

CHAPTER 1

A REVIEW ON THE APPLICATIONS OF  
FUNCTIONALIZED POLYMERS IN  
ORGANIC SYNTHESIS

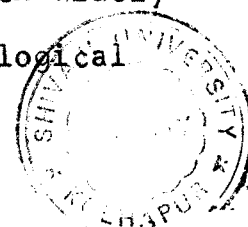
## CHAPTER I

### A REVIEW ON THE APPLICATIONS OF FUNCTIONALIZED POLYMERS IN ORGANIC SYNTHESIS

#### INTRODUCTION

Discovery and applications of new reagents has been one of the most fascinating aspects of synthetic organic chemistry. The study of reactive polymers is an area which until recently had been largely neglected. Polymer chemists tended to study the preparation and physical properties of polymers and this, of course, led to the growth of the plastic industry. Organic chemists, on the other hand, tended to concentrate on studies of relatively small, well-defined molecules or on studies of natural polymers, and synthetic reactive polymers were hardly studied. The last ten to fifteen years have seen the rise in popularity of the simple yet far-reaching idea of attaching chemically reactive species to insoluble supports. Applications have been found in organic chemistry, inorganic chemistry, biochemistry and biology.

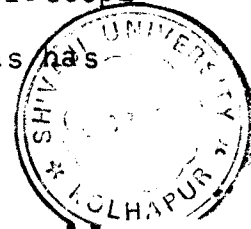
Since the mid 1960s, synthetic macromolecules have also been increasingly recognized as organic species, capable of behaving as organic reactants and susceptible, under appropriate conditions, to all the chemical transformations of smaller organic species. Ion-Exchange resins had previously been widely examined as acid and base catalysts<sup>1</sup>, though no technological



application appears to have developed at that time. The re-discovery of polymers as organic molecules and their use in organic synthesis was made by Merrifield in 1963<sup>2</sup>, when he introduced his "solid phase technique" for the synthesis of peptides, in which an insoluble cross-linked macromolecule was used as a protecting group, simultaneously providing a Facile method for isolating and purifying the product of each condensation step. Since that announcement functionalized polymers have found widespread application in organic synthesis and related fields<sup>3-8</sup>. They have been employed as stoichiometric reagents, as catalysts, as protecting groups, as substrate carriers, in analytical chemistry, in ion exchange, in the detection of reaction intermediates, in chromatography, in biologically and pharmacologically active systems, in the immobilization of enzymes and cells, in the application of dyes and colorants, and in the field of agricultural chemicals.

#### Structure and Properties of Functionalized Polymers :

A functionalized polymer in the present context is a synthetic macromolecule to which are chemically bound functional groups which can be utilized as reagents, catalysts, protecting groups etc. The macromolecule can be a linear species capable of forming a molecular solution in a suitable solvent, or alternatively a cross-linked species, or so-called resin, which though readily being solvated by a suitable solvent remains macroscopically insoluble. Of the two approaches the use of resins has



been more widespread because of the practical advantages accruing from their insolubility. Active functional groups may be incorporated into polymer chains (i) by direct polymerization and copolymerization of monomers containing the desired functional groups, (ii) by chemical modification of a performed polymer, and (iii) by a combination of (i) and (ii). A difficulty with the first method is that considerable manipulation of ~~of~~ the copolymerization procedure may be necessary to ensure a good yield of the required copolymer and, in the case of resins, to ensure also a satisfactory physical form. In the second method commercially available resins of high quality are normally employed and the desired functional groups introduced by using standard organic synthetic procedures. While this generally ensures a product with a good physical form, the derivatization reactions required must be as free of side reactions as possible. Even so the polymer prepared in this way rarely have every repeat unit functionalized, and the distribution of groups may not be uniform. Standard elemental analysis with supporting infrared absorption spectra generally provides satisfactory evidence for chemical modification and allows calculation of the degree of substitution or functionalization of polymeric species, quoted in milliequivalents per gram of polymer. In some circumstances other analytical procedures<sup>9</sup>, including detailed structural analysis by nuclear magnetic resonance spectroscopy<sup>10</sup>, can be applied, depending on the nature of the polymer and the chemical transformations involved.

