_2$Ph 185

Preparation of Polymeric Sulfonium Salts 186
  +
  a. P-S(CH$_3$)$_2$ $^\text{-SO}_4$CH$_3$ 186
  b. P-S(CH$_3$)$_2$ $^\text{-SO}_3$F 186
  c. P-S(CH$_3$)Ph $^\text{-SO}_3$F 186
  +
  d. P-S(Et)$_2$ $^\text{-SO}_4$Et 188
  e. P-S(Et)$_2$ $^\text{-SO}_3$F 188
  f. P-S(Et)Ph $^\text{-SO}_4$Et 188
  g. P-S(CH$_2$Ph)$_2$ $^\text{-SO}_3$CF$_3$ 188
Reactions of $\text{P}-\text{S}(\text{CH}_3)_2^-\text{SO}_3\text{F}$ with Ketones using t-BuOK as Base

a. Reaction with PhCOCH$_2$CH$_3$ to give Ph(Et)-C=C(CH$_3$)$_2$

b. Reaction with PhCOPh to give (Ph)$_2$C=C(CH$_3$)$_2$

c. Reaction of recycled $\text{P}-\text{S}(\text{CH}_3)_2^-\text{SO}_3\text{F}$ resins

Reactions of $\text{P}-\text{S}(\text{CH}_3)_2^-\text{SO}_3\text{F}$ with Aldehydes using Phase Transfer Catalysis

a. Reaction with PhCHO to PhCH=C=CH$_2$

b. Reaction with PhCOCH$_3$ to give Ph(CH$_3$)$_2$C=C(CH$_3$)$_2$

c. Reaction with CH$_3$(CH$_2$)$_9$CHO to give CH$_3$(CH$_2$)$_9$C=C(CH$_3$)$_2$

d. Reaction with trans-Ph-CH=CH-CHO to give trans-Ph-CH=CH=CH$_2$

Reactions of $\text{P}-\text{S}(\text{CH}_3)_2^-\text{SO}_3\text{F}$ with Ketones using Phase Transfer Catalysis

a. Reaction with PhCOCH$_2$CH$_3$ to give Ph(CH$_3$)$_2$C=C(CH$_3$)$_2$

b. Reaction with PhCOCH$_3$ to give Ph(CH$_3$)$_2$C=C(CH$_3$)$_2$

c. Reaction with PhCOCH$_3$ to give Ph(CH$_3$)$_2$C=C(CH$_3$)$_2$

d. Reaction with PhCOCH$_3$ to give Ph(CH$_3$)$_2$C=C(CH$_3$)$_2$

Preparation of Ph(CH$_3$)$_2$C=C(CH$_3$)$_2$ from Ph$(\text{CH}_3)$C=CH$_2$

Reaction of $\text{P}-\text{S}(\text{CH}_3)_2^-\text{SO}_3\text{F}$ with PhCH$_2$COCH$_3$

a. With t-BuOK in DMSO as base
b. Under phase transfer conditions

Preparation of \( \text{PhCH}_2(\text{CH}_3)C\stackrel{0}{\text{CH}}_2 \)

Reactions of \( \text{P-S(CH}_3\text{)Ph}^-\text{SO}_3\text{F} \) under Phase Transfer Conditions

a. Reaction with PhCHO

b. With PhCOCH_3

Reaction of \( \text{P-S(CH}_3\text{)}_2^-\text{SO}_4\text{CH}_3 \) under Phase Transfer Conditions

Regeneration of \( \text{P-S(CH}_3\text{)}_2^-\text{SO}_3\text{F} \)

Reactions of \( \text{P-S(Et)}^+\text{SO}_3\text{Et} \) under Phase Transfer Conditions

a. with PhCHO to give Ph\( \text{CH}_2\text{-CH-CH}_3 \)
b. with PhCHO to give Ph\( \text{CH}_2\text{-CH-CH}_3 \)
c. with PhCOCH_2CH_3

d. with PhCOCH_3

Reactions of \( \text{P-S(CH}_3\text{)}_2^-\text{SO}_3\text{F} \) under Phase Transfer Conditions

a. with PhCHO to give Ph\( \text{CH}_2\text{-CH-CH}_3 \)
b. with PhCHO to give Ph\( \text{CH}_2\text{-CH-CH}_3 \)
c. with PhCOCH_3 to give Ph\( \text{CH}_3\text{C}\stackrel{0}{\text{CH}}_3 \)
d. with PhCOCH_2CH_3 to give Ph\( \text{CH}_3\text{CH}_2\text{C}\stackrel{0}{\text{CH}}_3 \)
e. with PhCOOPh to give (Ph)_2\( \text{C}_\text{CH}-\text{CH}_3 \)

Preparation of trans-1-methyl-2-phenyl oxirane

Preparation of cis-1-methyl-2-phenyl oxirane

Regeneration of \( \text{P-S(Et)}^+\text{SO}_3\text{F} \)

Regeneration of \( \text{P-S(Et)}^+\text{SO}_4\text{Et} \)
Reactions of \( \text{P-S(CH}_2\text{Ph)Ph} \) \( \text{SO}_3\text{CF}_3 \) 212

a. with PhCHO to give PhCH=—CHPh under Phase Transfer conditions 212

b. with PhCHO to give PhCH=CHPh using LDA as base 212

c. with CHO to give PhCH=CH=CH using LDA as base 213

d. Reaction with Ketones using LDA as base 214

e. Regeneration of \( \text{P-S(CH}_2\text{Ph)Ph} \) \( \text{SO}_3\text{CF}_3 \) 214

Preparation of cis-stilbene oxide 214

Reactions of \( \text{P-S(CH}_2\text{-CH=CH}_2\text{Ph} \) \( \text{SO}_3\text{CF}_3 \) 215

a. with PhCHO under phase transfer conditions 215

b. with PhCHO to give PhCH=CH-CH=CH using LDA as base 215

c. with PhCOPh using LDA as base 215

d. Regeneration of \( \text{P-S(CH}_2\text{CH=CH}_2\text{Ph} \) \( \text{SO}_3\text{CF}_3 \) 216

Preparation of PhCH=CH-CH=CH 216

Claims to Original Research 218

Publications Arising from this Thesis 219

References 221
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>FIGURE</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Flask for Anhydrous Reactions of Polymers</td>
</tr>
<tr>
<td>2</td>
<td>$^{13}$C NMR Spectra of $\text{P-CH}_3$ Substituted meta and para (D.F. = 0.50)</td>
</tr>
<tr>
<td>3</td>
<td>Infrared Spectrum of $\text{P-CH}_2\text{OCOCH}_3$</td>
</tr>
<tr>
<td>4</td>
<td>Infrared Spectrum of $\text{P-CH}_2\text{OH}$</td>
</tr>
<tr>
<td>5</td>
<td>Infrared Spectrum of $\text{P-CH}_2\text{O-Ph-CHO}$</td>
</tr>
<tr>
<td>6</td>
<td>Infrared Spectrum of $\text{P-CH}_2\text{CH(CN)}_2$</td>
</tr>
<tr>
<td>7</td>
<td>Infrared Spectrum of $\text{P-CH}_2\text{CH(COOEt)}_2$</td>
</tr>
<tr>
<td>8</td>
<td>Infrared Spectrum of $\text{P-SH}$</td>
</tr>
<tr>
<td>9</td>
<td>Infrared Spectrum of $\text{P-OH}$</td>
</tr>
<tr>
<td>10</td>
<td>Infrared Spectrum of $\text{P-CH}_2\text{S(CH}_2\text{)}_2\text{PhNO}_2$</td>
</tr>
<tr>
<td>11</td>
<td>Infrared Spectrum of $\text{P-O-CH}_2\text{-CH=CH}_2$</td>
</tr>
<tr>
<td>12</td>
<td>Infrared Spectrum of $\text{P-CH(CN)CH}_2\text{CN}$</td>
</tr>
<tr>
<td>13</td>
<td>Oxidation of Cyclopentanol (1.7 mmoles) in 4 ml Cyclohexane at 77° using 2 g of Resin: Comparison of PVPCC with Chromate Ion Exchange Resin</td>
</tr>
<tr>
<td>14</td>
<td>Infrared Spectrum of $\text{P-S(CH}_3\text{)}_2\text{SO}_3\text{F}$</td>
</tr>
<tr>
<td>15</td>
<td>$^1$H NMR Spectrum of $\text{CH-CH}_2\text{CH}_2\text{O}$</td>
</tr>
<tr>
<td>16</td>
<td>$^{13}$C NMR Spectrum of $\text{CH-CH}_2\text{CH}_2\text{O}$</td>
</tr>
<tr>
<td>17</td>
<td>$^1$H NMR Spectrum of PhCH$_2$(CH$_3$)$_2$CH$_2$</td>
</tr>
<tr>
<td>18</td>
<td>$^{13}$C NMR Spectrum of PhCH$_2$(CH$_3$)$_2$CH$_2$</td>
</tr>
<tr>
<td>19</td>
<td>$^1$H NMR Spectrum of PhCH$_2$(CH$_3$)$_2$CH$_2$</td>
</tr>
<tr>
<td>20</td>
<td>$^1$H NMR Spectrum of PhCH$_2$(CH$_3$)$_2$CH$_2$</td>
</tr>
<tr>
<td>21</td>
<td>$^{13}$C NMR Spectrum of PhCH$_2$(CH$_3$)$_2$CH$_2$</td>
</tr>
<tr>
<td>22</td>
<td>$^1$H NMR Spectrum of Ph(CH$_3$)$_2$CH$_2$</td>
</tr>
<tr>
<td>FIGURE</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>23</td>
<td>$^1$H NMR Spectrum of Ph(CH$_3$CH$_2$)$_2$C$^0$CH$_2$</td>
</tr>
<tr>
<td>24</td>
<td>$^1$H NMR Spectrum of PhCH$^\equiv$CH=CH$_2$</td>
</tr>
</tbody>
</table>
### LIST OF TABLES

<table>
<thead>
<tr>
<th>TABLE</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>44</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
</tr>
<tr>
<td>7</td>
<td>64</td>
</tr>
<tr>
<td>8</td>
<td>66</td>
</tr>
<tr>
<td>9</td>
<td>70</td>
</tr>
<tr>
<td>10</td>
<td>73</td>
</tr>
<tr>
<td>11</td>
<td>74</td>
</tr>
<tr>
<td>12</td>
<td>76</td>
</tr>
<tr>
<td>13</td>
<td>81</td>
</tr>
<tr>
<td>14</td>
<td>86</td>
</tr>
<tr>
<td>15</td>
<td>87</td>
</tr>
<tr>
<td>16</td>
<td>90</td>
</tr>
<tr>
<td>17</td>
<td>93</td>
</tr>
<tr>
<td>18</td>
<td>145</td>
</tr>
<tr>
<td>19</td>
<td>147</td>
</tr>
<tr>
<td>20</td>
<td>149</td>
</tr>
</tbody>
</table>

- Functional Polymers from $\text{[P-CH}_2\text{Cl}$
- Functional Polymers from $\text{[P-Li}$
- Polymers as Supports in Organic Synthesis
- Polymeric Reagents
- Reaction of $\text{[P-CH}_2\text{Cl}$ with nucleophiles under phase transfer conditions
- Reaction of $\text{[P-CH}_2\text{Cl}$ with 1,4-butanedithiol
- Direct Lithiation of Crosslinked Polystyrene
- Chemical Shifts in $^{13}\text{C}$ NMR Spectra of $\text{o, m, and p}$-Methyl Polystyrene and of CH$_3$I Quenched[P-Li
- Bromination of 1% Crosslinked Polystyrene
- Chemical Shifts in $^{13}\text{C}$ NMR spectra of polystyrene and standard o, m and p-bromopolystyrenes
- Chemical Shifts in $^{13}\text{C}$ NMR of partially halogenated polystyrenes
- Carboxylation of Lithiated Polystyrenes
- Reactions of Lithiated Resin
- Preparation of $\text{[P-SH}$ from $\text{[P-Br}$
- Preparation of $\text{[P-SH}$ by Direct Lithiation
- Preparation of $\text{[P-OH}$ by Direct Lithiation
- Phase Transfer Reactions on Miscellaneous Polymers
- Bromination of Alkenes with PVPHP
- Bromination of Ketones with PVPHP
- Reaction of alcohols with a 12-fold excess of PVPCC in methylene chloride at room temperature
Oxidation of cinnamyl alcohol with PVPCC: influence of solvent and of temperature on the extent of reaction as a function of time

Determination of the reactivity as a function of the amount of PVPCC

Reaction of PVPCC with various alcohols

Determination of the consumption of oxidizing agent and reactivity of partially spent PVPCC

Activity of recycled PVPCC: Oxidation of cinnamyl alcohol in cyclohexane at 80°

Comparison of PVPCC and Amberlyst A-26 Chromate Ion Exchange Resin: Oxidation of cyclopentanol

Reactions of Polymeric Methyl Sulfonium Salts with Aldehydes and Ketones under phase transfer catalysis

Preparation of Polymeric Sulfides and Sulfonium Salts

Ethylidene transfer reactions under phase transfer catalysis

Preparation of Polymeric Sulfides and Sulfonium Salts
### LIST OF SCHEMES

<table>
<thead>
<tr>
<th>SCHEME</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Synthesis of an Insect Sex Attractant on a Polymer Support</td>
</tr>
<tr>
<td>2</td>
<td>Synthesis of a Threaded Macrocycle on a Polymer Support</td>
</tr>
<tr>
<td>3</td>
<td>Synthesis of Optically Active α-Hydroxy Acids</td>
</tr>
<tr>
<td>4</td>
<td>Selective Functionalization of Sugars with $\text{P} \text{~B(OH)}_2$</td>
</tr>
<tr>
<td>5</td>
<td>Use of Polymers in Studies of Reaction Mechanisms</td>
</tr>
<tr>
<td>6</td>
<td>Cyclobutadiene Trapping on Polymer</td>
</tr>
<tr>
<td>7</td>
<td>The Mono-Alkylation and Acylation of Esters on Polymeric Supports</td>
</tr>
<tr>
<td>8</td>
<td>A Polymer Bound Benzyne</td>
</tr>
<tr>
<td>9a</td>
<td>Oxidation of Alcohols with a Polymeric Reagent</td>
</tr>
<tr>
<td>9b</td>
<td>Homologation of Iodides on Polymer Support</td>
</tr>
<tr>
<td>10</td>
<td>A Polymeric Reagent for Peptide Bond Formation</td>
</tr>
<tr>
<td>11</td>
<td>A Nucleoside Coupling Reagent</td>
</tr>
<tr>
<td>12</td>
<td>Reaction Mechanism of $\text{P} \text{-IF}_2$</td>
</tr>
<tr>
<td>13</td>
<td>Photo-oxidation with $\text{P} \text{-CH}_2$-Rose Bengal</td>
</tr>
<tr>
<td>14</td>
<td>Sequential Cyclooligomerization and Hydrogenation of Butadiene</td>
</tr>
<tr>
<td>15</td>
<td>Chemical Modification of $\text{P} \text{-CH}_2$Cl by Phase Transfer Catalysis.</td>
</tr>
<tr>
<td>16</td>
<td>Site-Site Interactions in the Reaction of $\text{P} \text{-CH}_2$Cl with Dithiols</td>
</tr>
<tr>
<td>17</td>
<td>Reactions of $\text{P} \text{-Li}$</td>
</tr>
<tr>
<td>18</td>
<td>Reactions of $\text{P} \text{-Li}$</td>
</tr>
<tr>
<td>19</td>
<td>Reactions of Polymeric Nucleophiles under Phase</td>
</tr>
<tr>
<td>SCHEME</td>
<td>PAGE</td>
</tr>
<tr>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>Transfer Catalysis</td>
<td>92</td>
</tr>
<tr>
<td>Reaction of $\text{CHO}$ under Phase Transfer Catalysis</td>
<td>96</td>
</tr>
<tr>
<td>Preparation, Use and Regeneration of PVPCC</td>
<td>152</td>
</tr>
<tr>
<td>Alkylidene Transfer Reactions using Polymeric Sulfonium Salts</td>
<td>164</td>
</tr>
</tbody>
</table>
ABSTRACT

The first part of this thesis describes the preparation of functional polymers by chemical modification of insoluble polystyrene resins. A series of new functional polystyrenes are prepared by the phase transfer catalysed nucleophilic displacement of chloride from \( \text{P}-\text{CH}_2\text{Cl} \) in a three phase system. The use of a similar system to control the degree of intraresin reaction in 1\% crosslinked \( \text{P}-\text{CH}_2\text{Cl} \) is also discussed. The preparation of \( \text{P}-\text{Br} \) and \( \text{P}-\text{Li} \) and their use in preparing a variety of functional polymers are studied. Several nucleophilic polymers are also prepared and their reactivity tested.

In part 2 of the thesis the preparation, use, and regeneration of polymeric reagents for halogenation, oxidation and alkylidene transfer reactions are described.
INTRODUCTION

Since the pioneering work of Merrifield, polymers have found wide application in organic chemistry as supports for polypeptide, polynucleotide and polysaccharide synthesis, as reagents or protecting groups in organic reactions and as supports for catalysts. The primary advantages of polymers in these applications result from their insolubility which simplifies the separation of products from excess reagents and by-products of the reaction.

REVIEW OF THE LITERATURE

1. Functionalization of Polystyrene

Polystyrene is one of the most commonly used polymers in this field and as a consequence, a considerable effort has gone into the preparation of derivatives containing the functional groups necessary for the attachment of a wide variety of organic and inorganic molecules to the polymer backbone. These functionalities may be incorporated by two methods: a) chemical modification of preformed polystyrene beads or, b) synthesis of the required monomer followed by copolymerization with varying amounts of styrene and divinylbenzene to give the desired degrees of substitution and crosslinking.

The choice of method depends upon the requirements of the application for which the polymer is intended. If a polymer with specific pore size, swelling properties, or bead stability is needed, then the chemical modification route is preferred as a wide variety of polystyrene resins with well defined properties are commercially available. Polymers used as supports for organic synthesis or as organic reagents are usually prepared in this way.
The polymerization of a functional monomer is the preferred route when no suitable reaction is available for the introduction of the desired functionality into the preformed polymer, or when a well controlled distribution of functional groups within the polymer is desired.

One of the most versatile functional polymers is chloromethylated polystyrene. Not only is it widely used as a solid support in polypeptide synthesis and as a ligand in homogeneous catalyst immobilization, but it is a key intermediate in the synthesis of a wide variety of other functionalities bound to the polystyrene ring. Some of the many functionalized polymers obtained from chloromethylated polystyrene $\text{P-CH}_2\text{Cl}$ are shown in Table 1.

Chloromethylation can be effected by one of two routes: reaction of styrene-divinylbenzene copolymer with paraformaldehyde and hydrogen chloride, or by reaction of the copolymer with chloromethyl methyl ether, chloromethyl ethyl ether, or bis (1,4chloromethoxy) butane in the presence of a Friedel-Crafts catalyst such as AlCl$_3$ or ZnCl$_2$. An extensive study of the reaction with chloromethyl methyl ether and SnCl$_4$ has been published. The reaction is accompanied by methylene bridging which increases the amount of crosslinking unless very pure grade reagents are used. Methylene bridging can also be reduced by using chloroform or carbon tetrachloride as a cosolvent. The degree of substitution is determined by catalyst and reagent concentrations, reaction time, and temperature.

The preparation of $\text{P-CH}_2\text{Cl}$ with very low degrees of functionalization for use in peptide synthesis has also been described.
### TABLE 1: Functional Polymers from \( \text{P}-\text{CH}_2\text{Cl} \)

<table>
<thead>
<tr>
<th>Polymer Structure</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{P}-\text{CHO} )</td>
<td>(16-18)</td>
</tr>
<tr>
<td>( \text{P}-\text{CO}_2\text{H} )</td>
<td>(16, 20)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}=\text{CH}-\text{CH}_2\text{OH} )</td>
<td>(17)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{CN} )</td>
<td>(16, 39)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{COOH} )</td>
<td>(16, 39)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{CH}_2\text{COOH} )</td>
<td>(21)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{OCMe} )</td>
<td>(16, 22-24)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{OH} )</td>
<td>(16, 18, 22, 23)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{S}(\text{CH}_3)_2\text{Cl}^+ )</td>
<td>(25-27)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{SC}^+\text{NH}^-\text{HCl} )</td>
<td>(29, 30)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{SH} )</td>
<td>(30)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{ON}(\text{CH}_3)_3\text{Cl}^- )</td>
<td>(33)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{NH}_2 )</td>
<td>(35, 38)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{OCHCH}_2\text{OH} )</td>
<td>(39)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{P}(\text{Ph})_2 )</td>
<td>(40)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{P}^\text{OH}_2 )</td>
<td>(41)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{OCHCH}_2\text{OR} )</td>
<td>(42)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{C}^\text{OH} )</td>
<td>(43)</td>
</tr>
<tr>
<td>( \text{P}-\text{CH}_2\text{OCCl} )</td>
<td>(44, 83)</td>
</tr>
</tbody>
</table>
Formylated polystyrene $\text{P}^-\text{CHO}$ can be made in good yield by oxidation of $\text{P}^-\text{CH}_2\text{Cl}$ with dimethyl sulfoxide$^{16-18}$. However oxidation with pyridine N-oxide fails to give the desired product$^{19}$. $\text{P}^-\text{CHO}$ is a useful intermediate in the synthesis of other functional polymers. For example oxidation with $\text{K}_2\text{Cr}_2\text{O}_7$ gives $\text{P}^-\text{COOH}^{16,20}$ and reaction with malonic acid followed by reduction with aluminum hydride gives the unsaturated polymeric alcohol $\text{P}^-\text{CH=CH-CH}_2\text{OH}$ used as a support in polysaccharide synthesis$^{17}$.

The cyano derivative $\text{P}^-\text{CH}_2\text{CN}$ is formed by reaction of $\text{P}^-\text{CH}_2\text{Cl}$ with KCN in dimethylsulfoxide, a reaction which is often complicated by partial oxidation to the corresponding aldehyde. Acid hydrolysis yields the corresponding carboxylic acid $\text{P}^-\text{CH}_2\text{COOH}^{16}$. The polymeric acid with one more carbon in the chain has been made by reaction of $\text{P}^-\text{CH}_2\text{Cl}$ with an organo lithium compound containing a protected carboxyl group, followed by acid hydrolysis$^{21}$ (eqn. 1)

$$\text{P}^-\text{CH}_2\text{Cl} + \text{LiCH}_2\text{CN} \rightarrow \text{P}^-\text{CH}_2\text{CH}_2\text{CNH}_2$$

Polymeric esters $\text{P}^-\text{CH}_2\text{OC-R}$ are easily made by reaction of acid salts with $\text{P}^-\text{CH}_2\text{Cl}$.$^{16,22,23}$ Soluble polystyrene esters have also been made using solid $\text{CH}_3\text{COOK}$ and 18-crown-6 as catalyst in benzene/acetonitrile solvent$^{24}$. Hydroxymethyl polystyrene $\text{P}^-\text{CH}_2\text{OH}$ can be produced by saponification of polymeric esters prepared as above,$^{16,22,23}$ $\text{P}^-\text{CH}_2\text{OH}$ has also been prepared by reduction of $\text{P}^-\text{COOH}^{18}$. 
The polymeric sulfonium salt \( \text{P-CH}_2\text{S}^+\text{Cl}_2 \) is made by addition of dimethyl sulfide to \( \text{P-CH}_2\text{Cl} \). This polymer is used as an ion exchange resin and as a protecting group in polypeptide synthesis.

A polymeric thiol group can be introduced by reaction of \( \text{P-CH}_2\text{Cl} \) with thiourea to give an isothiouronium salt \( \text{P-CH}_2\text{SC}\text{NH}_2\text{HCl} \) followed by basic hydrolysis to give the free thiol \( \text{P-CH}_2\text{SH} \). Although the yield in this reaction appears to be high by elemental analysis, the polymer was not very reactive in subsequent chemical reactions, the maximum yield being 45%.

A polymer containing a hydroquinone moiety has been prepared by a modified Friedel-Crafts reaction (eqn. 2) and was shown to possess redox properties.

\[
\text{P-CH}_2\text{Cl} + \begin{array}{c}
\text{OH} \\
\text{OH}
\end{array} \xrightarrow{\text{ZnCl}_2} \begin{array}{c}
\text{OH} \\
\text{OH}
\end{array}
\] (eqn. 2)

The synthesis and application of similar polymers has been reviewed.

Anion exchange polymers of the type \( \text{P-CH}_2\text{NR}_3\text{Cl} \), derived from \( \text{P-CH}_2\text{Cl} \) and amines, are very widely used and many types of resins are commercially available. The synthesis of anion exchange resins has been reviewed.

Resins containing \( \text{-CH}_2\text{NH}_2 \) groups have been synthesized by reaction of \( \text{P-CH}_2\text{Cl} \) with ammonia or amines. However these reactions lead to crosslinking and an improved procedure involving reaction of \( \text{P-CH}_2\text{Cl} \) with potassium phthalimide followed by hydrazine reduction was developed. (eqn 3).
Several methods for preparing $\text{P-CH}_2\text{NH}_2$ directly from polystyrene are also available.\textsuperscript{38}

The polymer supported dihydroxy ether $\text{P-CH}_2\text{OCH}_2\text{CH}_2\text{OH}$ was prepared as shown (eqn. 4) and is used as a protecting group for aldehydes.\textsuperscript{86,87}

Polymeric phosphines $\text{P-CH}_2\text{P(Ph)}_2$ have been prepared by reaction of $\text{P-CH}_2\text{Cl}$ with $\text{LiP(Ph)}_2$.\textsuperscript{40} These polymers are useful as ligands in the formation of supported transition metal catalysts.

Phosphoric acid containing polymers $\text{P-CH}_2\text{P(OH)}_2$ useful as ion exchange resins, are prepared by reaction of $\text{P-CH}_2\text{Cl}$ with trialkyl phosphite followed by hydrolysis.\textsuperscript{41}

Polymeric phenol ethers are formed in a manner analogous to the reaction of monomeric benzyl chlorides with phenols in the presence of base.\textsuperscript{42} (eqn 5).
A polymer containing cyclopentadiene units \( \text{P}-\text{CH}_2\text{C}_5 \) has been made by reaction of \( \text{P}-\text{CH}_2\text{Cl} \) with cyclopentadienyl anion \(^43\). This polymer is useful as a ligand in the synthesis of resin-bound catalysts.

A methylchloroformylated resin \( \text{P}-\text{CH}_2\text{OCCl} \) used as a solid support in peptide synthesis, is made by first transforming \( \text{P}-\text{CH}_2\text{Cl} \) to the hydroxymethylated polymer as previously discussed \(^18,24\) and then reacting with phosgene \(^44\).

Another useful intermediate in the chemical modification of polystyrene is polystyryllithium \( \text{P}-\text{Li} \) (Table 2). In general, one of two methods is used for generating this reactive species: a) direct lithiation using a mixture of n-butyllithium and \( \text{N},\text{N},\text{N}',\text{N}'\text{-tetramethylethylenediamine (TMEDA)} \), or b) the metal-halogen exchange reaction between halogenated polystyrene and n-butyllithium.

The direct lithiation procedure was first used by Chalk \(^45\) for soluble polystyrene. Due to the reactivity of the n-BuLi:TMEDA complex, reactions must be run in hydrocarbon solvents such as cyclohexane. Although this is not a disadvantage in the case of soluble polystyrene, it presents difficulties in the extension of the reaction to swelleable crosslinked polystyrene where a solvent with good swelling properties is desirable. Thus, for soluble polystyrene, a degree of functionalization (DF) of 0.2 could be obtained after 4 hours at room temperature, while for a 1% crosslinked resin, reaction for two days at 60°C gave a DF of only 0.1 \(^46\). A macroreticular resin, in which swelling should not be a problem, gave a DF of 0.16 under the same conditions.

Kinetic studies have shown that a 1:1 TMEDA:n-BuLi complex is the active species in the metalation reaction \(^47\). n-BuLi alone is completely unreactive.
Two studies on the position of lithium substitution on the ring have reported conflicting results. The first, involving quenching with D$_2$O, suggests 20% ortho and 80% para substitution$^{45}$. The second, a $^{13}$C NMR study of $^{13}$CH$_3$I quenched polymer, shows 2:1 meta to para substitution for a 5% functionalized polymer.$^{48}$

The lithiation of halogenated polystyrene with n-BuLi was first studied by Braun using soluble poly(iodostyrene)$^{49-51}$. This reaction has been widely applied to crosslinked polystyrenes using mainly brominated resins.$^{52-57}$ Thus, one of the primary problems in applying this procedure is making a suitable brominated polystyrene precursor.

A large number of bromination procedures have been reported. In most cases these have been catalytic brominations using bromine and ferric chloride$^{58}$, iodine$^1$, iron powder$^{60}$, pyridine$^{52}$ or mercuric acetate.$^{52}$ Other preparations use stoichiometric amounts of thallium triacetate$^{53}$ or boron trifluoride$^{61}$ to effect the bromination.

The ferric chloride catalysed reaction has been used to prepare resins with up to 4 mequiv/g of Br.$^{58}$ However, un-reproducible results have been reported$^{53,54}$, and highly coloured non-homogeneous products have been obtained.$^{56}$

Homogeneous, visually clean brominated polymers exhibiting good reactivity have been obtained using stoichiometric amounts of thallium (III) acetate$^{53-56}$ in a reaction patterned after the aromatic thallation-halogenation reaction developed by Taylor & McKillop$^{62}$. A major drawback of this procedure is that extensive washing of the polymer is necessary to remove the large amounts
of sparingly soluble and toxic thallium salts produced in the reaction. Another problem is the high cost of the thallic acetate used.

Most iodopolystyrenes are prepared by copolymerization of styrene and p-iodostyrene. However a procedure is available for the complete iodination of the preformed polymer, involving reaction with iodine, iodine pentoxide, and sulfuric acid in nitrobenzene at 90° for 50 hours. However lower degrees of functionalization may be difficult to obtain.

\[ \text{(P-Li)} \] has also been made from a polystyryl mercury compound (eqn. 6).

\[
\begin{align*}
\text{(P)} & \xrightarrow{\text{Hg(OCCF}_3)_2} \text{(P-HgOCCF}_3) & \xrightarrow{(\text{Me})_4\text{NCl}} \text{(P-HgCl)} & \xrightarrow{n-\text{BuLi}} \text{(P-Li)} \\
\end{align*}
\]

Some of the functionalized polymers resulting from reactions with \text{(P-Li)} are shown in Table 2.

Introduction of carboxyl groups into lithiated polystyrene can be accomplished either by bubbling CO\text{\textsubscript{2}} into a suspension of the lithiated resin, or by reacting the resin with a slurry of dry ice in THF. The latter method is preferred as a large excess of CO\text{\textsubscript{2}} is necessary to prevent formation of side products such as ketones or tertiary alcohols. The degree of substitution can be determined by reaction of the carboxyl groups with n-BuLi followed by back titration of excess reagent with acid.

Braun has prepared a large number of soluble polystyrene derivatives from soluble \text{(P-Li)}. Reaction with aldehydes and ketones yields secondary and tertiary alcohols. The reaction of \text{(P-Li)} with sulfur yields a thiol, with dimethyl formamide yields \text{(P-CHO)}, and with nitriles produces ketones. Ketones have also been formed by reaction of \text{(P-Li)} with an excess of acylhalide.
**TABLE 2: Functional Polymers from P-Li**

<table>
<thead>
<tr>
<th>Functional Group</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-COOH</td>
<td>(46, 47)</td>
</tr>
<tr>
<td>P-C-R</td>
<td>(50)</td>
</tr>
<tr>
<td>P-SH</td>
<td>(66)</td>
</tr>
<tr>
<td>P-CHO</td>
<td>(51)</td>
</tr>
<tr>
<td>P-C-OH</td>
<td>(51, 13)</td>
</tr>
<tr>
<td>P-C-OH</td>
<td>(46, 57)</td>
</tr>
<tr>
<td>P-P(Ph)_2</td>
<td>(60, 61)</td>
</tr>
<tr>
<td>P-SMe</td>
<td>(55)</td>
</tr>
<tr>
<td>P-MgBr</td>
<td>(56)</td>
</tr>
<tr>
<td>P-B(OH)_2</td>
<td>(52, 59, 68-71)</td>
</tr>
</tbody>
</table>
A trityl alcohol group has been introduced into crosslinked polystyrene by reaction of benzophenone with \( \text{P}-\text{Li} \). Substituted benzophenones have also been used. These polymers are useful in the protection of alcohols and in polynucleotide synthesis.

An important and widely used polystyrene derivative is the polymeric analogue of triphenylphosphine \( \text{P}-\text{P} \). Reaction of \( \text{P}-\text{Li} \) with chlorodiphenylphosphine yields the desired product. Alternatively, reaction of \( \text{P}-\text{Br} \) with lithium diphenylphosphide can be used. However, in this case it is sometimes difficult to react all the bromine and the product is contaminated with starting material.

Polymeric sulfides are made by reaction of \( \text{P}-\text{Li} \) with dialkyldisulfides. For example, \( \text{P}-\text{SCH}_3 \) is made in this way for use as a polymeric reagent.

For applications in which \( \text{P}-\text{Li} \) is less suitable than a Grignard reagent, a procedure has been developed to effect the conversion using freshly prepared \( \text{MgBr}_2 \) in ether.

Boronic acid resins \( \text{P}-\text{B(OH)}_2 \) have been prepared by reaction of \( \text{P}-\text{Li} \) with trimethyl or tributylborate followed by acid hydrolysis. These polymers have been used as polyol and sugar protecting groups.

Friedel-Crafts acylation is a useful reaction for the introduction of carbonyl containing moieties into polystyrene resins. For example, the polymer bound trityl alcohols discussed previously have also been prepared by acylation of polystyrene followed by reaction with a Grignard reagent (eqn 7).

\[
P + \text{ClC}^\text{Ph} \xrightarrow{\text{AlCl}_3} \text{P}^\circ \text{C}^\text{Ph} \xrightarrow{\text{PhMgBr}} \text{P}^\circ \text{C}^\text{Ph} \quad \text{(eqn. 7)}
\]

Carboxylated resins, \( \text{P}-\text{COOH} \), have also been made via a variety of Friedel-Crafts acylations. For example, acylation with o-chlorobenzoyl
chloride and cleavage with potassium t-butoxide gives \( \text{PCOOH} \) in good yield. The ortho substituent facilitates and directs the cleavage reaction. (eqn. 8).

Sulfonated polystyrene \( \text{PSO}_3\text{H} \) is widely used in the preparation of cation exchange resins and has also been used as a catalyst in such acid catalysed reactions as esterification and hydrolysis. They have been prepared using sulfuric acid alone, sulfuric acid/perchloroethylene, and chlorosulfuric acid in \( \text{CH}_2\text{Cl}_2 \).  

Nitration of polystyrene is carried out using \( \text{HNO}_3 \) and \( \text{H}_2\text{SO}_4 \) in a manner similar to that used to prepare monomeric aromatic nitrates to give \( \text{PNO}_2 \). Reduction leads to the corresponding amine \( \text{PNH}_2 \). Phosphorylated polymers, used as ion exchange resins, are prepared by Friedel-Crafts reaction of polystyrene with phosphorous trichloride. (eqn. 9).

Other phosphoric acid containing polymers can be made by Friedel-Crafts alkylation using alkylation agents containing a dialkylphosphonate group.
An interesting polymer-bound diene can be made from polystyrene by Birch reduction. (eqn 10). This polymer is used as a ligand in the synthesis of a polymer supported catalyst.

2. Polymers as Supports in Organic Synthesis

The solid phase method of synthesis was developed almost simultaneously by Merrifield and Letsinger for the preparation of peptides on polymer supports. Although these first applications yielded very small peptides, the technique has been extended to the synthesis of polypeptides as large as Ribonuclease A by adding one residue at a time to the polymer-supported peptide chain. Polynucleotides and polysaccharides have also been synthesized in this way by a series of repetitive steps.

The main advantage of the solid phase method is the great simplification of experimental procedure which results from the attachment of the product to an insoluble support. Excess reagents and by-products may be removed at each step by washing and filtering rather than by the laborious purification techniques necessary in classical methods of synthesis. The loss of yield that results from the purification of intermediates at each step is also eliminated.

The advantages which make the solid phase synthesis of biological macromolecules attractive also apply to more "ordinary" organic syntheses and polymer supports have been used in a wide variety of such applications.
### TABLE 3: Polymers as Supports in Organic Synthesis

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Use</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-CH₂COCl</td>
<td>monoprotection of diols</td>
<td>84, 85</td>
</tr>
<tr>
<td>P-CH₂OCH₂CH-OH</td>
<td>monoprotection of aromatic dialdehydes</td>
<td>86, 87</td>
</tr>
<tr>
<td>P-CH₂Cl</td>
<td>monoprotection of diols</td>
<td>46, 68</td>
</tr>
<tr>
<td>P-CCl</td>
<td>synthesis of insect sex attractants</td>
<td>93 - 98</td>
</tr>
<tr>
<td>P-CH₂OH</td>
<td>monoprotection of diacid chlorides</td>
<td>89, 90</td>
</tr>
<tr>
<td>P-CH₂CO-Ο-NO₂</td>
<td>monoprotection of diamines</td>
<td>91, 92</td>
</tr>
<tr>
<td>P-CH₂Cl</td>
<td>threaded macrocycle synthesis</td>
<td>100</td>
</tr>
<tr>
<td>P-CO-CHO</td>
<td>unsymmetrical tetraaryl-porphyrin synthesis</td>
<td>101</td>
</tr>
<tr>
<td>P-CHO</td>
<td>protecting group in carbohydrate synthesis</td>
<td>102, 103</td>
</tr>
<tr>
<td>P-B(OH)₂</td>
<td>selective diol protecting group in preparation of partially derivatized polyols and carbohydrates</td>
<td>52, 68, 70, 71</td>
</tr>
<tr>
<td>P-C-O</td>
<td>synthesis of optically active α-hydroxy acids</td>
<td>104</td>
</tr>
<tr>
<td>P-CH₂OCH₂C-NH₂</td>
<td>synthesis of optically active 2-alkyl cyclohexanones</td>
<td>105</td>
</tr>
</tbody>
</table>
The monoprotection of symmetrical difunctional molecules using polymeric supports has been extensively studied, mostly by Leznoff and coworkers. Solution methods give rise to product mixtures containing unreacted, mono-, and difunctionalized molecules, which are often difficult to separate. This problem can be solved by using attacking reagents bound to insoluble polymer supports. The monoprotected molecules can then be "fished out" of the large excess of unreacted starting material by filtration and washing of the solid support. The polymer-bound molecule is then functionalized on its free end and released from the polymer to give an unsymmetrical product. Occasionally some starting material is attached to the polymer at both ends, yielding a symmetrical product. However, the desired unsymmetrical product is usually much less contaminated than would be the case using solution techniques.

In addition to double coupling, low resin capacities, loss of activity on recycling the polymers, or incomplete functionalization or cleavage reactions can limit the usefulness of this method in some cases.

Monoprotected symmetrical diols bound to polymers have been used in the synthesis of insect sex attractants and carotenoids. An interesting example of the ability of polymeric supports to "fish out" minor components of reaction mixtures is the synthesis of hooplanes or threaded macrocycles. A macrocycle attached to a polymer is mixed with 1,10-decanediol, and trityl chloride is then added to trap the minute fraction of diol molecules which had become threaded through the ring. After seventy cycles a 6% yield of the hooplane is obtained.
SCHEME 1: Synthesis of an Insect Sex Attractant on a Polymer Support

\[ \Phi-C-Cl \xrightarrow{\text{HO(CH\textsubscript{2})\textsubscript{n}OH}} \Phi-C-O(CH\textsubscript{2})\textsubscript{n}OH \xrightarrow{\text{MeSO\textsubscript{2}Cl}} \Phi-C-O(CH\textsubscript{2})\textsubscript{n}OSO\textsubscript{2}Me \]

\[ \text{LiC}≡\text{C(CH\textsubscript{2})\textsubscript{m}CH\textsubscript{3}} \xrightarrow{m=1,3} \Phi-C-O(CH\textsubscript{2})\textsubscript{n}C≡\text{C(CH\textsubscript{2})\textsubscript{m}CH\textsubscript{3}} \xrightarrow{\text{HCl/H\textsubscript{2}O}} \Phi-C-\text{OH} + \text{HO(CH\textsubscript{2})\textsubscript{n}C≡\text{C(CH\textsubscript{2})\textsubscript{m}CH\textsubscript{3}}} \]

1) H\textsubscript{2}/Pd
2) Ac\textsubscript{2}O

SCHEME 2: Synthesis of a Threaded Macrocycle on a Polymer Support

\[ \Phi-\text{CH\textsubscript{2}Cl} + \xrightarrow{\text{OC(CH\textsubscript{2})\textsubscript{2}COCH}} \Phi-\text{CH\textsubscript{2}OC(CH\textsubscript{2})\textsubscript{2}COCH(CH\textsubscript{2})\textsubscript{28}} \]

1) HO(CH\textsubscript{2})\textsubscript{10}OH
2) Wash
70 cycles

NaHCO\textsubscript{3} → NaOH → OC(Ph)\textsubscript{3} + \Phi-\text{CH\textsubscript{2}OH}
A similar principle is used in the synthesis of unsymmetrical tetraarylporphyrins on solid phase. Reaction of p-tolualdehyde and pyrrole in the presence of \[ \text{CHO} \] yields large amounts of symmetrical tetra-tolylphorphyrin in solution and a 2-4% yield of unsymmetrically substituted product attached to the polymer.

Polymer supports have also been used in asymmetric synthesis. For example, a polymer bound sugar has been used to induce asymmetry in the synthesis of \( \alpha \)-hydroxy acids (Scheme 3). The product was obtained in higher chemical and optical yields than for the same reaction in solution. The synthesis of optically active 2-alkyl cyclohexanones has also been accomplished on solid phase with chemical and optical yields which compare favourably with those obtained for the solution phase reaction.

Polymers have also found application as protecting groups in carbohydrate synthesis. An aldehyde containing resin \[ \text{CHO} \] has been used to form acetals with glucose and other sugars. The unprotected groups can then be modified before releasing the sugar by acid hydrolysis.

Another polymer useful for the selective protection of carbohydrates, as well as other cyclic and acyclic polyols, is polystyrylboronic acid (Scheme 4). This polymer has also been used to separate cis-trans mixtures of cyclic diols by selective binding with the cis isomer.