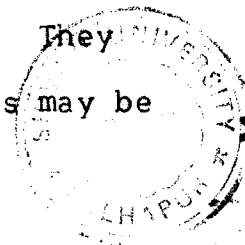
Functionalized polymeric supports must possess a structure which permits adequate diffusion of reagents into the reactive sites, a phenomenon which depends on the extent of swelling or solvation, the effective pore size and pore volume, and the chemical and mechanical stability of the resins under the conditions of a particular chemical reaction or reaction sequence. These in turn depend on the degree of cross-linking of the resin and the conditions employed during preparation of the resin. Three main types of resins<sup>9</sup> can be identified; (a) microporous or gel-type resins; (b) macroporous resin, and (c) macroreticular resins.

Microporous species are prepared from a vinyl monomer and a difunctional vinyl comonomer in the absence of any additional solvating media. In the dry state they are microporous, with polymer chains being separated by typical solid-state intermolecular distances. On contact with a good solvent a soft gel network is formed with the generation of considerable porosity depending on the degree of cross-linking. Where the latter is  $\leq 1\%$ , swollen resins generally have low mechanical stability and readily fragment even under carefully handling. In contrast, commercially available microporous resins with  $> 8\%$  cross-linking are mechanically very stable, but unfortunately give rise to acute diffusional limitations resulting in slow and incomplete reactions. In practice resins of  $\sim 2\%$  cross-link ratio provide a satisfactory compromise generally allowing adequate penetration by most reagents and yet retaining sufficient mechanical stability to provide ease

of handling. Copolymer beads made by suspension polymerization of 98 % styrene and 2 % divinyl benzene isomers have found very wide application as a result of these factors.

Very similar properties can arise with macroporous resins. These are prepared as before but with the inclusion of an inert solvent. Where the solvent solvates both monomer and polymer a fully expanded network is formed with a considerable degree of porosity<sup>11</sup>. Removal of the solvent causes a reversible collapse of the matrix, and in the dry state such materials are similar to microporous resins. In order to achieve mechanical stability in the solvent swollen state it is usual to employ larger quantities of difunctional comonomer in the preparation, upto  $\sim$  20 %. Materials of this type are not readily available from commercial sources.

Where the solvent employed during polymerization is a good solvent for the monomers but a precipitant for the polymer, the term macroreticular is generally employed to describe the product<sup>12</sup>. The latter is a highly porous rigid material which retains its overall shape and volume when the precipitant is removed. Again it is normal to use a larger quantity of difunctional comonomer, and in the case of some chromatographic applications styrene resins with  $>$  50 % divinylbenzene content are employed<sup>13</sup>. This enables such products to be subjected to high pressures,  $\sim$  1000 psi, in high-performance liquid chromatography conditions. The structure of these resins is quite different from the previous two. They have a large and permanent pore volume, and reaction sites may be



regarded as being located on a permanent interior surface of the resin. Such materials are available from a number of commercial sources. Macroporous species have also been prepared in the presence of large inert molecules which subsequently can be washed away to create permanent voids<sup>14</sup>.

#### Advantages and Disadvantages in Using Functionalized Polymers :

Having a reagent or substrate attached to an insoluble support has several practical advantages which include the following :

(i) Reaction work-up is simplified because the supported species are easily separated from the non-supported species by filtration. This may make it possible to avoid exposing the reaction product(s) to water or to avoid a chromatographic separation in the reaction work-up.

(ii) If the use of an excess of a reagent results in a greater reaction yield, then an excess can be used without causing separation problems.

(iii) When a polymer-supported reagent is used, the spent reagent is easily recovered and can possibly be recycled. This is very important economically and can make it worthwhile to prepare complex supported reagents.

(iv) If the reaction proceeds virtually to completion, so that filtration and washing of the polymer are all that is required to work-up the reaction, it becomes feasible to automate the

process. This has obvious industrial attractions.

(v) If a reaction proceeds very readily it can possibly be carried out using a column of the supported reagent or substrate and passing the other reactants down the column in turn.

(vi) Since cross-linked polymers are insoluble and non-volatile, they are nontoxic and odourless. Hence carrying out reactions involving, for example, thiols or selenium compounds on polymer supports is a way of making the reactions environmentally more acceptable.

The practical advantage of attaching catalysts to insoluble supports are similar to the above and they have long been recognized and industrially exploited. Thus, the reaction products are easily separated from the catalyst and the latter is available for re-use. Catalysts on insoluble supports can be used in flow systems. The vast majority of supported catalysts used commercially employ some sort of ill-defined physical interaction between the catalyst and the support. Indeed the structural nature of the actual catalytic species in these preparations is in many instances unknown. It is concerned with soluble catalysts which have been 'heterogenized' by being chemically bound to an appropriately functionalized support.

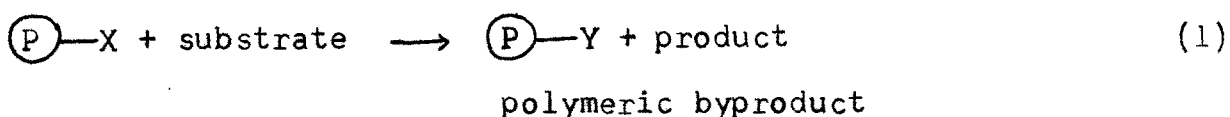
Balancing the above advantages there are also a number of important disadvantages. Probably the most important of these, is the likely additional time and cost in synthesizing a supported reagent or catalyst. This may well be offset by the potential



advantages, and certainly in the case of regenerable and recyclable species this objection essentially disappears. The occurrence of slow reactions and poor yields, however, can seldom be accommodated, and these can be problems, however, appropriate choice of support and reaction conditions can overcome this problem. The ultimate capacity of a functionalized polymer is also restricted, and may be important in preparative organic chemistry involving stoichiometric quantities of supported reagents. Difficulties in characterization of reactions on polymers can also arise. Finally in the use of functionalized polymers there always exists the additional chemical option of a side reaction with the polymer itself. A number of classic cross-linking side reactions have been identified<sup>15,16</sup>, but many other low yields may well be associated with intrapolymeric reactions, which have never been recognized, let alone characterized. Despite these drawbacks, a large number of systems have been developed, and considerable scope now exists for their exploitation in routine synthetic chemistry.

#### Polymer Supported Reagents :

A polymer supported reagent is a reactive organic group bound to a macromolecular support and used in stoichiometric quantities to achieve the chemical modification of an added substrate (reaction 1)



Such groups may be attached to polymeric carriers by physical adsorption or by chemical bonding. Physically adsorbed species are generally unsatisfactory since in use the components tend to dissociate, and they are therefore unsuitable for column or cyclical application.

Resins containing peroxacid residues, eg (1.1), can be prepared readily from formyl- or carboxyl-substituted polystyrene resins<sup>17,18</sup>. Tri- and di-substituted alkenes are generally epoxidized in good yield by these resins<sup>18</sup> and sulphides, including penicillins and oxidized deacetoxycephalosporins, are efficiently oxidized to sulphoxides and/or sulphones<sup>19</sup>. Penicillin G, (1.2) has been oxidized in 91 percent yield by passing a solution in acetone down a column of the resin<sup>19</sup>. An advantage of these resins is that they can be used with equal facility with acidic substrates, for there is no difficulty in separating the acidic product from spent peroxyacid as there can be when monomeric peroxyacids are used. The spent resin can be recycled<sup>17,19</sup>.

The Moffat oxidation (carbodi-imide, dimethyl sulphoxide (DMSO),  $H^+$  catalyst) converts alcohols to aldehydes under mild conditions but separating the aldehyde from the ureas which are also formed can present problems. These can be overcome by using the carbodi-imide resin (1.3)<sup>20</sup>. The spent resin can be recycled but with some loss of activity.