Solid supports have also been used in mechanistic studies for the detection of reactive intermediates. A polymer bound precursor releases a reactive intermediate into the surrounding solution from which it is trapped in a second polymer (Scheme 5). For example, the existence of cyclobutadiene as a discrete species has been demonstrated in this way. (Scheme 6). This technique has also been used to elucidate the mechanism of the imidazole
SCHEME 3: Synthesis of Optically Active α-Hydroxy Acids

SCHEME 4: Selective Functionalization of Sugars with P-B(OH)₂
SCHEME 5: **Use of Polymers in Studies of Reaction Mechanisms**

solid phase

- \( \text{precursor} \) → \( \text{P}_1 \) → \( \text{P}_2 \) - adduct

solution

- [reactive intermediate]

solid phase

- \( \text{P}_2 \) - trap

SCHEME 6: **Cyclobutadiene Trapping on Polymer**

\[
\begin{align*}
\text{P}-\text{SO}_2\text{NH} & \quad \text{Fe(CO)}_4\text{H}_4 \\
\text{NCH}_2 & \quad \text{oxidant}
\end{align*}
\]

SCHEME 7: **The Mono-Alkylation and Acylation of Esters on Polymeric Supports**

\[
\begin{align*}
\text{P}-\text{CH}_2\text{Cl} + \text{R}_1\text{CH}_2\text{CO}_2\text{H} & \rightarrow \text{P}-\text{CH}_2\text{OC}-\text{CH}_2\text{R}_1 \\
\text{P}-\text{CH}_2\text{OC}-\text{CHR}_1 & \rightarrow \text{P}-\text{CH}_2\text{OC}-\text{CHR}_1\text{-CR}_2 \\
\text{R}_2\text{X} & \rightarrow \text{P}-\text{CH}_2\text{OC}-\text{CHR}_1\text{R}_2
\end{align*}
\]
catalyzed aminolysis of nitrophenyl esters,\textsuperscript{107} and the Fries rearrangement\textsuperscript{108}.

One of the primary controversies in the use of polymer supports is the amount of site isolation obtained. One of the advantages claimed for this type of synthesis is that the rigid polymer matrix imparts infinite dilution conditions to the reaction, and many workers have used this effect to generate reactive or unstable species separated from other groups on the resin. However, at least as many examples exist in which intraresin reactions can and do occur, indicating that the polymer chains possess a good deal of mobility. "Site isolation" has been used in the monoacylation\textsuperscript{109} and alkylation of esters. (Scheme 7). No self-condensation was observed for low concentrations of ester on the polymer. However, increasing the polymer capacities\textsuperscript{109} or increasing the time interval before quenching the ester enolate\textsuperscript{111} leads to some intraresin reaction.

Another example where site isolation seems to be achieved is in the generation of a polymer-bound benzyne\textsuperscript{112}. (Scheme 8). Monomeric benzyynes are instantly converted to biphenylene derivatives; however the polymer bound benzyne species had a half life of $\sim$ 50 seconds and did not form dimers on decomposition, i.e. site isolation was maintained.

This result contrasts with others obtained using resins with the same degree of functionalization and crosslinking. Using $\text{P-CH}_2\text{COOH}$, up to 58\% intraresin anhydride formation was observed\textsuperscript{113,114}. Similarly, in the Dieckmann cyclization on polymer supports, the yield of dimer was far greater than that of the desired cyclononanone\textsuperscript{113,115}. (eqn. 11).

\begin{equation}
\text{P-CH}_2\text{SC(C}_2\text{H}_8\text{CN} \xrightarrow{\text{base}} \text{minor} + \text{major} \quad (\text{eqn. 11})
\end{equation}
SCHEME 8: A Polymer Bound Benzyne

\[
P - C - C l + H O - C H _ 2 C H _ 2 O C O _ 2 E t \rightarrow P - C - O C H _ 2 C H _ 2 \]

\[
Pb(OAc)_4 \rightarrow P - C - O C H _ 2 C H _ 2 \]

\[+ 2N_2 \]

SCHEME 9a: Oxidation of Alcohols with a Polymeric Reagent

\[
P - S - C H _ 3 C l ^ - + H O ( C H _ 2 ) _ 7 O H \xrightarrow{E t _ 3 N} O H C - ( C H _ 2 ) _ 5 C H O + H O ( C H _ 2 ) _ 6 C H O + P - S C H _ 3 \]

\[(1) \quad (20)\]

SCHEME 9b: Homologation of Iodides on Polymer Support

\[
P - S C H _ 3 \xrightarrow{n-BuLi} P - S C H _ 2 Li \xrightarrow{D A B C O} I ( C H _ 2 ) _ 4 I \]

\[
P - S C H _ 2 ( C H _ 2 ) _ 4 I + P - S - C H _ 2 ( C H _ 2 ) _ 4 C H _ 2 - S - P \]

\[\xrightarrow{N a I / C H _ 3 I} P - S C H _ 3 + I ( C H _ 2 ) _ 5 I \]

\[(1) \]

\[
P - S C H _ 3 + I ( C H _ 2 ) _ 6 I \]

\[(3) \]
Again the difference appears to be in the time frame\(^{112,114}\). While the polymer chain mobility may be negligible over several benzyne half-lives (110 - 150 sec), it is not over a longer time interval.

Other examples of site isolation are: the lack of dimer formation in polymer bound titanocene\(^{116}\), the stability of \(\text{P-CH}_2\text{Fe(CO)}_2\text{H}\)\(^{117}\), and the lack of metal cluster formation on irradiation of \(\text{P-CH}_2\text{Co(CO)}_2\)\(^{117}\). (These observations were made in poor swelling solvents or no solvent). However many rhodium complexes with \(\text{P-P(Ph)}_2\) are known in which more than one polymeric phosphine group is complexed with the metal\(^{110,118-120}\).

Several results suggest that the presence of positively charged species on the polymer increase the site isolation by decreasing chain mobility. The reaction of \(\text{P-S-CH}_2\text{Cl}^+\) with diols gave approximately a 20:1 ratio of mono-to di-oxidized product\(^{55}\) (Scheme 9a). A similar polymer with a negative rather than a positive charge gave \(~75\%\) of the doubly reacted product\(^{121}\) (Scheme 9b). Similarly in the reaction of \(\text{P-CH}_2\text{Cl}\) with 1 equivalent of \(\text{N,N,N',N'}\text{tetramethylethlenediamine}\) only half of the chlorine was displaced\(^{122}\) (eqn 12).

\[
2 \text{P-CH}_2\text{Cl} + (\text{CH}_3)_2\text{N(CH}_2\text{)}_2\text{N(CH}_3\text{)}_2 \rightarrow \text{P-CH}_2\text{Cl} + \text{P-CH}_2\text{N(CH}_2\text{)}_2\text{NCl}^-
\]

(eqn. 12)

Another set of experiments suggests that chain mobility, and therefore the degree of intraresin reaction, is determined by the swelling properties of the solvent used\(^{123}\). Thus, in a poor swelling solvent such as benzene, \(\text{P-P(Ph)}_2\) forms a 1:1 complex with \(\text{Co(NO)}(\text{CO})_3\). On addition of xylene, a good swelling solvent for this system, the 2:1 complex is rapidly formed. This result is observed
for 20% crosslinked polystyrene as well as the 2% crosslinked material.

The effects of solvent and charge on polymer mobility were shown to be interrelated using electron paramagnetic resonance spectroscopy to measure the rotational motion of a polymer bound nitroxide radical. In poor swelling solvents the correlation time $T$ was the same as for the dry polymer, but in good swelling solvents $T$ was reduced by a factor of up to 100. Introduction of positively charged species onto the polymer backbone changed these results dramatically. Previously good solvents such as THF and ethyl acetate gave the same $T$ value as the dry polymer, while two previously poor solvents, ethanol and 1-propanol, swelled the polymer and gave very low $T$ values. Evidently the effect of positive charges on site isolation is the result of an alteration in the swelling properties of the polymer.

In summary, it appears as if polystyrene matrices are not inherently rigid even at 20% crosslinking. However, site isolation can be achieved using short reaction times, low concentrations, and non-swelling solvents.

3. Polymers as Reagents in Organic Synthesis

The use of polymeric reagents in organic synthesis affords the same advantages observed in the use of polymeric supports, the chief of these being the ease of isolation of the product from the reaction mixture. In the case of solid supports, the excess reagents and by-products were filtered away from the polymer-attached product, while in the case of polymeric reagents, the product is found in the liquid phase with the excess reagent and by-products bound to the solid polymer.

However, the requirements for a good polymeric reagent are somewhat different from those desired for a solid support. Supports for solid phase synthesis often
Have very low capacities to prevent interference between the reactive groups in the growing molecules, and the value of the product is often such that the cost of discarding the polymer support at the end of the synthesis is negligible. For polymeric reagents, on the other hand, a high capacity is desirable to allow the reaction to proceed on a practical scale, and the ability of the reagent to be easily regenerated is critical since the reactions are, in general, simple ones carried out on relatively inexpensive substrates that could not justify the expense of discarding a custom-made polymer after one use. In addition, the reaction should go to completion and produce a single product to make extra purification steps unnecessary.

Polymeric reagents have been developed for such processes as epoxidation, oxidation, reduction, acylation, halogenation and Wittig reactions. (Table 4).

A polymeric analogue of perbenzoic acid \( \text{PJ}-\text{C}_2\text{O}_2\text{H} \) has been used to epoxidize olefins and to oxidize amines to N-oxides and sulfides to sulfoxides or sulfones. For example, penicillins are oxidized to the S-oxides in good yields (eqn 13).

\[
\begin{align*}
\text{R}_1^* & \quad \text{H} & \quad \text{N} & \quad \text{CO}_2\text{R}_3 \quad \xrightarrow{\text{P}-\text{COO}_2\text{H}} \quad \text{R}_1 \quad \text{R}_2^* & \quad \text{H} & \quad \text{S} & \quad \text{CH}_3 & \quad \text{CO}_2\text{R}_3
\end{align*}
\]

(eqn 13)

The resin is easily regenerated by treatment with hydrogen peroxide using a sulfonic acid catalyst.

Several polymeric reagents have been employed in the oxidation of alcohols. Reaction of polymer bound thianisole \( \text{P}-\text{SCH}_3 \) with chlorine yielded a chlorosulfonium reagent \( \text{P}-\text{SC}_\text{Cl}^- \) which oxidizes primary alcohols to aldehydes. This reagent was particularly useful in oxidizing sensitive
<table>
<thead>
<tr>
<th>Polymer</th>
<th>Use</th>
<th>Recycling</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \overset{0}{P} )-COOH</td>
<td>- epoxidation of olefins</td>
<td>Yes</td>
<td>125 - 127</td>
</tr>
<tr>
<td></td>
<td>- oxidation of amines and sulfides</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \overset{C}{P} )-SCH(_3)Cl(^-)</td>
<td>- oxidation of alcohols to aldehydes</td>
<td>Yes</td>
<td>60</td>
</tr>
<tr>
<td>( \overset{+}{P} )-SCH(_3)</td>
<td>- inhibition of peroxide formation</td>
<td></td>
<td>129</td>
</tr>
<tr>
<td></td>
<td>in ethers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \overset{+}{P} )-N((Me)_3)HCrO(_4)(^-)</td>
<td>- oxidation of alcohols</td>
<td>Yes</td>
<td>130</td>
</tr>
<tr>
<td>( \overset{+}{P} )-CH(_2)N((Me)_3)(^2)</td>
<td>- oxidation of alkyl halides to</td>
<td>Yes</td>
<td>154</td>
</tr>
<tr>
<td></td>
<td>carbonyl compounds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \overset{H}{P} )-Sn-Bu</td>
<td>- reduction of carbonyl compounds to</td>
<td>No</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>alcohols and alkyl halides to</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>alkanes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \overset{\text{N.BH}_3}{P} )</td>
<td>reduction of carbonyl compounds</td>
<td>Yes</td>
<td>131, 132</td>
</tr>
<tr>
<td>( \overset{\text{CH}_2N(\text{Me})_3BH}_4^-)</td>
<td>compounds to alcohols</td>
<td>Yes</td>
<td>133</td>
</tr>
<tr>
<td>( \overset{\text{BH}_3}{P} )-SCH(_3)</td>
<td>- acylating agent for amines and</td>
<td>Yes</td>
<td>134</td>
</tr>
<tr>
<td></td>
<td>alcohols</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \overset{\text{COC-Ph}}{P} )</td>
<td>- acylating agent for amines and</td>
<td>?</td>
<td>135</td>
</tr>
<tr>
<td></td>
<td>carboxylic acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \overset{\text{SO}_2\text{COC-Ph}}{P} )</td>
<td>- acylating agent for alcohols and</td>
<td>?</td>
<td>136, 137</td>
</tr>
<tr>
<td></td>
<td>amines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \overset{\text{NO}_2\text{OH}}{P} )</td>
<td>- synthesis of peptide bonds</td>
<td>?</td>
<td>140</td>
</tr>
<tr>
<td>( \overset{\text{SO}_2\text{Cl}}{P} )</td>
<td>- nucleoside coupling</td>
<td>?</td>
<td>141, 142</td>
</tr>
<tr>
<td>Polymer</td>
<td>Use</td>
<td>Recycling</td>
<td>Reference</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>-CH₂N(CH₃)₃X⁻</td>
<td>- halogen-halogen exchange</td>
<td>?</td>
<td>143</td>
</tr>
<tr>
<td></td>
<td>X = F⁻, Cl⁻, Br⁻</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- nucleophilic substitutions on alkyl halides</td>
<td>?</td>
<td>144, 145</td>
</tr>
<tr>
<td>P-IF₂</td>
<td>- preparation of gem difluorides from 1,1-diphenyl olefins</td>
<td>Yes</td>
<td>146, 147</td>
</tr>
<tr>
<td>P-ICl₂</td>
<td>- preparation of 1,2-dichloroalkanes from olefins</td>
<td>Yes</td>
<td>148</td>
</tr>
<tr>
<td>P-P(Ph)₂/CCl₄</td>
<td>- conversion of alcohols to alkyl halides, amides and oximes to nitriles and imidoyl chlorides, and carboxylic acids to acid chlorides</td>
<td>?</td>
<td>149 - 152</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- bromination of alkenes and phenyl alkanes</td>
<td>Yes</td>
<td>155, 156</td>
</tr>
<tr>
<td>P-mercaptoproline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-C=NBr</td>
<td>- allylic bromination</td>
<td>Yes</td>
<td>157</td>
</tr>
<tr>
<td>P-P(Ph)₂</td>
<td>- cleavage of ethers to alkyl halides</td>
<td>Yes</td>
<td>158</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-P(Ph)₂CH₂RX⁻</td>
<td>- Wittig reaction</td>
<td>Yes</td>
<td>159 - 163</td>
</tr>
<tr>
<td>P-CH₂N=C=NCH(CH₃)₂</td>
<td>- dehydration agent</td>
<td>partially</td>
<td>164, 165</td>
</tr>
<tr>
<td></td>
<td>- Moffatt oxidation reagent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-AlCl₃</td>
<td>- dehydrating agent for preparation of ethers and esters</td>
<td>?</td>
<td>166, 167</td>
</tr>
<tr>
<td>Polymer</td>
<td>Use</td>
<td>Recycling</td>
<td>Reference</td>
</tr>
<tr>
<td>-------------</td>
<td>------------------------------------------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>P-SO$_2$N$_3$</td>
<td>diazo group transfer agent</td>
<td>?</td>
<td>168</td>
</tr>
<tr>
<td>P-SeCl</td>
<td>preparation of α,β- unsaturated ketones</td>
<td>No</td>
<td>169</td>
</tr>
<tr>
<td>P-CH$_2$-Rose bengal</td>
<td>photosensitizer for generation of singlet oxygen</td>
<td>Yes</td>
<td>170, 171</td>
</tr>
</tbody>
</table>

TABLE 4: (Continued) Polymeric Reagents
compounds such as prostaglandin intermediates. Regeneration of the reagent could be accomplished in one step. $\text{P}_2\text{S}-\text{CH}_3$ has also been used in the prevention of peroxide formation in ethers\textsuperscript{129}.

Another oxidizing agent is formed by reaction of chromium trioxide with anion exchange resins to give $\text{P}_2\text{N}$(Me)$_3$HCrO$_4$\textsuperscript{130}. This reagent produces aldehydes and ketones from alcohols in good yields and is said to be regenerable.

A polymeric N-oxide $\text{P}_2\text{CH}_2\text{N}$(CH$_3$)$_2$\textsuperscript{154} oxidizes alkyl bromides and iodides to aldehydes and ketones in better yields than the monomeric reagent\textsuperscript{172}. The polymer is easily recycled by reaction with $\text{H}_2\text{O}_2$.

An organotin dihydride polymeric reagent $\text{P}_2\text{Sn}-\text{Bu}$ has been described for use in the reduction of aldehydes and ketones to alcohols and of alkyl halides to alkanes.\textsuperscript{56} Unfortunately the reagent could not be restored to its initial activity on regeneration and therefore could not be recycled.

Reusable reducing agents could be made by complexing sodium borohydride with poly(4-vinyl pyridine)\textsuperscript{131,132} or anion exchange resins\textsuperscript{133}, or by reacting diborane with $\text{P}_2\text{CH}_2\text{SCH}_3$\textsuperscript{134}. These polymeric borohydride analogues reduced aldehydes and ketones to alcohols in good yields.

Several polymeric anhydrides have been synthesized and their use as acylating agents studied. The benzoic anhydride polymer $\text{P}_2\text{COC-Ph}$ formed by reaction of $\text{P}_2\text{C}-\text{Cl}$ with benzoic acid successfully acylated amines and alcohols\textsuperscript{135}. A resin contained mixed carbonic - carboxylic anhydride functions $\text{P}_2\text{CH}_2\text{OOCOCPh}$ made by reaction of $\text{P}_2\text{CH}_2\text{OH}$ first with phosgene then benzoic acid, is
useful in preparing amides and anydrides. For example, 7-aminocephalosporanic acid is N-acylated in 75% yield with this reagent. Mixed sulfonic-acetic anhydride resins \( \text{SO}_2\text{OC}-\text{CH}_3 \) have also been prepared and used as acylating agents for alcohols and amines.

Reagents for adding amino acid residues to peptides (Scheme 10) and for nucleoside coupling (Scheme 11) have been prepared.

Anion exchange resins \( \text{CH}_2\text{N(CH}_3)_3\) with a variety of counterions have been used to effect such \( S_N^2 \) type reactions as halogen/halogen exchange and the synthesis of nitriles, phenol ethers, and nitro compounds from alkyl halides in good yields without side reactions.

The preparation of gem-difluoro compounds from 1,1-diphenyl olefins has been accomplished using polystyryliodine(III)difluoride (eqn. 14):

\[
\begin{align*}
\text{P-I} & \overset{\text{XeF}_2}{\rightarrow} \text{P-IF} \\
\text{HF} & \rightarrow \text{P-I + Ph-F} \\
\text{Ph} & \rightarrow \text{Ph-F} \\
\text{R} & \rightarrow \text{Ph-H}
\end{align*}
\quad (\text{eqn. 14})
\]

The rearrangement is believed to take place via an electrophilic attack on the olefin by the iodine followed by a phenyl group migration (Scheme 12). The reagent is recycled without loss of activity.

The chlorine analogue of this reagent \( \text{P-ICl}_2 \) also converts alkenes to dichlorides; however, in this case cis-1,2-dichloroalkanes are obtained.

Alkyl chlorides have been prepared from alcohols in excellent yields using the equivalent reagents \( \text{P-Ph}_2/\text{CCl}_4 \) or \( \text{P-Ph}_2\text{Cl}_2 \).
SCHEME 10: A Polymeric Reagent for Peptide Bond Formation

\[
\begin{align*}
\text{P-CH}_2-\text{NO}_2 & \rightarrow \text{O} \text{R} \text{ClC-CH-NH(Pg)} \rightarrow \text{P-CH}_2-\text{NO}_2 \\
\text{H}_2\text{NCHR'-C peptide} & \rightarrow \text{P-CH}_2-\text{NO}_2 + (\text{Pg})\text{HNCHRC-NHCHR'-C peptide}
\end{align*}
\]

(Pg = Protecting group)

SCHEME 11: A Nucleoside Coupling Reagent

\[
\begin{align*}
\text{P-SO}_2\text{Cl} + \text{HOPO} & \rightarrow \text{Et thymine} \rightarrow \text{P-SO}_2\text{PO} \text{Et thymine} \\
\text{Ph CO Ph thymine} & \rightarrow \text{P-SO}_3\text{H} + \text{Ph-CO Ph thymine}
\end{align*}
\]
SCHEME 12: Reaction Mechanism of $\text{P} - \text{IF}_2$

$\text{P} - \text{I} - \text{F}$ \[ \xrightarrow{\text{HF}} \] $\text{P} - \text{I} - \text{F} \cdot \text{HF}$ \[ \xrightarrow{\text{F}^-} \] $\text{P} - \text{I} - \text{CHR-C-Ph}$ \[ \xrightarrow{\text{F}^-} \] $\text{RCH-C-Ph}$

$\text{P} - \text{IF}_2$ \[ \xrightarrow{(-\text{HF}, \text{F}^-)} \] $\text{P} - \text{I} - \text{CHR-C-Ph}$ \[ \xrightarrow{(-\text{P} - \text{I}, \text{F}^-)} \] $\text{RCH-C-Ph}$

SCHEME 13: Photo-oxidations with $\text{P} - \text{CH}_2$-Rose Bengal

$\text{P} - \text{CH}_2\text{Cl}$ + NaOOC$\text{O-C-Ph}$ $\xrightarrow{\text{DMF}}$ $\text{P} - \text{CH}_2\text{OC}$ \[ \text{[P-CH}_2\text{-Rose Bengal]} \]

$\text{P} - \text{CH}_2$-Rose Bengal $\xrightarrow{\text{hv}}$ $\text{P} - \text{CH}_2$-Rose Bengal$^1$

$\text{P} - \text{CH}_2$-Rose Bengal$^1$ $\xrightarrow{\text{hv}}$ $\text{P} - \text{CH}_2$-Rose Bengal$^3$

$\text{P} - \text{CH}_2$-Rose Bengal$^3$ + $\text{O}_2$ $\xrightarrow{\text{hv}}$ $\text{P} - \text{CH}_2$-Rose Bengal + $\text{O}_2$

$\text{O}_2$ + $\text{OPh}$ $\xrightarrow{\text{hv}}$ $\text{OPh}$ (95%)
The \( \text{P}_2\text{P(Ph)} \) produced can be regenerated with phosgene. These reagents also convert primary amides and aldoximes to nitriles, secondary amides and ketoximes to imidoyl chlorides and carboxylic acids to acid chlorides. For example,

\[
\text{P}_2\text{P(Ph)}_2 + \text{CCl}_4 + \text{R}_1\text{CNHR}_2 \rightarrow \text{R}_1\text{C}_{\text{NHR}}^\text{Cl} + \text{P}_2\text{P(Ph)}_2 + \text{CHCl}_3
\]

(eqn. 15)

The analogous bromine reagent \( \text{P}_2\text{P(Ph)}_2\text{Br}_2 \) is made by reaction of the phosphine polymer with \( \text{Br}_2 \). This reagent cleaves ethers to give two alkyl bromides. The phosphine oxide polymer produced is reduced to the phosphine with trichlorosilane.

Several other brominating agents have also been described. The polymeric equivalent of N-bromosuccinimide reacts with alkenes to give 1,2-dibromoalkanes. However the reaction with cumene (2-phenylpropane) gave a mixture of three products, all different from those obtained using N-bromosuccinimide.

The reagent \( \text{P}_2\text{C(Ph)=NBr} \) made by reacting \( \text{P}_2\text{Li} \) with benzonitrile and then bromine, brominated olefins in the allylic position in moderate yield.

Polymer bound analogues of triphenylphosphine have been used in Wittig reactions. (eqn. 16).

\[
\text{P}_2\text{P(Ph)}_2 + \text{RCH}_2\text{X} \rightarrow \text{P}_2\text{P-CH}_2\text{RX}^- + \text{Ph} + \text{P}-\text{CHR}
\]

(eqn. 16)
Cis-trans stereoselectivity can be achieved by controlling the lithium salt concentration, or by varying the stability of the ylide.

A polymeric carbodiimide reagent \( \text{P-CH}_2\text{N=NCH(CH}_3\text{)}_2 \) has been used as a dehydrating agent and in the Moffatt oxidation. The polymeric urea formed is regenerated to the carbodiimide with tosyl chloride. However, some loss of activity is observed due to formation of N-acylurea rearrangement product.

A polystyrene-\( \text{AlCl}_3 \) complex has been prepared and used as a dehydrating agent to prepare ethers and esters. The advantage of this polymeric reagent is that it is no longer water sensitive, as the \( \text{AlCl}_3 \) is protected by the hydrophobic polystyrene matrix. The active agent is made accessible by swelling the polymer in an organic solvent.

Another reagent whose stability is increased by attachment to a polymer is tosyl azide. The monomeric reagent is detonated by shock, while the polymer is non-explosive and indefinitely stable at room temperature. The reagent is used to transfer diazo groups to \( \beta \)-dicarbonyl compounds (eqn 16).

\[
\text{P-SO}_2\text{N}_3 + \text{RCCH}_2\text{CR}' \xrightarrow{\text{E}_3\text{N}} \text{RC-C-CR')}\text{N}_2 + \text{P-SO}_2\text{NH}_2
\]

Several selenium reagents have been described and used in typical reactions. For example \( \text{P-SeCl} \) is used to prepare \( \alpha,\beta \)-unsaturated ketones (eqn. 17).

\[
\text{P-SeCl} + \text{CH}_3\text{O} \xrightarrow{} \text{P-Se} + \text{H}_2\text{O}_2 \quad \text{P-SeOH} + \text{CH}_3\text{O}
\]
The reagent is not recycled.

Several polymer bound photo-sensitizers, such as \( \text{P}-\text{CH}_2\text{-Rose Bengal} \) capable of generating singlet oxygen on irradiation have been made and used in a variety of photo-oxidation reactions (Scheme 13)\(^{170,171}\). These polymer-bound sensitizer dyes have several advantages over their monomeric counterparts. They can be used in solvents in which the unbound dye is insoluble, they are significantly more stable towards bleaching, and they can be easily removed from the reaction mixture by filtration and can be recycled with no loss of activity.

4. Polymers as Catalysts and Catalyst Supports

The first polymeric catalysts used were the ion exchange resins, which can be used in acid or base catalysed reactions. Acidic \( \text{P}-\text{SO}_3\text{H} \) resin is used to catalyse such processes as the hydrolysis of esters and amides\(^{173,174}\), and the formation of acetics, methyl glycosides\(^{175}\), esters\(^{177}\), and amides\(^{178}\). Basic resins \( \text{P}-\text{CH}_2\text{~N}^+(\text{CH}_3)_3\text{OH}^- \) have been used in the hydrolysis\(^{179}\) and formation\(^{180}\) of esters, and in aldol, Michael,\(^{182}\) and malonic ester\(^{183}\) reactions.

Polymers have also been applied to phase transfer catalysis. A solid polymer is used to transfer ions from an aqueous to an organic layer in a process called "triphase catalysis." For example, polymers of the type \( \text{P}-\text{CH}_2\text{N}^+(\text{R})_3\text{Cl}^- \) \(^{184,185}\) and \( \text{P}-\text{NRBr}^- \), in which \( R \) is a large alkyl group, catalyze the nucleophilic displacement of \( \text{Br}^- \) by \( \text{CN}^- \) in an alkyl bromide.

Another approach to triphase catalysis is the use of "solid phase cosolvents" such as \( \text{P}-\text{CH}_2\text{O(CH}_2\text{CH}_2\text{O)}_n\text{CH}_3 \) \((n_{av} = 13)\). Such polymers have been
shown to contain both water and the organic solvent within the swollen matrix under triphase conditions. These polymers even catalyse the reaction between a solid and a liquid phase successfully (eqn 18).

\[
\text{KOPh}_{(\text{solid})} + \text{Br-(CH}_2\text{)}_3\text{CH}_3 \xrightarrow{\text{Toluene}} \text{PhO-(CH}_2\text{)}_3\text{CH}_3
\]

The yields and reaction rates are equal to or better than those obtained with the corresponding soluble poly(ethylene glycol monomethyl ether).

Another solid phase cosolvent which exhibits the same properties as its monomeric counterpart is the polymer-bound analogue of hexamethylphosphoramide \(\text{P}-\text{CH}_2\text{N(CH}_3\text{)}_3\text{P}[\text{N(CH}_3\text{)}_2\text{]}_2\). This polymer catalyses the alkylation of phenols and heterocyclic nitrogen compounds and after five reaction cycles showed no loss of activity.

The use of polymers as supports for transition metal complexes used as catalysts has generated wide interest. One of the main difficulties with the soluble catalysts is the need to separate the products from the catalyst and recover and recycle the often expensive metal complex. A second problem is that these compounds are often air and moisture sensitive. Linking these homogeneous catalysts to solid supports renders the recovery problem trivial, and the polymer often increases the stability of the complexes towards such poisons as water and oxygen.

Solid-supported catalysts can be made: a) by first synthesizing the desired ligands, either by chemical modification of the preformed polymer, or by
SCHEME 14: Sequential Cyclooligomerization and Hydrogenation of Butadiene

\[
\begin{align*}
\text{butadiene} & \xrightarrow{\text{catalyst}, 110^\circ \text{C}} \text{cyclooctatetraene} + \text{cyclooctane} + \text{cycloocta-1,5-diene} \\
& \xrightarrow{\text{H}_2, 350 \text{ psi}, 50^\circ \text{C}} \text{cycloheptatriene} + \text{cyclooctane} + \text{cycloocta-1,5-diene}
\end{align*}
\]
polymerization of a suitable functional monomer, followed by coordination of the metal complex by the conventional methods of organometallic synthesis, or b) by synthesizing a monomer containing the desired organometallic group and polymerizing it. The possibility that the transition metal could interfere with the polymerization reaction makes the first method the preferred one in most cases.

Polymer-bound transition metal complexes have been used to catalyze such reactions as hydrogenation, hydrosilylation, hydroformylation, isomerization, carbonylation, and oligomerization. For example, polymer bound titanocene $\text{P}-\text{CH}_2\text{CH}_2\text{Ti}-\text{O}$ catalyses the hydrogenation of olefins and because it contains coordinatively unsaturated sites which are stabilized by the polymer it is more active than its non-supported analogue. The polymeric Wilkinson's catalyst $[\text{P-(P(Ph)_2)}_n-\text{RhCl}(\text{P(Ph)_2})_m (m + n = 3)$ is a hydrogenation and hydrosilylation catalyst. Two other rhodium complexes $[\text{P-(P(Ph)_2)}_2-\text{RhCl}(\text{CO})]$ and $[\text{P-(P(Ph)_2)}_2-\text{RhH(CO)}(\text{P(Ph)_3})]$ are used in hydroformylation reactions.

An interesting variation of the polymer supported catalysis technique is to attach two catalysts to a single support and perform several reactions on a substrate in one pot. For example a polymer containing $[\text{P-(P(Ph)_2)}_2 \text{Ni(CO)}_2$, a cyclooligomerization catalyst, and $[\text{P-(P(Ph)_2)}_2 \text{RhCl}(\text{P(Ph)_3})_x$, a hydrogenation catalyst, are used to catalyze two sequential reactions on butadiene (Scheme 14).

5. Other Applications of Functionalized Polymers

Polymers containing biologically active molecules have been developed for applications in which controlled release or non-release of the reactive moiety to the environment is desired. For example, polymers with pesticide
or herbicide pendant groups have been designed for slow continuous release of the killing agent to reduce the quantity and number of applications of the biocide required to produce the desired effect. Paints containing polymer bound fungicides are protected from mildew formation without the problems of reduction of activity and pollution of the environment caused by leaching of these toxic compounds from the painted surface, serious drawbacks to the use of monomeric fungicides to prevent damage to the paint.

The activity of the Food and Drug Administration in the United States against food additives which are suspected carcinogens has led to the development of polymeric food dyes, antioxidants, and sweeteners. These polymer-bound additives are not absorbed from the digestive tract because of their high molecular weights, and are therefore less likely to have adverse health effects than their readily absorbed monomeric analogues.

Polymers containing molecules with pharmacological activity are under investigation for use in medicine. Polymers with antibacterial, antasilicosis, antiviral, and anticancer activity have already been synthesized.

Polymer immobilized enzymes have been used for such applications as biochemical analysis using enzyme electrodes, affinity chromatography, and sequential organic synthesis.
PART 1

Synthesis of Functional Polymers
RESULTS AND DISCUSSION

The success of functional polymers in many applications rests on having a good polymer, possessing reactive functional groups which are easily accessible to the substrates, and free from groups which could promote undesired reactions. However, although the reactions used in the functionalization of insoluble resins are similar to those carried out on soluble materials, they are often more difficult to control and the insolubility of the polymer makes removal of unreacted starting material and unwanted side products from the desired polymer impossible. Thus, it is often difficult to know exactly what groups are present on the polymer and in what concentrations; while infrared spectroscopy and elemental analysis can give a good indication of the success of a functionalization reaction, the main criterion is the reactivity of the functional polymer in the application for which it was intended.

A major portion of this thesis involved the development of reliable methods for the preparation of a wide variety of functional polymers bearing reactive and easily accessible groups by the chemical modification of preformed polymers. We are mainly interested in reactions using 1% cross-linked swellable polystyrene resins although we have also studied macroreticular polystyrenes. A degree of functionalization (D.F.) of 0.2 - 0.4 (i.e. with 20-40% of the aromatic rings substituted) is desirable for the following reasons. Overcrowding of the functional groups on the polymer, which could cause interference in subsequent steps is avoided, yet the concentration of reactive groups is still high enough that a reaction can be carried out
on a practical scale without having to use large amounts of resin.

The first step in the synthesis of functional polymers by chemical modification is the removal of impurities from the starting resin. The presence of surface contaminants on the preformed polymer could prevent the introduction of certain types of functional groups. For example, analysis of the commercial polystyrene, Biobeads SX-1 showed that it contained 145 p.p.m of aluminum, probably left over from the alumina used as a stabilizing agent in the emulsion polymerization. The presence of metallic groups such as aluminum could interfere with reactions such as the metal-halogen exchange reaction between $\text{P-Br}$ and n-BuLi. In fact, we observed substantial improvement in the yield of this reaction after extensive washing with acids, bases and organic solvents had reduced this residual aluminum to $\sim 50$ p.p.m. However, as 5-10% weight losses were typically obtained after such washings, other impurities or soluble polymer chains were also removed from the crosslinked polymer and these could also account for the improvement in reactivity of the polymer. Trace analyses of the washed polymer showed that it was remarkably free from contamination, containing no sulfur, nitrogen or oxygen and less than 0.1% halogen. Macroreticular resins are less sensitive to surface impurities than the swellable resins because of their much larger surface areas; however they are often less reactive and give lower reaction yields than their swellable counterparts for other reasons.

**Chemical Modification of $\text{P-CH}_2\text{Cl}$ by Phase Transfer Catalysis.**

The preparation and reactions of chloromethylated polystyrene have been extensively studied, as $\text{P-CH}_2\text{Cl}$ was for many years the polymer most often used in solid phase synthesis, and it is still a very versatile
starting material for the preparation of a large number of functionalized polymers (Table 1).

The chloromethyl group of $\text{P-CH}_2\text{Cl}$ provides a reactive handle on the polymer which can subsequently be transformed into a wide variety of more complex functional groups by the conventional reactions of organic synthesis, such as the displacement of chloride from the chloromethyl groups by nucleophiles. However in a number of cases the reactions are accompanied by undesired side reactions and the functional yields are low. Since the polymers cannot be purified once they have been prepared, it is desirable to use very simple systems in the functionalization reactions to avoid all side reactions whenever possible.

We had previously used phase transfer catalysis for the generation of reactive intermediates on insoluble polymers (see Part 2 of this thesis) and found that reactions involving such three phase systems proceeded in remarkably clean fashion to give excellent yields of products without appreciable formation of side products. Thus, the use of phase transfer catalysis in the preparation of new functionalities on polymers by reaction with $\text{P-CH}_2\text{Cl}$ seemed to hold promise. We have carried out a number of nucleophilic substitutions on $\text{P-CH}_2\text{Cl}$ using a variety of C-, S- and O- nucleophiles under phase transfer conditions to test this hypothesis and have found that excellent yields of functional polymers could be obtained (Table 5 and Scheme 15). In general, the reaction involved a three phase system consisting of two liquid phases, an organic swelling agent and an aqueous solution of the nucleophile, and the solid polymer in the presence of a phase transfer catalyst.
SCHEME 15: Chemical Modification of \( P - CH_2 Cl \) by Phase Transfer Catalysis

\[
\begin{align*}
\text{VIII} & : P - CH_2 S - (CH_2)_4 - SH \\
\text{VII} & : P - CH_2 - S - (CH_2)_3 - CH_3 \\
\text{VI} & : P - CH_2 - C = N \\
\text{IV, V} & : P - CH_2 - O - X \\
\text{IV} & : X = -CHO \\
\text{V} & : X = -NO_2
\end{align*}
\]
Table 5  Reaction of CHCl with nucleophiles under phase transfer conditions

<table>
<thead>
<tr>
<th>Starting Resin meq/g</th>
<th>Swelling agent</th>
<th>Catalyst</th>
<th>Reagent</th>
<th>Temp. (days)</th>
<th>Time</th>
<th>Structure of Product</th>
<th>Product Analysis (meq/g)</th>
<th>Product D.F.</th>
<th>Functional Yield %b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>A</td>
<td>Adogen 464 CH₃COOK</td>
<td>100</td>
<td>4</td>
<td>D-CH₂OOCOCH₃</td>
<td>0 - 1.70 (ester)</td>
<td>0.200</td>
<td>98</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>A</td>
<td>(Bu)₄NCl  CH₂COOK</td>
<td>100</td>
<td>4</td>
<td>D-CH₂OOCOCH₃</td>
<td>0 - 1.70 (ester)</td>
<td>0.200</td>
<td>98</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>B</td>
<td>Adogen 464 CH₃COOK</td>
<td>80</td>
<td>4</td>
<td>D-CH₂OOCOCH₃</td>
<td>0.08 - 1.66 (ester)</td>
<td>0.198</td>
<td>96 (100)</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>C</td>
<td>Adogen 464 CH₂COOK</td>
<td>25</td>
<td>4</td>
<td>D-CH₂OOCOCH₃</td>
<td>1.03 - -</td>
<td>0.205</td>
<td>8 (100)</td>
</tr>
<tr>
<td>2.1</td>
<td>0.24</td>
<td>D</td>
<td>(Bu)₄NOH  CH₃(CH₂)₃SH NaOH</td>
<td>65</td>
<td>2</td>
<td>D-CH₂S(CH₂)₃CH₃</td>
<td>0 - 1.92 (S)</td>
<td>0.24</td>
<td>100</td>
</tr>
<tr>
<td>2.1</td>
<td>0.24</td>
<td>A</td>
<td>(Bu)₄NOH  CH₃(CH₂)₃SH NaOH</td>
<td>65</td>
<td>2</td>
<td>D-CH₂S(CH₂)₃CH₃</td>
<td>0 - 1.90 (S)</td>
<td>0.24</td>
<td>100</td>
</tr>
<tr>
<td>2.1</td>
<td>0.24</td>
<td>D</td>
<td>(Bu)₄NOH  CH₃(CH₂)₃SH NaOH</td>
<td>25</td>
<td>1</td>
<td>D-CH₂S(CH₂)₄SH</td>
<td>0 - 3.50 (S)</td>
<td>0.23</td>
<td>95</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>B</td>
<td>Adogen 464 NaCN</td>
<td>80</td>
<td>4</td>
<td>D-CH₂CN</td>
<td>trace 1.84 -</td>
<td>0.205</td>
<td>100</td>
</tr>
<tr>
<td>2.6</td>
<td>0.310</td>
<td>C</td>
<td>Adogen 464 NaCN</td>
<td>80</td>
<td>3</td>
<td>D-CH₂CN</td>
<td>0.4 2.3 -</td>
<td>0.250</td>
<td>81 (100)</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>A</td>
<td>(Bu)₄NOH  HO-CH₂CHO KOH</td>
<td>80</td>
<td>3</td>
<td>D-CH₂OCH₂CHO</td>
<td>0 - 3.06 (O)</td>
<td>0.200</td>
<td>98</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>A</td>
<td>(Bu)₄NOH  HO-NO₂ KOH</td>
<td>85</td>
<td>2</td>
<td>D-CH₂O-NO₂</td>
<td>0 - 1.52 4.47 (O)</td>
<td>0.203</td>
<td>99</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>A</td>
<td>Adogen 464 CH₂(CN)₂ KOH</td>
<td>90</td>
<td>5</td>
<td>D-CH₂CN</td>
<td>trace 3.3 -</td>
<td>0.200</td>
<td>98</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>A</td>
<td>Adogen 464 CH₂(COEt)₂ KOH</td>
<td>90</td>
<td>5</td>
<td>D-CH₂O-COEt</td>
<td>0.10 - 4.8</td>
<td>0.158</td>
<td>77 (81)</td>
</tr>
<tr>
<td>1.8</td>
<td>0.205</td>
<td>A</td>
<td>Adogen 464 CH₂(CN)COOEt KOH</td>
<td>90</td>
<td>5</td>
<td>D-CH₂C-CN</td>
<td>0.09 1.4 2.76</td>
<td>0.181</td>
<td>88 (92)</td>
</tr>
</tbody>
</table>

a)  A = o-dichlorobenzene; B = 1,2-dichloroethane; C = dichloromethane; D = benzene
b)  % conversion given in parenthesis
a) Preparation of \( \text{P-CH}_2\text{O-CO-CH}_3 \)

The first reaction we studied was the replacement of chloride by acetate, a reaction which had been carried out successfully by Ayres and Mann\(^{16}\) using potassium acetate in dimethyl sulfoxide. However, our experience with reactions of \( \text{P-CH}_2\text{Cl} \) in DMSO indicates that the oxidation of \( \text{P-CH}_2\text{Cl} \) to the aldehyde \( \text{P-CHO} \) was always a competing reaction.

The reaction of \( \text{P-CH}_2\text{Cl} \) with a concentrated aqueous solution of potassium acetate under phase transfer conditions was partially successful, but did not result in complete displacement of chloride when carried out at room temperature using dichloromethane as the organic solvent. However, when the reaction was carried out at higher temperatures using o-dichlorobenzene or 1,2-dichloroethane as solvent, essentially quantitative conversion of \( \text{P-CH}_2\text{Cl} \) into \( \text{P-CH}_2\text{O-CO-CH}_3 \) was observed. The product contained no residual chlorine and the infrared spectra showed large bands at 1750 and 1235 cm\(^{-1}\), characteristic of \( \text{C=O} \) and \( \text{C-O} \) absorptions. Saponification of the polymeric ester with excess base followed by back titration with acid indicated that the degree of functionalization of the polymer was essentially identical to that of the starting \( \text{P-CH}_2\text{Cl} \) polymer.

b) Preparation of \( \text{P-CH}_2\text{OH} \)

Hydroxymethyl polystyrene \( \text{P-CH}_2\text{OH} \) can be made by saponification of the polymeric acetate using a conventional two phase procedure\(^{22,23}\) or in a three phase system using aqueous sodium or potassium hydroxide and \((\text{Bu})_4\text{NOH}\) or Adogen 464 as catalyst. However, this two step synthesis is
rather time consuming, so an attempt was made to find a procedure that did not require the isolation of any intermediates in the synthesis of \( P \)-CH\(_2\)OH. The direct displacement of chloride by hydroxide ion in \( P \)-CH\(_2\)Cl was unsuccessful using phase transfer catalysis, as was the case in previous attempts to perform this reaction using conventional conditions. We have however succeeded in carrying out the one-pot conversion of chloromethyl polystyrene to the hydroxymethyl derivative using a three phase system consisting of \( P \)-CH\(_2\)Cl suspended in \( o \)-dichlorobenzene or 1,2-dichloroethene and an aqueous solution of hydroxide and acetate ions in the presence of a phase transfer catalyst such as \((Bu)\(_4\)NOH. After processing the reaction mixture, the infrared spectrum of the polymer exhibited a large hydroxyl and no carbonyl adsorption, which would have been present if any acetylated groups remained on the polymer. This reaction is described as a one-pot rather than a one-step reaction as we believe that it was the acetate ion which effected displacement of chloride, and that the acetylated polymer underwent saponification as soon as it was formed, both acetate and hydroxide ions being transported by the phase transfer catalyst.

Chlorine analysis of the final product revealed that only approximately 90-95% of the chlorine had been removed from the polymer, suggesting that some of the chloromethyl groups were located in inaccessible positions within the resin. This finding was somewhat puzzling because quantitative replacement of chloride by a variety of nucleophiles including acetate ion could be obtained easily under phase transfer conditions. The reason for this incomplete removal of chlorine became apparent when the reaction was carried out using soluble chloromethylated polystyrene as a polymer substrate. After a short time of reaction, the soluble polystyrene began to
form a gel, indicating that a crosslinking reaction was occurring. The final product of the reaction was completely insoluble in common organic solvents and still contained some chlorine. This crosslinking was due to displacement of chloride ion by \( \text{P}-\text{CH}_2\text{O}^- \), the species formed in the saponification reaction. Attack of this species on a unit of acetylated polymer produced no net change in the polymer composition, while attack on a chloromethylated unit resulted in crosslinking (eqn. 19).

\[
\text{P}-\text{CH}_2\text{Cl} + \text{OCH}_2\text{P} \rightarrow \text{P}-\text{CH}_2\text{OCH}_2\text{P} + \text{Cl}^- \quad (\text{eqn. 19})
\]

This crosslinking reaction probably occurred also in the case of the 1% crosslinked polystyrene, as site-site interactions within the polymer can be extensive in this type of resin. To avoid this undesirable crosslinking and obtain quantitative replacement of chloride in the formation of \( \text{P}-\text{CH}_2\text{OH} \), the reaction was carried out in one-pot under phase transfer conditions by first adding the acetate ion. Then after several hours when formation of the acetylated polymer was complete, adding hydroxide to the aqueous phase led smoothly to the desired hydroxymethyl polymer with complete removal of chlorine and without additional crosslinking.

c) Reaction of \( \text{P}-\text{CH}_2\text{Cl} \) with other O-nucleophiles

The nucleophilic displacement of chloride from \( \text{P}-\text{CH}_2\text{Cl} \) by oxygen nucleophiles under phase transfer conditions was further tested by reaction with phenolate ions derived from p-hydroxybenzaldehyde and p-nitrophenol (Table 5 and Scheme 15). In both cases virtually complete removal of chlorine
from \( \text{P-CH}_2\text{Cl} \) was observed and the expected products \( \text{P-CH}_2\text{O-CHO} \) and \( \text{P-CH}_2\text{O-NO}_2 \) were obtained in 98% and 99% yields respectively. These polymers were characterized by elemental analysis and infrared spectroscopy. \( \text{P-CH}_2\text{O-CHO} \) showed characteristic infrared absorptions at 2755 (aldehyde C-H), 1695 (C=O) and 1150 (C-O) cm\(^{-1}\). \( \text{P-CH}_2\text{O-NO}_2 \) showed absorptions at 1345 and 855 cm\(^{-1}\) due to the NO\(_2\) groups and C-O absorptions at 1165 and 1005 cm\(^{-1}\). Soluble polymers with similar functionalities have been prepared in excellent yields by a classical route and showed similar infrared spectra \(^{42}\).  

d) Reaction of \( \text{P-CH}_2\text{Cl} \) with C-nucleophiles

The reactivity of \( \text{P-CH}_2\text{Cl} \) in a three phase system with various carbon nucleophiles has also been tested and excellent results were obtained in most cases. Reactions of this type have occasionally been used to produce more complicated functional polymers from \( \text{P-CH}_2\text{Cl} \) using conventional techniques but low functional yields are often obtained. For example, the best published procedure for the preparation of a dinitrile containing polymer, used in the synthesis of a metal ion complexing agent, involved reaction of \( \text{P-CH}_2\text{Cl} \) with malononitrile in DMF using ethoxide ion as base (eqn. 20) \(^{206}\).

\[
\text{P-CH}_2\text{Cl} + \text{CH}_2(\text{CN})_2 \xrightarrow{\text{EtO}^- \text{DMF}} \text{P-CH}_2\text{CH(CN)CH(CN)}
\]  

(eqnn 20).

However only 30% of the chloromethyl groups could be transformed into the dinitrile using this procedure. On the other hand, essentially complete conversion of \( \text{P-CH}_2\text{Cl} \) could be achieved using phase transfer catalysis and a 98% yield of \( \text{P-CH}_2\text{CH(CN)}_2 \) was obtained after 2-3 days of reaction at 80°. \(^{207}\)
The polymer showed a sharp CN absorption band at 2200 cm\(^{-1}\) in its infrared spectrum. This malononitrile polymer could be reduced to give the ion complexing polymer \([\text{P}-\text{CH}_2\text{CH(CH}_2\text{NH}_2)_2]\) in excellent yield.

Similar reactions were also carried out under phase transfer conditions with ethyl cyanomalonate and diethylmalonate to give \([\text{P}-\text{CH}_2\text{CH(CN)COOEt}]\) and \([\text{P}-\text{CH}_2\text{CH(COOEt)}_2]\) in satisfactory functional yields of 88% and 77% respectively. In these cases, the final polymer still contained a small but measurable amount of chlorine. It is however interesting to note that in both of these reactions no hydrolysis of the ester was observed, as confirmed by the infrared spectra of the two polymers which did not exhibit any absorption bands corresponding to carboxylic acid groups but showed strong ester bands at 1745 and 1740 cm\(^{-1}\) respectively.

In contrast, the reaction of \([\text{P}-\text{CH}_2\text{Cl}]\) with acetyl acetone under phase transfer conditions gave ambiguous results. The expected product was \([\text{P}-\text{CH}_2\text{CH(CO-CH}_3)_2]\) but when the reaction was carried out using 1,2-dichloroethane as solvent the polymer which was obtained showed two carbonyl bands in the IR, a large one at 1740 cm\(^{-1}\) and a smaller shoulder at 1710 cm\(^{-1}\). When o-dichlorobenzene was used as solvent the product exhibited a single moderately sized C=O absorption at 1710 cm\(^{-1}\). In both cases the removal of chlorine from the polymer was almost complete, but conversion of the carbonyl groups of the two polymers to oximes gave products which contained much less nitrogen than would have been expected for \([\text{P}-\text{CH}_2\text{CH(CO}\text{CH}_3)_2]\). This apparent low yield of diketone may be explained by the formation of variable amounts of enol ethers by intraresin reaction between polymer bound diketone and \([\text{P}-\text{CH}_2\text{Cl}]\) (eqn. 21).
The presence of two C=O bonds in the infrared spectra would then be explained by the existence of two types of carbonyl groups in the product, the desired functionality $\text{P-CH}_2\text{CH}(\text{CO-CH}_3)_2$, and the side product $\text{P-CH}_2\text{C} = \text{C(\text{CH}_3)OCH}_2\text{P}$. This possible explanation could be tested by reaction of $\text{P-CH}_2\text{Cl}$ with 3-methyl-2,4-pentanedione which has only one abstractable proton (eqn. 22).

In this case only one C=O band should be observed in the infrared spectrum, and the nitrogen content of the oxime formed from the product should be
greater than the chlorine content of the starting \( \text{P-CH}_2\text{Cl} \), expressed in mequiv/g. This experiment has yet to be carried out.

e) Preparation of \( \text{P-CH}_2\text{CN} \)

The preparation of cyanomethyl polymer \( \text{P-CH}_2\text{CN} \) from \( \text{P-CH}_2\text{Cl} \) can be accomplished by a nucleophilic displacement of chloride by cyanide ion. The reaction with potassium cyanide in DMSO has been described\(^{16} \), but as is always the case when DMSO is used in reactions of \( \text{P-CH}_2\text{Cl} \), some oxidation of the chloromethyl groups also occurred. We have carried out this transformation using sodium cyanide in a two-phase system with DMF as the solvent, or under phase transfer conditions (Table 5). In both cases excellent yields were obtained and the \( \text{P-CH}_2\text{CN} \) produced was free of contamination by aldehyde. The polymeric nitrile obtained has a very sharp CN absorption band at 2260 cm\(^{-1} \) in its infrared spectrum.

f) Reaction of \( \text{P-CH}_2\text{Cl} \) with an N-nucleophile

A test reaction of \( \text{P-CH}_2\text{Cl} \) with a nitrogen nucleophile under phase transfer conditions was unsuccessful. The treatment of \( \text{P-CH}_2\text{Cl} \) with potassium hydroxide and phthalimide in such a system for up to four days produced a polymer in which most of the chlorine still remained and which showed no carbonyl bands in the infrared spectrum in the region corresponding to the desired phthalimide polymer.

A similar reaction with potassium phthalimide in DMF has been used by Sparrow\(^{37} \) to produce a crosslinked amine polymer \( \text{P-CH}_2\text{NH}_2 \) by hydrazine hydrate reduction of the polymeric phthalimide. This reaction
was performed using a \( \text{P}-\text{CH}_2\text{Cl} \) with a very low degree of functionalization and no yield was reported for either step. We have carried out these reactions successfully with highly functionalized \( \text{P}-\text{CH}_2\text{Cl} \) resins using the same two phase conditions in an overall yield of > 99% for the two step process.

g) Reaction of \( \text{P}-\text{CH}_2\text{Cl} \) with S-nucleophiles

The reaction of \( \text{P}-\text{CH}_2\text{Cl} \) with S-nucleophiles in three phase systems gave results comparable to those obtained with C-nucleophiles. Displacement of chloride by butanethiol or methanethiol in the presence of aqueous hydroxide ion, using \((\text{Bu})_4\text{NOH}\) as phase transfer catalyst, was complete and the polymeric sulfides \( \text{P}-\text{CH}_2\text{S(CH}_2\text{)}_3\text{CH}_3 \) and \( \text{P}-\text{CH}_2\text{SCH}_3 \) were obtained in quantitative yields. (Table 5 and Scheme 15). These sulfides, when converted to the sulfoxides with hydrogen peroxide in acetic anhydride, can potentially be used as oxidizing agents. 154

The reaction of \( \text{P}-\text{CH}_2\text{Cl} \) with a difunctional nucleophile such as a dithiol can be used as a probe of the extent of site-site interactions in polymers. One of the attractive features which has often been associated with the use of insoluble polymers was their ability to provide isolation of reactive sites, which affords a good alternative to the use of high dilution in the study of reactions involving symmetrical bifunctional molecules or in the study of highly reactive sites. A number of reports have confirmed that polymer supports provide much more isolation of reactive sites than would normally be obtained in solution chemistry, and very reactive species have been successfully isolated on polymer supports when the concentration of functional groups was kept low ( < 0.5 mequiv/g)
and the reaction conditions were carefully controlled. However, other reports show that, at least with lightly crosslinked polymer matrices, intraresin site isolation is generally not achieved. 39, 113-115, 121, 208

This problem of control of site-site interactions in swellable polymers led us to investigate the reaction of 1% crosslinked P-CH₂Cl, having a relatively high degree of functionalization, with 1,4-butanedithiol in the presence of base 209.

In such a system, it was expected that, should the reactive sites be isolated on the polymer, each chlorine atom would be replaced by a species containing two atoms of sulfur, while reaction at both extremities of the dithiol would result in the replacement of each chlorine atom by a single atom of sulfur (eqn. 23).

\[
\text{P-CH}_2\text{Cl} + \text{HS(-CH}_2\text{)}_4\text{SH} \rightarrow \text{P-CH}_2\text{S(CH}_2\text{)}_4\text{SH} + \text{P-CH}_2\text{S(CH}_2\text{)}_4\text{SCH}_2\text{P}
\]

Thus a measure of the sulfur-content of the polymer, after complete removal of the chlorine, would allow for the calculation of the extent of site-site interaction as follows:

Polymer (1000 g) contains \(T\) styrene units, of which \(X\) are unsubstituted (unit mol. wt. 104), \(Y\) are singly bound (unit mol. wt. 238) and \(Z\) are doubly bound (unit mol. wt. 177) so:

\[1000 = X(104) + Y(238) + Z(177)\]

and \(X + Y + Z = T\)
Since the degree of functionalization is .244 in this case (starting \( \text{P-CH}_2\text{Cl} \) had 2.1 mequiv/g of Cl)

\[
Y + Z = 0.244T
\]

and

\[
X = 0.756T
\]

From the sulfur analysis \( S \), (expressed in mequiv/g) we get:

\[
S = 2Y + Z
\]

thus

\[
T = (S - Y) / 0.244
\]

Substituting for \( X, Z \) and \( T \) in the first equation gives:

\[
499S - 438Y = 1000
\]

or:

\[
Y = (1000 - 499S) / 438
\]

The percent of double coupling, which is a measure of the extent of intraresin reaction is then given by:

\[
100 \frac{Z}{Y + Z}
\]

The reaction of \( \text{P-CH}_2\text{Cl} \) with S-nucleophile such as butanethiol was known to be complete, so no complications due to unreactive sites within the polymer were expected.

When the reaction was carried out with \( \text{P-CH}_2\text{Cl} \) and 1,4-butanedithiol in DMF with a molar ratio of polymer functional groups: base: dithiol of 0.8: 1: 4.6, a polymer containing no chlorine and a sulfur content corresponding to 62% double and 38% single coupling was isolated (Table 6 expt. 1). Varying the amount of base with respect to dithiol gave a certain degree of control over the extent of intraresin reaction observed (Table 6, expts. 2,3); however, even with a very high dithiol: base ratio a considerable amount of double coupling was observed. These experiments clearly confirm that site-site interactions can be extensive in 1% cross-linked polystyrene resins.
<table>
<thead>
<tr>
<th>Exp. #</th>
<th>Reaction of $\text{P-CH}_2\text{Cl}$ with 1,4-butanedithiol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Molar Ratio</td>
</tr>
<tr>
<td></td>
<td>$\text{P-CH}_2\text{Cl}$/base/dithiol</td>
</tr>
<tr>
<td>1</td>
<td>0.8 : 1 : 4.6</td>
</tr>
<tr>
<td>2</td>
<td>0.2 : 1 : 0.69</td>
</tr>
<tr>
<td>3</td>
<td>0.73 : 1 : 11.7</td>
</tr>
<tr>
<td>4</td>
<td>0.05 : 1 : 0.5</td>
</tr>
<tr>
<td>5</td>
<td>0.11 : 1 : 0.68</td>
</tr>
<tr>
<td>6</td>
<td>0.11 : 1 : 0.68</td>
</tr>
<tr>
<td>7</td>
<td>0.15 : 1 : 1.3</td>
</tr>
<tr>
<td>8</td>
<td>0.15 : 1 : 2.6</td>
</tr>
</tbody>
</table>
The problem which must therefore be faced is how can site-site interactions be avoided in the many applications of solid phase synthesis in which monoreaction of a symmetrical difunctional molecule is required. The answer to this question will, of course, vary depending on the type of reaction being considered. In our case, a solution could be found through consideration of the reactive species which may be involved in the formation of $\text{P-CH}_2\text{S(CH}_2\text{)}_4\text{SH}$ and $\text{P-CH}_2\text{S(CH}_2\text{)}_4\text{SCH}_2\text{P}$ (Scheme 16). A casual inspection of the reactions leading to these two species would suggest that reaction of monothiolate $\text{HS(CH}_2\text{)}_4\text{S}^-$ with $\text{P-CH}_2\text{Cl}$ would lead to single coupling, while reaction of the dithiolate $\text{S(CH}_2\text{)}_4\text{S}^-$ would be responsible for the double coupling. Obviously this explanation was not satisfactory as shown by the case in which 26% double coupling was obtained even though the high ratio of dithiol to base ensured that few dithiolate anions were present. (Table 5 expt. 3). An alternative route leading to intraresin reaction could proceed through proton transfer involving the polymer bound thiol $\text{P-CH}_2\text{S(CH}_2\text{)}_4\text{SH}$ and free monothiolate ion to yield the polymer bound thiolate $\text{P-CH}_2\text{S(CH}_2\text{)}_4\text{S}^-$ which could react with a second chloromethyl site in the polymer to give double coupling (Scheme 16).

In order to limit the formation of doubly bound species, the formation of polymer bound thiolate had to be prevented, both through control of the number of dithiolate anions present in the medium and of the proton exchange reaction. This control could be achieved through the use of a three phase system in which most of the reactive thiolate ions are kept in the aqueous layer away from the polymer. The polymer phase was swollen in benzene and an aqueous solution containing NaOH and 1,4-butanedithiol was added.
SCHEME 16: Site-site interactions in the reaction of \( \text{P-CH}_2\text{Cl} \) with dithiols

\[
\begin{align*}
\text{I} & : \text{P-CH}_2\text{Cl} + \text{HS-S}^\ominus \rightarrow \text{P-CH}_2\text{-S}^\ominus\text{SH} \\
\text{II} & : \text{P-CH}_2\text{-S}^\ominus\text{SH} \text{ (single coupling)} \\
\text{III} & : \Theta_{\text{S-S}}^\ominus \text{P-CH}_2\text{-S}^\ominus\text{S}^\ominus \\
\text{IV} & : \text{P-CH}_2\text{-S}^\ominus\text{S}^\ominus\text{S}^\ominus\text{CH}_2\text{-P} \text{ (double coupling)}
\end{align*}
\]
A phase transfer catalyst such as (Bu)$_4$NOH was used to carry the reactive thiolate species into the organic layer. Using this approach, only a small amount of thiolate can ever be present in the organic phase, and in addition, since it is known that dianions are transported less easily under phase transfer conditions than monoanions$^{211}$, the influence of the dithiolate on the reaction should be greatly reduced. Our results seemed to confirm this expectation, as illustrated by the reaction carried out in DMF and under phase transfer conditions with the same base to dithiol ratio (Table 6, expts 2,5) in which double coupling was drastically reduced using the three phase system (39% vs 94%). Double coupling could be reduced to $\sim$5% by a modest increase in the base to dithiol ratio (Table 6, expts 7,8). Since phase transfer reactions are best carried out with fairly concentrated aqueous phases, it was not practical to test the reaction under conditions in which the base: dithiol ratio would approach the value of 1:12 used to reduce double coupling in DMF (Table 6, expt 3). Under such phase transfer conditions essentially no double coupling would be expected; however, when the amount of base was drastically reduced, the phase transfer reaction became very slow and, after 24 hr. the polymer still contained appreciable amounts of unreacted chlorine.

Double coupling could be increased to $\sim$87% by using a 2:1 ratio of base to dithiol to convert all the dithiol to the dianion (Table 6, expt 4). This overcame the preference of the phase transfer catalyst for singly over doubly charged species and ensured that only polymer bound thiolate (P)-CH$_2$S(CH$_2$)$_4$S was formed. In addition, the proton exchange reaction was suppressed since there was no thiol present to donate a proton to the polymer bound thiolate to give (P)-CH$_2$S(CH$_2$)$_4$SH. Thus, a large percentage of double coupling was expected and observed.
In this system, the extent of intraresin reaction can be reliably and reproducibly controlled by a simple variation in the reaction conditions. In general, reduction of double coupling is the aim as, for example, in the preparation of mono derivatives of symmetrical difunctional molecules. However, occasionally large amounts of double binding are desirable to anchor a polyfunctional molecule firmly to the polymer and this can also be provided using this method.

The use of phase transfer catalysis to control the amount of site-site interactions can be applied to other substrates containing groups such as hydroxyl and carboxyl, which are reactive in nucleophilic displacements only in their anionic forms.

h) Preparation of P-CH₂SH

P-CH₂SH has been prepared by reaction of P-CH₂Cl with thiourea to give an isothiouronium salt P-CH₂S-C\(^{\text{NH₂-HCl}}\), followed by reaction with base to give the thiomethylated polystyrene in a functional yield of 89%. However, subsequent reactions with this polymer proceeded only in yields of 20-45%, which suggested that a large proportion of the sulfur in the original polymer may not have been present as thiol groups.

We have reinvestigated this reaction with 1% crosslinked P-CH₂Cl using the same procedure for the preparation of the isothiouronium salt but different conditions for the second, more critical step, in which the thiol is formed. The reaction with the hydroxide ion was carried out using phase transfer conditions under an inert atmosphere to prevent the formation of disulfides through interaction between the functional groups on the polymer. Using this procedure, P-CH₂SH was obtained in better than
95% functional yield, based on elemental analysis. The infrared spectrum of the polymer contained an absorption due to SH centered at 2580 cm\(^{-1}\), and a test reaction with the polymer showed that all the thiol groups were reactive (see p. 89 in this thesis).

If however, the polymeric isothiouronium salt was treated with base under phase transfer conditions without the exclusion of atmospheric oxygen, the resulting polymer contained a large amount of sulfur, which indicated a very high functional yield, but showed no SH band in the infrared spectrum. If this polymer was then treated with lithium aluminum hydride to reduce any disulfide bonds, the SH absorption reappeared. This observation showed once again that extensive site-site interactions do exist in 1% crosslinked polystyrene due to the mobility of the polymer chains. In applications involving \(\text{P}-\text{CH}_2\text{SH}\) in basic medium, it is essential that all reactions be carried out under inert atmosphere to prevent formation of disulfides, which decrease the reactivity of the polymer.

**Preparation and Reactions of Lithiated Polystyrene \(\text{P}^{-}\text{Li}\)**

Polystyryl lithium \(\text{P}^{-}\text{Li}\) is another widely used starting material in the preparation of chemically modified polystyrene resins. Two main reaction routes have been studied for the production of \(\text{P}^{-}\text{Li}\): the direct lithiation of polystyrene with N,N,N',N'-tetramethylethylenediamine (TMEDA) -n-butyllithium complexes and the metal-halogen exchange reaction between \(\text{P}^{-}\text{Br}\) and excess n-BuLi.

a) \(\text{P}^{-}\text{Li}\) by Direct Lithiation

The direct lithiation of insoluble polystyrene resins by reaction with a 1:1 complex of n-BuLi and TMEDA has been reported by Fyles and Leznoff\(^{46}\). This method is attractive as it is a rapid, one-step preparation which does not require the use of an already functionalized polymer as starting material.
However the degree of functionalization obtained in this reaction was quite low, usually less than 0.11 for 2% crosslinked polystyrene.

We investigated this reaction further with the aim of increasing the degree of functionalization since, in a number of applications, it would be desirable to obtain more highly substituted resins. Our procedure involved the reaction of an amine-n-butyllithium complex with a 1% crosslinked resin at 65-70°C in a non-polar solvent. A specially designed reaction flask (Fig. 1) was used to allow removal of excess reagent and washing of the lithiated resin with fresh solvent under anhydrous conditions. The minimum degree of functionalization was determined by quenching the washed \( \text{P-Li} \) with a slurry of dry ice in THF to give a carboxylated resin \( \text{P-COOH} \). This reaction was a good probe to determine the extent of the lithiation reaction as it was known to proceed in good yield, and the carboxyl groups produced could be accurately titrated using an excess of a standard n-BuLi solution and back titrating with aqueous standard acid using phenolphthalein as indicator. However, we found that the literature procedure for this titration was not satisfactory for the high concentrations of carboxyl groups obtained in our reactions, as the benzene used as a swelling agent isolated the polymer, which contained some excess n-BuLi, from the aqueous titrating agent. The trapped excess base, plus the phenolphthalein indicator, gave the polymer a pink colour which did not disappear even when more than one equivalent of acid had been added. Using anhydrous tetrahydrofuran as the swelling agent in the reaction between \( \text{P-COOH} \) and n-BuLi and quenching the excess reagent with EtOH rather than water gave a solvent system
FIGURE 1: Flask for Anhydrous Reactions of Polymers

SEPTUM INLET → TO CONDENSER, DRYING TUBE, etc...

INERT GAS INLET

OUTLET

FRITTED GLASS FILTER
which was sufficiently miscible with water that the aqueous acid could reach all the unreacted base and sharp end points were obtained in the titration.

The results obtained in the direct lithiation study are shown in Table 7. As can be seen, the best results were obtained using TMEDA complexes in a non-polar hydrocarbon solvent such as cyclohexane or heptane. An increase in the molar ratio of TMEDA to n-BuLi from 0.7:1 to 1.9:1 did not change the degree of functionalization, while shorter reaction times produced a noticeable decrease. However, increasing the reaction time beyond 4 hours had no further effect on D.F.. Aromatic solvents such as benzene or polar solvents such as THF were unsuitable for the reaction. In a second series of experiments, triethylenediamine (TEDA) was used as the complexing agent instead of TMEDA, but the reaction was quite sluggish and a reaction time of 24 hr was required to achieve a functionalization of 1.1 mequiv/g of P-COOH.

In our experiments with TMEDA-n-BuLi complexes, we observed that a degree of functionalization of 0.23 seemed to be the maximum which could be obtained after carboxylation. This same limit was also observed in the preparation of other functional groups from P-Li prepared by direct lithiation (p88, this thesis). Presumably this was due to the fact that the solvents which must be used for the reaction were unable to swell the resin and the penetration of the relatively bulky TMEDA-n-BuLi complex into the pores of the resin was severely limited and only the most accessible sites on the polymer could be lithiated.

Two conflicting reports on the position of substitution of the aromatic rings of soluble polystyrene in the direct lithiation reaction have appeared in the literature. A deuteration study by Chalk indicated that the substitution occurred at the ortho and para positions in a 1:4 ratio while
Table 7

Direct Lithiation of Crosslinked Polystyrene

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Polystyrene (mequiv.)</th>
<th>Amine used (mmoles)</th>
<th>n-BuLi (mmoles)</th>
<th>reaction conditions</th>
<th>P-COOH mequiv/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclohexane</td>
<td>27</td>
<td>TMEDA (25)</td>
<td>34</td>
<td>65°, 4.5h</td>
<td>2.0</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>25</td>
<td>TMEDA (25)</td>
<td>27</td>
<td>70°, 1.5h</td>
<td>1.4</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>25</td>
<td>TMEDA (56)</td>
<td>30</td>
<td>67°, 4h</td>
<td>2.0</td>
</tr>
<tr>
<td>heptane</td>
<td>26</td>
<td>TMEDA (25)</td>
<td>27</td>
<td>68°, 3h</td>
<td>1.52</td>
</tr>
<tr>
<td>Benzene</td>
<td>26</td>
<td>TMEDA (25)</td>
<td>27</td>
<td>70°, 3.5h</td>
<td>0.15</td>
</tr>
<tr>
<td>Tetrahydrofuran</td>
<td>24</td>
<td>TMEDA (25)</td>
<td>35</td>
<td>75°, 3h</td>
<td>0</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>30</td>
<td>TEDA (24)</td>
<td>25</td>
<td>65°, 3h</td>
<td>0.4</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>19</td>
<td>TEDA (18)</td>
<td>18</td>
<td>70°, 4h</td>
<td>0.6</td>
</tr>
<tr>
<td>cyclohexane</td>
<td>24</td>
<td>TEDA (22)</td>
<td>32</td>
<td>70°, 24h</td>
<td>1.1</td>
</tr>
</tbody>
</table>

a TMEDA = tetramethylethylenediamine; TEDA = triethylenediamine.
a $^{13}\text{CH}_3\text{I}$ quenching study by Evans showed substitution in the meta and para positions in a 2:1 ratio. Since the methyl iodide quenching study was carried out under conditions which gave a very low degree of functionalization (0.05), we decided to reinvestigate this reaction to see if an increase in the degree of functionalization would result in a change in the substitution pattern.

We prepared soluble lithiated polystyrenes by direct lithiation using a variety of bases (n-BuLi, t-BuLi), complexing agents (TMEDA, TEDA) and reaction conditions, and quenched them with methyl iodide to give $^{\text{P}}\text{-CH}_3$ with degrees of functionalization in the range 0.19 - 0.5. Study of the methylated polystyrenes by $^{13}\text{C}$ NMR spectroscopy confirmed the results of Evans and co-workers. In every case, regardless of the degree of functionalization or of the metalating complex used, the polymer showed aromatic substitution in the meta and para positions in a 2:1 ratio (Table 8, Fig. 2).

b) $^{\text{P}}$-Li by Bromination-Lithiation

The failure of the direct lithiation procedure to give high degrees of functionalization led us to consider the more laborious two step procedure for generating $^{\text{P}}$-Li. The halogenation-lithiation route developed by Braun for soluble polystyrene had been used by several groups to prepare lithiated polystyrene from $^{\text{P}}$-Br. The method is not without its problems however, as the literature procedures for the bromination of polystyrene leave something to be desired, and the metalation reactions are often incomplete, leaving unreacted functional groups on the polymer which may prove troublesome in further reactions or in the characterization of the polymers.
TABLE 8: Chemical Shifts in $^{13}$C NMR Spectra of Standard o,m and p-Methyl Polystyrene and of CH$_3$I Quenched F-Li Polymer

<table>
<thead>
<tr>
<th>Structure</th>
<th>Polymeric Methyl Polystyrene$^a$</th>
<th>m-Methyl Polystyrene$^a$</th>
<th>p-Methyl Polystyrene$^a$</th>
<th>Methyl Polystyrene$^b$ From Direct Lithiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon Atom#</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>143.8</td>
<td>145.4-146.5</td>
<td>142.6-143.0</td>
<td>145.3-145.9</td>
</tr>
<tr>
<td>2</td>
<td>136.4</td>
<td>128.4-129.1</td>
<td>127.7</td>
<td>126.3-128.6</td>
</tr>
<tr>
<td>3</td>
<td>130.5</td>
<td>137.1-137.3</td>
<td>128.7</td>
<td>137.1-137.2</td>
</tr>
<tr>
<td>4</td>
<td>125.8-126.2</td>
<td>126.5-126.9</td>
<td>134.6-134.8</td>
<td>134.6-134.8</td>
</tr>
<tr>
<td>5</td>
<td>125.8-126.2</td>
<td>127.8-128.2</td>
<td>128.7</td>
<td>126.3-128.6</td>
</tr>
<tr>
<td>6</td>
<td>125.8-126.2</td>
<td>124.7-124.8</td>
<td>127.7</td>
<td>126.3-128.6</td>
</tr>
<tr>
<td>7</td>
<td>43.8-47.0</td>
<td>42.6-44.2</td>
<td>42.7-44.5</td>
<td>41.1-44.5</td>
</tr>
<tr>
<td>8</td>
<td>34.3-34.9</td>
<td>40.5-40.6</td>
<td>40.1-40.7</td>
<td>40.5</td>
</tr>
<tr>
<td>9</td>
<td>18.3-19.2</td>
<td>21.5</td>
<td>21.1</td>
<td>21.4</td>
</tr>
</tbody>
</table>

a) data from reference 48.

b) The left hand side column corresponds to the meta substituted and the right hand side column applies to the para substituted polystyrene. Where one line is observed for both isomers in the spectrum only one entry is made.
FIGURE 2: $^{13}$C NMR Spectrum of (±)-Cl$_3$ Substituted meta and para (d.f.=0.50)
We have reinvestigated both the bromination and lithiation steps of this sequence in order to develop a reliable procedure for preparing \( \text{P}-\text{Li} \) in high functional yields without any residual \( \text{P}-\text{Br} \) as contaminant\(^{210}\). The first step in this process is the preparation of reactive \( \text{P}-\text{Br} \) with the desired degree of substitution. The method used most often in the literature involves the reaction of the insoluble polystyrene resin with bromine in the presence of ferric chloride as catalyst. However, this reaction has been reported to give unreproducible results\(^{53,54}\) and the degree of functionalization obtained cannot be predicted in advance. In addition coloured products of low quality and lacking homogeneity\(^{56}\) are sometimes obtained which can be partially or completely unreactive towards lithiation by n-BuLi\(^{13}\).

A more reliable procedure involves the reaction of polystyrene with a stoichiometric amount of thallic acetate followed by displacement of the thallium on the aromatic ring by bromine\(^{53-56}\) (eqn. 24).

\[
\text{P} \quad \text{Tl(OAc)}_3 \quad \text{P-Tl(OAc)}_2 \quad \text{Br}_2 \quad \text{P-Br + Tl(OAc)}_2\text{Br} \quad \text{(eqn. 24)}
\]

The drawbacks of this method are its cost, as large amounts of thallic acetate are used (eg. 100 g of \( \text{Tl(OAc)}_3 \cdot \frac{1}{2} \text{H}_2\text{O} \) for 50 g polymer) and the difficulties experienced in the removal of the sparingly soluble thallium (III) salts produced in the reaction from the solid polymer. For example when we prepared polystyryl bromide using this method, an extensive washing procedure,
including a six day extraction of the polymer with methanol using a Soxhlet extractor, was necessary to purify the polymer. Removal of these impurities is critical, as we have observed that thallium salts act as Friedel-Crafts catalysts and can promote undesired reactions on the polymer in later steps.

We studied the bromination of cross-linked polystyrene with the aim of developing a reliable, convenient, and inexpensive procedure for the preparation of clean and homogeneous polymers with a readily predictable degree of functionalization. As can be seen from Table 9, the ferric chloride catalyzed reaction gave reasonably consistent results when the bromination was carried out in refluxing carbon tetrachloride in the dark. The degree of substitution could be controlled by varying the amount of bromine used in the reaction. Although high degrees of functionalization could be obtained using an excess of bromine, polybromination was not observed under the reaction conditions. Protecting the reaction mixture from light prevented the formation of benzylic bromination products by light initiated free radical pathways.

Even better results could be obtained using thallic acetate, in catalytic rather than stoichiometric amounts, to promote the bromination reaction. The disappearance of bromine at CCl₄ reflux temperature was rapid, and the polymers obtained were almost colourless and had a cleaner appearance than those obtained using the ferric chloride catalyst. Control of the degree of functionalization presented no problem, as virtually all of the bromine added was incorporated in the polymer (Table 9). The progress of the reaction was independent of the amount of thallic acetate used; thus very small amounts of the catalyst could be employed and extensive washing of the
<table>
<thead>
<tr>
<th>Exp.</th>
<th>Catalyst</th>
<th>molar ratio catalyst/PS</th>
<th>molar ratio Bromine/PS</th>
<th>mequiv. Bromine per gram</th>
<th>Degree of Functionalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>FeCl₃</td>
<td>1:77</td>
<td>1.12:1</td>
<td>4.97</td>
<td>0.85</td>
</tr>
<tr>
<td>2</td>
<td>FeCl₃</td>
<td>1:61</td>
<td>1.12:1</td>
<td>5.32</td>
<td>0.96</td>
</tr>
<tr>
<td>3</td>
<td>FeCl₃</td>
<td>1:37.5</td>
<td>0.39:1</td>
<td>2.87</td>
<td>0.39</td>
</tr>
<tr>
<td>4</td>
<td>Tl(OAc)₃</td>
<td>1:9.6</td>
<td>0.42:1</td>
<td>2.89</td>
<td>0.39</td>
</tr>
<tr>
<td>5</td>
<td>Tl(OAc)₃</td>
<td>1:270</td>
<td>0.11:1</td>
<td>1.03</td>
<td>0.11</td>
</tr>
<tr>
<td>6</td>
<td>Tl(OAc)₃</td>
<td>1:105</td>
<td>0.21:1</td>
<td>1.76</td>
<td>0.21</td>
</tr>
<tr>
<td>7</td>
<td>Tl(OAc)₃</td>
<td>1:366</td>
<td>0.25:1</td>
<td>2.06</td>
<td>0.25</td>
</tr>
<tr>
<td>8</td>
<td>Tl(OAc)₃</td>
<td>1:50</td>
<td>0.41:1</td>
<td>2.66</td>
<td>0.35</td>
</tr>
<tr>
<td>9</td>
<td>Tl(OAc)₃</td>
<td>1:62</td>
<td>0.44:1</td>
<td>3.10</td>
<td>0.43</td>
</tr>
<tr>
<td>10</td>
<td>Tl(OAc)₃</td>
<td>1:94</td>
<td>0.88:1</td>
<td>5.07</td>
<td>0.88</td>
</tr>
<tr>
<td>11</td>
<td>TlCl₃</td>
<td>1:58</td>
<td>1.25:1</td>
<td>6.05ᵇ</td>
<td>&gt;1</td>
</tr>
<tr>
<td>12</td>
<td>TlCl₃</td>
<td>1:68</td>
<td>1.16:1</td>
<td>5.16</td>
<td>0.91</td>
</tr>
<tr>
<td>13</td>
<td>TlCl₃</td>
<td>1:78</td>
<td>0.4:1</td>
<td>2.95</td>
<td>0.40</td>
</tr>
<tr>
<td>14</td>
<td>TlCl₃</td>
<td>1:61</td>
<td>0.43:1</td>
<td>3.15</td>
<td>0.43</td>
</tr>
<tr>
<td>15</td>
<td>Tl salt³</td>
<td>-</td>
<td>0.48:1</td>
<td>3.19</td>
<td>0.44</td>
</tr>
</tbody>
</table>

a) Typical reaction conditions were as follows: reaction in CHCl₃ 1 hour at room temperature followed by 1 3/4 hours at reflux.

b) Reaction at reflux temperature for 24 hours.

c) Thallium salt recovered from exp. 4
product to remove thallium salt impurities was no longer necessary.

To test if other thallium (III) salts were also useful catalysts, the reaction was attempted using TlCl₃ as a catalyst. In every case, the bromination results were comparable to those obtained with Tl(OAc)₃. Polybromination could be achieved but only using an excess of bromine and a 24 hour reflux period. Even the insoluble thallium salt, recovered from the extraction of P-Br made with a stoichiometric amount of Tl(OAc)₃, proved an excellent catalyst in the reaction. This result is not surprising though, as the active agent in the catalytic thallium (III) acetate reaction must be of similar structure.

Other catalysts such as ZnCl₂ and SnCl₄ were tried but were not very reactive and gave polymers with low degrees of functionalization.

An interesting result was obtained when the bromination reaction was carried out in acetic acid; the reaction mixture containing the polymer gradually became homogeneous as the polymer dissolved. Cleavage of the polymer was extensive as evidenced by the low viscosity ([η] = 0.155, 30°C, toluene) of the brominated polymer after 1 day of reaction. This depolymerization was, however, only observed when acetic acid was used in conjunction with the TlCl₃ or FeCl₃ catalyst.

The iodination of cross-linked polystyrene with thallic trifluoroacetate and iodine could not be converted to a catalytic reaction as the thallium (III) trifluoroacetate was reduced to a thallium (I) salt during the reaction. Thus the degree of functionalization of the P-I obtained depends upon the amount of Tl(OOCF₃)₃ used (eqn. 25).
\[
\text{P} + \text{Tl}[(\text{OCOCF}_3)_3] \rightarrow \text{P}-\text{Tl}[(\text{OCOCF}_3)_2] + \text{CF}_3\text{COOH} \rightleftharpoons \text{I}_2 \rightarrow \text{P}-\text{I} + \text{TlI} + 2\text{CF}_3\text{COO}^- \\
(\text{eqn. 25}).
\]

Once again, the large amount of \(\text{Tl}[(\text{OCOCF}_3)_3]\) required and the necessity of removing the insoluble thallium salts produced are major drawbacks to the use of this procedure to prepare \(\text{P}-\text{I}\).

The exact position of substitution on the aromatic rings of polystyryl bromides and iodides made by these methods was studied using \(^{13}\text{C}\) NMR spectroscopy on soluble polymers prepared by similar routes. Authentic samples of soluble o, m, and p-bromopolystyrenes were made by free radical polymerization of the corresponding ring-brominated styrenes.

Soluble polystyrene of molecular weight 20,000 was brominated using \(\text{FeCl}_3\) or \(\text{Tl}(\text{OAc})_3\) as catalyst and the \(^{13}\text{C}\) NMR spectra of the resulting brominated polymers (Table 10) were compared with those of polystyrene and the pure samples of o, m, and p-polystyryl bromide (Table 11). In both cases, the \(^{13}\text{C}\) NMR spectra of the polymers prepared by catalytic bromination showed only signals due to unreacted polystyrene units or p-bromopolystyrene units; no trace of any ortho or meta substitution could be seen.

Soluble \(\text{P}-\text{I}\) was prepared by reaction of soluble polystyrene with an equimolar amount of thallic trifluoroacetate and iodine. In this case, removal of the insoluble by-products presented no problems as they could be filtered from the soluble polymer. Although \(^{13}\text{C}\) NMR spectra of authentic samples of o, m and p-poly(iodostyrene) were not available, the substitution pattern of \(\text{P}-\text{I}\) made with \(\text{Tl}[(\text{OCOCF}_3)_3]\) could be determined by comparing
TABLE 10  Chemical shifts in $^{13}$C-NMR spectra of polystyrene and standard o, m, and p-bromopolystyrenes.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Polystyrene</th>
<th>o-bromopolystyrene</th>
<th>m-bromopolystyrene</th>
<th>p-bromopolystyrene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure</td>
<td>(C—C)</td>
<td>(C—C)</td>
<td>(C—C)</td>
<td>(C—C)</td>
</tr>
<tr>
<td>Carbon Atom #</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>$145.34$</td>
<td>$143.6$</td>
<td>$146.9, 146.6$</td>
<td>$143.3$</td>
</tr>
<tr>
<td>2.</td>
<td>$127.99 - 127.76$</td>
<td>$132.7$</td>
<td>$129.96, 129.50$</td>
<td>$129.37$</td>
</tr>
<tr>
<td>3.</td>
<td>$127.99 - 127.76$</td>
<td>$127.42$</td>
<td>$122.43$</td>
<td>$131.44$</td>
</tr>
<tr>
<td>4.</td>
<td>$125.7$</td>
<td>$127.42$</td>
<td>$129.96, 129.50$</td>
<td>$119.84$</td>
</tr>
<tr>
<td>5.</td>
<td>$127.99 - 127.76$</td>
<td>$125.48$</td>
<td>$129.96, 129.50$</td>
<td>$131.44$</td>
</tr>
<tr>
<td>6.</td>
<td>$127.99 - 127.76$</td>
<td>$127.42$</td>
<td>$126.17$</td>
<td>$129.37$</td>
</tr>
<tr>
<td>7.</td>
<td>$42.4 - 45.5^a$</td>
<td>$41.1 - 45.2^a$</td>
<td>$41.8 - 44.9^a$</td>
<td>$41.0 - 44.3^a$</td>
</tr>
<tr>
<td>8.</td>
<td>$40.75$</td>
<td>$38.42$</td>
<td>$40.53$</td>
<td>$40.28$</td>
</tr>
</tbody>
</table>

$^a$ Broad band.
TABLE 11: Chemical shifts\(^a\) in \(^{13}\text{C}\)-NMR of partially halogenated polystyrenes.