Another mild oxidant for converting alcohols to aldehydes or ketones is thioanisole and chlorine followed by triethylamine.

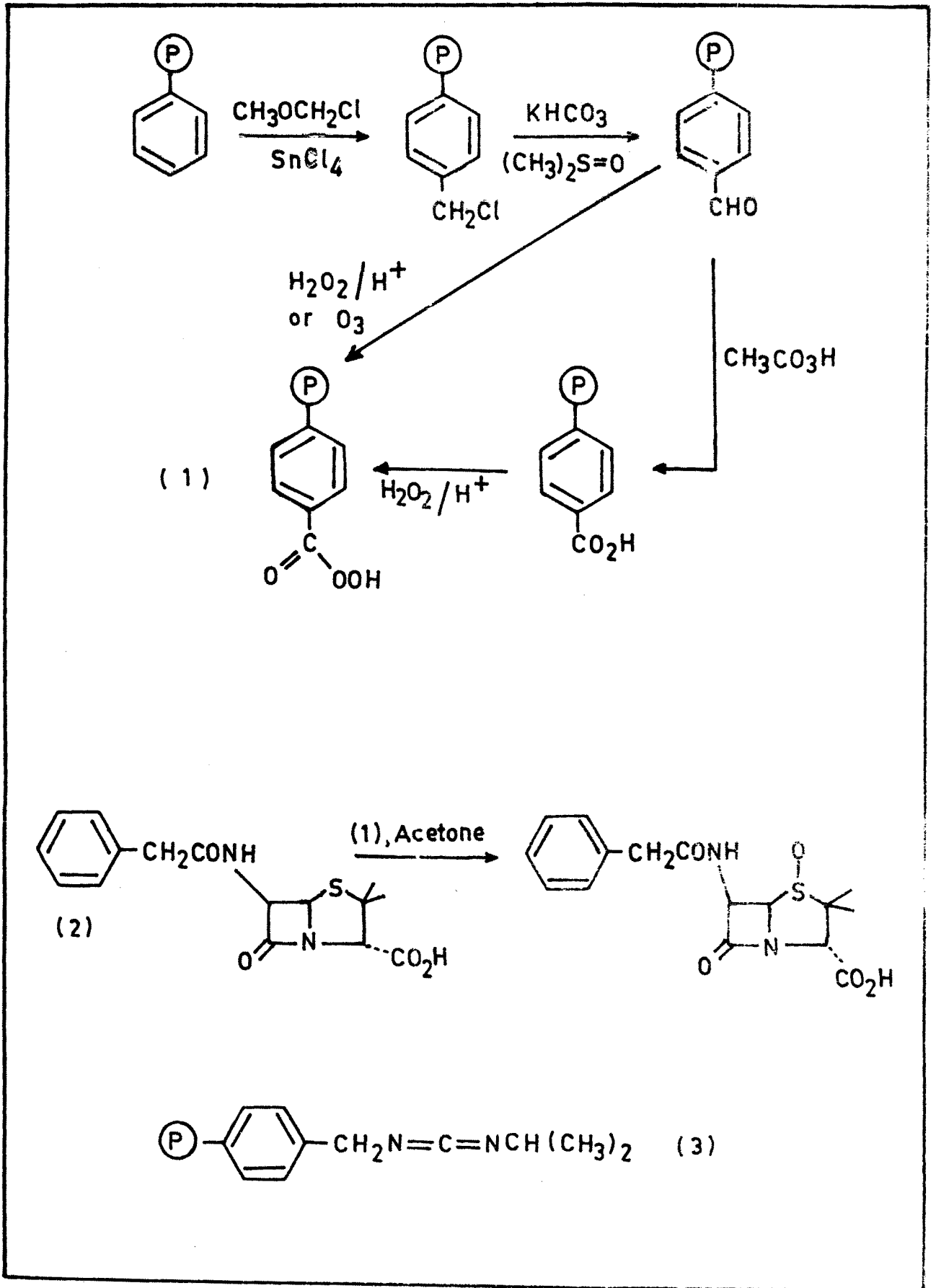


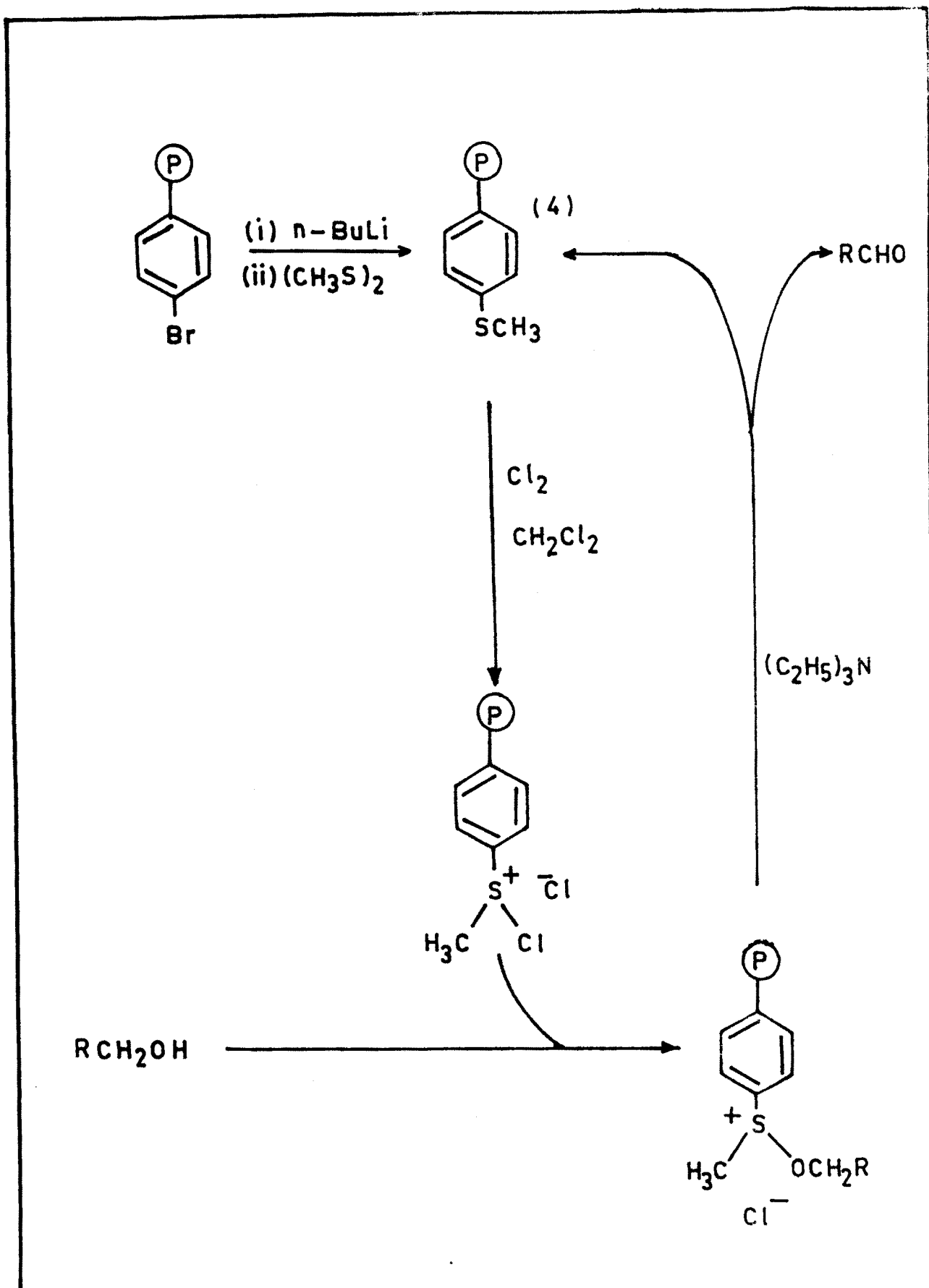
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Resin (2.4) can be employed in place of thioanisole and has the advantage that the resin is odourless and is readily recovered for re-use<sup>21</sup> (see chart 2). The substrate becomes attached to the resin in the first step and is released in the second, consequently, if the sulphide residues on the resin are sufficiently remote and the resin is inflexible, only one hydroxyl group of a substrate with two or more hydroxyl groups should be oxidised. This possibility has been investigated using a macroreticular resin with 1,7-heptanediol as the substrate. The best selectivity achieved was a hydroxyaldehyde to dialdehyde ratio of 23:1, but, unfortunately, the yield of hydroxyaldehyde was then only 50 percent.