<table>
<thead>
<tr>
<th>Method of Preparation</th>
<th>FeCl(_3) Catalyzed Bromination</th>
<th>Tl (OAc)(_3) Catalyzed Bromination</th>
<th>Tl (O-CO-CF(_3))(_3) Catalyzed Iodination(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.F</td>
<td>0.65</td>
<td>0.40</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Carbon Atom #

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>143.6 - 144.2</td>
<td>144.6 - 145.1</td>
<td>144.62 - 145.14 (146.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>127.62, 128.27</td>
<td>129.28</td>
<td>127.59, 128.14</td>
<td>129.3.</td>
<td>127.60, 128.16</td>
<td>129.63 (130.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>127.62, 128.27</td>
<td>131.29</td>
<td>127.59, 128.14</td>
<td>131.12</td>
<td>127.60 128.16</td>
<td>137.10 (138.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>126.07</td>
<td>119.65</td>
<td>125.86</td>
<td>119.39</td>
<td>125.85</td>
<td>90.82 (93.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>127.62, 128.27</td>
<td>131.29</td>
<td>127.59, 128.14</td>
<td>131.12</td>
<td>127.60, 128.16</td>
<td>137.10 (138.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>127.62, 128.27</td>
<td>129.28</td>
<td>127.59, 128.14</td>
<td>129.31</td>
<td>127.60, 128.16</td>
<td>129.63 (130.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>41.1 - 44.9 (Br)</td>
<td>42.4 - 45.4 (Br)</td>
<td>41.5 - 45.9 (Br)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>40.2 - 40.3</td>
<td>40.38</td>
<td>40.43</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) For each method of synthesis the left hand side column corresponds to the unsubstituted units and the right hand side column applies to the halogenated styrene units. Where one line is observed a single entry is made.

\(^b\) Number in parenthesis correspond to calculated values for p-iodopolystyrene (see ref 214). Calculated values for m-iodopolystyrene did not fit with the measured data.
the $^{13}$C NMR spectrum obtained for this polymer with that calculated for m-and p-polystyryl iodide using the method of Stothers. Not surprisingly, the substitution seemed to occur exclusively in the para position (Table 10).

We have used the insoluble polystyryl bromides, prepared by the catalytic brominations described above, to produce lithiated polystyrene by reaction with n-BuLi under a variety of conditions, and have found that the outcome of the reaction varied considerably, depending on the type of polymer used, its degree of bromination, and the solvent used in the lithiation.

Brominated macroreticular resins were found to react completely with an excess of n-BuLi in tetrahydrofuran, even when the starting resin contained a large proportion of brominated aromatic rings. In contrast, the extent of lithiation of 1% cross-linked resins in THF depended upon the degree of functionalization. Almost complete removal of bromine could be accomplished in one reaction with n-butyllithium for polymers containing 1-1.5 mequiv Br/g. However, more substituted resins required several successive treatments with this reagent to displace all the bromine. For example, a polymer containing three mequiv. of bromine per gram, when allowed to react with excess n-BuLi in THF and quenched in methanol, yielded a product which still contained 1.9 mequiv Br/g. A second treatment under the same conditions reduced the bromine content to 0.6 mequiv/g and a third treatment effected complete removal of the bromine.

A second study which used the quenching of the $^P$-Li with dry ice to give $^P$-COOH was then undertaken. The results of this carboxylation study confirmed that THF was not an ideal solvent for the lithiation of swellable $^P$-Br polymers (Table 12). Cyclohexane also gave incomplete removal
Table 12: Carboxylation of Lithiated Polystyrene

<table>
<thead>
<tr>
<th>Starting resin Br, mequiv/g</th>
<th>Molar ratio BuLi/Br</th>
<th>Solvent</th>
<th>Product COOH, mequiv/g</th>
<th>Product Br, mequiv/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.89</td>
<td>4:1</td>
<td>THF</td>
<td>1.4</td>
<td>1.53</td>
</tr>
<tr>
<td>2.89</td>
<td>3:1</td>
<td>Cyclohexane</td>
<td>1.3</td>
<td>1.45</td>
</tr>
<tr>
<td>2.89</td>
<td>3:1</td>
<td>Benzene</td>
<td>2.9</td>
<td>0</td>
</tr>
<tr>
<td>2.78</td>
<td>2.4:1</td>
<td>Toluene</td>
<td>2.7</td>
<td>0</td>
</tr>
</tbody>
</table>
of the bromine, while reaction in benzene or toluene proceeded quantitatively to give $\text{CHO}_2$, uncontaminated by any residual $\text{Br}_2$.

The difference in behavior between cyclohexane and benzene or toluene could be explained by considering the swelling properties of these solvents. In benzene or toluene, the 1% crosslinked resin was fully swollen which allowed easy penetration of the n-BuLi into the interior of the polymer beads, while in cyclohexane the resin was only partially swollen, and therefore a number of reactive sites were located in pores which were inaccessible to the reagent.

This explanation could not account for the difference of reactivity between tetrahydrofuran and benzene or toluene however, as all three solvents have excellent swelling properties. It seemed more likely that the explanation lay in the polar nature of the tetrahydrofuran solvent which could increase the ionic repulsions between the negative charges on the partially lithiated polymer and the n-butyllithium and limit the accessibility of the reagent to the unreacted sites in this way.

A comparison of the bromination-lithiation versus the direct lithiation procedure would indicate that the one-step preparation is the method of choice, because of its ease and rapidity, for applications in which the amount and the position of substitution on the aromatic ring is not critical. However, the more laborious but more versatile bromination-lithiation route is preferred when careful control over the degree of functionalization is required, or when steric factors are likely
to play a part in the subsequent reactions of the polymer, since the bromination procedure can give predictable results over a wide range of degrees of functionalization and the substitution pattern is exclusively para. In addition, since the resin is fully swollen during the bromination reaction, a more even distribution of the functional groups on the polymer would be expected than in the case of the direct lithiation, which takes place in a non-swelling solvent. This would be an advantage at higher degrees of substitution where overcrowding of the functional groups can occur.

c) Reactions of \( (\text{P}) - \text{Li} \)

To test the reactivity of the polystyryllithium resin and to explore its application to the preparation of polystyrene resins containing various functional groups, a number of reactions were studied. (Schemes 17 and 18). In all these cases, the lithiated resin was prepared in situ using the reaction flask shown in Fig. 1 from \( (\text{P}) - \text{Br} \), since this procedure allowed the calculation of a functional yield for each reaction. For the reactions shown in Scheme 17, the yield could be estimated by titration (for \( (\text{P}) - \text{COOH} \)) or by elemental analysis. Derivatives of the products formed in the reactions shown in Scheme 18 had to be prepared as shown before yields could be determined. The yields obtained in these reactions are shown in Table 13.

The reaction of \( (\text{P}) - \text{Li} \) with dry ice to give \( (\text{P}) - \text{COOH} \) has already been described and the preparation of \( (\text{P}) - \text{SH} \) will be discussed in the next section.

Polymeric sulfides can be prepared by reaction of \( (\text{P}) - \text{Li} \) with dialkyl-disulfides. We have used this reaction to prepare a series of polymeric
SCHEME 17: Reactions of \(\text{P}-\text{Li}\)
SCHEME 18: Reactions of $\text{P-Li}$

I $\rightarrow$ XIII $\rightarrow$ XIV $\rightarrow$ XV

I $\rightarrow$ XI $\rightarrow$ XIV

I $\rightarrow$ XII $\rightarrow$ XV
<table>
<thead>
<tr>
<th>Precursor $\mathbf{P}$-Br</th>
<th>mequiv./g</th>
<th>degree of functionalization</th>
<th>Reagent</th>
<th>Product structure $^b$</th>
<th>mequiv./g</th>
<th>degree of functionalization</th>
<th>functional yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.89</td>
<td>0.39</td>
<td></td>
<td>$\text{CO}_2$</td>
<td>II $\mathbf{P}$-COOH</td>
<td>2.9</td>
<td>0.35</td>
<td>90%</td>
</tr>
<tr>
<td>2.8</td>
<td>0.37</td>
<td></td>
<td>$\text{S}_8$</td>
<td>III $\mathbf{P}$-SH</td>
<td>2.37</td>
<td>0.27</td>
<td>73%</td>
</tr>
<tr>
<td>3.1</td>
<td>0.43</td>
<td></td>
<td>$\text{CH}_3\text{S-SCH}_3$</td>
<td>IV $\mathbf{P}$-SCH$_3$</td>
<td>2.6</td>
<td>0.31</td>
<td>72%</td>
</tr>
<tr>
<td>2.89</td>
<td>0.39</td>
<td></td>
<td>$\text{B}(\text{OCH}_3)_3$</td>
<td>V $\mathbf{P}$-B(OH)$_2$</td>
<td>3.15</td>
<td>0.38</td>
<td>97%</td>
</tr>
<tr>
<td>2.89</td>
<td>0.39</td>
<td></td>
<td>$\text{C}_6\text{H}_5$-N=C=O</td>
<td>VI $\mathbf{P}$-CO-NH-$\text{C}_6\text{H}_5$</td>
<td>2.2</td>
<td>0.31</td>
<td>80%</td>
</tr>
<tr>
<td>3.1</td>
<td>0.43</td>
<td></td>
<td>$\text{Si(CH}_3)_2\text{Cl}_2$</td>
<td>VII $\mathbf{P}$-Si($\text{CH}_3)_2\text{Cl}$</td>
<td>2.2</td>
<td>0.28</td>
<td>65%</td>
</tr>
<tr>
<td>2.8</td>
<td>0.37</td>
<td></td>
<td>$\text{ClP(C}_6\text{H}_5)_2$</td>
<td>VIII $\mathbf{P}$-P($\text{C}_6\text{H}_5)_2$</td>
<td>1.92</td>
<td>0.31</td>
<td>84%</td>
</tr>
<tr>
<td>1.76</td>
<td>0.21</td>
<td></td>
<td>Br$\text{CH}_2\text{CH}_2\text{Br}$</td>
<td>IX $\mathbf{P}$-CH$_2\text{CH}_2\text{Br}$</td>
<td>1.13</td>
<td>0.14</td>
<td>67%</td>
</tr>
<tr>
<td>2.8</td>
<td>0.37</td>
<td></td>
<td>(CH$_3)_2\text{N-CHO}$</td>
<td>X $\mathbf{P}$-CHO</td>
<td>2.3$^c$</td>
<td>0.26</td>
<td>70%</td>
</tr>
<tr>
<td>2.89</td>
<td>0.39</td>
<td></td>
<td>$\text{CH}_2\text{-CH}_2$</td>
<td>XI $\mathbf{P}$-CH$_2\text{CH}_2\text{OH}$</td>
<td>2.8$^c$</td>
<td>0.33</td>
<td>85%</td>
</tr>
<tr>
<td>2.8</td>
<td>0.37</td>
<td></td>
<td>$\text{C}_6\text{H}_5$-CO-$\text{C}_6\text{H}_5$</td>
<td>XII $\mathbf{P}$-C($\text{C}_6\text{H}_5)_2$OH</td>
<td>1.4$^c$</td>
<td>0.20</td>
<td>54%</td>
</tr>
</tbody>
</table>

$^a$ Reactions performed using 1% crosslinked brominated polystyrene using n-butyllithium in benzene for the lithiation.

$^b$ Numerals refer to structures shown in schemes 17 and 18.

$^c$ Calculated from the elemental analysis of a derivative; see scheme 18.
sulfides with different alkyl groups to serve as precursors for polymeric sulfonium salts (see Part 2 of this thesis).

Treatment of \( \text{P}^-\text{Li} \) with an excess of trimethyl borate and hydrolysis gave a polymeric boronic acid \( \text{P}^-\text{B(OH)}_2 \), which is a useful selective protecting group for polyhydroxy compounds such as sugars.\(^{52,70,71}\)

Reaction of \( \text{P}^-\text{Li} \) with isocyanates yields polymeric amides, for example (eqn 26).

\[
\text{P}^-\text{Li} + \text{N}=\text{C}=\text{O} \rightarrow \text{P}^-\text{C}=\text{N}=\text{O} \rightarrow \text{P}^-\text{C}=\text{NH} \quad \text{(eqn 26)}.
\]

The polymeric N-chloroamide \( \text{P}^-\text{CO-N-Ph} \), which is formed from this product by reaction with t-butyl hypochlorite, can be used as an oxidizing agent\(^{154}\) for alcohols or sulfides.

Silicon containing polymers of the type \( \text{P}^-\text{Si(CH}_3)_2\text{Cl} \) could be obtained by reaction of \( \text{P}^-\text{Li} \) with dichlorodimethylsilane. Preliminary experiments showed that this polymer had potential utility as a protecting group in the preparation of mono derivatives of symmetrical diols (eqn 27).

\[
\begin{align*}
\text{P}^-\text{Si-Cl} + \text{HO-OH} & \xrightarrow{\text{pyridine}} \text{P}^-\text{Si-O-OH} \\
\text{P}^-\text{Si-O-OCPh} & \xrightarrow{\text{H}_2\text{O}} \text{P}^-\text{Si-OH} + \text{HO-OC-Ph} \\
\text{P}^-\text{Si-O-OCPh} & \xrightarrow{\text{H}_2\text{O}} \text{P}^-\text{Si-OH} + \text{HO-OC-Ph} \\
\text{P}^-\text{Si-O-OCPh} & \xrightarrow{\text{H}_2\text{O}} \text{P}^-\text{Si-OH} + \text{HO-OC-Ph} \\
\end{align*}
\quad \text{(eqn 27)}
\]

The polymeric silyl chloride could be regenerated with thionyl chloride. However, as this polymer showed no special advantages over the existing polymeric trityl chloride diol protecting group\(^{46,67}\), its development was not
continued.

Reaction of \( \text{P-Li} \) with chlorodiphenylphosphine yields the polymeric analogue of triphenylphosphine \( \text{P-P(Ph)}_2 \) in good yield. This polymer has found use as a polymeric Wittig reagent and is widely employed as a ligand in the preparation of polymer supported transition metal catalysts.\(^8\)

The reaction of \( \text{P-Li} \) with 1,2 dibromoethane gives a product containing 1.1 mequiv Br/g. The rather low functional yield of this reaction (Table 13) with 1% cross-linked resins could be accounted for by an intraresin reaction of the type shown (eqn 28).

\[
\begin{align*}
\text{P-Li} \quad &\text{BrCH}_2\text{CH}_2\text{Br} \quad \rightarrow \quad \text{P-CH}_2\text{CH}_2\text{Br} \quad \rightarrow \quad \text{P-Li} \quad \text{P-CH}_2\text{CH}_2-P \quad \text{ (eqn. 28)}
\end{align*}
\]

A polymer containing trityl chloride was prepared by reaction of \( \text{P-Li} \) with benzophenone followed by reaction with acetyl chloride to give \( \text{P-C(Ph)}_2\text{Cl} \). However, the functional yield was only moderate (Table 13), possibly due to steric problems with the bulky benzophenone molecule. Trityl polymers with much larger degrees of functionalization have been prepared by Friedel-Crafts acylation of polystyrene with benzoyl chloride followed by a Grignard reaction with phenyl magnesium bromide.\(^67\) \( \text{P-C(Ph)}_2\text{OH} \) has also been made by reaction of benzophenone with \( \text{P-Li} \) made via the direct lithiation procedure.\(^46\)

Reaction of \( \text{P-Li} \) with dimethyl formamide gave a polymeric aldehyde \( \text{P-CHO} \) which was characterized as the oxime (Scheme 18). Thus the yield reported (Table 13) should be taken as a minimum as an additional step was required to give the analysis. \( \text{P-CHO} \) has been used as a protecting group for sugars.\(^102,103\)
The lithiated resin reacted with ethylene oxide at low temperature to give a polymeric alcohol\(-\text{CH}_2\text{CH}_2\text{OH}\) which was characterized as its 3,5-dinitrobenzoate derivative in good yields. This polymer has potential utility as a solid support.

**Preparation of Nucleophilic Polymers from [P]-Li**

Chloromethylated resins have been so widely used as polymer supports because substrate molecules can be easily attached to them by nucleophilic displacement of chloride from the polymer. The reverse reaction, the attachment of molecules to polymers by displacement of a leaving group on the substrate by a nucleophilic polymer is seldom achieved as very few suitable polymeric nucleophiles are available. The preparation of several functional polymers which have potential as nucleophilic supports for example\([\text{P}]-\text{CH}_2\text{SH}, [\text{P}]-\text{CH}_2\text{OH}\) and \([\text{P}]-\text{CH}_2\text{CH}_2\text{OH}\), has already been described in this thesis. Two polymers containing phenol or thiophenol groups have been made from lithiated polystyrene which should prove very useful as polymeric supports in view of their ability to generate powerful nucleophiles which could react with various substrates under very mild conditions.

a) Preparation of [P]-SH

The reaction of polystyryl lithium, prepared via either the direct lithiation or the bromination lithiation procedure, with elemental sulfur yielded a polymer containing sulfur attached directly to the aromatic rings of the polymer. When \([\text{P}]-\text{Li}\) derived from \([\text{P}]-\text{Br}\) was reacted with an excess of sulfur, the product often contained more sulfur than was theoretically possible as calculated from the bromine
content of the precursor. This indicated that in addition to the desired thiol, di- and poly-sulfides were formed. To obtain the desired polymeric thiol, the polymer was reduced with lithium aluminum hydride under reflux to eliminate all sulfur-sulfur bonds (eqn. 29).

\[
\text{P-Li} + \text{S}_x \rightarrow \text{P-S}_x \text{H} + \text{P-S}_x \text{P} \rightarrow \text{P-SH} \quad \text{(eqn 29)}
\]

Our first experiments were performed using a large excess of sulfur, which had to be removed from the polymer by solvent extraction prior to the reduction. This excess was not necessary, as the yields obtained in the preparation of \( \text{P-SH} \) by the bromination-lithiation route, using only one equivalent of sulfur per equivalent of bromine in the starting material, were practically identical to those obtained using a large excess of sulfur (Table 14). In a typical experiment involving equivalent amounts of \( \text{P-Li} \) and sulfur, approximately 83% of the sulfur became attached to the polymer. After reduction of the sulfur-sulfur bonds, approximately 73% of the sulfur remained attached to the polymer, indicating that \( \sim 10\% \) of the original sulfur had not been directly attached to the aromatic rings of the polymer. The transformation of \( \text{P-Br} \) into \( \text{P-SH} \) was generally achieved in yields of 70-75% over a wide range of degrees of functionalization (Table 14) and thus the reaction could produce predictable results.

In the preparation of \( \text{P-SH} \) by direct lithiation of polystyrene, best results are obtained using a 1:1 ratio of base to polymer (Table 15, expt. 1). Lowering the amount of base or sulfur relative to polymer resulted in a decrease in the degree of functionalization (Table 15, expt. 2,3). In an attempt to increase the amount of substitution, we substituted t-BuLi
## TABLE 14  PREPARATION OF \( \text{P}-\text{SH} \) from \( \text{P}-\text{Br} \)

<table>
<thead>
<tr>
<th>( \text{P}-\text{Br} )</th>
<th>Sulfur mequiv</th>
<th>ratio ( \text{P}-\text{Br} / \text{S} )</th>
<th>( \text{P}-\text{SH} )</th>
<th>Functional Yield ( % )</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.F. ( a )</td>
<td>mequiv/g</td>
<td>scale(g)</td>
<td>% S</td>
<td>mequiv/g</td>
</tr>
<tr>
<td>0.115</td>
<td>1.02</td>
<td>21</td>
<td>150</td>
<td>1:7</td>
</tr>
<tr>
<td>0.15</td>
<td>1.3</td>
<td>18</td>
<td>94</td>
<td>1:4</td>
</tr>
<tr>
<td>0.19</td>
<td>1.60</td>
<td>16</td>
<td>250</td>
<td>1:10</td>
</tr>
<tr>
<td>0.37</td>
<td>2.82</td>
<td>35</td>
<td>100</td>
<td>1:1</td>
</tr>
<tr>
<td>0.42</td>
<td>3.1</td>
<td>22</td>
<td>800</td>
<td>1:12</td>
</tr>
<tr>
<td>0.42</td>
<td>3.1</td>
<td>20</td>
<td>62</td>
<td>1:1</td>
</tr>
</tbody>
</table>

\( a \) Degree of functionalization: fraction of aromatic rings carrying the substituent

\( b \) Calculated from the number of mequiv. of \( \text{P}-\text{Br} \) and \( \text{S} \)

\( c \) (Final D.F./Initial D.F) x 100
Table 15  
PREPARATION OF $\mathbb{P}$-SH BY DIRECT LITHIATION

<table>
<thead>
<tr>
<th>Exp. #</th>
<th>Base complex</th>
<th>Ratio polystyrene:base:sulfur</th>
<th>Reaction conditions</th>
<th>S analysis mequiv./g.</th>
<th>D.F.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>nBuLi:TMEDA</td>
<td>1:1:0.49</td>
<td>4hr,60°</td>
<td>1.98</td>
<td>0.22</td>
</tr>
<tr>
<td>2</td>
<td>nBuLi:TMEDA</td>
<td>1.62:1:0.49</td>
<td>4hr,65°</td>
<td>1.40</td>
<td>0.15</td>
</tr>
<tr>
<td>3</td>
<td>nBuLi:TMEDA</td>
<td>1.62:1:0.24</td>
<td>4hr,65°</td>
<td>1.01</td>
<td>0.11</td>
</tr>
<tr>
<td>4</td>
<td>tBuLi:TMEDA</td>
<td>1.62:1:0.49</td>
<td>4hr,RT</td>
<td>1.07</td>
<td>0.115</td>
</tr>
<tr>
<td>5</td>
<td>tBuLi:TMEDA</td>
<td>1.62:1:0.98</td>
<td>4hr,RT</td>
<td>0.94</td>
<td>0.10</td>
</tr>
<tr>
<td>6</td>
<td>tBuLi:TMEDA</td>
<td>1.62:1:0.49</td>
<td>4hr,65°</td>
<td>0.98</td>
<td>0.105</td>
</tr>
</tbody>
</table>
for n-BuLi as base but found that a decrease in functionalization resulted, a result in marked contrast with that obtained for soluble polystyrene (p.117 this thesis).

It should be noted that the maximum degree of functionalization obtained by the direct lithiation was 0.22, almost exactly the same as that obtained in the preparation of $\text{P}-\text{COOH}$ using this route (p. 63 this thesis.). In general, the bromination-lithiation procedure was preferred as it allowed better control of the degree of functionalization and more highly substituted polymers could be obtained.

b) Preparation of $\text{P}-\text{OH}$

We have prepared hydroxypolystyrene by the addition of oxygen to a suspension of polystyryl lithium in dry benzene or cyclohexane at room temperature (eqn. 30).

\[
\begin{align*}
\text{P}-\text{Li} + \text{O}_2 & \rightarrow \text{P}-\text{O}_x\text{H} \\
\text{P}-\text{OH} + \text{NaHSO}_3 & \rightarrow \text{P}-\text{OH} 
\end{align*}
\]  

(eqn. 30)

This reaction was easier to carry out than the corresponding preparation of $\text{P}-\text{SH}$, as an excess of oxygen could be used without adversely affecting the ease of purification of the product. Although the reaction seemed to form little hydroperoxide, the polymers were routinely washed with sodium bisulfite to ensure their reduction to the desired hydroxyl polymers (eqn. 30). The infrared spectrum of $\text{P}-\text{OH}$ included large hydroxyl absorptions and the polymer reacted easily with benzoyl chloride to yield the corresponding benzoate in which the hydroxyl bands had disappeared and had been replaced by a large band at 1740 cm$^{-1}$.

As was the case for the corresponding polystyryl mercaptan, the transformation of $\text{P}-\text{Br}$ into $\text{P}-\text{OH}$ proceeded in approximately 75% yield.
We have also studied the preparation of \( \text{P}-\text{OH} \) using the direct lithiation route. Once again the maximum degree of functionalization obtained was 0.23. (Table 16). However, in every case, the reaction of the lithiated resin with oxygen was found to give a higher degree of functionalization than had been obtained for the sulfur quenching reaction under the same conditions (Table 15, 16). This may be due to an increased ease of access of oxygen to the reactive sites as compared with sulfur. Especially striking is the contrast between reactions carried out with t-BuLi-TMEDA where a D.F. of 0.10 was obtained with sulfur quenching (Table 15 exp. 5), while oxygen quenching gave a D.F. of 0.19 (Table 16, exp.3) under similar conditions.

The best procedure reported in the literature for the preparation of \( \text{P}-\text{OH} \) involved the co-polymerization of p-acetoxystyrene, styrene and divinyl benzene followed by removal of the acetyl groups with hydrazine hydrate. There has been no previous report of the preparation of \( \text{P}-\text{OH} \) by chemical modification of polystyrene.

Reactions of Polymeric Nucleophiles using Phase Transfer Catalysis

The reactivity of the polymeric nucleophiles prepared above were determined by test reactions of the polymers with substrates containing groups that could allow easy calculation of the yield from elemental analysis of the product. For example, the activity of \( \text{P}-\text{CH}_2\text{SH} \) (p.59 this thesis) as a nucleophile was determined by reaction with p-nitrophenethyl bromide using phase transfer conditions, under inert atmosphere to prevent disulfide
<table>
<thead>
<tr>
<th>Base complex</th>
<th>Ratio polystyrene:base:O₂</th>
<th>Reaction conditions</th>
<th>O analysis mequiv./g.</th>
<th>D.F.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 n-BuLi:TMEDA</td>
<td>0.95:1:large excess</td>
<td>4h, 65°</td>
<td>2.18</td>
<td>0.23</td>
</tr>
<tr>
<td>2 n-BuLi:TMEDA</td>
<td>1.62:1:large excess</td>
<td>4h, 65°</td>
<td>1.57</td>
<td>0.17</td>
</tr>
<tr>
<td>3 t-BuLi:TMEDA</td>
<td>1.62:1:large excess</td>
<td>4h, 65°</td>
<td>1.80</td>
<td>0.19</td>
</tr>
<tr>
<td>4 t-BuLi:TMEDA</td>
<td>1.62:1:large excess</td>
<td>4h, RT</td>
<td>1.30</td>
<td>0.14</td>
</tr>
</tbody>
</table>
bond formation within the polymer. (Scheme 19). Analysis of the product showed that the ratio of sulfur to nitrogen was 1:1, indicating that complete reaction of $\text{P-CH}_2\text{SH}$ to give $\text{P-CH}_2\text{S(CH}_2\text{)}_2\text{PhNO}_2$ had been obtained. (Table 17).

A similar reaction of the polymeric phenolate, generated from $\text{P-OH}$ under phase transfer conditions, with p-nitrophenethyl bromide gave $\text{P-O-CH}_2\text{CH}_2\text{-PhNO}_2$ in close to 90% functional yield. The reaction of $\text{P-OH}$ with allyl bromide using a three phase system gave a product in which no hydroxyl absorption remained in the infrared spectrum. However, attempts to characterize the product by bromination of the double bond to yield the dibromide were inconclusive, as the final product contained more bromine than expected, probably due to some allylic bromination. (Table 17, Scheme 19).

Test reactions of $\text{P-SH}$ with p-nitrophenethyl bromide showed that only 70-75% of the sulfur on the polymer was reactive. This unreactive sulfur was probably not present as the disulfide as the polymers had been reduced with lithium aluminum hydride and the same conditions were used as for the reaction of $\text{P-CH}_2\text{SH}$ in which no disulfide formation was observed. It was more likely that the unreactive sulfur was present as an intrapolymeric sulfide $\text{P-S-P}$, as sulfide formation is a known side reaction of the reaction of organo lithium reagents with sulfur$^{213}$.

An interesting reaction of $\text{P-SH}$ is the nucleophilic displacement of bromide from a symmetrical molecule like 1,4-dibromobutane under phase transfer conditions. (Scheme 19). Two products could be obtained depending upon the extent of site-site interactions in the polymer. Site isolation would give $\text{P-S-(CH}_2\text{)}_4\text{Br}$ as a product while intraresin reaction would produce $\text{P-S(CH}_2\text{)}_4\text{S-P}$. Thus an evaluation of the amount of double coupling in this system could be obtained from the analytical data on the bromine and sulfur.
SCHEME 19: Reactions of Polymeric Nucleophiles under Phase Transfer Catalysis

\[
\begin{align*}
\text{P}-\text{CH}_2\text{SH} & \rightarrow \text{P}-\text{CH}_2\text{S-C}\text{H}_2\text{CH}_2\text{O-NO}_2 \\
\text{XV} & \quad \text{XVI} \\
\text{P}-\text{O-CH}_2-\text{CH} = \text{CH}_2 & \leftarrow \text{P}-\text{OH} \rightarrow \text{P}-\text{O-CH}_2\text{CH}_2\text{O-NO}_2 \\
\text{XVIII} & \quad \text{XVII} \quad \text{XIX} \\
\text{P}-\text{S-CH}_2\text{CH}_2\text{O-NO}_2 & \quad \text{XXI} \\
\text{XXII} & \quad \text{P}-\text{S-(CH}_2\text{)_4-Br} \\
\text{XXIII} & \quad \text{P}-\text{S-(CH}_2\text{)_4-S-P} \\
\text{XX} & \quad \text{XXIV} \\
\text{XXV} & \\
\text{P}-\text{CH}_2\text{-CN} & \rightarrow \text{P}-\text{CH-CN} \\
\text{VI} & \quad \text{XXVI}
\end{align*}
\]
<table>
<thead>
<tr>
<th>Starting resin</th>
<th>Swelling</th>
<th>Catalyst</th>
<th>Reagent</th>
<th>Temp.</th>
<th>Time (days)</th>
<th>Structure of Product</th>
<th>Product Analysis meq/g</th>
<th>Product</th>
<th>Functional</th>
</tr>
</thead>
<tbody>
<tr>
<td># D meq/g D.F. agent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II 1.70 0.20 A (Bu)_4NOH KOH</td>
<td></td>
<td></td>
<td></td>
<td>85</td>
<td>2</td>
<td>(P)-CH₂OH</td>
<td>- - -</td>
<td>0.20&lt;sup&gt;c&lt;/sup&gt;</td>
<td>100</td>
</tr>
<tr>
<td>XII 3.60 0.42 B TEBAC</td>
<td></td>
<td></td>
<td>KCN</td>
<td>70</td>
<td>1.5</td>
<td>(P)-CH-OCH₂-COCH₃</td>
<td>2.42 -</td>
<td>- 0.33</td>
<td>79</td>
</tr>
<tr>
<td>XII 3.60 0.42 B TEBAC</td>
<td></td>
<td></td>
<td>KCN</td>
<td>45</td>
<td>1.5</td>
<td>(P)-CH-OCH₂-COCH₃</td>
<td>4.04 -</td>
<td>- 0.34</td>
<td>81</td>
</tr>
<tr>
<td>XV 2.04 0.24 A Adogen 464</td>
<td></td>
<td></td>
<td>(Bu)₄NOH</td>
<td>75</td>
<td>2</td>
<td>(P)-CH₂SCH₂CH₂-COCH₃</td>
<td>1.58 1.58</td>
<td>- 0.24</td>
<td>100</td>
</tr>
<tr>
<td>XVII 2.18 0.235 A (Bu)₄NOH</td>
<td></td>
<td></td>
<td>BrCH₂CH₂-CO₂NaOH</td>
<td>50</td>
<td>3</td>
<td>(P)-CH₂SCH₂CH₂-COCH₃</td>
<td>1.51 -</td>
<td>- 0.209</td>
<td>89</td>
</tr>
<tr>
<td>XVII 2.18 0.235 A Adogen 464</td>
<td></td>
<td></td>
<td>BrCH₂CH₂-CO₂NaOH</td>
<td>65</td>
<td>3</td>
<td>(P)-CH₂SCH₂CH₂-COCH₃</td>
<td>- - -</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XX 2.50 0.28 D (Bu)₄NI</td>
<td></td>
<td></td>
<td>BrCH₂CH₂-CO₂NaOH</td>
<td>25</td>
<td>1</td>
<td>(P)-SCH₂CH₂-COCH₃</td>
<td>1.37 1.86</td>
<td>- -</td>
<td>73</td>
</tr>
<tr>
<td>XX 2.50 0.28 D (Bu)₄NI</td>
<td></td>
<td></td>
<td>Br(CH₃)₂Br</td>
<td>25</td>
<td>1</td>
<td>(P)-S(CH₃)₂Br</td>
<td>- - 1.23 (Br)</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>XX 2.12 0.235 D (Bu)₄NOH</td>
<td></td>
<td></td>
<td>CIC₂H₂CH₂OH</td>
<td>65</td>
<td>1.2</td>
<td>(P)-S(CH₂CH₂OH)CH₂CH₂OH</td>
<td>- 1.7 2.3 (0)</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>VI 2.50 0.29 A Adogen 464</td>
<td></td>
<td></td>
<td>CIC₂H₂CN</td>
<td>25</td>
<td>4</td>
<td>(P)-CHCN</td>
<td>2.06 -</td>
<td>- 0.26</td>
<td>88</td>
</tr>
</tbody>
</table>

a) A = O-dichlorobenzene; B = 1,2-dichloroethane; D = Benzene; b) TEBAC = Triethylbenzyl ammonium chloride; c) Calculated from saponification and esterification experiments. d)Numerals refer to structures shown in Schemes 15, 19, and 20.
content of the product, once a correction for the unreactive sulfur in the polymer had been made. The analytical results from the reaction of (P)-SH with p-nitrophenethyl bromide and 1,4-dibromobutane could be compared directly as the products have essentially the same functional group molecular weights. Reaction of (P)-SH with p-nitrophenethyl bromide gave a product containing 1.37 mequiv N/g (Table 17). Thus if no double coupling occurred, the reaction of the same (P)-SH with 1,4-dibromobutane would give 1.37 mequiv/g of bromine. However, the product obtained on reaction with an excess of 1,4-dibromobutane contained only 1.23 mequiv Br/g., indicating that the reaction gave ∼10% double coupling, a relatively low value for 1% crosslinked resins. These results could only be deemed to be accurate to within ±5% because of the uncertainty in the amount of unreactive sulfur in the polymer.

The reaction of (P)-SH with 2-chloroethanol under phase transfer conditions also gave rise to two products, as the polymeric alcohol (P)-SCH₂CH₂OH initially formed could react with more 2-chloroethanol in a Williamson type synthesis (Scheme 19). The final product of the reaction contained more oxygen than sulfur (Table 17). It should be noted however that a long chain polyether of the type (P)-S-(CH₂CH₂O)ₙCH₂CH₂OH could find useful applications as an ion complexing agent.

(P)-SCH₂CH₂OH could be prepared more satisfactorily under classical two phase conditions by formation of the polymeric thiolate, followed by removal of the excess base and addition of 2-chloroethanol. This polymer when oxidized to the sulfone (P)-SO₂CH₂CH₂OH, can be used to prepare mono derivatives of symmetrical diacid chlorides.
The polymeric nitrile \( \text{P}-\text{CH}_2\text{CN} \), prepared as previously described (p.51), was also tested as a nucleophile. Reaction with chloroacetonitrile in a three phase system gave the dinitrile \( \text{P}-\text{CH(CN)CH}_2\text{CN} \) in 88% yield. The dinitrile polymer showed two sharp CN bands at 2200 cm\(^{-1}\) and 2250 cm\(^{-1}\) in its infrared spectrum. Other experiments under slightly different conditions gave the same results, indicating that the polymeric trinitrile, which would be formed by reaction of the second acidic hydrogen of the starting polymer, was not obtained. The lack of reactivity of the second proton may be due to steric problems.

**Nucleophilic Additions to \( \text{P}-\text{CHO} \) under Phase Transfer Conditions**

The reactivity of \( \text{P}-\text{CHO} \) towards nucleophiles under phase transfer conditions was tested by reaction with cyanide ion, with trapping of the cyanohydrin intermediate as the cyanohydrin acetate \( \text{P}-\text{CH(CN)OCOCH}_3 \) or the cyanohydrin ether \( \text{P}-\text{CH(CN)OCH}_2\text{-PhNO}_2 \) (Scheme 20).

The addition of cyanide to \( \text{P}-\text{CHO} \) in the presence of acetic anhydride gave a product which contained a very strong ester band at 1755 cm\(^{-1}\) but no aldehydic CH or CO bands in the infrared spectrum. Since it was expected that acetic anhydride would be rapidly hydrolyzed by the very alkaline aqueous cyanide solution, this reagent was added slowly over the course of the reaction.

When the addition of cyanide to \( \text{P}-\text{CHO} \) was carried out in the presence of p-nitrobenzyl bromide as trapping agent the infrared spectrum of the product showed new absorptions due to the NO\(_2\) group, replacing the aldehydic bands. Both addition reactions proceeded in \( \sim 80\% \) functional yield, calculated from the nitrogen analyses (Table 17).
SCHEME 20: Reaction of (P)-CHO under Phase Transfer Catalysis

XII

||
|---|---|
| (P)-CH=O | (P)-CH-O-C-CH$_3$
|     | C≡N  |

XIII

||
|---|---|
| (P)-CH=O | (P)-CH-O-CH$_2$-NO$_2$
|     | C≡N  |

XIV
EXPERIMENTAL

The resins used in this research were a solvent-swellable 1% divinylbenzene-styrene copolymer Bio-beads SX-1 purchased from Bio-Rad Laboratories and a macroreticular resin, Amberlite XE - 305, purchased from British Drug House. THF, used in anhydrous reactions, was purified by distillation from lithium aluminum hydride while benzene and toluene were dried by distillation from calcium hydride; cyclohexane was dried over molecular sieves. Solvents used to wash the polymers were histological grade or better and were recycled after use. All other chemicals were reagent grade and used without further purification unless specified. Infrared spectra were recorded on Beckman IR-20A or Pye-Unicam SP 1100 spectrophotometers using potassium bromide pellets. Proton NMR spectra were recorded on Varian T60 or Varian HA-100 spectrometers operating at 60 MHz and 100 MHz respectively. $^{13}$C NMR spectra were recorded using a Varian CFT 80 spectrometer operating at 20 MHz in Fourier transform mode with $^1$H noise decoupling. Elemental analyses were performed by MHW Laboratories, Chemalytics Inc., Galbraith Laboratories or in this laboratory (halogen and sulfur analyses only) using a Parr peroxide bomb with 200-300 mg samples of resin.

Washing of Cross-Linked Polystyrene Resins

Polystyrene (Bio-beads SX-1 108.70 g) was washed for 30-60 min. at 60-80°C with each of the following: 1N NaOH, 1N HCl, 2N NaOH-dioxane (1:2), 2N HCl-dioxane(1:2), H$_2$O and DMF. The polymer was then washed at room temperature with each of the following: 2N HCl in methanol, H$_2$O, methanol, methanol-CH$_2$Cl$_2$ (1:3), methanol-CH$_2$Cl$_2$ (1:10), and methanol. The resin was then dried under
vacuum at 50-70°C for several hours to give 100.1 g of polystyrene.

**Analysis:** C 92.18 %, H 7.69 %, halogen 0.1 %, N none, S none, O none.

All SX-1 resins used in this work were washed in this way.

**Calculation of the degree of functionalization (D.F.) and of the functional yield**

To calculate the degree of functionalization of a substituted polystyrene resin \( \mathbf{P} - X \), which carries a substituent \( X \) on a fraction of its aromatic rings, analytical data on the polymer must be available. The elemental analysis of a heteratom present in \( X \) can easily be transformed into a capacity expressed in mequiv \( X/g \).

Using this capacity, the D.F. can be calculated in one of two ways. The first method involves the calculation of the total number of styrene units, substituted and unsubstituted, in the polymer as follows: assuming that the capacity of the polymer is \( A \) mequiv/g, then the mass of substituent groups \( X \) in 1000 mg of polymer is \( A (B-1) \) mg where \( B \) is the molecular weight of the substituent \( X \). The mass of the polystyrene residues in 1000 mg of polymer is:

\[
1000 - A(B-1) \text{ mg}
\]

and the number of polystyrene residues in 1000 mg of polymer is:

\[
C = \frac{1000 - A(B-1)}{104} \text{ mequiv/ g}
\]

The degree of functionalization is the number of mequiv. of functional group \( (A) \) divided by the number of mequiv of polystyrene residues \( (C) \) in 1 g of
The functional polymer.

\[ \text{D.F. } = \frac{A}{C} \]

The second method involves the calculation of the mass of a repeating unit of the polymer. A substituted polymer \( \text{P-X} \) with a capacity of \( A \) mequiv/g would contain one substituted polystyrene residue and an unknown number of unsubstituted polystyrene residues per repeating unit. In 1000 mg of polymer the mass of the repeating unit \( B \) is:

\[ B = \frac{1000}{A} \]

and the number of unsubstituted polystyrene residues \( C \) is:

\[ C = \frac{(B-\text{M.W. substituted polystyrene residue})}{104} \]

Since one repeating unit contains one substituted residue and \( C \) unsubstituted residues then:

\[ \text{D.F. } = \frac{1}{1 + C} \]

The functional yield of a polymer reaction is calculated by comparing the D.F's of the starting resin and the product:

\[ \text{functional yield} = \frac{\text{D.F. product}}{\text{D.F. starting material}} \times 100 \]

Preparation of \( \text{P-CH}_2\text{Cl} \)

Chloromethylated polystyrene was made by a modification of the procedure of Pepper. Polystyrene (Bio-beads SX-1, 50 g) was swollen in 250 ml of \( \text{CHCl}_3 \) and
100 ml chloromethyl methyl ether. After two hours of stirring at room temperature, the reaction mixture was cooled to 0°C and 6 ml of SnCl₄ in 80 ml CH₃OCH₂Cl were added dropwise. After one-half hour of stirring at 0° and one-half hour at room temperature the pinkish reaction mixture was filtered, washed with dioxane, MeOH (2 times), dioxane/H₂O/HCl (8:2:1), methanol, dioxane/H₂O (1:1), H₂O, acetone, and methanol, and dried under vacuum to give 56.1 g of white polymer containing 2.1 mequiv of Cl/gram. Higher degrees of functionalization can be obtained by increasing the reaction time or the amount of SnCl₄ used. Chloromethyl ethyl ether can be substituted for chloromethyl methyl ether but in this case, the SnCl₄ catalyst and the chloromethylation agent are added sequentially rather than together to prevent formation of a brown tar from the ether.

Preparation of \( \text{P}-\text{CH}_2\text{OCHO}_3 \)

a) In dichloromethane solvent

\( \text{P}-\text{CH}_2\text{Cl} \) (SX-1, 1.8 mequiv/g, 1.03 g) in 7 ml CH₂Cl₂ was stirred with 0.4 g Adogen 464 and 3 g potassium acetate in 5 ml water at room temperature for 4 days. The resin was filtered, washed with methanol, water (3 times), THF/H₂O, THF, acetone, CH₂Cl₂, and methanol and dried to give 0.81 g of polymer which contained 1.03 mequiv/g of Cl.

b) In o-dichlorobenzene solvent

To 0.969 g of \( \text{P}-\text{CH}_2\text{Cl} \) (SX-1, 1.8 mequiv/g) in 8 ml o-dichlorobenzene were added 0.3 g Adogen 464 and 3 g potassium acetate in 5 ml of water. The mixture was placed in an oil bath at 100° and stirred magnetically for 4 days. After filtration the polymer was washed repeatedly with methanol,
water, THF-H2O 3:1, THF, acetone, dichloromethane, methanol. After drying overnight at 60° under vacuum, the polymer weighed 1.006 g and its infrared spectrum had large bands at 1750 and 1235 cm⁻¹. The saponification equivalent of II was determined by treating the polymer with an excess of aqueous potassium hydroxide in a heterogeneous mixture consisting of approx. 0.5 g polymer with 5 ml aqueous KOH and 15 ml THF with 0.05 g of tetrabutylammonium hydroxide, at 75° for 24 hours. After back titrating with 0.1 N HCl, it was determined that the polymer contained 1.70 mequiv of ester per gram for a functional yield of 98%. (Fig. 3)

Preparation of (P)-CH₂OH

a) Conversion of (P)-CH₂OCOCH₃ to (P)-CH₂OH in a three phase system:

The reaction was carried out on 2.04 g of (P)-CH₂OCOCH₃ prepared as above, swollen in 14 ml o-dichlorobenzene, and stirred with 0.25 ml of 40% tetrabutylammonium hydroxide solution and 5 g KOH in 5 ml H₂O for 48 hours at 85°C. The polymer was then washed with THF, H₂O (3 times), THF, acetone, CH₂Cl₂ and MeOH and dried to give 1.91 g of product which had an infrared spectrum which contained no carbonyl absorption and showed hydroxyl bands at 3460 and 3635 cm⁻¹.

b) Phase transfer reaction with simultaneous addition of acetate and hydroxide ions:

The reaction was carried out in a 3-phase system consisting of 1.1 g of (P)-CH₂Cl (1.8 mequiv/g) suspended in 10 ml 1,2-dichlorobenzene with 0.3 g of a 40% aqueous solution of tetrabutylammonium hydroxide, 3 g of potassium acetate and 2 g potassium hydroxide in 6 ml water. The mixture was stirred vigorously at 85° for 2 days, then filtered and washed thoroughly as above. After drying
the polymer weighed 1.05 g. Its IR spectrum included a large hydroxyl and no carbonyl absorption. A small amount of chlorine (0.1 mequiv/g) remained on the polymer. (Fig. 4)

Similar results were obtained when the reaction period was extended to 5½ days.

c) Phase transfer reaction with successive addition of acetate and hydroxide ions:

The reaction was carried out as above, except for the addition of potassium hydroxide which was made after 24 hours of reaction of the polymer with aqueous potassium acetate. Adogen 464 was used as the phase transfer catalyst. The reaction proceeded smoothly to yield a hydroxymethyl polymer which contained no remaining chloride.

d) Hydroxymethylation of soluble polystyrene

To a solution of 1.5 g of chloromethylated polystyrene (soluble, $\overline{M_n} = 20,000$, 4.4 mequiv/g) was added a mixture of 0.3 g 40% aqueous tetrabutylammonium hydroxide, 3 g potassium acetate and 3 g sodium hydroxide in 6 ml H$_2$O. The heterogeneous mixture was stirred rapidly at 85° and a polymer gel was observed to form slowly. After two days of reaction the polymer was collected by filtration and was found to be insoluble in common organic solvents such as benzene, chloroform, or dioxane. After washing with water, methanol, THF/water 3:1, THF, water, acetone, and dichloromethane, the polymer was dried (1.04 g).

The dry polymer had a large hydroxyl absorption in its IR spectrum and still contained 0.3 mequiv chlorine/g.

Preparation of $\text{P-CH}_2\text{O-CHO}$

$\text{P-CH}_2\text{Cl}$ (1.8 mequiv/g, 1 g) was stirred in 15 ml o-dichlorobenzene with 5 g
p-hydroxybenzaldehyde, 0.1 ml tetrabutylammonium hydroxide 40% solution, and 2.3 g KOH in 5 ml H₂O at 80°C for 3 days. After washing with THF, H₂O (3 times), THF, acetone, CH₂Cl₂ and methanol and drying, the product (1.15 g) contained 3.06 mequiv O/g for a functional yield of 98%. The infrared spectrum of the polymer contained bands at 2755 (aldehydic CH), 1695 (C=O) and 1150 (C-O) cm⁻¹. The polymer contained no remaining chlorine. (Fig. 5)

Preparation of (P)-CH₂O\(\text{NO}_2\)

The reaction involved stirring (P)-CH₂Cl (1.8 mequiv/g, 1 g) with 15 ml o-dichlorobenzene, 0.1 ml 40% (Bu)₄NOH solution, 6 g p-nitrophenol and 4.2 g KOH in 11 ml H₂O for 2 days at 85°. After washing as above and drying, the product weighed 1.18 g and contained 1.52 mequiv/g of N and 4.47 mequiv/g of O for a functional yield of 99%. The infrared spectrum had bands at 1345, 855 (NO₂), 1165 and 1005 (C-O) cm⁻¹.

Preparation of (P)-CH₂CH(CN)₂

The reaction was carried out by stirring (P)-CH₂Cl (1.8 mequiv/g, 1.02 g) in 11 ml o-dichlorobenzene with 0.2 g Adogen 464, 3 g malononitrile and 2.5 g KOH in 6 ml H₂O at 90° for 5 days. After standard workup, the product (1.05 g) contained 3.3 mequiv/g of N for a functional yield of 98%. The infrared spectrum showed a sharp absorption at 2200 cm⁻¹(CN). (Fig. 6)

Preparation of (P)-CH₂CH(CH₂NH₂)₂

The reaction involved 0.93 g of (P)-CH₂CH(CN)₂, prepared above, in 25 ml of dry tetrahydrofuran with 0.5 g LiAlH₄. After 24 hours reflux, the excess reducing agent was destroyed by addition of excess aqueous HCl. After disappearance of the aluminum salts, the polymer was collected on filter, washed repeatedly with water, 10% NaOH, dioxane-water (4:1), THF, dichloromethane
and methanol. After drying the polymer weighed 0.88 g. Its infrared spectrum included a NH band at 3400 cm⁻¹.

Preparation of [(P)-CH₂CH(CN)COOEt]

The reaction involved stirring [(P)-CH₂Cl (1.8 mequiv/g, 1.1 g)] in 7 ml o-dichlorobenzene with 0.4 g Adogen 464, 3 g ethyl cyanoacetate and 3 g KOH in 5 ml H₂O at 90° for 5 days. After standard workup, the product (1.1 g) contained 1.4 mequiv/g of N, 2.76 mequiv/g of O and 0.09 mequiv/g of residual Cl for a functional yield of 88% and a conversion of 92%. The infrared spectrum contained absorptions at 2220 (CN) and 1750 (ester) cm⁻¹.

Preparation of [(P)-CH₂CH(COOEt)₂]

[(P)-CH₂Cl (1.8 mequiv/g, 1.05 g)] was stirred with 10 ml o-dichlorobenzene, 0.4 g Adogen 464, 3 g diethyl malonate and 3 g KOH in 6 ml H₂O for 5 days at 90°. After standard workup, 1.07 g product were obtained which contained 4.8 mequiv O/g and 0.10 mequiv/g of residual chlorine for a functional yield of 77% and a conversion of 81%. The infrared spectrum had a band due to the ester group at 1745 cm⁻¹. (Fig. 7)

Reaction of [(P)-CH₂Cl with CH₂(COCH₃)₂]

a) [(P)-CH₂Cl (2.5 mequiv/g, 0.99 g)] in 7.0 ml 1,2-dichloroethane was reacted with 0.4 g Adogen 464, 3 g KOH in 6 ml water and 2 ml acetylacetone at 70°. After 1 day of reaction, 1 ml of acetyl acetone was added and the reaction was continued for a second day. The resin was then washed with methanol, water, THF, acetone, CH₂Cl₂ and methanol. After drying under vacuum, 1.00g of polymer was obtained.
FIGURE 7  Infrared Spectrum of \( \text{P}^+\text{OH}_2\text{CH(COOEt)}_2 \)
which contained no residual chlorine. The infrared spectrum containing two carbonyl absorptions at 1740 and 1710 cm\(^{-1}\).

The product obtained above (0.60 g) was treated with hydroxylamine hydrochloride (1.5 g) in 15 ml pyridine at 90°C for 3 days and then washed with \(\text{H}_2\text{O}\) (3 times), THF, \(\text{Et}_2\text{O}\), \(\text{CH}_2\text{Cl}_2\) and MeOH. The polymer obtained contained 1.23 mequiv/g of N and showed oxime bands in the infrared spectrum at 1635 and 3415 cm\(^{-1}\) as well as some residual C=O absorption at 1740 cm\(^{-1}\).

b) In o-dichlorobenzene

\(\text{P}-\text{CH}_2\text{Cl}\) (2.58 mequiv Cl/g, 4.1 g) was stirred in 50 ml o-dichlorobenzene with 0.5 g Adogen 464, 4 g NaOH in 13 ml \(\text{H}_2\text{O}\) and 5 ml of acetylacetone for 1 day at 70°C. 4 ml of acetylacetone were then added and the reaction continued for another day. The product was filtered and washed as above to give 4.0 g of polymer which showed a C=O band at 1710 cm\(^{-1}\) in the infrared spectra and contained only 0.16 mequiv/g of Cl.

Treatment of this product (0.82 g) with 2.5 g hydroxylamine hydrochloride in 15 ml pyridine for 3 days at 87°C, followed by washing with \(\text{H}_2\text{O}\) (3 times), THF, \(\text{Et}_2\text{O}\), \(\text{CH}_2\text{Cl}_2\) and MeOH, gave a polymeric oxime containing 0.71 mequiv/g of N. The infrared spectrum showed oxime absorptions at 3500 and 3620 cm\(^{-1}\).

Preparation of \(\text{P}-\text{CH}_2\text{CN}\)

a) In DMF solvent

A suspension of 30 g \(\text{P}-\text{CH}_2\text{Cl}\) (2.43 mequiv/g) and 9 g NaCN in 250 ml dimethylformamide was stirred at 75-80°C for 4 hours. The mixture was filtered and the polymer washed with water, methanol, water, dioxane-water(4:1), DMF,
dioxane, acetone, chloroform, and finally methanol. After drying under vacuum overnight at 80°, 28.66 g of polymer were obtained. The polymer had a sharp CN band in its infrared spectrum at 2280 cm^{-1} and contained 3.35% N or 2.4 mequiv CN per gram.

b) In a three phase system,

The reaction was carried out by stirring 1 g \( \text{P}-\text{CH}_2\text{Cl} \) (1.8 mequiv Cl/g) with 8 ml 1,2-dichloroethane, 0.2 g Adogen 464 and 3 g NaCN in 7 ml \( \text{H}_2\text{O} \) at 80° for 4 days. After washing as above the product (1.07 g) contained 1.84 mequiv N/g for a functional yield of 100%. The infrared spectrum had a CN band at 2280 cm^{-1}. A similar reaction carried out at 25° for 3 days in dichloromethane solvent with \( \text{P}-\text{CH}_2\text{Cl} \) (2.6 mequiv/g) gave a polymer containing 2.3 N/g and 0.4 mequiv Cl/g for a functional yield of 81% and a conversion of 100%.

Attempted Reaction of \( \text{P}-\text{CH}_2\text{Cl} \) with \( \text{HN} \) under phase transfer conditions

\( \text{P}-\text{CH}_2\text{Cl} \) (Bio-beads SX-1, 1.8 mequiv/g, 2.07 g) was stirred in 25 ml 1,2-dichloroethane with 0.3 ml 40% tetrabutylammonium hydroxide solution, 2 g KOH in 5 ml \( \text{H}_2\text{O} \) and 3 g phthalimide at 70° for two days. Filtering and washing the product with \( \text{H}_2\text{O} \) (3 times), THF, acetone, \( \text{CH}_2\text{Cl}_2 \) and \( \text{MeOH} \) gave 2.07 g of polymer which contained 1.4 mequiv/g of Cl and contained no phthalimide C=O bands in its infrared spectrum.

Preparation of \( \text{P}-\text{CH}_2\text{N} \) in a two phase system

\( \text{P}-\text{CH}_2\text{Cl} \) (Amberlite XE-305, 3.62 mequiv Cl/g, 25.0 g) was added to 200 ml DMF and 20 g potassium phthalimide, and the reaction mixture was stirred at 80°
for 18 hours. After filtering, washing with DMF, H₂O (3 times) and MeOH (3 times), and drying under vacuum, 35.8 g of product was obtained which showed strong phthalimide absorptions at 1710 and 1745 cm⁻¹.

A similar experiment with 21.1 g (P)-CH₂Cl (Bio-beads SX-1, 2.6 mequiv/g) gave 29.0 g of product which had the same infrared spectrum described above.

Preparation of (P)-CH₂NH₂

(Amberlite XE-305, 35.8 g) was treated overnight with 19.0 ml of hydrazine hydrate in 125 ml of refluxing ethanol. After washing with EtOH (2 times), 1N HCl (3 times), dioxane/ H₂O/HCl (8:1:1), 2N NaOH (2 times), H₂O (4 times), MeOH (3 times) and drying, 24.8 g of resin was obtained which showed no C=O absorptions and a large NH₂ band at 3400 cm⁻¹ in the infrared spectrum. The polymer contained no residual Cl and 3.97 mequiv N/g for a functional yield of 100%.

A similar experiment using 1% crosslinked phthalimide polymer gave a product with the same infrared spectrum and containing 2.73 mequiv N/g for a functional yield of > 99%.

Preparation of (P)-CH₂S(CH₂)₃CH₃

The reaction involved stirring 1.5 g of (P)-CH₂Cl (2.1 mequiv/g) in 15 ml benzene, 0.1 ml of tetrabutylammonium hydroxide 40% solution, 5 ml butanethiol and 1.5 g NaOH in 5 ml H₂O. The reaction was carried out under a nitrogen atmosphere at 65° for two days. After washing with THF, THF/H₂O/HCl (2:1:1), H₂O (3 times), THF, acetone, CH₂Cl₂ and MeOH, the product obtained (1.6 g) contained 1.92 mequiv/g of S and no chlorine, for a functional yield of 100%.
(P)-CH₂SCH₃ could be prepared in similar fashion substituting methane-thiol for the butanethiol.

Reaction of (P)-CH₂Cl with 1,4-butanedithiol

a) In DMF solvent

(P)-CH₂Cl (2.1 mequiv/g, 1.37 g) in 25 ml DMF was reacted with 0.2 g sodium methylate and 2 ml 1,4-butanedithiol for 1 day at room temperature under nitrogen. After washing as above, 1.48 g of polymer containing 2.64 mequiv S/g and no residual chlorine were obtained. This corresponded to 62% double coupling. A similar experiment with 0.99 g polymer, 0.55 g NaOMe, and 0.6 ml 1,4-butanedithiol gave a polymer (1.04 g) containing 2.11 mequiv S/g for 94% double coupling. Another experiment with 1.03 g polymer, 2.7 mequiv base and 1 ml dithiol resulted in a polymer containing 3.19 mequiv/g of sulfur, corresponding to 26% intraresin reaction.

b) In a three phase system

A typical three phase reaction was carried out as follows: to a suspension of 1.40 g of chloromethylated polymer (2.1 mequiv/g) in 15 ml of benzene were added 0.8 g of NaOH in 6 ml of H₂O, 0.13 g of a 40% aqueous solution of tetrabutylammonium hydroxide and 6 ml of 1,4-butanedithiol. The mixture was stirred vigorously under nitrogen at room temperature for 22 hr and filtered, and the polymer was washed with THF-HCl-H₂O (2:1:1), H₂O, THF, acetone, dichloromethane, and methanol. After drying in vacuo, the polymer weighed 1.57 g and contained a trace of chlorine and 3.50 mequiv/g sulfur, corresponding to only 5% double coupling.
Other experiments under the same conditions with varying base to dithiol ratios gave different amounts of intraresin reaction. Reaction of (P)-CH₂Cl (2.1 mequiv/g 1.47 g) with 0.8 g of NaOH and 3 ml 1,4-butanedithiol gave 1.61 g of polymer containing 3.23 mequiv S/g (23% double coupling). Reaction of 1.31 g (P)-CH₂Cl with 1 g of NaOH and 2 ml of dithiol gave 1.49 g of product containing 3.01 mequiv S/g (39% double coupling). 1.38 g (P)-CH₂Cl, 2.1 g NaOH and 3 ml 1,4-butanedithiol (2:1 ratio) resulted in a product (1.44 g) in which 87% of the sites were double coupled (2.23 mequiv S/g).

Preparation of (P)-CH₂SH

A suspension of 25 g of (P)-CH₂Cl (2.1 mequiv/g, D.F. = 0.244) and 17 g of thiourea in 350 ml of THF and 100 ml of ethanol was stirred and heated to reflux for two days. The resin was then washed with water followed by THF and benzene to remove all excess soluble reagents and by-products. After this washing, the polymer was suspended in 300 ml benzene and a solution of 0.4 g tetrabutylammonium iodide and 15 g sodium hydroxide in 20 ml of boiled distilled water was added. The 3 phase mixture was then stirred at 80° under nitrogen for two days. After filtration the resin was washed with THF, water, THF-water-HCl 5:1:1, water, THF, acetone, methylene chloride, and finally methanol. After drying under vacuum, 24.18 g of (P)-CH₂SH was obtained. The infrared spectrum of the polymer included an SH band centered at 2580 cm⁻¹. Analysis: Cl, none; S, 2.04 mequiv/g (D.F. = 0.234) for a functional yield of 96%.
Preparation of $\text{P}-\text{CH}_2\text{SSCH}_2\text{P}$

When a similar reaction was performed with 6.27 g of $\text{P}-\text{CH}_2\text{Cl}$ (1.8 mmole/g, D.F. = 0.205) and 3.72 g of thiourea followed by reaction with 5 g sodium hydroxide and 0.18 g tetrabutylammonium iodide in 7 ml of distilled water (not deoxygenated) under normal atmosphere, 6.14 g of a polymer containing 5.8% S (1.81 mequiv/g) were obtained. The polymer, which showed no SH absorption in its IR spectrum, was thought to be the disulfide $\text{P}-\text{CH}_2\text{S-S-CH}_2\text{P}$. This assumption was supported by the fact that following LiAlH$_4$ reduction the polymer exhibits an SH absorption in the IR spectrum. The functional yield in this reaction was essentially quantitative.

Preparation of $\text{P}$-Li by Direct Lithiation

All lithiation reactions and reactions involving lithiated resin intermediates were carried out under inert atmosphere using a specially designed flask equipped with a coarse porosity fitted glass filter (Fig. 1). This one piece reaction vessel allowed the addition or removal of solvents and excess reagents or by-products, the washing of the resin, etc., without transfer or exposure to the atmosphere.

a) with TMEDA:

Washed polystyrene (Bio-beads SX-1, 2.8 g, 27 mequiv) was suspended in 20 ml of dry cyclohexane containing 4 ml (25 mmole) of TMEDA and 13.5 ml n-BuLi (2.5 N) were added. The reaction mixture turned red gradually during 4.5 hr of heating at 65°. After the liquid phase was removed, the resin was rinsed
twice to yield the desired \( \text{P}-\text{Li} \), which was quenched by addition of a slurry of dry ice in anhydrous THF. After washing with THF/H\(_2\)O/HCl (2:1:1), H\(_2\)O (3 times), MeOH, THF/H\(_2\)O, THF, cyclohexane, MeOH and drying, 2.93 g of carboxylated resin containing 2.0 mequiv COOH/g were obtained.

Increasing the amount of TMEDA relative to n-BuLi had no effect upon the efficiency of the reaction and the product still contained 2.0 mequiv/g of COOH groups.

A similar experiment using 2.57 g of polymer, 17 ml n-BuLi (1.6 N) and 4 ml TMEDA, but with a reaction time of 1\(\frac{1}{2}\) hour at 70\(^\circ\) yielded 2.75 g of \( \text{P}-\text{COOH} \) containing only 1.4 mequiv/g of acid.

Reaction of polystyrene (2.73 g) with 17 ml n-BuLi (1.6 N) and 4 ml TMEDA for 4 hour at 65\(^\circ\) in 35 ml heptane gave 2.93 g of \( \text{P}-\text{COOH} \) with a functionalization of 1.5 mequiv/g indicating that heptane was somewhat less effective than cyclohexane as a solvent for this reaction. Benzene and THF were unsuitable solvents, giving almost no reaction under the same conditions.

b) with TEDA

Polystyrene (3.14 g), 2.71 g triethylenediamine, and 10 ml n-BuLi (2.5 N) were reacted 3 hr at 65\(^\circ\) in 40 ml of cyclohexane. After removing the liquid phase and washing the product twice with cyclohexene, the lithiated resin was quenched with dry ice and after washing as before, 3.17 g of a product containing 0.4 mequiv/g of COOH groups were obtained. Increasing the reaction time to 4 hr yielded a resin containing 0.6 mequiv COOH/g and after 24 hour, the product contained 1.1 mequiv. of functional groups per gram.
Preparation of Soluble $\text{P-CH}_3$ from $\text{P-Li}$: Determination of Position of Substitution in Direct Lithiation Reaction

a) Methylation of Polystyrene with n-BuLi-TMEDA and Methyl Iodide

Polystyrene ($M_n$ 20,000, 2.5 g) was dissolved in 125 ml cyclohexane and 4 ml TMEDA and 10 ml n-BuLi (2.6 N) were added. The reaction was stirred under $N_2$ at room temperature for 4 hours and 6 ml of methyl iodide were added, and allowed to react for 16 hours. The reaction mixture was then poured into excess methanol and the precipitate was collected and redissolved in $\text{CH}_2\text{Cl}_2$. The solution was filtered and reprecipitated in MeOH. After filtering and drying, 1.87 g of polymer was obtained. Proton NMR showed the degree of functionalization be be 0.19.

$^{13}$C-NMR showed the substitution pattern to be meta and para in a 2:1 ratio. A similar experiment in which the polystyryl lithium was formed by heating at 65°C for 4 hours resulted in a polymer with 27% of the rings substituted by Me groups. $^{13}$C-NMR showed the same substitution pattern described above.

b) Methylation of Polystyrene with t-BuLi-TMEDA and Methyl Iodide

Polystyrene ($M_n$ 20,000, 2.5 g) was dissolved in 150 ml cyclohexane and 4 ml TMEDA and 23 ml t-BuLi (1.2 N) were added. After 1 hour under $N_2$ at room temperature, 6 ml $\text{CH}_3\text{I}$ were added and the reaction mixture was stirred 1½ hour. An isolation procedure similar to that described above yielded 1.24 g of a polymer with a degree of functionalization of 0.50. $^{13}$C-NMR showed a meta:para ratio of 2:1.

A similar experiment using 2.5 g polystyrene, 3.1 g TEDA, 23 ml t-BuLi and heating to 50°C for 2 hours yielded 1.54 g of polymer with a degree of functional-
ization of 0.19 and a meta:para ratio of 2:1.

**Preparation of (P)-Br by Thallation-Bromination**

Polystyrene (Bio-beads SX-1, 24.21 g) and thallic acetate (10.0 g) were suspended in carbon tetrachloride and the reaction was protected from light. Bromine (5.3 ml) was added dropwise and the reaction mixture was stirred in the dark at room temperature for 2 hours and a reflux for 1 hour. Copious evolution of HBr was observed. After 1 hour of reflux, no free bromine was left in the reaction mixture which was then filtered and washed with EtOH, dioxane/3N HCl (4:1), dioxane/H₂O (3:2), H₂O, MeOH (3 times), THF/H₂O (7:3), THF, Et₂O and benzene. On drying under vacuum 33.55 g of beige polymer was obtained, greater than the theoretical yield of 32.1 g, which shows the product to be still contaminated by thallium salts. Extraction of the polymer for 6 days with methanol resulted in a weight loss of 1.51 g; this purified product contained 2.9 mequiv of Br/gram. A small amount of insoluble material (~0.5 g) could be separated from the methanol solvent; it contained 14.5% Br and was probably a mixed salt of thallium like Tl(OAc)₂ Br.

**Preparation of (P)-Br by catalytic bromination**

a) with FeCl₃

Washed polystyrene (Bio-beads SX-1, 2.4 g) was suspended in 20 ml carbon tetrachloride containing 0.1 g FeCl₃ and the reaction vessel was protected from light. Bromine (0.5 ml) in 5 ml CCl₄ was added dropwise and the reaction mixture was stirred for 1 hour at room temperature and 1½ hr at reflux. The resin was washed with CCl₄, acetone, THF and MeOH and dried under vacuum to give 3.11 g of polymer containing 2.87 mequiv Br/g for a D.F. of 0.39. Higher degrees of functionalization could be obtained.
using more bromine but the reaction was less predictable. For example, reaction of 5 g polymer with 3 ml bromine as above gave a product containing 5.32 mequiv Br/g, while a second reaction using the same quantities of polymer, bromine, and catalyst, but a longer reaction time of 6 hr at RT and 17 hr at reflux gave a product containing only 4.97 mequiv/g of Br.

b) with Tl(OAc)$_3$

To a suspension of 20 g of washed resin in 300 ml of carbon tetrachloride was added 1.18 g of thallic acetate. The reaction mixture was stirred in the dark for 30 min, then 13.6 ml of bromine in 20 ml carbon tetrachloride were added slowly. After stirring one hour at room temperature in the dark, the mixture was heated to reflux for 1.5 hours. The reaction mixture, which had lost all the coloration due to free bromine, was collected on filter and washed with carbon tetrachloride, acetone, acetone-water (2:1), acetone, benzene, and methanol. After drying under vacuum, 26.3 g of resin containing 3.10 mequiv. of bromine per gram were obtained (24.8% Br). Thus the resin obtained in this preparation had functional groups on 43% of the aromatic rings (theory 44%). Brominated polystyrenes with a Br content of 1-5 mequiv/g can be reliably obtained using this method by varying the relative amounts of bromine and polystyrene added to the reaction mixture (Table 9). This reaction was also useful for the preparation of macroreticular $\text{P}^\text{Br}$. Thus 94.3 g polystyrene (Amberlite XE-305) in 650 ml CCl$_4$ containing 0.73 g Tl(OAc)$_3$ was reacted with 28 ml Br$_2$ to give after processing, 128.9 g of polymer containing 3.48 mequiv/g of bromine.
c) With TlCl$_3$

Washed polystyrene (Bio-beads SX-1, 2.40 g) was suspended in 30 ml of CCl$_4$ containing 0.13 g TlCl$_3$, and 0.5 ml Br$_2$ in 5 ml CCl$_4$ was added in the dark. After 1 hr of reaction at room temperature and 1½ hr at reflux, the polymer was washed as usual and dried to give 3.08 g of product containing 2.95 mequiv Br/g. Higher bromine contents could be obtained using more Br$_2$ and longer reaction times.

If acetic acid was added to the reaction mixture, extensive depolymerization of the resin was observed. For example, reaction of 5.45 g of polymer in 50 ml CCl$_4$ and 30 ml acetic acid containing 0.33 g TlCl$_3$ with 3.1 ml Br$_2$ in the dark at reflux temperature for 1 day gave a homogeneous reaction mixture which was precipitated in MeOH to give 7.34 g of a soluble polymer with a bromine content of 3.85 mequiv/g and a viscosity [η] of 0.115 at 30°C in toluene.

Preparation of P-I

Polystyrene (Bio-beads SX-1, 3.2 g) in 30 ml CCl$_4$ was reacted with 10 ml of Tl(OCOCF$_3$)$_3$ solution (0.8 N) for 1 hour at room temperature and then 3.16 g I$_2$ was added slowly over 45 min with exclusion of light. After 1 hr of reflux the polymer was filtered, washed with CCl$_4$, acetone, THF and MeOH and extracted for 6 days with H$_2$O and then for 3 days with acetone. After drying, 5.0 g of polymer containing 2.85 mequiv I/g was obtained. This product was probably still contaminated with thallium salts as the theoretical yield was 4.8 g.
Preparation of Soluble o, m, and p-polystyrylbromide

To a solution of 2 g o-bromostryrene in 25 ml toluene was added 0.05 g of azobisisobutyronitrile. The mixture was stirred under nitrogen at 90° for 2 days. After concentration of the solution, the polymer was precipitated by pouring into 200 ml methanol. After filtration the polymer was washed three times with methanol, then dried under vacuum to yield 1.5 g of poly-(o-bromostyrene). Poly-(m-bromostyrene) and poly(p-bromostyrene) were prepared in the same way.

Bromination of Soluble Polystyrene with FeCl₃ Catalyst

To a solution of 2.5 g polystyrene in 30 ml CCl₄ were added 0.1 g FeCl₃ and 1 ml bromine. The reaction was allowed to proceed in the dark for 3 days at room temperature with stirring. After filtration, the polymer was precipitated by pouring the reaction mixture into an excess of methanol. After filtration and washing with methanol, the polymer was redissolved in methylene chloride, reprecipitated in methanol, collected on filter and dried under vacuum. The dried polymer weighed 2.13 g and contained 4.18 mequiv of bromine/g for a D.F. of 0.65.

Bromination of Soluble Polystyrene with Tl(OAc)₃ Catalyst

To a solution of 7.5 g polystyrene in 100 ml carbon tetrachloride was added 0.2 g thallic acetate. Bromine (1.8 ml) was added dropwise while the polymer was stirred in the dark at reflux temperature. After 2 hours, the mixture was cooled and the polymer precipitated by pouring into excess methanol.
The polymer was redissolved in dichloromethane, the solution filtered to remove any solid impurity and finally poured in methanol to reprecipitate the polymer. After drying, 8.08 g of polymer were obtained; analysis indicated 2.96 mequiv of bromine/g for a D.F. of 0.40.

Iodination of Polystyrene with Tl(OOCF$_3$)$_3$ and Iodine

To a solution of 4 g of polystyrene in 125 ml carbon tetrachloride were added 15 ml of an 0.8 M solution of thallic trifluoroacetate. The mixture was stirred at room temperature for 1 hour and 3 g of iodine were added portionwise while the solution was heated, letting the iodine color disappear between additions. After addition of 3 g, the iodine color remained and the mixture was refluxed for an additional 1 hour. After filtration to remove precipitated thallous iodide, the polymer was precipitated by pouring in methanol. After washing with methanol and hot water, the polymer was disssolved in dichloromethane, then reprecipitated in methanol. After drying the polymer weighed 4.1 g and contained 2.1 mequiv. iodine/g for a D.F. of 0.30.

Lithiation of 1% Crosslinked P-Br in THF Followed by Methanol Quenching

A brominated resin (2.45 g) (3 mequiv Br/g) was swollen in 30 ml of dry THF and 4 ml of 2.5 M n-BuLi in hexane were added. After 1½ hr at room temperature, the liquid phase was removed and 30 ml of dry THF were added followed by 4.5 ml of 2.5 M n-BuLi in hexane. The reaction mixture was stirred and heated to 65-70°C for 1½ hr. After removal of the liquid phase, a new 30-m1 portion of dry THF was added followed by 3 ml of methanol. The brown coloration of the polymer disappeared instantly. After filtration,
the polymer was washed with THF, methanol, THF-water (2:1), water, THF-water (2:1), THF, and finally methanol. After drying 2.23 g of polymer was obtained. Elemental analysis for bromine revealed that the polymer still contained 1.95 mequiv of Br/g. The above reaction sequence was repeated using 1.81 g of the polymer recovered above (1.95 mequiv Br/g) and two successive additions of 2.5 M n-BuLi (3 ml at room temperature, and 3.5 ml at 65-70°C). After quenching with methanol and washing as above, 1.61 g of a resin containing 0.68 mequiv Br/g was obtained. After a third treatment with two successive portions of n-BuLi (2 ml at room temperature, then 3 ml at 65-70°C) followed by quenching with methanol and washing, the resin was found to have lost all its bromine.

Lithiation of 1% Crosslinked (P)-Br followed by CO2Quenching

a) in tetrahydrofuran

A stirred suspension of 1.73 g of brominated resin (2.89 mequiv/g) in 20 ml of dry THF was treated with 5 ml of 1.6 M n-BuLi in hexane for 1.5 h at room temperature. The liquid phase was removed and 20 ml of dry THF were added followed by 3 ml of 1.6 M n-BuLi; after 1 h of stirring at room temperature, the liquid phase was again removed and a third portion of 20 ml of dry THF and 4 ml of 1.4 M t-BuLi was added. After 1 h of stirring at room temperature, the liquid phase was removed, the resin was washed twice with dry THF, and a slurry of powdered dry ice in dry THF was added. After washing twice with THF-2N HCl (3:1), the resin was washed further as described above, then dried to yield 1.59 g of a resin which still contained 1.53 mequiv of Br/g. In addition, acid-base titration of the resin showed that it contained 1.4 mequiv of -COOH group per gram.
b) in cyclohexane

The lithiation was carried out by heating a suspension of 2.04 g of brominated resin (2.89 mequiv/g) in 20 ml of cyclohexane with 10 ml of 1.6 M n-BuLi in hexane at 68°C for 3 h. After quenching with solid carbon dioxide in THF, washing and drying, 1.92 g of a resin containing 1.45 mequiv Br/g and 1.3 mequiv -COOH/g was obtained.

c) in benzene or toluene

The lithiation was carried out using 2.04 g of brominated resin (2.89 mequiv/g), swollen in 30 ml of dry benzene, by adding 10 ml of 1.6 M n-BuLi and stirring the suspension at 60°C for 3 h. After quenching with powdered carbon dioxide in THF, washing, and drying, 1.86 g of a polymer containing 2.9 mequiv of -COOH per gram was obtained. The infrared spectrum of the polymer included very broad hydroxyl and carbonyl absorptions. Similar results were obtained using toluene as solvent.

Preparation of $\text{P}-\text{SCH}_3$ from $\text{P}-\text{Li}$

$\text{P}-\text{Li}$ was prepared by reacting 10 g $\text{P}-\text{Br}$ (Bio-beads SX-1, 3.1 mequiv/g) with an excess of n-BuLi in benzene. After cooling and removal of the liquid phase, the lithiated resin was washed twice with dry benzene. The resin was suspended in 100 ml anhydrous THF and 11 ml of dimethyl disulfide was added with stirring. After 15 min at room temperature and 30 min at 65°C, the resin was filtered and washed successively with THF, ether, THF-water, (2:1), water, THF, benzene and methanol. After drying, 8.64 g of product was obtained containing 2.6 mequiv S/g and no bromine.
Preparation of \((P)-B(\text{OH})_2\) from \((P)-\text{Li}\)

\((P)-\text{Li}\) was prepared as above from 15 g of brominated polystyrene (2.78 mequiv/g). The resin was suspended in 150 ml of dry THF and 18 ml of trimethyl borate was added. After stirring at room temperature overnight, the liquid phase was removed and the resin washed with THF. After addition of 140 ml of dioxane, 12 ml of water, and 36 ml of HCl, the mixture was heated to 60°C with stirring for 1.5 hr. The resin was then collected on a filter and washed repeatedly with dioxane-water (3:1), dioxane, acetone, and finally methanol. The dry resin weighed 12.96 g and its infrared spectrum included a large hydroxyl absorption.

Anal. B, 3.4\%(3.15\,\text{mequiv/g}).

Preparation of \((P)-\text{CO-NHPh}\) from \((P)-\text{Li}\)

The lithiated resin was prepared as above from 1.91 g of brominated polystyrene (2.89 mequiv./g). The resin was swollen in 20 ml of dry benzene and 3 ml of phenyl isocyanate were added. After 15 min stirring at room temperature, the mixture was stirred at 65° for 30 min. The resin was collected on filter and washed successively with ethanol, THF, water, THF-water (2:1), THF, ether and finally methanol. After drying, 2.13 g of product were obtained. The infrared spectrum showed a large carbonyl absorption at 1650 cm\(^{-1}\) and NH peaks at 3380 cm\(^{-1}\) and 3300 cm\(^{-1}\).

Analysis: N, 3.04\% (2.2\,\text{mequiv/g}); Br, none.
Preparation of \( \text{P-Si(CH}_3\text{)}_2\text{Cl} \)

\( \text{P-Li} \) was prepared as above from 2.46 g of brominated polystyrene (3.1 mequiv./g). The resin was suspended in 35 ml of dry benzene and 4 ml of dichlorodimethylsilane were added. After 45 min. at room temperature, the polymer was collected on filter and washed repeatedly with dry benzene to yield \( \text{P-Si(CH}_3\text{)}_2\text{Cl} \) which could be used directly without further purification (removal of lithium chloride). For analytical purposes the chloride was hydrolyzed to the corresponding silanol by addition of water in pyridine. After washing with pyridine, THF, THF-water (3:1), water, THF, benzene, and finally ether, the resin was dried under vacuum to yield 2.45 g of a resin which exhibited large hydroxyl absorptions at 3600 and 3380 cm\(^{-1}\), and bands at 1250 cm\(^{-1}\) (Si-C), 820 cm\(^{-1}\) (Si-OH), 770 cm\(^{-1}\) (Si-C).

Analysis: Si, 6.16% (2.2 mequiv./g).

Use of \( \text{P-Si(CH}_3\text{)}_2\text{Cl} \) as an Alcohol Protecting Group

\( \text{P-Si(CH}_3\text{)}_2\text{Cl} \) prepared as above from 2.46 g \( \text{P-Br} \) (3.1 mequiv/g) was suspended in 20 ml dry pyridine and 2 ml butanediol was added. After 1½ hr at room temperature, the resin was filtered, washed 2 times with pyridine and suspended in fresh pyridine (20 ml) containing 4 ml benzoyl chloride. After 2½ days at room temperature, the resin was washed with pyridine, benzene and dry THF to remove excess reagents. These washings were discarded, and the product was removed from the polymer by hydrolysis with THF/H\(_2\)O. After washing the resin further with THF and ether, the
filtrates were combined and evaporated to give 0.16 g yellow oil which contained some of the desired HO(CH_2)_4OC-Ph as well as some impurities as shown by its NMR spectrum. No attempts were made to purify the product, improve the capacity of the resin or optimize the yields.

The polymer, when recovered and dried showed an infrared spectrum consistent with the structure $\text{P-Si(CH}_3)_2\text{OH}$. The polymer could be regenerated using thionyl chloride. Thus 2.13 g of spent polymer treated with 5 ml SOCl_2 in 10 ml CHCl_3 for 20 hr at RT and washed with benzene and CH_2Cl_2 gave 2.07 g of polymer containing 1.8 mequiv Cl/g.

**Preparation of $\text{P-P(Ph)}_2$ from $\text{P-Li}$**

The lithiated resin was prepared from 2.49 g of brominated polystyrene (2.8 mequiv/g). The resin was suspended in 30 ml of dry THF and 5 ml of chlorodiphenylphosphine was added. After 1.75 hr at room temperature the resin was collected on a filter and washed as above for $\text{P-SCH}_3$. After drying the resin weighed 2.87 g.

Anal. P, 5.96% (1.92 mequiv/g); Br, none.

**Preparation of $\text{P-CH}_2\text{CH}_2\text{Br}$ from $\text{P-Li}$**

$\text{P-Li}$ was prepared from 2.30 g of brominated polystyrene (1.76 mequiv/g) and was added to a solution of 7 ml of 1,2-dibromoethane in 40 ml of dry benzene and the mixture was stirred at room temperature for 2.5 hr. After filtration the resin was washed as described above and dried to give 2.19 g of polymer containing 1.13 mequiv Br/g.
Preparation of \( \text{P-CHO} \) from \( \text{P-Li} \)

\( \text{P-Li} \) was prepared from 2.6 g of brominated polystyrene (2.8 mequiv/g). The resin was suspended in 35 ml of dry THF and 5 ml of N,N-dimethylformamide was added with stirring. After 1.75 hr at room temperature, the resin was collected on a filter and washed with THF-water (2:1), THF-water-HCl (8:2:1), water, THF-water, (2:1), THF and finally methanol. After drying, the resin weighed 2.25 g. The ir spectrum included absorptions at 2720 and 1690 cm\(^{-1}\).

For analytical purposes the oxime was prepared by reaction of 0.79 g of \( \text{P-CHO} \) with 1 g of hydroxylamine hydrochloride in 10 ml of pyridine. After 4 hr at 90°C, the resin was washed successively with pyridine, water, THF-water (2:1), THF, benzene, dichloromethane, and methanol. After drying 0.8 g of resin was obtained. The ir spectrum of \( \text{P-CH=NOH} \) showed a large hydroxyl absorption at 3350 cm\(^{-1}\) and no residual carbonyl absorption.

Anal. N, 3.1\%(2.2 mequiv/g)

The minimum degree of functionalization of \( \text{P-CHO} \) could be calculated from this analysis and corresponded to 2.3 mequiv of aldehyde functional group per gram.

Preparation of \( \text{P-CH}_2\text{CH}_2\text{OH} \) from \( \text{P-Li} \)

\( \text{P-Li} \) was prepared from 1.73 g of brominated polystyrene (2.89 mequiv/g). The resin was suspended in 25 ml of dry THF at -50°C and 8 ml of condensed ethylene oxide was added. The mixture was allowed to reach room temperature gradually (1 hr) and the resin was collected on a filter, then washed.
successively with THF-water (3:1) THF-water-HCl(8:2:1), water, THF, methanol, and finally ether. After drying, the resin weighed 1.49 g and exhibited a large hydroxyl absorption in the ir spectrum.

For analytical purposes the 3,5-dinitrobenzoate was prepared by reaction of 0.46 g of (F)-\( \text{CH}_2\text{CH}_2\text{OH} \) with 0.63 g of 3,5-dinitrobenzoyl chloride in 10 ml of dry pyridine. After 1½ hr at 85°C, the resin was filtered and washed as described above to yield 0.66 g of (p)-\( \text{CH}_2\text{CH}_2\text{O-CO-Ph(NO}_2)_2 \). The ir spectrum included a large carbonyl absorption at 1730 cm\(^{-1}\). Anal. N, 5.07% (3.62 mequiv N/g). The minimum degree of functionalization could be calculated from this analysis and corresponded to 2.80 mequiv of -\( \text{CH}_2\text{CH}_2\text{OH} \) functional group per gram.

Preparation of (F)-C(Ph)_2OH from (P)-Li

(P)-Li was prepared from 13 g of brominated polystyrene (2.8 mequiv/g). The lithiated resin was suspended in 100 ml of dry THF and 11 g of benzophenone in 40 ml of THF was added. An exothermic reaction occurred immediately. After 2 hr at room temperature the resin was collected on a filter and washed as described above. After drying under vacuum, 14.24 g of product was obtained. The infrared spectrum of (P)-C(Ph)_2OH included large hydroxyl absorptions at 3430 and 3580 cm\(^{-1}\). The chloride (P)-C(Ph)Cl was prepared by reaction with acetyl chloride. The polymeric alcohol (13.8 g) was suspended in 500 ml benzene and the system was dried by azeotropic distillation of ~125 ml benzene. The reaction mixture was cooled to 70° and 25 ml acetyl chloride was added. After 3½ hr reaction at 70° and 18 hr at room temperature, the resin was filtered
and washed with benzene, \( \text{CH}_2\text{Cl}_2 \) (3 times) and petroleum ether 30-60(3 times). The dried polymer weighed 14.5 g and contained 1.46 mequiv Cl/g. Complete disappearance of the hydroxyl absorption was observed indicating that the reaction was complete.

Preparation of \( (\text{P})\text{-SH} \) from \( (\text{P})\text{-Li} \)

a) via bromination-lithiation

Bromination of 1% crosslinked polystyrene was carried out as described earlier using the thallium (III) catalyzed bromination. The brominated resin was lithiated, then allowed to react with elemental sulfur using an equimolar amount of functional polymer and sulfur as follows: to 35 g of \( (\text{P})\text{-Br} \) (2.82 mequiv/g); D.F. = 0.377) swollen in 300 ml of dry benzene were added 125 ml (200 mequiv.) of n-butyllithium. After heating at 70° for two hours, the solvent was removed and the lithiated polymer was washed twice with dry benzene. After addition of 300 ml of dry THF and 3.2 g (100 mequiv) of sulfur, the mixture was stirred at 60° overnight. After filtration, the resin was washed with THF, THF/water/HCl 6:1:1, then water. The resin was then placed in a Soxhlet and extracted with THF for 3 days. After a last wash with methanol, the polymer was dried in vacuo. The dry resin (29.9 g) had an infrared spectrum which included an SH band at 2560 cm\(^{-1}\) and contained 8.77% sulfur (2.74 mequiv/g suggesting a D.F. of 0.313) for an apparent functional yield of 83%.
The resin was then suspended in 250 ml dry THF and treated with 2 g LiAlH₄ under reflux for 5 hours. After cooling, excess hydrochloric acid was added to destroy all remaining hydride and dissolve the inorganic salts. The resin was then washed thoroughly with THF/water/HCl(6:1:1), THF/water(4:1), water, methanol, dichloromethane and finally, ether. The dry polymer contained 7.6% sulfur (2.37 mequiv/g; D.F. = 0.27) for a functional yield of 73%. A second treatment with lithium aluminum hydride did not cause any further loss of sulfur or change in the infrared spectrum of the polymer (Fig. 8).

b) via direct lithiation with TMEDA and n-BuLi or t-BuLi

15 g of 1% crosslinked polystyrene were lithiated using 37 ml of 2.6N n-BuLi and 15 ml TMEDA in 125 ml of dry cyclohexane. The reaction was allowed to proceed for 4 hours at 60°C with stirring. After filtration, the lithiated resin was washed twice with dry cyclohexane, and 150 ml anhydrous THF and 1.5 g sulfur were added. After stirring overnight at room temperature, the polymer was filtered and washed with THF/HCl/H₂O(2:1:1), then H₂O. After extraction with THF in a Soxhlet for 2 days to remove excess sulfur, the resin was dried, then reduced by reaction with 2.5 g LiAlH₄ in 300 ml anhydrous THF for 4 hours at reflux. After addition of 3N HCl to dissolve all aluminium salts, the polymer was collected on filter and washed with water, THF, acetone, dichloromethane, and finally methanol. After drying, 14.6 g of polymer containing 1.4 mequiv sulfur/g were obtained. A similar reaction using 5 g resin, 7.5 ml n-BuLi and 0.72 g sulfur gave a polymer with 1.96 mequiv sulfur/g.

A reaction carried out with 15 g of polymer, 15 ml TMEDA, 80 ml t-BuLi (1.2N) and 125 ml cyclohexane for 4 hours at 65°C, followed by addition of
FIGURE 8: Infrared Spectrum of S-SH
1.5 g sulfur and reduction as above gave a polymer containing 0.98 mequiv sulfur/g.

**Preparation of (P)-OH from (P)-Li**

a) via bromination-lithiation

The reaction was carried out in one-pot using the reaction vessel shown in Figure 1. To 5.2 g of (P)-Br (3.14 mequiv/g) in 50 ml dry benzene was added 15 ml n-BuLi (2.6M) and the suspension was stirred under nitrogen atmosphere at 55° for 2.5 hours. After filtration, the polymer was washed twice with dry benzene under nitrogen and after addition of 60 ml dry THF, oxygen was bubbled through the mixture for 20 hours. The polymer was filtered and washed thoroughly with methanol, 5% NaHSO₃, H₂O, THF, acetone, dichloromethane, and methanol. After drying, 4.3 g of a polymer containing 2.86 mequiv oxygen/g was obtained. The IR spectrum of the polymer included a large hydroxyl absorption at 3590 and 3500 cm⁻¹. (Fig. 9)

b) via direct lithiation with TMEDA and n-BuLi or t-BuLi

To a suspension of 5.1 g 1% crosslinked polystyrene in 40 ml cyclohexane were added 7.6 ml TMEDA and 35 ml n-BuLi (1.6N). After stirring for 4 hours at 65° under nitrogen, the polymer was filtered and washed twice with cyclohexane. After addition of 60 ml cyclohexane, oxygen was bubbled through the reaction mixture for 20 hours. After filtration and washing as above, the polymer was dried to yield 5.3 g of a material containing 3.49% oxygen (2.18 mequiv/g).

A similar reaction carried out on 10 g of polymer in 100 ml cyclohexane with 10 ml TMEDA and 53 ml t-BuLi (1.2N) under nitrogen for 4 hr at 60° gave a product which after washing and drying contained 1.80 mequiv oxygen/g.
FIGURE 9 Infrared Spectrum of (Z)-OH
Reaction of \( (\text{P})\text{-CH}_{2}\text{SH} \) with p-nitrophenethyl bromide under phase transfer conditions

To 0.83 g of \( (\text{P})\text{-CH}_{2}\text{SH} \) prepared previously (2.04 mequiv/g) in 15 ml of o-dichlorobenzene were added 0.4 g Adogen 464, 3 g p-nitrophenethyl bromide and 2 g of NaOH in 3 ml \( \text{H}_{2}\text{O} \). The mixture was stirred for 2 days at 75°C under nitrogen atmosphere. After filtration the polymer was collected on filter and washed repeatedly with acetone, \( \text{H}_{2}\text{O} \), THF, THF/\( \text{H}_{2}\text{O} \)/HCl (2:1:1), \( \text{H}_{2}\text{O} \), THF, acetone, dichloromethane and finally methanol. The polymer obtained (1.07 g) contained 1.58 mequiv S/g and 1.58 mequiv N/g for an essentially quantitative conversion. The IR spectrum of the final product showed no -SH absorption and contained -NO\(_2\) peaks at 1355 and 1530 cm\(^{-1}\). (Fig. 10)

Preparation of \( (\text{P})\text{-OCH}_{2}\text{CH}_{2}\text{CH}=\text{CH}_{2} \)

\( (\text{P})\text{-OH} \) (2.18 mequiv/g, 0.84 g) was stirred in 12 ml o-dichlorobenzene with 0.2 g Adogen 464 and 2 g KOH in 5 ml \( \text{H}_{2}\text{O} \), and 2 g p-nitrophenethyl bromide were added in small portions over 24 hr. After 3 days of reaction at 50° and a standard workup, the product (0.97 g) contained 1.51 mequiv. N/g for a functional yield of 89%. The infrared spectrum had no OH bands but contained NO\(_2\) absorptions at 1345 and 1520 cm\(^{-1}\).
hydroxyl band in the infrared spectrum. An attempt to characterize the product by conversion to the dibromide \( \text{P-O-CH}_2\text{CHBr-CH}_2\text{Br} \) was carried out as follows: 0.32 g of polymer was swollen in 7 ml \( \text{CCl}_4 \) and 1.2 ml ethanol. A solution of 0.4 ml of bromine in 5 ml \( \text{CCl}_4 \) was added to the stirred suspension. After 6 hours stirring in the dark, the polymer was washed as usual. The dry polymer (0.33 g) contained 4.2 mequiv of bromine/g. (Fig. 11)

Preparation of \( \text{P-S-CH}_2\text{CH}_2\text{O-NO}_2 \)

\( \text{P-SH} \) (2.5 mequiv/g, 57 g) in 15 ml benzene was stirred with 0.08 g tetrabutylammonium iodide, 1 g NaOH in 12 ml \( \text{H}_2\text{O} \) and 2 g p-nitrophenethyl bromide for 1 day at room temperature under nitrogen. After workup, 0.73 g of polymer containing 1.86 mequiv/g of S and 1.37 mequiv/g of N was obtained.

Reaction of \( \text{P-SH} \) with 1,4-dibromobutane

\( \text{P-SH} \) (2.5 mequiv/g, 51 g) in 15 ml benzene was reacted with 2 ml 1,4-dibromobutane, 0.08 g \((\text{Bu})_4\text{NI}\), and 1 g NaOH in 2 ml \( \text{H}_2\text{O} \) for 1 day at room temperature under nitrogen. After workup, 0.607 g of polymer containing 2.05 mequiv/g of S and 1.22 mequiv/g of Br was obtained.

Reaction of \( \text{P-SH} \) with 2-chloroethanol

\( \text{P-SH} \) (2.5 mequiv/g, 1.04 g) in 15 ml o-dichlorobenzene was stirred with 0.4 g Adogen 464, 3 g KOH in 5 ml \( \text{H}_2\text{O} \) and 1 ml 2-chloroethanol at 78°C for 2 days under nitrogen. After processing, 1.13 g of polymer containing 2.51 mequiv/g of O and 2.03 mequiv/g of S was obtained. The infrared spectrum showed a large hydroxyl absorption at 3500 cm\(^{-1}\) but no SH band.
FIGURE 11: Infrared Spectrum of $\text{P} \text{-OCH}_2\text{CH} = \text{CH}_2$
Preparation of $\text{P-CH(CN)CH}_2\text{CN}$

The reaction involved stirring $\text{P-CH}_2\text{CN}$ (2.50 mequiv/g, 1.03 g) in 8 ml o-dichlorobenzene with 0.12 ml 40% (Bu)$_4$NOH solution, and 2.5 g NaOH in 5 ml H$_2$O and adding 1 ml 2-chloroacetonitrile slowly over 2 days. After 4 days of reaction at room temperature, the product was washed with THF, H$_2$O (3 times), THF, acetone, CH$_2$Cl$_2$ and MeOH and dried to give 1.11 g of polymer containing 4.11 mequiv N/g. The infrared spectrum contained two sharp CN bands at 2200 and 2250 cm$^{-1}$. The reaction carried out under the same conditions in dichloromethane gave identical results. (Fig. 12)

Preparation of $\text{P-CH(CN)OCOCH}_3$

The reaction was carried out by stirring 0.97 g of $\text{P-CHO}$ (3.60 mequiv/g) swollen in 12 ml 1,2-dichloroethane with 0.1 g benzyltriethylammonium chloride and 3 g KCN in 4 ml H$_2$O and adding 4 ml acetic anhydride over a 24 hour period. After 1 1/2 days at 70°, the product was worked up as previously described to give 1.13 g of polymer containing 2.42 mequiv/g of N for a 79% functional yield. The infrared spectrum included a small band at 2230 cm$^{-1}$ (CN) and a large band at 1770 cm$^{-1}$ (ester).

Preparation of $\text{P-CH(CN)OCH}_2\text{NO}_2$

$\text{P-CHO}$ (3.6 mequiv/g 1.03) in 10 ml 1,2-dichloroethane was stirred with 0.2 g benzyltriethylammonium chloride and 1 g KCN in 3 ml H$_2$O and 1.5 ml p-nitrobenzyl bromide was added over 24 hrs. After 1 1/2 days at 70°, the reaction was processed as before to give 1.28 g polymer containing 4.04 mequiv N/g for a functional yield of 81%. The infrared spectrum included a CN band at 2220 cm$^{-1}$. 
FIGURE 12: Infrared Spectrum of \( \text{H}^+ - \text{CH(ON)CH}_2\text{CN} \)
PART 2

Polymeric Reagents
RESULTS AND DISCUSSION

The second part of this thesis is concerned with the preparation and application of several polymeric reagents. Polymeric reagents are generally used in single step reactions and derive their main advantages from their insolubility. Thus, reactions can often be driven to completion by using an excess of reagent, since both the unspent reagent and the polymeric by-product can be separated easily from the desired product of the reaction. In addition to being insoluble, polymeric reagents should be stable and easy to prepare, have a capacity sufficient for use on a practical scale and have a reactivity comparable to that of the monomeric reagent. Polymeric reagents must also be designed in such a way that the spent reagent can be easily regenerated to its initial activity in one, or at most two, steps. The ability of the polymer to be regenerated is critical, since few reactions could justify the use of a custom-made polymer which would be discarded after the reaction had been carried out.

It was our aim in undertaking this work to prepare polymeric reagents for such processes as halogenation, oxidation and alkylidene transfer reactions which met the criteria for good polymeric reagents described above.

Poly(vinylpyridinium hydrobromide perbromide): A Brominating Agent

Several halogenated polymers have been prepared for use as reagents in bromination reactions. However, these reagents can give mixtures of products and the yields are at best moderate. We have prepared a polymeric brominating agent analogous to the monomeric reagent pyridinium hydrobromide perbromide, and have tested its
reactivity in simple bromination reactions.\(^{215}\)

Pyridinium hydrobromide perbromide is a reagent which can be used instead of free bromine for the bromination of alkenes or ketones. The crystalline reagent is easier to handle than liquid bromine and can be measured more accurately in micro quantities; also it is often more selective than bromine.\(^{216}\) The polymeric reagent poly(vinylpyridinium hydrobromide perbromide) (PVPHP) in addition to these advantages, is completely insoluble so purification of the product is greatly simplified. The polymeric reagent is as reactive as its monomeric counterpart and can be stored for long periods of time without loss of activity and can be fully regenerated in a simple fashion.

a) Preparation of PVPHP

The first step in the synthesis of the reagent is the preparation of cross-linked polyvinylpyridine by copolymerization of varying amounts of 4-vinylpyridine divinylbenzene and in some cases styrene. Reaction conditions had to be found that would produce a polymer consisting of small porous beads with good mechanical stability. The normal technique of pearl copolymerization was not satisfactory as 4-vinylpyridine is very soluble in water and the polymer formed in large glassy chunks rather than as discrete beads. Adding a non-water-miscible solvent for 4-vinylpyridine, such as styrene or toluene creates an emulsion and allows the polymerization to take place within the organic droplets rather than in the water, producing an insoluble polymer with the desired physical properties. 2% Crosslinked bead polymers containing 47% and 98% vinylpyridine units were prepared in this way.

The polyvinylpyridine beads were reacted first with an excess of hydrogen bromide, then with excess bromine to give PVPHP in 75-85% yield (eqn 31) as a stable
odourless orange solid.

\[ \text{CH} = \text{CH}_2 \quad \text{CH} = \text{CH}_2 \quad \text{CH} = \text{CH}_2 \quad \text{CH} = \text{CH}_2 \]

initiator

1) HBr

2) Br\(_2\)

HBr\(_3\)\(^-\) (eqn 31)

b) Reaction of PVPHP with Alkenes and Ketones

The reactivity of the reagent was determined by using it to brominate a series of alkenes and ketones. Although reactions involving the monomeric reagent are typically performed in acetic acid,\(^2\) PVPHP reacted only sluggishly in this solvent. The reagent was completely unreactive in solvents like chloroform or carbon tetrachloride which are frequently used in brominations involving free bromine. In contrast, PVPHP reacted rapidly with alkenes and ketones in methanol. The reactions could be followed visually, as the reagent changed gradually from orange to cream as its bromine was consumed.

The reaction of PVPHP with simple alkenes generally gave excellent yields of the dibrominated products. (Table 18). A 10-40% excess of polymeric reagent in methanol was used to ensure complete conversion and usually the reaction was complete after 1-2 hours. In the reaction with cis-stilbene, a 94% yield of the dl-dibromide was obtained, a result which was in agreement with that obtained for the monomeric reagent.\(^2\) Reaction of cis-stilbene with free bromine was less selective and gave a mixture of dl- and meso-dibromides in lower overall yield.\(^2\)

The other alkenes tested gave satisfactory yields of dibrominated alkanes as the only product, except cinnamyl alcohol which gave two products in addition to some starting material. This reaction was stopped after 15 min as longer reaction times seemed to increase the proportion of side product.
Table 18: Bromination of Alkenes with PVPHP\(^a\).

<table>
<thead>
<tr>
<th>ALKENE</th>
<th>REACTION TIME HR.</th>
<th>PRODUCT</th>
<th>YIELD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cis-stilbene</td>
<td>1</td>
<td>d1-stilbene dibromide</td>
<td>94</td>
</tr>
<tr>
<td>cyclohexene</td>
<td>1.5</td>
<td>1,2-dibromocyclohexane</td>
<td>88</td>
</tr>
<tr>
<td>1,7-octadiene</td>
<td>1.5</td>
<td>1,2,7,8-tetrabromooctane</td>
<td>87</td>
</tr>
<tr>
<td>cinnamyl alcohol</td>
<td>0.25</td>
<td>3-phenyl-2,3-dibromopropanol</td>
<td>46(^b)</td>
</tr>
<tr>
<td>cinnamic acid</td>
<td>1.5(^c)</td>
<td>3-phenyl-2,3-dibromopropanoic acid</td>
<td>89</td>
</tr>
</tbody>
</table>

\(^a\) Reaction at room temperature unless otherwise noted.

\(^b\) Yield after column chromatography; 15% starting material recovered.

\(^c\) Reaction in refluxing methanol.
Separation of the product mixture by column chromatography gave a 46% yield of the desired 3-phenyl-2,3-dibromopropanol, 15% of recovered starting material and ~20-25% of an unidentified side product.

The reaction of PVPHP with ketones gave excellent yields of the corresponding α-bromides (Table 19). Only in the case of 1-phenyl-2-propanone was any residual starting material observed and in all cases only one brominated product was obtained.

The spent polymeric reagent was separated easily from the desired product after reaction and the isolation step consisted of a filtration, followed by repeated washing of the resin to extract any product which might have remained in the pores, and evaporation of the combined filtrates to give the product, which usually did not require further purification. The polymeric reagent could be regenerated easily by washing with NaOH, followed by reaction with HBr and bromine. The recycled resins were as reactive as the original material even after several reaction cycles.

Poly(vinylpyridinium chlorochromate): An Oxidizing Agent

Polyvinylpyridine could also be used to prepare a second polymeric reagent, poly(vinylpyridinium chlorochromate) (PVPCC) which could oxidize alcohols to aldehydes and ketones.

a) Preparation of PVPCC

The reagent could be easily prepared by addition of a stoichiometric amount of chromium trioxide and concentrated hydrochloric acid to a suspension of polyvinylpyridine (2% crosslinked, D.F. = 0.98) in water.
TABLE 19: BROMINATION OF KETONES WITH PVPHP<sup>a</sup>

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Reaction time hr.</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O=C=O</td>
<td>3.5</td>
<td>O=C=O&lt;sub&gt;Br&lt;/sub&gt;</td>
<td>100</td>
</tr>
<tr>
<td>C-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>3.5</td>
<td>C-CH&lt;sub&gt;2&lt;/sub&gt;Br</td>
<td>99</td>
</tr>
<tr>
<td>C-CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>0.7&lt;sup&gt;b&lt;/sup&gt;</td>
<td>C-CH-CH&lt;sub&gt;3&lt;/sub&gt;&lt;sub&gt;Br&lt;/sub&gt;</td>
<td>100</td>
</tr>
<tr>
<td>CH&lt;sub&gt;2&lt;/sub&gt;-C-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>1</td>
<td>CH-C-CH&lt;sub&gt;3&lt;/sub&gt;&lt;sub&gt;Br&lt;/sub&gt;</td>
<td>80&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction at room temperature unless otherwise noted.

<sup>b</sup> Reaction in refluxing methanol.

<sup>c</sup> Product contains 20% of starting material.
After 1 hr the orange resin was washed free of unbound material with water. The capacity of the resin was determined in two ways: indirectly by titration of the wash water to determine the amount of the original chromate not attached to the resin, or directly by titration of the chromate released from the PVPCC resin by treatment with 2 N NaOH. Both methods gave comparable results; however as the direct method was more versatile and could also be used with partially spent resins, it was the method of choice for all determinations. The PVPCC resins made in this way usually contained 3.5-3.9 mmoles of oxidizing agent per gram of dried polymer. The reagent could be used freshly prepared or could be dried and stored; however the dry reagent had to be soaked briefly in water before use to restore reactivity to its original level.

b) Reaction of PVPCC with alcohols

The first attempts to use this reagent were made using conditions similar to those described by Corey and Suggs for the corresponding monomeric reagent\textsuperscript{219}. However, the reaction in dichloromethane was found to be very sluggish and a large excess of PVPCC was necessary to obtain reasonable rates and yields of carbonyl compounds (Table 20). More polar oxygenated solvents such as ether or tetrahydrofuran were found to be even less suitable, as a marked decrease in reaction rate was observed in these solvents. In contrast, non-polar hydrocarbons such as benzene, or better, heptane or cyclohexane, gave satisfactory results with the rate or reaction increasing with a decrease in solvent polarity. (Table 21). Best results at room temperature were obtained using cyclopentane, the solvent with the lowest polarity. As mentioned before, the presence of a small amount of water within the resin was
TABLE 20: Reaction of alcohols with a 12-fold excess of PVPCC in methylene chloride at room temperature.

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Time (days)</th>
<th>% Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>cinnamyl alcohol</td>
<td>&lt;0.5</td>
<td>100</td>
</tr>
<tr>
<td>1-phenylethanol</td>
<td>2</td>
<td>78</td>
</tr>
<tr>
<td>1-hexanol</td>
<td>3</td>
<td>91</td>
</tr>
<tr>
<td>4-methyl-4-pentene-2-ol</td>
<td>3</td>
<td>61</td>
</tr>
<tr>
<td>3-hexanol</td>
<td>4</td>
<td>86</td>
</tr>
<tr>
<td>cyclopentanol</td>
<td>3.5</td>
<td>100</td>
</tr>
<tr>
<td>2-octanol</td>
<td>4</td>
<td>76</td>
</tr>
</tbody>
</table>
TABLE 21: Oxidation of cinnamyl alcohol with PVPCC\textsuperscript{a}: influence of solvent and of temperature on the extent of reaction as a function of time.

<table>
<thead>
<tr>
<th>Time (min.)</th>
<th>Dichloromethane (25^\circ)</th>
<th>Cyclopentane (25^\circ)</th>
<th>Tetrahydrofuran (25^\circ) (80^\circ)</th>
<th>Benzene (25^\circ) (80^\circ)</th>
<th>Cyclohexane (25^\circ) (80^\circ)</th>
<th>Heptane (80^\circ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>15%</td>
<td>56%</td>
<td>9%</td>
<td>15%</td>
<td>38%</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>32%</td>
<td>82%</td>
<td>15%</td>
<td>26%</td>
<td>54%</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>46%</td>
<td>91%</td>
<td>18.5%</td>
<td>31%</td>
<td>65%</td>
<td>92.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>180</td>
<td>79%</td>
<td>-</td>
<td>26.5%</td>
<td>45%</td>
<td>86%</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction of 1.7 mmole of alcohol with 1.9 g of PVPCC in 10ml of the solvent indicated.
also necessary for good reactivity. For practical purposes, cyclohexane was the solvent of choice.

As expected, increases in temperature (Table 21) or in molar ratio of resin to substrate (Table 22) resulted in increases in rates of oxidation. The reaction was rapid in cyclohexane at 80°C with 4.5 or 2.2:1 ratios of chlorochromate to alcohol (Table 22, entries 1,2) but when the reaction was attempted with a smaller amount of resin, the reaction proceeded rapidly to 50% conversion then slowed down considerably, presumably due to lack of accessibility of the reactive sites (Table 22, entry 3). When a similar reaction was carried out with a partially loaded resin in which only approximately 25% of the vinylpyridine units were transformed into the chlorochromate, the reaction proceeded smoothly to completion, due to the greater accessibility of the reactive sites (Table 22, entry 4). In this experiment the ratio of oxidizing agent to alcohol was approximately 1.1:1.

PVPCC was effective in the oxidation of various types of alcohols: allylic, benzylic, secondary or primary (Table 23). Preferred reaction conditions included the use of an excess of PVPCC in cyclohexane at 80°C to increase the rate of reaction and carry the oxidation to completion to facilitate the workup procedure. The product isolation and purification steps were made easy by the fact that no products of overoxidation, soluble chromium salts or other impurities were found in the reaction mixture once the oxidation was complete. Thus, the carbonyl compounds could be obtained by a simple filtration, followed by washing the resin to extract all the product and evaporation of the solvent. The use of the PVPCC reagent is summarized in Scheme 21.

Although the results reported were obtained using a 4.5:1 ratio of oxidizing agent to alcohol, titrations of the resin before and after the oxidations showed
SCHEME 21: Preparation, Use, and Regeneration of PVPCC

1) HCl or HNO₃
2) NaOH or KOH

\[
\begin{align*}
\text{HCl or HNO}_3 & \quad 2) \text{NaOH or KOH} \\
\text{R-CH-R'} & \quad 1.7 \text{ mmoles} \\
\text{OH} & \quad 80^\circ \text{C} \\
\text{R-C} & \quad 90-100\% \\
\text{R'= H or alkyl} & \\
\text{Cr}^{\text{III}} & \quad 5.9 \text{ mmoles} \\
\text{Partially Spent} & \quad \text{Reagent} \\
\text{HCl wash} & \quad 1) \text{HCl wash} \\
\text{CrO}_3 & \quad 2) \text{CrO}_3 (2 \text{ mmoles})
\end{align*}
\]
Table 22: Determination of the reactivity as a function of the amount of PVPCC.

<table>
<thead>
<tr>
<th>Entry #</th>
<th>Weight of PVP&lt;sup&gt;a&lt;/sup&gt;</th>
<th>mmoles of chlorochromate</th>
<th>mmoles of alcohol&lt;sup&gt;b&lt;/sup&gt;</th>
<th>% conversion 16 min</th>
<th>36 min</th>
<th>56 min</th>
<th>90 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 g</td>
<td>7.7</td>
<td>1.7</td>
<td>96</td>
<td>99+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>0.5 g</td>
<td>3.8</td>
<td>1.7</td>
<td>87</td>
<td>95</td>
<td>97</td>
<td>99+</td>
</tr>
<tr>
<td>3</td>
<td>0.25g</td>
<td>1.9</td>
<td>1.7</td>
<td>51</td>
<td>53</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>4&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1 g</td>
<td>1.9</td>
<td>1.7</td>
<td>38</td>
<td>61</td>
<td>71</td>
<td>81</td>
</tr>
</tbody>
</table>

<sup>a</sup> Amount of PVP used in the preparation of PVPCC

<sup>b</sup> All the reactions were carried out with cinnamyl alcohol in 5ml cyclohexane at 75°

<sup>c</sup> Reaction with partially loaded (25%) PVP; this reaction reached completion in 20 hrs
<table>
<thead>
<tr>
<th>Alcohol</th>
<th>mmoles</th>
<th>g PVPCC</th>
<th>Solvent, ml</th>
<th>Temperature</th>
<th>Time</th>
<th>Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinnamyl alcohol</td>
<td>1.7</td>
<td>1.9</td>
<td>cyclohexane, 10</td>
<td>80</td>
<td>36min</td>
<td>100%</td>
</tr>
<tr>
<td>Cyclohexanol</td>
<td>1.7</td>
<td>2.0</td>
<td>cyclohexane, 4</td>
<td>75</td>
<td>24 hr</td>
<td>94%</td>
</tr>
<tr>
<td>1-Butanol</td>
<td>1.7</td>
<td>2.0</td>
<td>cyclohexane, 4</td>
<td>75</td>
<td>4.5hr</td>
<td>90%</td>
</tr>
<tr>
<td>Benzyl alcohol</td>
<td>1.7</td>
<td>1.9</td>
<td>cyclohexane, 4</td>
<td>75</td>
<td>15min</td>
<td>95%</td>
</tr>
<tr>
<td>1-Phenyl-ethanol</td>
<td>1.7</td>
<td>2.0</td>
<td>cyclohexane, 10</td>
<td>80</td>
<td>3.5hr</td>
<td>96%</td>
</tr>
<tr>
<td>Cyclopentanol</td>
<td>1.7</td>
<td>1.9</td>
<td>cyclohexane, 4</td>
<td>77</td>
<td>3.5hr</td>
<td>82%</td>
</tr>
</tbody>
</table>

TABLE 23: Reaction of PVPCC with various alcohols.
that less than 1 molar equivalent of the polymeric reagent was actually consumed in the reaction. A polymer used in the oxidation of an alcohol under these conditions still contained enough active reagent to be reused without regeneration in further oxidation reactions (Table 24). However, washing the resin with cyclohexane and water to remove the oxidized product after each cycle was necessary, as the active sites on the polymer became coated by the oxidized material and were inaccessible to fresh substrate. Thus, when the oxidation of 1.7 mmole of cinnamyl alcohol was carried out with 7.7 mmole of PVPCC, the reaction was complete within 36 min, and the partially spent reagent still contained 6.2 mmol of chlorochromate. After washing to remove the cinnamaldehyde, three further oxidations were carried out as shown in Scheme 21. After four successive oxidations involving a total of 6.8 mmole of alcohol, the resin still contained 1.9 mmole of chlorochromate for a net consumption of 5.8 mmole. This indicated that the actual consumption of oxidizing agent was of the order of 0.85 molar equivalent, a value which was quite close to the theoretical value of 0.66. It should be noted however, that the rate of the oxidation reaction decreased in the third and fourth oxidations (Table 24).

c) Regeneration of PVPCC

The spent polymeric reagent, used in one or several oxidations, could be regenerated easily to polyvinylpyridine by complete removal of the chromium salts using consecutive washings with hydrochloric acid and sodium or potassium hydroxide. (Scheme 21). The recycled polyvinylpyridine, which was slightly darker than the starting PVP resin, could then be treated with chromic anhydride and hydrochloric acid to produce a PVPCC resin with an activity comparable to
Table 24: Determination of the consumption of oxidizing agent and reactivity of partially spent\textsuperscript{a} PVPCC.

<table>
<thead>
<tr>
<th>Reaction cycle\textsuperscript{b}</th>
<th>mmoles PVPCC</th>
<th>mmoles alcohol</th>
<th>16 min</th>
<th>36 min</th>
<th>56 min</th>
<th>120 min</th>
<th>420 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.7</td>
<td>1.7</td>
<td>96</td>
<td>99+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>6.2\textsuperscript{c}</td>
<td>1.7</td>
<td>92</td>
<td>99+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>1.7</td>
<td>57</td>
<td>83</td>
<td>92</td>
<td>99</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>1.7</td>
<td>32</td>
<td>47</td>
<td>59</td>
<td>83</td>
<td>99</td>
</tr>
<tr>
<td>5</td>
<td>1.9\textsuperscript{d}</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Reaction of PVPCC prepared from 1 g PVP with successive portions of cinnamyl alcohol.

\textsuperscript{b} Each cycle consists of an oxidation followed by a wash with cyclohexane then water.

\textsuperscript{c} Data obtained in a parallel experiment.

\textsuperscript{d} Amount of chlorochromate remaining on the resin after four successive oxidations.
that of the original material. The reagent recycled four times was found to show no loss of reactivity or capacity (Table 25). It would be expected that the polymeric reagent could withstand many more reaction cycles as no chemical degradation of the polymer was observed. The limiting factor would be the mechanical stability of the polymer beads, as repeated handling could result in the formation of fine particles which, although reactive, are much harder to handle than spherical beads of well defined sizes. In the case of our PVPCC resin, only a small amount of powdery material was produced in five reaction cycles and the only losses which were observed were mechanical losses of less than 2% per cycle due to the repeated transfers of the polymer.

An alternate regeneration procedure aimed at the selective removal of the spent chromium salt by soaking in HCl after reaction was not successful, as some of the unreacted CrO$_3$ was leached from the polymer and not all of the spent reagent sites were freed from Cr(III) salts. Thus, 2 g PVPCC (7.7 mmole) was used to oxidize 1.7 mmole of cinamaldehyde. Washing the partially spent resin (6.1 mmole) with 100 ml of 1.5 N HCl released 1.2 mmole of CrO$_3$ into solution. The polymer was then reacted completely with 2 mmole CrO$_3$ to give a polymer containing a total of 6.8 mmole CrO$_3$, showing that at least 0.8 mmole of spent Cr(III) salts had been removed. However, when the same quantity of another resin which had been partially regenerated with HCl in this way was reacted with 5 mmole of CrO$_3$, only slightly more than 2 mmole were absorbed, showing that some sites on the regenerated polymer still contain Cr(III) salts (≈0.7 mmole).

d) Comparison of PVPCC with a similar oxidizing agent

A somewhat similar polymeric reagent to PVPCC has been prepared by reaction of Amberlyst A-26 ion exchange resin with chromic acid. This reagent was claimed to be regenerable although little experimental data were given and no mention of the capacity of the reagent after regeneration was made.
Table 25: Activity of recycled PVPCC: Oxidation of cinnamyl alcohol in cyclohexane at 80°. a

<table>
<thead>
<tr>
<th>Resin Cycle</th>
<th>Capacity</th>
<th>% conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>16 min.</td>
</tr>
<tr>
<td>1</td>
<td>3.58 d</td>
<td>97</td>
</tr>
<tr>
<td>2</td>
<td>3.60</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>3.86</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>3.70</td>
<td>93</td>
</tr>
<tr>
<td>5</td>
<td>3.65</td>
<td>95</td>
</tr>
</tbody>
</table>

a 1.7 mmole alcohol with 1.9 g of PVPCC in 10 ml of cyclohexane
b Each cycle consists of: preparation of PVPCC, oxidation, and regeneration to PVP.
c Capacity expressed in mmole of chlorochromate per gram of resin.
d In other runs, the initial capacity of PVPCC varied from 3.5 to 3.95 mmole/g.
A comparison of PVPCC and the chromate ion exchange resin was made using 7.7 mmole of each reagent for the oxidation of 1.7 mmole of cyclopentanol at 77° (Table 26, Fig 13). The two reagents were comparable in their initial reactivity but the reaction with PVPCC required much less time to reach completion than that with the chromate ion exchange resin. Both reagents are quite similar in their ease of preparation and their handling however, and the major difference between them would probably be the better efficiency of the PVPCC which consumed less CrO₃ and was fully regenerable.

Polymeric Sulfonium Salts: Alkyldiene Transfer Agents

We have prepared a number of polymeric sulfonium salts which could be used to prepare epoxides from aldehydes and ketones. The reaction of sulfonium salts with carbonyl compounds is quite well known and involves the generation of a sulfur ylide which attacks the carbonyl group (eqn 32).

\[
\begin{align*}
R^+S^+\text{-CH}_2\text{R}^'\text{X}^- & \xrightarrow{\text{base}} R^+S^-\text{-CHR}^' \\
R^+S^+\text{-CHR}^'\text{CR}_1\text{R}_2 & \xrightarrow{\text{R}^1\text{C} = 0} \text{RSR} + \text{R}^'\text{CH} \quad \text{(eqn 32)}
\end{align*}
\]

Two attempts to adapt this reaction to polymeric reagents have been reported in the literature but neither was particularly successful. The first involved preparation of a sulfonium salt by reaction of dimethyl sulfide with \(P\text{-CH}_2\text{Cl}\) (eqn 33).
FIGURE 3: Oxidation of Cyclopentanol (1.7 mmoles) in 4 ml Cyclohexane at 77° using 2 g of Resin: Comparison of PVPCC with Chromate Ion Exchange Resin.
Table 26: Comparison of PVPCC and Amberlyst A-26 Chromate Ion Exchange Resin: Oxidation of Cyclopentanol.\(^a\)

<table>
<thead>
<tr>
<th>REACTION TIME (min)</th>
<th>PVPCC % CONVERSION(^b)</th>
<th>AMBERLYST A-26 % CONVERSION(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>6.2</td>
<td>9.4</td>
</tr>
<tr>
<td>16</td>
<td>12.2</td>
<td>16.5</td>
</tr>
<tr>
<td>22</td>
<td>15.8</td>
<td>19.9</td>
</tr>
<tr>
<td>29</td>
<td>18.8</td>
<td>26.6</td>
</tr>
<tr>
<td>36</td>
<td>24.2</td>
<td>28.9</td>
</tr>
<tr>
<td>48</td>
<td>31.0</td>
<td>35.9</td>
</tr>
<tr>
<td>60</td>
<td>37.5</td>
<td>41.1</td>
</tr>
<tr>
<td>75</td>
<td>45.9</td>
<td>47.6</td>
</tr>
<tr>
<td>90</td>
<td>52.4</td>
<td>-</td>
</tr>
<tr>
<td>105</td>
<td>57.8</td>
<td>-</td>
</tr>
<tr>
<td>120</td>
<td>-</td>
<td>57.6</td>
</tr>
<tr>
<td>135</td>
<td>66.9</td>
<td>-</td>
</tr>
<tr>
<td>165</td>
<td>74.5</td>
<td>-</td>
</tr>
<tr>
<td>180</td>
<td>76.6</td>
<td>-</td>
</tr>
<tr>
<td>210</td>
<td>81.7</td>
<td>68.3</td>
</tr>
<tr>
<td>22 hr.</td>
<td>100</td>
<td>85.7</td>
</tr>
</tbody>
</table>

\(^a\) Reaction of 7.7 mmole of resin with 1.7 mmole of cyclopentanol in 4 ml of cyclohexane at 77°.

\(^b\) Percent of cyclopentanone in the reaction mixture as measured by GLC.
However, this polymeric sulfonium salt had two types of hydrogens α to sulfur and therefore two sulfur ylides could be formed. Abstraction of a hydrogen from one of the methyl groups would lead to the desired epoxide (eqn 33). However, abstraction of a benzylic hydrogen, the preferred process, gave a polymer bound epoxide with accompanying removal of sulfur from the polymer. Reaction of this polymeric reagent with benzaldehyde gave only a small yield of the desired styrene oxide, and the sizeable loss of sulfur meant that the spent polymer could not be regenerated.

The second attempt involved the preparation of a polymeric thioanisole by copolymerization of p-vinyl-thioanisole and divinylbenzene, and reaction with dimethyl sulfate to give a sulfonium salt in which the only abstractable protons were on the methyl groups. (eqn 34) 222.
However, as is often the case with polymers made in this way, the reagent was not very reactive and a 10 fold excess was necessary to obtain a 75% yield of styrene oxide from benzaldehyde. In addition, the polymer, when regenerated by reaction with dimethylsulfate, was completely unreactive and therefore could not be recycled.

In order for polymeric sulfonium salts to be useful as reagents, they must be both reactive and easily and completely regenerable. In an effort to overcome the problem of lack of reactivity, we prepared the sulfonium salts by chemical modification of swellable 1% crosslinked polystyrene beads (Scheme 22).

a) Preparation of Polymeric Sulfonium Salts

The first step in the synthesis of polymer-bound sulfonium salts was the preparation of polymeric sulfides by reaction of polystyryllithium with dialkyldisulfides as previously described in Part 1 of this thesis. Polymeric sulfides containing methyl, ethyl, phenyl and benzyl groups were prepared in this way in functional yields of 74-88% (Table 27). Because the sulfur was attached directly to the aromatic rings of the polystyrene, the polymeric sulfides were deactivated towards alkylation and only very strong alkylating agents such as alkyl fluorosulfonates and dialkyl sulfates could react to give the desired sulfonium salts. These reactions were generally very satisfactory for the preparation of methyl and ethyl containing sulfonium salts except in the case of the reaction of $\text{P-S-Ph}$ with diethyl sulfate, in which the alkylating agent was not powerful enough to overcome the strong deactivating effect of two phenyl groups on the sulfide (Table 27).
Scheme 22: Alkylidene Transfer Reactions using Polymeric Sulfonium Salts

\[ (-\text{CH-CH}_2-) \_n \rightarrow \text{n-BuLi} \rightarrow (-\text{CH-CH}_2-) \_n \rightarrow \text{RSSR} \rightarrow (-\text{CH-CH}_2-) \_n \rightarrow \text{R}^\prime \text{CH}_2\text{X} \rightarrow (-\text{CH-CH}_2-) \_n \rightarrow \text{Regeneration} \rightarrow \text{R}^\prime \text{CH}_2\text{X} \]

- \( R = \text{CH}_3, \text{CH}_2\text{CH}_3, \text{phenyl}, \text{benzyl} \)
- \( R' = \text{H}, \text{CH}_3, -\text{CH=CH}_2, \text{phenyl} \)
- \( X = \text{FSO}_3^-, \text{SO}_4\text{CH}_2\text{R}', \text{SO}_3\text{CF}_3^- \)
Table 27: Preparation of Polymeric Sulfides and Sulfonium Salts

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Starting Material</th>
<th>Reagent</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>(P)-SCH₂₃</td>
<td>(P)-Br</td>
<td>n-BuLi/(CH₃S)₂</td>
<td>78</td>
</tr>
<tr>
<td>(P)-S-CH₂CH₃</td>
<td>(P)-Br</td>
<td>n-BuLi/(CH₃CH₂S)₂</td>
<td>74</td>
</tr>
<tr>
<td>(P)-SCH₂Ph</td>
<td>(P)-Br</td>
<td>n-BuLi/(PhCH₂S)₂</td>
<td>87</td>
</tr>
<tr>
<td>(P)-SPh</td>
<td>(P)-Br</td>
<td>n-BuLi/(PhS)₂</td>
<td>88</td>
</tr>
<tr>
<td>(P)-S(CH₃)₂SO₄CH₃</td>
<td>(P)-SCH₃</td>
<td>(CH₃)₂SO₄</td>
<td>97</td>
</tr>
<tr>
<td>(P)-S(CH₃)₂SO₃F</td>
<td>(P)-SCH₃</td>
<td>CH₃SO₃F</td>
<td>92</td>
</tr>
<tr>
<td>(P)-S(Et)₂SO₄Et</td>
<td>(P)-S-Et</td>
<td>(Et)₂SO₄</td>
<td>~85</td>
</tr>
<tr>
<td>(P)-S(Et)₂SO₃F</td>
<td>(P)-SEt</td>
<td>Et SO₃F</td>
<td>96</td>
</tr>
<tr>
<td>(P)-S(Et)PhSO₄Et</td>
<td>(P)-SPh</td>
<td>(Et)₂SO₄</td>
<td>~23</td>
</tr>
<tr>
<td>(P)-S(CH₂Ph)₂SO₃CF₃</td>
<td>(P)-S-CH₂Ph</td>
<td>PhCH₂SO₃CF₃</td>
<td>61</td>
</tr>
<tr>
<td>(P)-S(CH₂Ph)PhSO₃CF₃</td>
<td>(P)-SPh</td>
<td>PhCH₂SO₃CF₃</td>
<td>92</td>
</tr>
<tr>
<td>(P)-S(CH₂CH=CH₂)PhSO₃CF₃</td>
<td>(P)-SPh</td>
<td>CH₂=CH-CH₂SO₃CF₃</td>
<td>92</td>
</tr>
</tbody>
</table>
The preparation of benzyl sulfonium salts presented more of a problem, as neither benzyl fluorosulfonate nor dibenzyl sulfate was available and benzyl bromide was not a strong enough alkylating agent. Benzyl triflate however, could be made by reaction of benzyl alcohol with trifluoromethanesulfonic anhydride with 2,4,6-trimethylpyridine as base at -78° and could be reacted with polymeric sulfides at -78° (eqn 35) to give the desired sulfonium salts in good yield (Table 27). The polymeric reagent was stable at room temperature.

\[
\text{PhCH}_2\text{OH} + \text{CF}_3\text{SO}_2\text{SO}_2\text{CF}_3 \rightarrow \text{PhCH}_2\text{OSO}_2\text{CF}_3 + \text{CF}_3\text{SO}_3^- + \text{N}
\]

\[
\text{R= Ph, CH}_2\text{Ph}
\]

In this case, the insolubility of the polymeric salt was especially advantageous, as the pyridinium salt formed during the preparation of the benzyl triflate was soluble and could not be removed by filtration of triflate solution. After reaction with the polymeric sulfide, however, it could be removed simply by filtering and washing the insoluble resin.

Although both \(\text{P}^-\text{S(CH}_2\text{Ph)}_2^-\text{SO}_3\text{CF}_3\) and \(\text{P}^-\text{S(CH}_2\text{Ph)}\text{Ph}^-\text{SO}_3\text{CF}_3\) were made, the monobenzyl salt was used almost exclusively in epoxidation reactions as rearrangements were possible side reactions when the dibenzyl salt was used (eqn 36).

\[
\text{P}^-\text{S(CH}_2\text{Ph)}^-\text{SO}_3\text{CF}_3 \xrightarrow{\text{base}} \text{P}^-\text{S(Ph)}^-\text{CHPh} \xrightarrow{\text{CH}} \text{P}^-\text{S(Ph)}^-\text{CHPh} \xrightarrow{\text{CH}} \text{P}^-\text{S(Ph)}^-\text{CHPh}
\]

(eqn 36)
Polymeric sulfonium salts containing allyl groups were prepared similarly in good yield by reaction of the allyl triflate with \( \text{P-SPh} \) at -78° (Table 27). Again the salt with abstractable protons in only one group was made to prevent rearrangements of the type shown in eqn 37.

\[
\begin{align*}
\text{P} & \quad \text{S} \quad \text{CHR} \\
\text{CH}_2R & \quad \text{X}^- \quad \text{base} \quad \text{P} & \quad \text{S} \quad \text{CHR} \\
\text{P} & \quad \text{S} \quad \text{CHR} \quad \text{base} \quad \text{P} & \quad \text{S} \quad \text{CHR} \quad \text{base} \quad \text{P} & \quad \text{S} \quad \text{CHR} \\
\end{align*}
\]

(eqn 37)

b) Reactions of Polymeric Methyl Sulfonium Salts

Our initial experiments in the epoxidation of carbonyl compounds with polymeric sulfonium salts were performed using the same conditions described by earlier workers, i.e. potassium t-butoxide as the base in DMSO solvent. The results showed that the problem of lack of reactivity of the resins had been overcome as good yields of epoxides could be obtained using only ~ 30% excess of polymeric reagent. However, the sulfonium salts still could not be regenerated completely. For example, reaction of benzophenone with \( \text{P-S(CH}_3)_2 \text{SO}_3F \) gave 1,1-diphenyloxirane in 83% isolated yield. The used resin was then regenerated with methyl fluorosulfonate and reacted again with benzophenone. The product obtained contained ~ 60% of the desired epoxide, as well as some starting material and several side products. When the recovered resin was reacted again with methyl fluorosulfonate and used in a third epoxidation reaction with benzophenone, no epoxide was obtained. Thus, generation of the sulfonium ylide with potassium t-butoxide in DMSO was not a suitable procedure as it caused degradation of the polymer which prevented its recycling. Other base-solvent systems, such as potassium t-butoxide in THF or dimethoxyethane
and n-BuLi in THF or toluene, were also tried but gave only poor yields in the epoxidation reaction.

Two reports on the use of phase transfer catalysis in the generation of sulfonium ylides were present in the literature at that time. The first study indicated that epoxides could be obtained in isolated yields of 85-90% from the reaction of aldehydes with (CH$_3$)$_3$SI$^+$ in the presence of concentrated NaOH with (Bu)$_4$NI as phase transfer catalyst. However, reaction of ketones under the same conditions gave very poor yields (< 35%).

The second report involved the reaction of a sulfonium salt containing a long alkyl chain, such as lauryldimethyl sulfonium chloride (C$_{12}$H$_{25}$S(CH$_3$)$_2$Cl$^-$), with aldehydes and ketones in the presence of concentrated NaOH. In this case the sulfonium salt was sufficiently lipophilic to act as its own phase transfer agent. Analysis of the workup mixtures by gas-liquid chromatography showed that yields of epoxides approaching 90% could be obtained from both aldehydes and ketones. A disadvantage of this procedure was that the products were contaminated by the non-volatile lauryl methyl sulfide formed in the reaction.

The phase transfer technique was applied to our polymeric sulfonium salts with great success. When $\mathbf{P}^+$S(CH$_3$)$_2$SO$_3$F in dichloromethane was reacted with a variety of aldehydes and ketones in the presence of concentrated NaOH with (Bu)$_4$NI or (Bu)$_4$NOH as phase transfer catalyst, essentially quantitative conversions to the epoxides were observed by GLC analysis. The epoxides were isolated, usually in excellent yields, and their structures were confirmed by NMR spectroscopy. No side products were observed in the reactions and the epoxides were generally clean, except occasionally for a small amount of phase transfer catalyst. The reactions took typically 1-4 days to reach
Table 28: Reactions of Polymeric Methyl Sulfonium Salts with Aldehydes and Ketones Under Phase Transfer Catalysis

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Carbonyl Compound</th>
<th>Product</th>
<th>Yield (%)</th>
<th>GLC</th>
<th>Isolated</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>PhCHO</td>
<td><img src="image" alt="PhCH-CH2" /></td>
<td>100</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>CHO</td>
<td><img src="image" alt="CHO" /></td>
<td>100</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>CH₃(CH₂)₉CHO</td>
<td><img src="image" alt="CH₃(CH₂)₉CH-CH2" /></td>
<td>100</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>t-Ph-CH=CH-CHO</td>
<td><img src="image" alt="t-Ph-CH=CH-CH2" /></td>
<td>-</td>
<td></td>
<td>93</td>
</tr>
<tr>
<td>+</td>
<td>Ph-CO-Ph</td>
<td><img src="image" alt="Ph-CO-Ph" /></td>
<td>100</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>Ph-CO-CH₂CH₃</td>
<td><img src="image" alt="Ph-CO-CH₂CH₃" /></td>
<td>100</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td><img src="image" alt="Ketone" /></td>
<td><img src="image" alt="Ketone" /></td>
<td>98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>PhCOCH₃</td>
<td><img src="image" alt="PhCOCH₃" /></td>
<td>100</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>PhCH₂COCH₃</td>
<td><img src="image" alt="PhCH₂COCH₃" /></td>
<td>?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>PhCOCH₃</td>
<td><img src="image" alt="PhCOCH₃" /></td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>PhCHO</td>
<td><img src="image" alt="PhCHO" /></td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>PhCOCH₃</td>
<td><img src="image" alt="PhCOCH₃" /></td>
<td>41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
completion at room temperature. The reaction time could be shortened by increasing the amount of phase transfer catalyst used, but this made the problem of contamination of the product by catalyst more serious and so was not advantageous.

The only limitation on the choice of the carbonyl compound was its stability under phase transfer conditions. Although compounds such as cyclohexanone, which contained enolizable hydrogens, and benzaldehyde, which can undergo a base catalyzed Cannizzaro reaction, were stable under the reaction conditions, compounds which contain very acidic α hydrogens, such as phenyl acetaldehyde PhCH₂CHO, were polymerized by an aldol type reaction (eqn 38).

\[
2 \text{Ph-CH}_2\text{CHO} \xrightarrow{\text{OH}^-} \text{Ph-CHO} + \text{PhCH}_2\text{CH}
\]

Phenyl-2-propanone was also polymerized by the same type of reaction under phase transfer conditions in the absence of polymeric sulfonium salt. However, in the presence of \(\text{P-S(CH}_3\text{)}_2^+\text{SO}_3\text{F}\), an unidentified product was formed in good yield, rather than the tar observed previously. Purification of the product by column chromatography produced no change in the NMR spectrum. Preparation of PhCH₂(CH₃)-C\(\text{CH}_2\) by an independent route confirmed that the product was not the desired epoxide. The same product was also formed in the reaction of PhCH₂COCH₃ with \(\text{P-S(CH}_3\text{)}_2^+\text{SO}_3\text{F}\) in DMSO with potassium t-butoxide as base.

Two other methyl containing polymeric sulfonium salts were tested in the epoxidation reaction under phase transfer conditions. The first, \(\text{P-S(CH}_3\text{)}_2^+\text{SO}_4\text{CH}_3\), behaved in the same manner as \(\text{P-S(CH}_3\text{)}_2^+\text{SO}_3\text{F}\) in the epoxidation of
acetophenone under identical conditions. (Table 28). The second, 
\[ \text{Ph} - S(\text{CH}_3)\text{Ph} - \text{SO}_3\text{F} \]
contained only one transferable methyl group and reacted much more sluggishly than the other two reagents, giving only a 41% conversion of acetophenone to \( \text{Ph}(\text{CH}_3) - C\text{CH}_2 \) under the same conditions. (Table 28).

The reagents could be regenerated simply by washing the recovered resins and reacting with methyl fluorosulfonate or dimethyl sulfate. No loss of capacity or reactivity was observed. For example, a portion of 
\[ \text{Ph} - S(\text{CH}_3)_2 - \text{SO}_3\text{F} \]
containing 1.9 mequiv/g of reagent was used and regenerated five times. On the fifth cycle the polymer was analysed and contained 1.8 mequiv/g.

c) Reactions of Polymeric Ethyl Sulfonium Salts

The phase transfer technique was also applied to the reaction of aldehydes and ketones with \( \text{P}-S(\text{Et})_2 - \text{SO}_4\text{Et} \) and \( \text{P}-S(\text{Et})_2 - \text{FSO}_3 \), two polymeric sulfonium salts differing only in the nature of the counterion. The reactions were followed by GLC as before and the epoxides were isolated and characterized by NMR spectroscopy. When the possibility of stereochemistry was present, 1:1 mixtures of the cis and trans isomers were obtained.

When the ethyl sulfonate salt \( \text{P}-S(\text{Et})_2 - \text{SO}_4\text{Et} \) was used as the polymeric reagent, the reaction was very sluggish. Complete conversion of aldehydes to epoxides could be accomplished but only after 12 days of reaction (Table 29). With ketones the reaction was unsatisfactory, giving conversions of less than 40% after 28 days of reaction. In contrast, reaction of the fluorosulfonate salt \( \text{P}-S(\text{Et})_2 - \text{FSO}_3 \) with both aldehydes and ketones gave excellent yields of epoxides after 1-5 days of reaction (Table 29).

A counterion effect is quite common in phase transfer catalysis and is believed to be due to the relative solubilities of the complex between the catalyst and the ion to be transported, in this case \( \text{OH}^- \), and the catalyst-counterion complex in the organic solvent. If the catalyst-counterion ion pair is too soluble in the organic layer, the counterion is preferentially
Table 29: Ethylidene Transfer Reactions under Phase Transfer Conditions

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Carbonyl Compound</th>
<th>Product</th>
<th>Yield(%) GLC</th>
<th>Yield(%) Isolated</th>
</tr>
</thead>
<tbody>
<tr>
<td>(P)-S(Et)$_2$-SO$_4$Et</td>
<td>Ph-CHO</td>
<td>PhCH[O]CH[\sim]CH[\sim]CH$_3$</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_4$Et</td>
<td>cyclo-COOH</td>
<td>cyclo[CH[O]CH[\sim]CH[\sim]CH$_3$</td>
<td>100</td>
<td>60</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_4$Et</td>
<td>Ph-CO-CH$_2$CH$_3$</td>
<td>Ph[C]OCH[\sim]CH[\sim]CH$_3$</td>
<td>17</td>
<td>-</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_4$Et</td>
<td>Ph-CO-CH$_3$</td>
<td>Ph[C]OCH[\sim]CH[\sim]CH$_3$</td>
<td>38</td>
<td>-</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_3$F</td>
<td>Ph-CHO</td>
<td>PhCH[O]CH[\sim]CH[\sim]CH$_3$</td>
<td>100</td>
<td>63</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_3$F</td>
<td>cyclo-COOH</td>
<td>cyclo[CH[O]CH[\sim]CH[\sim]CH$_3$</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_3$F</td>
<td>Ph-CO-CH$_3$</td>
<td>Ph[C]OCH[\sim]CH[\sim]CH$_3$</td>
<td>99</td>
<td>59</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_3$F</td>
<td>Ph-CO-CH$_2$CH$_3$</td>
<td>Ph[C]OCH[\sim]CH[\sim]CH$_3$</td>
<td>94</td>
<td>70</td>
</tr>
<tr>
<td>(P)-S(Et)$_2$-SO$_3$F</td>
<td>Ph-CO-Ph</td>
<td>Ph$_2$[C]OCH-CH$_3$</td>
<td>&gt;99</td>
<td>96</td>
</tr>
</tbody>
</table>
extracted from the water layer and insufficient OH\(^-\) is transported to maintain the reaction. This could explain the difference in reactivity between the two polymeric sulfonium salts as one would expect \((\text{Bu})_4\text{N}^+\text{SO}_3\text{Et}\) to be much more soluble in organic solvents than \((\text{Bu})_4\text{N}^+\text{SO}_3\text{F}\). A similar counterion effect was observed in the phase transfer reaction of soluble sulfonium salts \(^{225,226}\). When the counterion was \(\text{I}^-\), which forms a soluble ion pair with the phase transfer catalyst, the reaction proceeded satisfactorily with aldehydes but gave poor yields with ketones \(^{225}\). When \(\text{Cl}^-\), which forms a much less soluble ion pair, was substituted for \(\text{I}^-\), good yields were obtained with ketones as well as aldehydes \(^{226}\).

Both \(\text{P}-\text{S-(Et)}_2\text{SO}_3\text{Et}\) and \(\text{P}-\text{S(Et)}_2\text{SO}_3\text{F}\) could be easily regenerated by reaction of the recovered \(\text{P}-\text{S-Et}\) resins with the appropriate alkylating agent. No loss of activity of the recycled reagents was observed in subsequent epoxidation reactions.

d) Reactions of Polymeric Benzyl Sulfonium Salts.

The benzylidene transfer reaction of \(\text{P}-\text{S(CH}_2\text{Ph)}\text{Ph}^-\text{SO}_3\text{CF}_3\) was tested under three phase conditions using benzaldehyde. The yield of epoxide was found to be lower than in previous cases, although all of the sulfonium salt was consumed. Analysis of the product by GLC showed that it contained benzyl alcohol, resulting from the \(S\_N\) displacement of polymeric phenyl sulfide from the sulfonium salt by \(\text{OH}^-\), which competes with ylide formation in this case (eqn 39).

\[
\text{P-S-(Ph)}^-\text{SO}_3\text{CF}_3 \quad \text{OH}^- \quad \text{P-SPh} \quad \text{PhCH}_2\text{OH} \\
\text{CH}_2\text{Ph} \quad \text{OH} \quad \text{(eqn 39)}
\]
In an effort to prevent the side reaction, the epoxidation reaction was performed in a two phase system with a non-nucleophilic base such as lithium diisopropylamide (LDA). Reasonable yields of epoxides could be obtained from reaction with benzaldehyde and cyclohexanecarboxaldehyde using this system. However, side products were often observed, and purification by column chromatography was then necessary. In addition, the reaction failed to give any epoxide with ketone substrates.

The recovered polymer could be regenerated to $\text{P}^+\text{S(CH}_2\text{Ph)}\text{Ph}^{-}\text{SO}_3\text{CF}_3$ by reaction with benzyl triflate. The regenerated reagent was as reactive as the original material.

These results indicate that further work is required to develop a polymeric sulfonium salt which will function effectively as a benzylidene transfer agent. The polymeric reagent presently available is probably quite satisfactory but conditions must be found to improve the ylide reaction itself.

e) Reactions of Polymeric Allyl Sulfonium Salt

The transfer of an allyl group from $\text{P}^+\text{S(CH}_2\text{-CH=CH}_2)\text{Ph}^{-}\text{SO}_3\text{CF}_3$ to benzaldehyde was attempted under three phase conditions, but the reaction was unsuccessful as indicated by GLC analysis which showed a very low conversion to epoxide (< 5%) after several days of reaction. The reaction gave better results when the ylide was generated at low temperature with LDA, although the yield was still quite low and the product was contaminated by starting material and other by-products, as shown by its NMR spectrum. The polymeric reagent failed to react with ketones under these conditions.

An authentic sample of $\text{PhCH-CH-CH=CH}_2$ was prepared by reaction of benzaldehyde with allyltetrahydrothiophenyl sulfonium bromide under phase transfer conditions. (eqn. 40)
The resin recovered from the epoxidation reactions could be regenerated to $\text{S}^-\text{(CH}_2\text{CH}=\text{CH}_2)\text{Ph}^-\text{SO}_3\text{CF}_3$ by reaction with allyl triflate as before.

Once again further work is necessary to find reaction conditions which will allow the efficient transfer of an allyl group from a polymeric sulfonium salt to a carbonyl compound. (eqn. 40)
EXPERIMENTAL

Gas chromatography was performed on a Gow-Mac Series 550 gas chromatograph with a thermal conductivity detector using helium as the carrier gas and 6 ft columns packed with 15% Carbowax 20 M on Chromasorb P or 4% SE-30 silicone oil on Chromasorb G. Other experimental details were as described in Part 1 of this thesis. The allyltetrahydrothiophenyl sulfonium bromide used in the synthesis of \( \text{PhCH} = \text{CH-CH}=\text{CH}_2 \) was kindly provided by Dr. T. Durst.

Preparation of Polyvinylpyridine (PVP)

a) 4-vinylpyridine-styrene-divinylbenzene copolymer

A 1 liter resin kettle was charged with 300 ml of degassed freshly boiled distilled water containing 1 g dissolved polyvinylalcohol (MW: 180,000-250,000), 6.4 g freshly distilled 4-vinylpyridine, 10.2 g freshly distilled styrene and 0.4 g divinylbenzene (DVB) (55% purity). Benzoyl peroxide (100 mg) was added and the mixture was stirred vigorously for 6 hr at 90° under nitrogen. The resulting polymer consisted of yellow lumps and white beads. The large pieces were unsuitable for use as polymeric reagents and were discarded. The white beads were washed with water, MeOH and benzene and dried under vacuum to give 8.9 g of polymer containing 4.56 mequiv/ g of N. (D.F. = 0.47).

b) 4-vinylpyridine-divinylbenzene (DVB) copolymer

A 2 liter resin kettle was charged with 600 ml of freshly boiled distilled water containing 2.4 g dissolved polyvinylalcohol (MW 180,000 - 250,000), 1.5 g divinylbenzene (55% purity) and 25 g freshly distilled 4-vinylpyridine dissolved in 50 ml toluene. Azobisisobutyronitrile (1g) was added and the reaction mixture was stirred vigorously for 2 days at 85° under nitrogen. The white beads obtained were washed with MeOH, H₂O, THF, acetone, CH₂Cl₂ and Et₂O, then
dried to give 24.9 g polymer containing 98% 4-vinylpyridine and 2% DVB. Most of the beads were of a mesh size (40 - 200) which was convenient for their direct use in the preparation of polymeric reagents.

**Preparation of Poly(vinylpyridinium hydrobromide perbromide) (PVPHP)**

4-Vinylpyridine-styrene-DVB copolymer (4.56 mequiv N/g, 1.49 g) was swollen in dioxane (25 ml) and the suspension was stirred for 1 hour with 25 ml of 48% hydrobromic acid. After cooling the mixture in ice water, 2 ml of bromine was added and the reaction mixture was stirred for an additional 4 hr. After filtration the bright orange resin was washed repeatedly with acetic acid and dichloromethane, then dried under vacuum to yield 3.1 g of polymer containing 5.6 mequiv Br/g or 1.97 mequiv functional group/g for a yield of 85%. The dry polymer still contained some water of hydration. PVPHP could be made similarly from the 4-vinylpyridine DVB copolymer (D.F. = 0.98) by reacting 20 g of resin in 60 ml dioxane with 30 ml 48% hydrobromic acid and 8.5 ml bromine as before to give 52.6 g of product containing 7.88 mequiv Br/g or 2.62 mequiv functional group/g for a functional yield of 75%.

**Bromination of Alkenes with PVPHP**

a) Preparation of d,l-stilbene dibromide from cis-stilbene

Cis-stilbene (0.97 g) was stirred with 2.95 g PVPHP (2.4 mequiv/g) in 21 ml of methanol at room temperature for 2 hours. The resin was then filtered and washed repeatedly with CHCl₃. Evaporation of the filtrates gave 1.7 g of crude d,l-dibromostilbene (94%). After recrystallization from methanol, the product had mp 111-113°C and its NMR spectrum contained peaks at 7.17 δ (5H, s), 4.97 δ (1H, d, J = 8 Hz) and 4.43 δ (1H, d, J = 8 Hz).

b) Preparation of 1,2-dibromocyclohexane from cyclohexene

Cyclohexene (0.98 g) in 22 ml methanol was treated with 4.0 g of
PVPHP (2.4 mequiv/g) for 1.5 hr at room temperature. The resin was filtered and washed with CHCl₃ and the combined filtrates were evaporated to give 2.55 g crude 1,2-dibromocyclohexane (88%) NMR: 4.5 δ (2H, broad singlet), 1.6-2.4 δ (8H, broad).

c) Preparation of 1,2,7,8-tetrabromooctane from 1,7-octadiene

1,7-octadiene (0.52 g) in 20 ml methanol was reacted with 1.97 g PVPHP (2.4 mequiv/g) for 1.5 hr at room temperature. Washing the resin and evaporating the filtrate gave 1.77 g of crude 1,2,7,8-tetrabromooctane (87%). The mass spectrum confirmed the presence of the tetrabromide. NMR: 3.5-4.1 δ (6H, m), 1.5-2.0 δ (8H, broad).


d) Preparation of 3-phenyl-2,3-dibromopropanol from cinnamyl alcohol.

Cinnamyl alcohol (1.65 g) in 25 ml methanol was reacted with 5.0 g PVPHP (2.4 mequiv/g) for 15 min. After processing as above, 3.1 g of a brown oil was obtained which contained ~55% of the desired product as well as 17% of starting material and ~29% of an unidentified side product as shown by NMR. This product, when chromatographed on silica gel (50 g) with benzene eluant, gave 0.24 g of starting material, 1.65 g of pure 3-phenyl-2,3-dibromopropanol (46%) and 0.47 g of an unidentified product. The NMR of the desired product has resonances at 7.32 δ (5H, s), 5.30 δ (1H, d, J = 11 Hz), 4.70 δ (1H, doublet of triplets, J = 11 Hz and 4 Hz), 4.28 δ (2H, d, J = 4 Hz), 2.11 δ (1H, broad).

e) Preparation of 3-phenyl-2,3-dibromopropanoic acid from cinnamic acid

Cinnamic acid (0.74 g) in 12 ml methanol was treated with 2.6 g PVPHP (2.4 mequiv/g) for 1.5 hr at room temperature and 1 hr at reflux. After processing as before, 1.37 g of crude 3-phenyl-2,3-dibromopropanoic acid was obtained (89%), NMR: 7.30 δ (5H, s), 5.30 δ (1H, d, J = 12 Hz), 4.80
δ (1H, d, J = 12 Hz) in CD$_3$OD solvent.

**Bromination of Ketones with PVPHP**

a) Preparation of 2-bromocyclohexanone

Cyclohexanone (1.1 g) in 23 ml methanol was reacted with 6.0 g PVPHP (2.4 mequiv/g) for 3.5 hr at room temperature. Washing the resin and evaporating the filtrate gave 2.0 g of crude product (100%). NMR: 4.36 δ (1H, broad triplet, J = 4 Hz), 1.8-2.4 δ (8H, m).

b) Preparation of α-bromoacetophenone

Acetophenone (1.02 g) in 23 ml methanol was stirred with 4.5 g PVPHP (2.4 mequiv/g) for 3.5 hr at room temperature. After workup, 1.68 g crude α-bromoacetophenone (99%) was obtained. NMR: 8.03 δ (2H, m), 7.60 δ (3H, m), 4.47 δ (2H, s)

c) Preparation of phenyl 1-bromoethyl ketone

Propiophenone (1.4 g) in 30 ml methanol was reacted with 5.7 g PVPHP (2.5 mequiv/g) for 40 minutes at reflux temperature. After processing as before 2.22 g of crude phenyl 1-bromoethyl ketone was obtained. (100% yield) NMR: 8.00 δ (2H, m), 7.53 δ (3H, m), 5.28 δ (1H, q, J=6Hz) 1.93 δ (3H, d, J = 6 Hz).

d) Preparation of bromobenzyl methyl ketone

1-Phenyl-2-propanone (1.35 g) in 25 ml methanol was treated with 5.15 g PVPHP (2.4 mequiv/g) for 1 hr at room temperature. After standard workup, 2.05 g of brown oil was obtained which was shown by NMR to be 80% of the desired product and 20% starting material. The NMR of the product mixture contained peaks due to bromobenzyl methyl ketone at 7.34 δ (5H, s), 5.40 δ
(1H, s), and 2.25 δ(3H, s) and phenyl-2-propanone peaks at 7.23 δ (5H, s), 3.67 δ (2H, s) and 2.12 δ (3H, s) in a 4:1 ratio. Some other small peaks due to impurities were also present.

**Regeneration of the Spent Reagent to PVPHP**

a) **Direct regeneration**

Used PVPHP (14 g, wet) in 30 ml dioxane was treated with 15.2 ml 48% hydrobromic acid and 7.3 ml bromine as before. After washing with acetic acid and CCl₄ and drying under vacuum, 19.0 g of regenerated reagent was obtained containing 7.26 mequiv Br/g or 2.42 mequiv functional group/g.

b) **Indirect regeneration**

Used PVPHP (14 g, wet) was soaked for 1 hr in 500 ml 1N NaOH, washed with H₂O, MeOH, and CCl₄ and dried under vacuum to give 8.1 g of dry PVP. This polymer was reacted with 8.7 ml 48% hydrobromic acid and 3.4 ml of bromine as before. After processing, 21.7 g of polymer was obtained containing 7.84 mequiv Br/g or 2.61 mequiv functional group/g.

**Preparation of PVPCC**

To 10 g of 2% crosslinked polyvinylpyridine resin (50-100 mesh) suspended in 20 ml water were added 9 g of chromic anhydride and 10 ml of concentrated hydrochloric acid. The mixture was stirred at room temperature for 1 hr, then filtered and the resin was washed with distilled water until the filtrate was clear. The resin was dried under vacuum at 60° for 5 hr to give 19.3 g of brown polymer containing 3.6 mmol of reagent per gram. Similar preparations gave PVPCC resins containing up to 3.95 mmole/g.

More usually, the PVPCC resins were used directly after air drying on the filter. Typically a PVPCC resin prepared from 1 g PVP, 0.92 g
CrO₃ and 1 ml concentrated HCl contained 7.5-7.9 mmole of chlorochromate after thorough washing with water and air drying. The fresh resin was bright orange. The capacity of the resin was determined by displacing the CrO₃ from the resin by reaction with 2N potassium hydroxide overnight, acidifying the solution with sulfuric and phosphoric acids, and titrating with a freshly prepared standard solution of ferrous ammonium sulfate using diphenylamine sulfonate as indicator.

Reaction of PVPCC with alcohols

a) Small scale procedure.

Typically, fresh, air dried PVPCC, prepared as described above from 1 g of PVP, was reacted with 1.7 mmole of alcohol in 4-10 ml of solvent (usually cyclohexane), with or without heating. Small aliquots were withdrawn at regular time intervals for chromatographic analysis on a column of 15% Carbowax 20M on chromosorb P. The percent conversion was calculated directly from the chromatograms after calibration. The data shown in Tables 20-25 were generated using this procedure. Occasionally, the reactions were carried out using less PVPCC for the same amount of alcohol (Table 22).

b) Reaction with dried PVPCC resins

PVPCC made from 1 g of PVP, 0.9 g CrO₃ and 1 ml concentrated HCl was washed and dried under vacuum to give 1.84 g of brown resin which was divided into two portions. The first portion (0.91 g) was suspended in 5 ml dry cyclohexane and reacted with 0.11 g cinnamyl alcohol (0.85 mmole) at 80°C. GLC analysis showed that even after 20 hr of reaction only 72% of the alcohol had been converted to the aldehyde and in addition, side products had been formed. The second portion of resin (0.92 g) was soaked for 10 minutes in distilled water, filtered and then reacted with 0.11 g cinnamyl alcohol in 5 ml cyclohexane at 80°C. GLC analysis showed almost 99% conversion to the aldehyde after 36 min and no side products were observed.
c) Larger scale reaction

Fresh PVPCC, prepared as above from 10 g of PVP, was reacted with 2.4 g of cinnamyl alcohol in 50 ml cyclohexane at 60°. After 60 min, GLC analysis showed that the reaction had essentially reached completion. The reaction mixture was filtered and the resin washed with ether and methylene chloride to extract the product. After evaporation of the solvent, 2.0 g of pure cinnamaldehyde (84%) was obtained. NMR: 9.63 δ (1H, d, J=7 Hz), 7.40 δ (1H, d, J=16 Hz), 7.37 δ, (5H, broad singlet), 6.63 δ (1H, doublet of doublets, J=16 Hz and 7 Hz)

d) Reaction with partially spent PVPCC

PVPCC (7.7 mmole) was prepared from 1.03 g of PVP and the required amounts of CrO₃ and HCl as described above. The resin was used immediately after washing with water for the oxidation of 1.7 mmole of cinnamyl alcohol in 5 ml of cyclohexane at 75°. The reaction was followed by GLC and was complete in 36 min. The resin, which had turned black in this first oxidation, was filtered and washed with cyclohexane to remove all the cinnamaldehyde. After rinsing with water and air drying on the filter, the resin was transferred quantitatively to a flask containing 1.7 mmole of cinnamyl alcohol in 5 ml of cyclohexane at 75°. This second oxidation proceeded rapidly and was complete in 36 min. After washing the resin with cyclohexane and water as above, a third oxidation of another 1.7 mmol of alcohol was carried out, requiring 2 hr to reach completion. The resin was again filtered and washed as above, then used in a fourth oxidation with another 1.7 mmole of cinnamyl alcohol. This fourth oxidation reached completion after 7 hr. After washing with cyclohexane, the resin was soaked in 2N potassium hydroxide overnight and the filtrate was titrated with standard ferrous ammonium sulfate in acidic
medium. The titration showed that the resin still contained 1.9 mmol of chlorochromate after four successive oxidations of 1.7 mmole portions of cinnamyl alcohol.

**Regeneration of PVPCC**

a) Standard procedure

The black spent reagent was regenerated by first washing sequentially with 2N hydrochloric acid and 2N sodium or potassium hydroxide until the washes were clear. This treatment effectively removed the chromium salts from the polymer and regenerated the PVP resin. The regenerated PVP was slightly darker than the original material but was unaffected in its ability to produce a satisfactory PVPCC reagent. After regeneration with \( \text{CrO}_3 \) and HCl, the darkened recycled PVPCC had an activity comparable to that of the fresh reagent, and its activity remained essentially constant through repeated oxidation-reduction cycles. The only losses which were observed were mechanical, typically 1-2%, due to the numerous transfers of wet polymer at the different stages of reaction or recycling.

b) Partial regeneration with HCl and \( \text{CrO}_3 \)

PVPCC made from 3 g of PVP as above was divided into three equal portions. The first portion was treated with NaOH and titrated as previously described; it contained 7.7 mmole of reagent. The second portion was reacted with 1.7 mmole cinnamyl alcohol in the usual way and the partially spent resin was titrated as above; it contained 6.1 mmole of unreacted chlorochromate. The third portion was reacted with 1.7 mmole of alcohol as before, and then soaked in 100 ml of 1.5 N HCl for several hours, filtered and washed with water. The combined filtrates were titrated and 1.2 mmole of reagent had been leached from the polymer. The resin was reacted for 1 hr with 2 mmole of \( \text{CrO}_3 \) then filtered and washed. Titration of the filtrate showed that virtually
all of the CrO₃ had been incorporated in the polymer. The regenerated PVPCC produced was treated with NaOH and titrated; it contained 6.8 mmole of reagent.

In a second experiment PVPCC (7.7 mmole) was reacted with 1.8 mmole of cinnamyl alcohol, then soaked in HCl overnight, filtered and washed. The polymer was then reacted with an excess of CrO₃ (5 mmol), washed, and used to oxidize 1.9 mmol of cinnamyl alcohol. The reaction was complete in 36 min. The partially spent reagent was treated with NaOH and titration of the filtrate showed that the resin contained 5.2-5.3 mmole of unreacted CrO₃. If however the regeneration with CrO₃ had been complete, it should have contained ~6 mmole of reagent. Therefore, this recycling procedure leaves ~0.7 mmole of the polymer unregenerated on the first cycle.

Comparison of PVPCC with Chromate Ion Exchange Resin

PVPCC (7.7 mmol) prepared as above and Amberlyst A-26 chromate ion exchange resin (7.7 mmol) prepared according to Cainelli were each reacted with 0.15 ml cyclopentanol in 4 ml cyclohexane at 77°C. The reactions were followed by GLC and the percentage of reaction was calculated (Table 26). The reaction with PVPCC was complete after 22 hr while the chromate ion exchange resin had only reached 86% conversion in that time.

Preparation of Polymeric Sulfides

a) \( \text{P} - \text{SCH}_3 \)

\( \text{P} - \text{Br} \) (Biobeads SX-1, 2.59 mequiv/g, 26 g) was suspended in 400 ml of anhydrous benzene in the reaction vessel shown in Fig. 1, and 100 ml n-BuLi (1.6N) was added. After 2 hrs of heating at 75° under nitrogen, the resin was filtered, washed twice with dry benzene, and 200 ml anhydrous THF containing 17 ml of dimethyl disulfide was added. The reaction mixture was heated at 65° for 2 hr, then left at room temperature overnight. The resin was filtered and washed with THF, THF/H₂O/HCl (2:1:1), H₂O (3 times), THF,
acetone, CH₂Cl₂ and MeOH. After drying 23.3 g of beige polymer were obtained containing 2.28 mequiv S/g for a functional yield of 78%.

b) \(\text{P}-\text{SCH₂CH₃}\)

Diethyl disulfide was prepared from 78 ml of ethyl mercaptan, 40 g NaOH in 120 ml water and 100 ml 30% hydrogen peroxide. The thiol was stirred in the aqueous base until a homogeneous solution was obtained and hydrogen peroxide was then added dropwise with cooling to 0°. The mixture was allowed to react overnight, then was extracted with ether. The ether extracts were washed with water, dried over MgSO₄ and evaporated to give an oil which was distilled to give 46.1 g of diethyl disulfide.

\(\text{P}-\text{Br}\) (3.13 mequiv/g, 30 g) in 300 ml benzene was reacted with 120 ml n-BuLi (1.6 N) as before, washed, and 28 ml of diethyl disulfide in 300 ml anhydrous THF were added. After processing as described above, 28.9 g of polymer were obtained containing 2.59 mequiv S/g for a functional yield of 74%.

c) \(\text{P}-\text{S-Ph}\)

Diphenyl disulfide was prepared as described above from 77 ml of benzenethiol, 30 g NaOH in 200 ml water and 75 ml of 30% hydrogen peroxide. The solid product was recrystallized from hot ethanol to give 55.8 g of diphenyl disulfide.

The polymeric phenyl sulfide was made as before from 23.5 g of \(\text{P}-\text{Br}\) (2.59 mequiv/g) in 250 ml benzene, 76 ml n-BuLi (1.6 N) and 21.0 g diphenyl disulfide in 250 ml THF. After standard workup, 25.5 g of polymer were obtained containing 2.19 mequiv/g of S for a functional yield of 88%.

d) \(\text{P}-\text{SCH₂Ph}\)

The polymeric benzyl sulfide was prepared from 13.5 g \(\text{P}-\text{Br}\) (2.59 mequiv/g) in 150 ml benzene, 44 ml n-BuLi (1.6 N) and 14.2 g of dibenzyl disulfide in 100 ml THF as before. After washing and drying the resin,
14.8 g of polymer were obtained containing 2.11 mequiv S/g for a functional yield of 87%.

**Preparation of Polymeric Sulfonium Salts**

a) $\text{P}^-\text{S}(\text{CH}_3)_2\text{SO}_4\text{CH}_3$

$\text{P}^-\text{SCH}_3$ (2.13 mequiv/g, 3.5 g) was suspended in 35 ml dimethyl sulfate and heated to 90° for 4 hr. After filtering, the resin was washed with ether, benzene, acetone, MeOH, benzene, ether (2 times) and dried to give 4.3 g of polymer containing 3.29 mequiv S/g or a functional yield of 97%. The infrared spectrum showed new absorptions at 1230 (vs), 155 (m), 1010 (s) and 570 (w) cm$^{-1}$.

b) $\text{P}^-\text{S-}(\text{CH}_3)_2\text{SO}_3\text{F}$

$\text{P}^-\text{SCH}_3$ (2.59 mequiv/g, 4.7 g) in 40 ml CH$_2$Cl$_2$ was reacted at room temperature with 5 ml methyl fluorosulfonate (Magic Methyl) for 2 days. The reaction mixture was filtered and washed with CH$_2$Cl$_2$, ether, MeOH, CH$_2$Cl$_2$ and ether. After drying, the polymer weighed 6.2 g and contained 3.79 mequiv S/g for a functional yield of 92%. The infrared spectrum showed new absorptions at 1265 (s), 1160 (m), and 570 (w) cm$^{-1}$.

(Fig. 14)

c) $\text{P}^-\text{S(\text{CH}_3)Ph}^-\text{SO}_3\text{F}$

$\text{P}^-\text{S-Ph}$ (2.03 mequiv/g, 3.85 g) in 40 ml CH$_2$Cl$_2$ was reacted with 5 ml of methyl fluorosulfonate for 5 days at room temperature. After washing as above, the polymer was dried to give 4.86 g of product containing 3.23 mequiv/g of S for a functional yield of 97%. 


FIGURE 14: Infrared Spectrum of \( \text{(} \text{D-} \text{S(CH}_3\text{)}_2 \text{SO}_3 \text{)} \)
d) \[ \overset{+}{\text{P}} \text{-S(Et)}_2^- \text{SO}_4 \text{Et} \]

\( \overset{+}{\text{P}} \text{-SEt} \) (2.51 mequiv/g, 6.7 g) suspended in 70 ml diethyl sulfate was stirred at room temperature for 1 day, then heated to 115° for 2 hr. After cooling, the reaction mixture was processed as above to give 8.9 g of polymer. The functional yield was estimated from the weight gain to be ~ 85%.

e) \[ \overset{+}{\text{P}} \text{-S(Et)}_2^- \text{SO}_3 \text{F} \]

\( \overset{+}{\text{P}} \text{-SEt} \) (2.59 mequiv/g, 7.8 g) in 70 ml \( \text{CH}_2\text{Cl}_2 \) was reacted with 7 ml ethyl fluorosulfonate at room temperature for 4 days. After standard workup 10.5 g of polymer was obtained containing 3.78 mequiv S/g for a functional yield of 96%.

f) \[ \overset{+}{\text{P}} \text{-S(Et)Ph}^- \text{SO}_4 \text{Et} \]

\( \overset{+}{\text{P}} \text{-S-Ph} \) (2.03 mequiv/g, 7.5 g) was reacted with 60 ml diethyl sulfate for 1 day at room temperature, 2 hr at reflux, then a further 2 days at room temperature. After processing as before, 8.1 g of polymer were obtained. The functional yield, estimated from the weight gain was only ~ 23%, showing that diethyl sulfate is not a strong enough reagent to completely alkylate the relatively unreactive polymeric phenyl sulfide.

g) \[ \overset{+}{\text{P}} \text{-S(CH}_2\text{Ph})_2^- \text{SO}_3 \text{CF}_3 \]

Trifluoromethanesulfonic anhydride (triflic anhydride) was made by reacting 108.8 g of trifluoromethanesulfonic acid with 85 g \( \text{P}_2\text{O}_5 \) at 130° and collecting the product which distills between 60-85° (71 g). \[ \text{229} \]

Benzyl triflate was prepared \[ \text{223} \] by adding 8.9 g of triflic anhydride in 10 ml \( \text{CH}_2\text{Cl}_2 \) dropwise to a solution of 3.8 g of 2,4,6-trimethylpyridine and 3.4 g of benzyl alcohol in 20 ml of \( \text{CH}_2\text{Cl}_2 \), which had been cooled to -78°C. After 30 min at -78°C, the benzyl triflate solution was added to 4.25 g of \( \overset{+}{\text{P}} \text{-SCH}_2\text{Ph} \) (2.10 mequiv/g) in 35 ml \( \text{CH}_2\text{Cl}_2 \) cooled in a dry ice bath.
After 4 days at -78°, the polymer was filtered and washed with CH$_2$Cl$_2$, ether, methanol, CH$_2$Cl$_2$ and ether and dried under vacuum at room temperature to give 6.08 g of product containing 2.12 mequiv S/g for a functional yield of 61%.

h) +S(Ph)CH$_2$Ph -SO$_3$CF$_3$

+$S$-Ph (2.19 mequiv/g, 7.3 g) was reacted for 1 day at -78° with benzyl triflate made as previously described from 5.85 g benzyl alcohol, 6.54 g 2,4,6-trimethylpyridine and 15.3 g triflic anhydride with a total of 80 ml of CH$_2$Cl$_2$ as solvent. After processing as above, 11.1 g of polymer was obtained containing 2.72 mequiv/g of S and 3.76 mequiv F/g for a functional yield of 92%.

i) +S(Ph)-CH$_2$CH=CH$_2$ -SO$_3$CF$_3$

Allyl triflate was made by reaction of 7.87 g of triflic anhydride with 1.31 g allyl alcohol and 1.84 g pyridine in 30 ml carbon tetrachloride at -35°. After 15 min the cold solution was filtered rapidly through sodium sulfate to remove the insoluble pyridine salt. The NMR spectrum of the reaction mixture in CCl$_4$ with no internal standard showed peaks at $\sim$ 5.8-6.4 $\delta$ (1H, m), $\sim$ 5.7 $\delta$ (1H, d, J = 4 Hz), $\sim$ 5.4 $\delta$ (1H, d, J = 5 Hz) and $\sim$ 5.0 $\delta$ (2H, d, J = 5 Hz), which was consistent with the structure of allyl triflate. The reagent was reacted immediately with 4.48 g of +S-Ph (2.19 mequiv/g) cooled in a dry ice-acetone bath. After 1 day at -78° the reaction was processed as usual to give 6.34 g of polymer containing 2.95 mequiv/g of S for a 92% functional yield.

Reactions of +S(CH$_3$)$_2$ -SO$_3$F with Ketones using t-BuOK as Base

a) Reaction with Ph-CO-CH$_2$CH$_3$ to give Ph(Et)C\[CH$_2$\]
and ether. The filtrates were combined and the aqueous layer was separated and washed twice with ether. The combined ether extracts were washed twice with water, dried over MgSO\(_4\) and evaporated to give 0.39 g of yellow oil (66% yield). The NMR spectrum of the product corresponded to the reported spectrum of the desired epoxide.\(^{229}\) NMR: 7.30 \(\delta\) (5H, s), 3.00 \(\delta\) (1H, d, J=6 Hz) 2.75 \(\delta\) (1H, d, J = 6 Hz) 1.64-2.46 \(\delta\) (2H, m), 0.93 \(\delta\) (3H, t, J = 8 Hz).

The spent reagent was washed with THF, THF/H\(_2\)O/HC\(_1\)(2:1:1), H\(_2\)O (3 times), THF, acetone, CH\(_2\)Cl\(_2\), and MeOH to give 3.22 g of recovered \([\text{P}}\text{-SCH}_3\) resin.

b) Reaction with Ph-CO-Ph to give \((\text{Ph})_2\text{-C \overset{\circ}{\longrightarrow}} \text{CH}_2\)

\(\text{P}^+\text{-S(\text{CH}_3)_2 \overset{\circ}{\longrightarrow}} \text{SO}_3\text{F}\) (1.4 mequiv/g, 4.1 g) and 0.95 g of benzophenone in 80 ml DMSO were reacted with 1.45 g potassium t-butoxide for 19 hr at room temperature. After processing as above, 0.93 g of product was obtained which contained \(\sim 10\%\) starting material and 90% of the desired epoxide (83% yield, 91% conversion). NMR of \((\text{Ph})_2\text{-C \overset{\circ}{\longrightarrow}} \text{CH}_2\): 7.27 \(\delta\) (10 H, s) and 3.23 \(\delta\) (2H, s). The spent reagent was washed as described above to yield 3.56 g of recovered \([\text{P}}\text{-SCH}_3\).

c) Reaction of recycled\([\text{P}}\text{-S(\text{CH}_3)_2 \overset{\circ}{\longrightarrow}} \text{SO}_3\text{F}\) resins

\(\text{P}^+\text{-SCH}_3\) (6.49 g), recovered from the above reactions, in 80 ml CH\(_2\)Cl\(_2\) was reacted with 4 ml of methyl fluorosulfonate for 2 days at room temperature. The resin was then filtered, washed with CH\(_2\)Cl\(_2\), Et\(_2\)O, MeOH, CH\(_2\)Cl\(_2\) and Et\(_2\)O and dried to give 7.23 of recycled polymeric sulfonium salt.

Recycled\([\text{P}}\text{-S(\text{CH}_3)_2 \overset{\circ}{\longrightarrow}} \text{SO}_3\text{F}\) (4.24 g) in 80 ml DMSO was reacted with 1.01 g of benzophenone and 1.9 g of potassium t-butoxide at room temperature for 1 day. The reaction mixture was treated as described above to give 1.04 g of oil which was shown by NMR to contain approximately 60% of the desired epoxide as well as some starting material and several unidentified side products.

The resin used in this reaction was recovered as described above to give
3.66 g of polymer which treated with 4.3 ml methyl fluorosulfonate in 50 ml CH₂Cl₂ for 3 days at room temperature and washed as usual to give 4.55 g of recycled sulfonium resin. This resin was reacted with 1.0 g of benzophenone and 1.37 g of potassium t-butoxide in 70 ml of DMSO at room temperature. Isolation of the product in the usual way gave 0.858 g of oil which contained none of the desired epoxide, according to its NMR spectrum.

Reactions of [P-S(CH₃)₂]⁺ FSO⁻ With Aldehydes Using Phase Transfer Catalysis

a) Reaction with Ph-CHO to give Ph-CH\textsuperscript{0}CH₂

[P-S(CH₃)₂]⁺ SO₃⁻ (recycled resin, 4.28 g) in 40 ml CH₂Cl₂ was stirred at room temperature with 84 mg (Bu)₄NI, 1.5 g NaOH in 1.5 ml H₂O and 0.3 ml benzaldehyde. After 3 days the reaction was complete as shown by GLC analysis. The reaction mixture was filtered and washed with CH₂Cl₂, ether and H₂O several times. The aqueous layer was separated and washed with CH₂Cl₂. The combined organic layers were washed once with water, dried over MgSO₄ and evaporated to give 0.334 g of colourless oil (97% yield) whose NMR spectrum was identical to that of an authentic sample of styrene oxide. NMR: 7.30 δ (5H, s), 3.9 δ (1H, m), 3.14 δ (1H, m), 2.81 δ (1H, m). The spent reagent was washed as before to give 3.53 g recovered resin.

b) Reaction with CHO to give CH\textsuperscript{0}CH₂

[P-S(CH₃)₂]⁺ SO₃⁻ (recycled resin, 5.04 g) in 50 ml CH₂Cl₂ was stirred with 0.2 ml of 40% (Bu)₄NOH solution, 5 g of NaOH in 9 ml water and 0.5 ml cyclohexanecarboxaldehyde at room temperature. The reaction was complete as shown by GLC after 1 day. Isolation of the product by the procedure described above gave 0.328 g of clear oil (63% isolated yield) whose \textsuperscript{1}H and \textsuperscript{13}C NMR spectra were consistent with the structure of the desired epoxide.
$^1$H NMR: 2.68-2.73 δ (2H, m), 2.50 δ(1H, m, J = 4 Hz), 1.73 δ( 5H, broad), 1.17 δ( 6H, broad). (Fig. 15)

$^{13}$C NMR: 56.59 δ(d, epoxide CH),45.86 δ(t, epoxide CH$_2$), 40.44 δ (broad, ring CH)$_2$29.76, 28.92, 26.43, 25.80, 25.63 δ( ring CH$_2$'s).(Fig. 16)

c) Reaction with CH$_3$(CH$_2$)$_9$CHO to give CH$_3$(CH$_2$)$_9$CH$_2$=

$^+$P-S(CH$_3$)$_2$ $^-$SO$_3$F (recycled resin 1.27 g) in 15 ml CH$_2$Cl$_2$ was stirred with 0.2 ml (Bu)$_4$N, 1 g NaOH in 2 ml water and 0.15 g undecanal for 1 day at room temperature. After standard workup, 0.12 g of clear oil was obtained (89% yield), whose NMR spectrum was in agreement with an authentic sample of 1,2 epoxy-dodecane. NMR: 2.9 δ(1H, broad), 2.7 δ(1H, m), 2.46 δ(1H, m), 1.27-1.47 δ(18H, broad), 0.96 (3H, broad). Recovered resin 0.93 g.

d) Reaction with trans-PhCH=CH-CHO to give trans-Ph-CH=CH-CH$_2$

$^+$P-S(CH$_3$)$_2$ $^-$SO$_3$F (recycled resin 3.1 g) in 40 ml CH$_2$Cl$_2$ was stirred with 0.3 ml 40% (Bu)$_4$NOH solution, 3 g NaOH in 6 ml water and 0.25 ml trans-cinnamaldehyde at -5° for 20 hr. The reaction mixture was worked up as usual to give 0.33 g of product whose proton NMR spectrum showed it to contain ~82% by weight of epoxide and ~18% by weight of phase transfer catalyst. Thus, the yield of epoxide is ~0.27 g (~93%). The proton NMR spectrum was in agreement with the literature.

$^1$H NMR: 7.34 δ(5H, s),6.82 δ (1H, d, J=16 Hz), 5.86 δ(1H, doublet of doublets, J= 8 Hz and 16 Hz),3.42-3.57 δ (1H, m), 2.98-3.12 δ(1H, m),2.68-2.80 δ(1H,m).

$^{13}$C NMR: 136.19 δ(s, ring C),134.47 δ(d, olefin CH),128.62, 128.04, 127.06, 126.44 δ(o,m,p ring CH's plus olefin CH),52.49δ (d, epoxide CH),49.08δ(t, epoxide CH$_2$).
FIGURE 15: 1H NMR Spectrum of $\text{D}_{2}$-DCl$_2$
Reactions of $\text{O}^+\text{S(CH}_3\text{)}_2\text{SO}_3\text{F}$ with Ketones using Phase Transfer Catalysis

a) Reaction with Ph-CO-Ph to give $(\text{Ph})_2\text{C}=\text{CH}_2$

$\text{O}^+\text{S(CH}_3\text{)}_2\text{SO}_3\text{F}$ (new resin, 2.13 g) in 15 ml CH$_2$Cl$_2$ was reacted with 0.16 g (Bu)$_4$NOH solution, 1.3 g NaOH in 2 ml H$_2$O and 0.25 g of benzophenone at room temperature. After stirring for 4 days, GLC analysis of the reaction mixture showed > 98% conversion to the epoxide. Processing the reaction in the standard way gave 0.26 g of product (96% yield). NMR: 7.27 $\delta$ (10H, s), 3.23 $\delta$ (2H, s). Recovered resin 1.61 g.

b) Reaction with Ph-CO-CH$_2$CH$_3$ to give Ph(\text{CH}_2\text{CH}_3)\text{C}=\text{CH}_2$

$\text{O}^+\text{S(CH}_3\text{)}_2\text{SO}_3\text{F}$ (new resin, 2.29 g) in 20 ml CH$_2$Cl$_2$ was stirred at room temperature with 0.08 g (Bu)$_4$NI, 1 g NaOH in 1 ml H$_2$O and 0.15 ml of propiophenone. The reaction was complete after 6 days and workup gave 0.16 g of clear oil (96% yield) whose NMR spectrum matched the published data for the desired epoxide. NMR: 7.20 $\delta$ (5H, s) 2.95 $\delta$ (1H, d, J=6 Hz), 2.68 $\delta$ (1H, d, J=6Hz), 1.60 - 2.30 $\delta$ (2H, m), 0.90 $\delta$ (3H, J=8 Hz). Recovered resin 1.88 g.

c) Reaction with $\text{CH}_2$ to give $\text{CH}_2$

$\text{O}^+\text{S(CH}_3\text{)}_2\text{SO}_3\text{F}$ (new resin, 1.28 g) in 10 ml CH$_2$Cl$_2$ was stirred with 0.15 ml 40% (Bu)$_4$NOH solution, 1 g of NaOH in 1.5 ml water and 0.1 ml of cyclohexanone at room temperature. The reaction had reached 98% conversion after 5 days as shown by GLC and the reaction mixture was processed to give 0.035 g of product. The isolated yield was low because of the low boiling point of the epoxide, which caused it to evaporate during the isolation procedure. The NMR of the product in CDCl$_3$ showed peaks at 2.60 $\delta$ (2H, s) and 1.57 $\delta$ (10H, s (broad)). The literature reports a chemical shift of 2.39 $\delta$ for the epoxide CH$_2$ protons in CS$_2$. The recovered resin weighed 0.97 g.
d) Reaction with Ph-CO-CH₃ to give Ph(CH₃)-C\(\overset{0}{\longrightarrow}\)CH₂

\(\text{P-S(CH₃)₂}^-\text{SO₃F (new resin, 1.95 g)}\) in 15 ml CH₂Cl₂ was stirred with 0.15 ml 40\% (Bu)₄NOH solution, 1.5 g NaOH in 2.5 ml water and 0.12 ml acetophenone at -5°C. The reaction was complete after 28 hr at this temperature and standard workup gave 0.126 g of product (94\% yield) whose NMR was comparable to that of a sample of the desired epoxide prepared by another route.

NMR: 7.30δ (5H, s), 2.92 δ(1H, d, J=6 Hz), 2.74 δ(1H, d, J=6 Hz), 1.69δ (3H, s). Recovered resin 1.47 g. When the reaction was performed at room temperature, the product was partially decomposed and side products were formed.

Preparation of Ph(CH₃)-C\(\overset{0}{\longrightarrow}\)CH₂ from Ph(CH₃)C=CH₂

α-Methylstyrene (1.2 g) in 25 ml CH₂Cl₂ was reacted with 2 g m-chloroperbenzoic acid at -5°C. After 5 days the reaction was complete and the reaction mixture was washed with 5\% NaHCO₃ and water to remove the m-chlorobenzoic acid. The organic layer was dried over MgSO₄ and evaporated to give 1.45 g of the epoxide, contaminated with a small amount of m-chlorobenzoic acid. NMR: 7.29 δ(5H, s), 2.93δ (1H, d, J=6 Hz), 2.75 δ(1H, d, J=6 Hz), 1.70 δ(3H, s).

Reaction of \(\text{P-S(CH₃)₂}^-\text{SO₃F with PhCH₂-CO-CH₃}\)

a) with t-BuOK in DMSO as base

\(\text{P-S(CH₃)₂}^-\text{SO₃F (1.4 mequiv/g, 3.87 g)}\) in 60 ml DMSO was reacted with 0.55 ml of phenyl-2-propanone and 1.37 g of potassium t-butoxide at room temperature for 1 day. After processing the reaction mixture as previously
described, 0.52 g of yellow oil was obtained which showed peaks in the NMR at 7.25 δ(5H, s), 3.65 δ(1H, q, J=6Hz), 2.53-2.93 δ(1H, m), 2.02 δ(3H, s), 1.38 δ(3H, d, J=6 Hz), 1.17 δ (ν1H, s). No change was observed after deuterium exchange. Purification of the product by column chromatography also produced no change in the NMR spectrum. This NMR did not correspond to that of the desired epoxide PhCH₂(CH₃)C―CH₂ made by a different route.

b) under phase transfer conditions.

®-S(CH₃)₂SO₃F (new resin, 1.8 g) in 20 ml CH₂Cl₂ was stirred with 0.07 g (Bu₄N), 1 g NaOH in 1 ml water, and 0.13 ml 1-phenyl-2-propanone at room temperature. After 48 hr, no starting material remained as shown by GLC analysis and the reaction mixture was processed in the usual way to give 0.145 g of a product which showed the same ¹H NMR spectrum as was described above. Recovered resin 1.70 g.

Phenyl magnesium bromide, made from 29 ml of benzyl chloride and 6 g of magnesium turnings in 150 ml dry ether, was cooled in an ice bath and 23 ml of chloropropanone were added dropwise. After ~15 hr at room temperature, the reaction mixture was cooled to 0° and 100 ml of 10% sulfuric acid was added slowly. The organic layer was separated and washed with 10% H₂SO₄, saturated NaCl solution and water, then dried over MgSO₄ and evaporated to give 41 g of yellow oil whose NMR spectrum was consistent with the structure.

OH
Ph-CH₂-C(CH₂Cl)-CH₃. NMR: 7.30 δ(5H, s), 3.44 δ(2H, s), 2.90δ (2H, s), 2.33 δ(1H, broad), 1.27 δ(3H, s).

The chlorohydrin obtained above in 100 ml of ethanol was cooled to 0° and 9.2 g KOH dissolved in 10 ml water and 30 ml ethanol was added dropwise with stirring. After several hours of reaction, 200 ml of water were added and
the reaction mixture was extracted with ether. The ether extracts were dried
over MgSO\(_4\) and evaporated to give 27 g of brown oil. Distillation gave
14.3 g of the desired epoxide (Bp. 82-84°/4 mm) \(^1\)H NMR: 7.24 \(\delta\)(5H, s),
2.83 \(\delta\)(2H, s), 2.60 \(\delta\)(2H, s) 1.26 \(\delta\)(3H, s) (Fig. 17)
\(^{13}\)C NMR: 129.58, 128.33, 126.58 \(\delta\)(aromatic C's), 53.23 \(\delta\)(t, epoxide CH\(_2\)),
43.15 \(\delta\)(t, benzyl CH\(_2\)) 20.87 \(\delta\)(q, CH\(_3\)). (Fig. 18)

Reactions of \(\overset{+}{(P)}-S(CH_3)Ph-\overset{+}{SO_3}F\) under Phase Transfer Conditions

a) Reaction with PhCHO

\(\overset{+}{(P)}-S(CH_3)Ph-\overset{+}{SO_3}F\) (1.5 mequiv/g, 1.54 g) in 20 ml CH\(_2\)Cl\(_2\) was stirred
with 0.15 g (Bu)\(_4\)NI, 1 g NaOH in 1 ml H\(_2\)O and 0.15 ml benzaldehyde
at room temperature and the reaction was followed by GLC. After 2 days
31% of the benzaldehyde had been converted to the epoxide and after 12
days 51% conversion had been attained. However, no further reaction was
observed after several more days. The product was not isolated. Recovered
resin 1 g.

b) with Ph-CO-CH\(_3\)

\(\overset{+}{(P)}-S(CH_3)Ph-\overset{+}{SO_3}F\) (1.4 mequiv/g 1.53 g) in 10 ml CH\(_2\)Cl\(_2\) was stirred
with 0.15 ml 40% (Bu)\(_4\)NOH solution, 1 g NaOH in 1.5 ml water and 0.1 ml
of acetophenone and the reaction was followed by GLC. After 3 days 41%
conversion had been attained. A parallel experiment using the same amount
of \(\overset{+}{(P)}-S(CH_3)_2\) \(\overset{+}{SO_3}F\) as the polymeric reagent had reached completion in the
same time.
Reaction of $\text{P-S(CH}_3\text{)}_2\text{SO}_4\text{CH}_3$ under Phase Transfer Conditions

$\text{P-S(CH}_3\text{)}_2\text{SO}_4\text{CH}_3$ (1.5 mequiv/g, 1.33 g) in 10 ml $\text{CH}_2\text{Cl}_2$ was stirred with 0.15 ml 40% $(\text{Bu})_4\text{NOH}$ solution, 1 g NaOH in 1.5 ml water and 0.12 ml of acetophenone at room temperature and the reaction was followed by GLC. After 3 days 93% of the acetophenone had reacted and after 6 days conversion had reached 98%. Isolation of the product in the standard way gave 0.06 g of yellow oil whose NMR showed that it contained the desired epoxide, as well as some side products resulting from the decomposition of the epoxide at room temperature. Recovered resin 0.95 g.

Regeneration of $\text{P-S(CH}_3\text{)}_2\text{SO}_3\text{F}$

Spent resin ($\text{P-SMe, 3.71 g}$), resulting from the reaction of $\text{P-S(CH}_3\text{)}_2\text{SO}_3\text{F}$ (3.79 mequiv S/g), was suspended in 50 ml $\text{CH}_2\text{Cl}_2$ and 3 ml $\text{CH}_3\text{SO}_3\text{F}$ were added. After 4 days at room temperature the resin was filtered, washed with $\text{CH}_2\text{Cl}_2$, ether, methanol, $\text{CH}_2\text{Cl}_2$ and ether and dried to give 4.37 g of regenerated reagent. This resin was used and regenerated 4 more times. On the fifth cycle the reagent was analyzed and contained 3.59 mequiv S/g. The polymer weighed 3.76 g showing that the mechanical losses amounted to approximately 4% per cycle.

The other methyl sulfonium salts could be regenerated similarly.

Reactions of $\text{P-S(Et}_2\text{)}_2\text{SO}_4\text{Et}$ under Phase Transfer Conditions

a) with Ph-CHO to give PhCH\text{CH-CH}_3

$\text{P-S(Et}_2\text{)}_2\text{SO}_4\text{Et}$ (~ 1.6 mequiv/g, 1.1 g) in 10 ml $\text{CH}_2\text{Cl}_2$ was stirred at room temperature with 0.05 g $(\text{Bu})_4\text{NI}$, 1 g NaOH in 1 ml water and 0.1 ml of benzaldehyde. The reaction was followed by GLC and was complete after 12 days. The product was isolated as usual to give 0.113 g of yellow oil (90% yield)
whose NMR spectrum showed it to be a 1:1 cis:trans mixture of the desired epoxide, by comparison to the NMR spectra of samples of cis and trans epoxide made by a different route.

NMR: 7.27-7.30 δ(5H, cis and trans), 4.03 δ(1/2H, d, J=4 Hz, cis), 3.53 δ(1/2H, d, J=2 Hz, trans), 3.32 δ(1/2H, quintet, J=4-5 Hz, cis), 3.00 δ(1/2H, quartet of doublets, J=2 Hz and 5 Hz, trans), 1.41 δ(1/2H, d, J=5 Hz, trans), 1.02 δ(1/2H, d, J=5 Hz, cis).

Recovered resin, 0.87 g.

b) with \(\text{CH} = \text{CH-CH}_3\) to give \(\text{CH} = \text{CH} = \text{CH-CH}_3\)

\(+P_4S(Et)_2SO_4Et (~1.6 \text{ mequiv/g, 2.11 g})\) in 20 ml CH2Cl2 was stirred with 0.07 g of (Bu)_4NI, 1 g NaOH in 1 ml of water and 0.15 ml cyclohexanecarboxaldehyde at room temperature. The reaction was followed by GLC and was complete after 12 days. Isolation of the product as usual gave 0.104 g of oil (60% isolated yield) whose NMR spectrum was consistent with a 1:1 cis:trans mixture of the desired epoxide.

NMR: 3.05 δ(1H, quintet, J=5 Hz, cis), 2.83 δ(1H, quartet of doublets, J=2 Hz and 5 Hz, trans), 2.60 δ(1H, broad, cis?), 2.40 δ(1H, broad, trans ?), 1.70 δ (5H, broad, cis and trans), 1.25 δ(3H, d, J=5 Hz, cis and trans), 1.13 δ (6H, broad, cis and trans). Recovered resin 1.77 g.

c) with Ph-CO-CH2CH3

\(+P_4S(Et)_2SO_4Et (~1.6 \text{ mequiv/g, 1.87 g})\) in 20 ml CH2Cl2 was stirred with 0.06 g (Bu)_4NI, 1 g NaOH in 1 ml water and 0.13 ml propiophenone at room temperature. The reaction was followed by GLC, but was very sluggish and after 28 days only 17% conversion had been reached. The product was discarded without isolation. Recovered resin \(\sim 1.5 \text{ g}\).
d) with Ph-CO-CH$_3$

\[
P-S(Et)_2-SO_4Et \ (\sim 1.6 \text{ mequiv/g, 2.11 g}) \text{ in } 20 \text{ ml } CH_2Cl_2 \text{ was stirred at room temperature with 0.07 g } (Bu)_4NI, 1 \text{ g } NaOH \text{ in 1 ml water and 0.15 ml acetophenone. The reaction was followed by GLC but was very sluggish and after 28 days a conversion of only 38% had been reached. The product was discarded without isolation. Recovered resin } \sim 1.7 \text{ g.}
\]

Reactions of \( P-S(Et)_2-SO_3F \) under Phase Transfer Conditions

a) with Ph-CHO to give Ph-CH=O-CH-CH$_3$

\[
P-S(Et)_2-SO_3F \ (1.8 \text{ mequiv/g, 1.31 g}) \text{ in } 10 \text{ ml } CH_2Cl_2 \text{ was stirred with 0.1 ml of 40% } (Bu)_4NOH \text{ solution, 1 g } NaOH \text{ in 1.5 ml water and 0.1 ml of benzaldehyde at room temperature. The reaction was followed by GLC and had reached 86% conversion after 1 day and was complete after 4 days. The product was isolated as usual to give 0.085 g of clear oil (63% isolated yield) whose NMR spectrum showed it to be a 1:1 cis:trans mixture of the desired epoxide, by comparison with the NMR spectra of samples of the cis and trans epoxide prepared by another route. NMR: 7.27 - 7.30 \delta (5H, cis, trans), 4.04 \delta (1\frac{1}{2}H, d, J=4.5 \text{ Hz, cis}), 3.55 \delta (1\frac{1}{2}H, d, J=2 \text{ Hz, trans}), 3.32 \delta (1\frac{1}{2}H, \text{ quintet, } J=5 \text{ Hz, cis}), 3.01 \delta (1\frac{1}{2}H, \text{ quartet of doublets, } J=2 \text{ Hz and 5.5 Hz, trans}), 1.44 \delta (1\frac{1}{2}H, d, J=5.5 \text{ Hz, trans}), 1.08 \delta (1\frac{1}{2}H, d, J=6 \text{ Hz, cis}). \text{ Recovered resin 0.99 g. (Fig. 19)}
\]

b) with CHO to give

\[
P-S(Et)_2-SO_3F \text{ (recycled resin 4.38 g) in } 55 \text{ ml } CH_2Cl_2 \text{ was stirred at room temperature with 0.25 ml 40% } (Bu)_4NOH \text{ solution, 4.6 g } NaOH \text{ in 7 ml water and 0.45 ml cyclohexanecarboxaldehyde. The reaction was complete after 1 day and 0.47 g of product (97% yield) was isolated. }^1H \text{ and } ^13C \text{ NMR spectra were consistent}
\]
with a 1:1 cis:trans mixture of the desired epoxide. $^1$H NMR: 2.99 $\delta$ (1 H, quintet, J=5 Hz, cis), 2.75 $\delta$ (1 H, quartet of doublets, J=2 Hz and 5 Hz, trans), 2.55 $\delta$(1 H, broad, cis ?), 2.38 $\delta$(1 H, broad, trans ?), 1.68 $\delta$(5H, broad, cis and trans), 1.24 $\delta$(3H, d, J=5 Hz, cis and trans), 1.14 $\delta$(6H, broad, cis and trans). The assignment of the peak at 2.55 $\delta$ to the cis isomer and that at 2.38 $\delta$ to the trans isomer is supported by the fact that the higher field resonance is the narrower of the two, as would be expected since J=2 Hz for the trans and J=5 Hz for the cis isomer. $^{13}$C NMR: 64.12 $\delta$ (d, epoxide CH $\alpha$ to ring, trans), 61.42 $\delta$(d, epoxide CH $\alpha$ to ring, cis), 53.17 $\delta$(d, epoxide CH $\alpha$ to CH$_3$, trans), 52.49 $\delta$(d, epoxide CH $\alpha$ to CH$_3$, cis), 40.14 $\delta$(broad, ring CH, trans), 36.47 $\delta$(broad, ring CH$_3$, cis), 30.76, 29.70, 29.19, 28.94 $\delta$(ring CH$_2$'s $\alpha$ to CH, cis and trans), 26.41, 25.83, 25.67 $\delta$(other ring CH$_2$'s, cis and trans), 17.88 $\delta$(q, CH$_3$ trans), 13.36 $\delta$(q, CH$_3$, cis). Resonances of cis and trans epoxides are assigned by analogy to cis and trans olefins, in which steric effects in the cis isomer move the carbon resonances to higher field relative to the trans. Recovered resin 2.95 g. (Fig. 20, 21)

c) with Ph-CO-CH$_3$ to give Ph(CH$_3$)C<sup>0</sup>CH$_3$ -P-S(Et)$_2$ $^-$SO$_3$F (recycled resin, 1.36 g) in 10 ml CH$_2$Cl$_2$ was stirred with 0.1 ml 40 % (Bu)$_4$NOH solutions, 1 g NaOH in 1.5 ml water and 0.12 ml of acetophenone at room temperature. The reaction was followed by GLC and was 99% complete after 2 days. The product was isolated as usual to give 0.087 g of oil (59% isolated yield). The NMR spectrum was consistent with a 1:1 mixture of the two isomers of the desired epoxide. NMR: 7.30 $\delta$(5H, s, Z plus E ), 3.15 $\delta$(4 H, q, J=5 Hz, Z isomer), 2.93 $\delta$(1 H, q, J=5 Hz, E isomer), 1.65 $\delta$(3H, s, Z plus E ), 1.41 $\delta$(1 H, d, J=5 Hz, E isomer). Recovered resin 0.99 g. (Fig. 22)
FIGURE 22: $^1$H NMR Spectrum of Ph(CH$_3$)$_2$CH-CH$_3$
d) with Ph-CO-CH\textsubscript{2}CH\textsubscript{3} to give Ph(CH\textsubscript{3}CH\textsubscript{2})C\textsubscript{0}CH-CH\textsubscript{3} |P|^{+}S(\text{Et})\textsubscript{2}^{-}SO\textsubscript{3}F (recycled resin, 1.31 g) in 10 ml CH\textsubscript{2}Cl\textsubscript{2} was stirred with 0.1 ml 40\% (Bu)\textsubscript{4}NOH solution, 1 g of NaOH in 1.5 ml water and 0.135 ml propiophenone at room temperature. The reaction was followed by GLC and had reached 94\% conversion after 5 days. Further reaction time did not increase the conversion. The product was isolated as usual to give 0.117 g of clear oil (70\% isolated yield). The NMR was consistent with a 1:1 mixture of the two isomers of the desired epoxide.

NMR: 7.30 \delta (5H, Z plus E), 3.16 \delta \left(\frac{1}{2} H, q, J=5 \text{ Hz}, Z \text{ isomer}\right), 2.95 \delta \left(\frac{1}{2} H, q, J=5 \text{ Hz}, E \text{ isomer}\right), 1.92-2.24 \delta (1H, m, Z \text{ plus E}), 1.51-1.84 \delta (1H, m, Z \text{ plus E}), 1.41 \delta (1\frac{1}{2} H, d, J=5 \text{ Hz}, E \text{ isomer}), 0.95 \delta (1\frac{1}{2} H, d, J=5 \text{ Hz}, \text{ Z isomer}), 0.89 \delta (3H, t, J=8 \text{ Hz}, Z \text{ plus E}). As was the case for Ph(CH\textsubscript{3}CH\textsubscript{2})C\textsubscript{0}CH\textsubscript{2} the methylene hydrogens of the ethyl group are nonequivalent. Recovered resin 0.95 g. (Fig. 23)

e) with Ph-CO-Ph to give (Ph)\textsubscript{2}C\textsubscript{0}CH-CH\textsubscript{3} |P|^{+}S(\text{Et})\textsubscript{2}^{-}SO\textsubscript{3}F (recycled resin, 1.23 g) in 10 ml CH\textsubscript{2}Cl\textsubscript{2} was stirred with 0.1 ml 40\% (Bu)\textsubscript{4}NOH solution, 1 g NaOH in 1.5 ml water and 0.186 g of benzophenone at room temperature. The reaction was followed by GLC and had reached 89\% conversion in 1 day. After 4 days the reaction was essentially complete, and the product (0.196 g) was isolated as usual (96\% yield). The NMR was consistent with the desired epoxide. NMR: 7.51 \delta (5H, s), 7.418 \delta (5H, s), 3.57 \delta (1H, q, J=6 \text{ Hz}), 1.20 \delta (3H, d, J=6 \text{ Hz}). Recovered resin 0.80 g.
FIGURE 23: $^1$H NMR Spectrum of Ph-(CH$_2$CH$_2$)C—CH-CH$_3$.
Preparation of trans-1-methyl-2-phenyl oxirane

trans-β-Methyl styrene (1.41 g) in 10 ml CH₂Cl₂ was reacted with 2.5 g of m-chloroperbenzoic acid for 3 1/2 hours at room temperature. The reaction mixture was washed with 10% Na₂SO₃ solution to destroy excess peracid, then with saturated NaHCO₃ solution and water. The organic layer was dried over MgSO₄ and evaporated to give 1.3 g of the desired trans epoxide.
NMR: 7.27 δ(5H, s), 3.57 δ(1H, d, J=2 Hz), 3.03 δ(1H, quartet of doublets, J=2 Hz and 5 Hz), 1.44 δ(3H, d, J=5 Hz).

Preparation of cis-1-methyl-2-phenyl oxirane

cis-β-Methyl styrene (0.9 g) in 15 ml CH₂Cl₂ was reacted with 2 g m-chloroperbenzoic acid for 20 hr at room temperature. The reaction was worked up as described above to give 1.0 g of the desired cis epoxide.
NMR: 7.30 δ(5H, s), 4.08 δ(1H, d, J=4 Hz), 3.34 δ(1H, quintet, J=5 Hz), 1.08 δ(3H, d, J=5 Hz).

Regeneration of P-S(Et)₂SO₃⁺

P-S(Et) (5.3 g), recovered from the reaction of P-S(Et)₂SO₃⁻ (1.8 mequiv/g) with carbonyl compounds, was suspended in 60 ml CH₂Cl₂ and reacted with 5 ml ethyl fluorosulfonate at room temperature for 3 days. After washing as usual, 7.0 g of regenerated resin was obtained. This resin was used successfully in further epoxidation reactions.
Regeneration of $\text{P}-\text{S(Et)}_2^-\text{SO}_4\text{Et}$

$\text{P}-\text{Set}$ (5.8 g), recovered from the reaction of $\text{P}-\text{S(Et)}_2^-\text{SO}_4\text{Et}$ with carbonyl compounds, was refluxed for 3 hr in 70 ml diethyl sulfate and then allowed to stand for 3 days at room temperature. After washing as usual, 7.6 g of regenerated resin was obtained.

Reactions of $\text{P}-\text{S(CH}_2\text{Ph)}\text{Ph}^-\text{SO}_3\text{CF}_3$

a) with PhCHO to give PhCH$\xrightarrow{0}$CHPh under phase transfer conditions

$\text{P}-\text{S(CH}_2\text{Ph)}\text{Ph}^-\text{SO}_3\text{CF}_3$ (2.09 g) in 20 ml CH$_2$Cl$_2$ was stirred with 0.3 ml benzaldehyde, 0.1 ml 40% (Bu)$_4$NOH solution and 1 g NaOH in 2 ml water for 3 days at room temperature. GLC analysis of the reaction mixture showed cis- and trans stilbene oxide as well as benzyl alcohol, starting material and a few other minor impurities. Isolation of the product as usual gave 0.58 g of yellow oil which contained a large proportion of (Bu)$_4$NOH as shown by its NMR spectrum. Purification of the product by column chromatography on 20 g silica gel with benzene eluant gave 0.28 g of a fraction containing mostly cis and trans-stilbene oxide in a ratio of 2:5, and 0.06 g of a fraction containing mostly benzaldehyde. The benzyl alcohol remained in the aqueous layer. The yield was ∼50%. Recovered resin 1.46 g. NMR: 7.37 δ(10H, s, trans), 7.20 δ(10H, s, cis), 4.37 δ(2H, s, cis), 3.88 δ(2H, s, trans). These assignments are in agreement with NMR spectra of authentic samples of trans$^\text{233}$ and cis-stilbene oxide.

b) with PhCHO to give PhCH$\xrightarrow{0}$CHPh using LDA as base

$\text{P}-\text{S(CH}_2\text{Ph)}\text{Ph}^-\text{SO}_3\text{CF}_3$ (1.25 mequiv/g, 1.84 g) was added to 0.72 ml diisopropylamine and 3 ml n-BuLi (1.6 N) in 16 ml dry THF at -60° under nitrogen. After ∼15 min, 0.1 ml benzaldehyde was added and the reaction was maintained at low temperature for several hours and then warmed to -10° overnight.
The product was isolated as usual to give 0.21 g yellow oil. The NMR spectrum showed the product to be cis-and-trans stilbene oxide with a small amount of impurity derived from diisopropylamine. Recovered resin 1.29 g.

In other experiments performed in the same way, more side products were obtained and purification by column chromatography was necessary. The yield of product relative to the reagent could be increased by using an excess of benzaldehyde, but the amount of side products was also increased.

\(\text{c) with } \text{CHO to give } \text{PhCH}^{-} \text{CH}^{0}\text{ using LDA as base}\)

\[\text{P}^{-}\text{S(CH}_2\text{Ph)Ph SO}_3\text{CF}_3 \text{ (recycled resin, 2.06 g) was added to a solution of 0.7 ml diisopropylamine and 3 ml n-BuLi (1.6 N) in } 20 \text{ ml anhydrous THF at } -60^{\circ}\text{ under nitrogen. After 15 min, 0.1 ml cyclohexancarboxaldehyde was added and the reaction was maintained at } -60^{\circ}\text{ for several hours, then allowed to warm gradually to } -10^{\circ}\text{ overnight. Isolation of the product as usual gave 0.16 g of oil which contained some of the desired epoxide, as well as large amounts of side products. Separation of the product by column chromatography on } 10 \text{ g silica gel with benzene eluant gave 0.04 g of a fraction containing } \sim 60\% \text{ of the desired product and } \sim 40\% \text{ of a fast moving by product derived from diisopropylamine. A second fraction (0.027 g) contained pure epoxide and the remainder (0.09 g), removed from the column with benzene-methanol (10:1), contained none of the desired product. Total yield of epoxide was } \sim 0.05 \text{ g or } 30\% \text{ with a cis to trans ratio of } 1:1. \text{ Recovered resin 1.41 g.}\]

NMR: 7.38 δ(5H,s), 4.13δ \(\frac{1}{2}\text{, H, d, J=4 Hz, cis}\), 3.73 δ\(\frac{1}{2}\text{H, d, J=2 Hz, trans}\), 2.77-3.07 δ(1H, broad, cis and trans), 0.97-2.20δ(11H, broad).
d) Reaction with ketones using LDA as base

\[
\text{P}^+\text{S(CH}_2\text{Ph)Ph}^-\text{SO}_3\text{CF}_3 (1.25 \text{ mequiv/g, 1.25 g}) \text{ was added to 0.6 ml diisopropylamine and 2.1 ml n-BuLi (1.6 N) in 12 ml THF at } -60^\circ \text{ under N}_2. \]

After 15 min, 0.1 ml propiophenone was added and the reaction was maintained at \(-60^\circ\) for several hours, then warmed to \(-10^\circ\) for 2 days. After processing as usual, 0.16 g of oil was obtained which was shown by NMR to contain mostly starting material with some impurities derived from the LDA. The amount of epoxide, if any, was very small. Similar results were obtained with acetophenone. Recovered resin 0.88 g.

e) Regeneration of \(\text{P}^+\text{S(CH}_2\text{Ph)Ph}^-\text{SO}_3\text{CF}_3\)

\(\text{P}^-\text{SPh}\) (4.1 g), recovered from epoxidation reactions with LDA as base, was treated with benzyl triflate, made from 4.13 g 2,4,6-trimethylpyridine, 3.66 g benzyl alcohol and 9.64 g triflic anhydride, at \(-78^\circ\) in \(\text{CH}_2\text{Cl}_2\) for 1 day as previously described. After standard workup, 6.0 g of regenerated reagent was obtained. \(\text{P}^-\text{SPh}\) (1.8 g) recovered from phase transfer reactions of \(\text{P}^+\text{S(CH}_2\text{Ph)Ph}^-\text{SO}_3\text{CF}_3\), was treated similarly with benzyl triflate, made from 2.58 g 2,4,6-trimethylpyridine, 2.29 g benzyl alcohol and 6.03 g triflic anhydride, to give 2.7 g of regenerated reagent.

**Preparation of cis-stilbene oxide**

Cis-stilbene (0.50 g) in 5 ml \(\text{CH}_2\text{Cl}_2\) was reacted with 0.56 g \(m\)-chloroperbenzoic acid at \(-5^\circ\) for 1 day. Ether (50 ml) was added to the reaction mixture, which was then extracted with 5\% NaHCO\(_3\) solution and water and dried over MgSO\(_4\). Evaporation of the solvent gave 0.527 g of cis-stilbene oxide (96%).
Reactions of $\text{P}^-\text{S}(\text{CH}_2\text{CH}=\text{CH}_2)\text{Ph}^-\text{SO}_3\text{CF}_3$

a) with PhCHO under phase transfer conditions

$\text{P}^-\text{S}(\text{CH}_2\text{CH}=\text{CH}_2)\text{Ph}^-\text{SO}_3\text{CF}_3$ (1.47 mequiv/g, 1.27 g) in 10 ml CH$_2$Cl$_2$ was stirred at room temperature with 0.1 ml 40% (Bu)$_4$NOH solution, 1 g NaOH in 1.5 ml water and 0.1 ml benzaldehyde. After 6 days of reaction, GLC analysis showed only a very small peak corresponding to the desired epoxide. The product was discarded and the polymer recovered (1.02 g).

b) with PhCHO to give PhCH=CH=CH=CH$_2$ using LDA as base

$\text{P}^-\text{S}(\text{CH}_2\text{CH}=\text{CH}_2)\text{Ph}^-\text{SO}_3\text{CF}_3$ (1.47 mequiv/g, 1.00 g) was added to 0.36 ml diisopropylamine and 1.5 ml n-BuLi (1.6 N) in 12 ml anhydrous THF at -70° under nitrogen. After 15 min, 0.15 g benzaldehyde was added and the reaction was maintained at low temperature for several hours before being allowed to warm to room temperature overnight. The product (0.095 g) was isolated as usual and its NMR spectrum showed it to contain ~30% of the desired epoxide as well as some starting material and some side-product derived from diisopropylamine.

NMR: 7.40 δ(5H, s), 5.27-5.70 δ(3H, m), 4.30 δ($\frac{1}{2}$H, d, J=4 Hz, cis), 3.82 δ($\frac{1}{2}$H, d, J=2 Hz, trans), 3.73 δ($\frac{1}{2}$H, broad, cis), 3.40 δ($\frac{1}{2}$H, doublet of doublets, J=2 Hz, and 6 Hz, trans).

c) with PhCOPh using LDA as base

$\text{P}^-\text{S}(\text{CH}_2\text{CH}=\text{CH}_2)\text{Ph}^-\text{SO}_3\text{CF}_3$ (1.47 mequiv/g, 1.93 g) was added to 0.72 ml diisopropylamine and 3 ml n-BuLi (1.6 N) in 18 ml anhydrous THF at -60° under nitrogen. After 15 min, 0.11 g benzophenone was added and the reaction was maintained for several hours at -60° before warming to -10° for 2 days. Isolation of the product gave 0.13 g of oil which contained mostly starting material with a small amount of impurity derived from LDA. No absorptions were observed in the NMR.
between 2.05 and 6.85 δ indicating that no epoxide was formed.

d) Regeneration of $\text{P}-\text{S(CH}_2\text{CH=CH}_2\text{)Ph}^+\text{SO}_3\text{CF}_3$

$\text{P}-\text{SPh}$ (4.59 g), recovered from the above reactions, was reacted at -78° in CH$_2$Cl$_2$ with allyl triflate, made as previously described from 1.31 g allyl alcohol, 1.84 g pyridine and 7.87 g triflic anhydride. After 1 day at -78° and 2 days at -15° the resin was washed as usual and dried to give 5.40 g of regenerated reagent.

Preparation of $\text{PhCH=CH-CH=CH}_2$

Benzaldehyde (2 ml) in 20 ml CH$_2$Cl$_2$ was stirred with 0.4 g benzyltriethylammonium chloride, 3 g NaOH in 3 ml water and 7.6 g of a 67% aqueous solution of allyltetrahydrothiophenyl sulfonium bromide at room temperature. After 10 min the reaction was complete as shown by NMR. The reaction mixture was extracted with CH$_2$Cl$_2$ twice and the combined organic extracts were washed with water, dried over MgSO$_4$ and evaporated to give 2.6 g of the desired epoxide in a cis to trans ratio of 1:2. NMR: 7.32-7.34 δ(5H, cis and trans), 5.24-5.92 δ (3H, m, cis and trans), 4.22 δ(1/3 H, d, J=4 Hz, cis). 3.75 δ(2/3 H, d, J=2 Hz, trans), 3.58-3.70δ(1/3 H, m, cis), 3.34δ (2/3 H, doublet of doublets, J=2 Hz and 6 Hz, trans). (Fig. 24)
CLAIMS TO ORIGINAL RESEARCH

- Development of thallium (III)salt catalysed bromination of polystyrene.
- Preparation of new functional polymers by reaction on lithiated polystyrene.
- Preparation of new functional polymers by chemical modification in a three phase system with phase transfer catalysis.
- Control of site interactions in the reaction of bifunctional molecules with 1% crosslinked functional polystyrenes.
- Preparation and reactions of nucleophilic polymers.
- Preparation and use of poly(vinylpyridinium hydrobromide perbromide) as a regenerable polymeric reagent.
- Preparation and use of poly(vinylpyridinium chlorochromate) as a regenerable polymeric reagent.
- Preparation and use of polymeric sulfonium salts as regenerable alkylidene transfer reagents.
- Use of phase transfer catalysis for the generation of ylides in a solid phase.


- M.J. Farrall and J.M.J. Fréchet, Reaction of Crosslinked Chloromethyl Polystyrene with 1,4-Butanediol; Site-Site Interactions and their Control; J. Am. Chem. Soc., 100, 7998 (1978).


- M.J. Farrall and J.M.J. Fréchet, Functionalization of Polystyrene Resins


REFERENCES


227. T. Durst, personal communication.