Several polymer supported selenium reagents have recently been prepared<sup>22</sup>. Use of these avoids the difficulties arising from the odour and the toxicity of low molecular weight selenium compounds.

Reactions of cross-linked poly-N-bromo succinimide (3.5) prepared by bromination of cross-linked polysuccinimide, with cumene in carbon tetrachloride, gives three major products, bromides (3.6), (3.7) and (3.8). Under similar conditions N-bromo succinimide reacts with cumene to give two major products, bromides (3.9) and (3.10).

It has been suggested that the difference arises because, in the vicinity of the polymer chain, the environment is polar and this favours dehydrobromination of the initial product (3.9) to

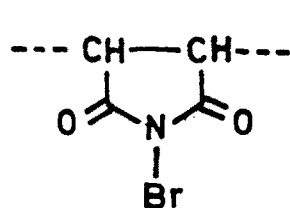


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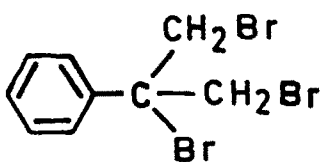
give  $\alpha$ -methyl styrene, which can then react with bromine (formed by reaction of hydrogen bromide and N-bromoamide) to give bromide (3.10). This, by further dehydrobrominations and brominations, is converted to the other products. In agreement it is found that N-bromosuccinimide reacts with cumene in acetonitrile (a more polar solvent than  $\text{CCl}_4$ ) to give bromide (3.6), and with ethyl benzene to give  $\alpha,\beta$ -dibromoethyl benzene.

A problem some times encountered in Witting reactions is separating the alkene from the triphenyl phosphine oxide that is produced. This can be avoided by using a resin containing triphenylphosphine residues in place of triphenylphosphine<sup>23</sup>. The phosphine (3.11) can be prepared<sup>24</sup> as shown in charts.

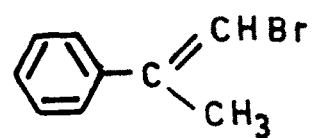
The reagent triphenylphosphine-carbon tetrachloride brings about many useful conversions under mild conditions<sup>25</sup>. As before, separation problems can be overcome using the phosphine resin (3.11) in place of triphenylphosphine. Alcohols give chlorides<sup>24,26,27</sup> acids give acid chlorides<sup>26</sup>, acids and amines give amides<sup>26,28</sup>, primary amides give nitriles<sup>29</sup> and secondary amides give imidoyl chlorides<sup>29</sup>. There is evidence that the polymer supported reactions with alcohols and with acids proceed mainly via reaction (3.12) in chart 3<sup>30</sup>. Hence a high proportion of the phosphorus containing residues on the resin can reach each other. This type of reaction is probably easier with a highly substituted flexible resin than it is in the monomeric reaction and may explain why the polymeric reactions proceed somewhat faster than those using triphenylphosphine (ca x13) or



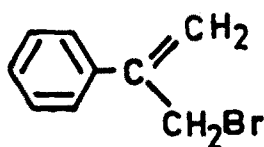
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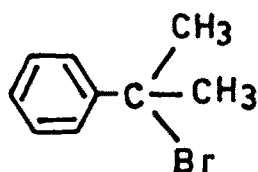
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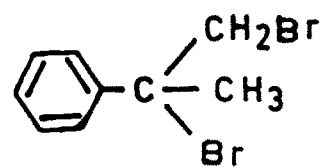
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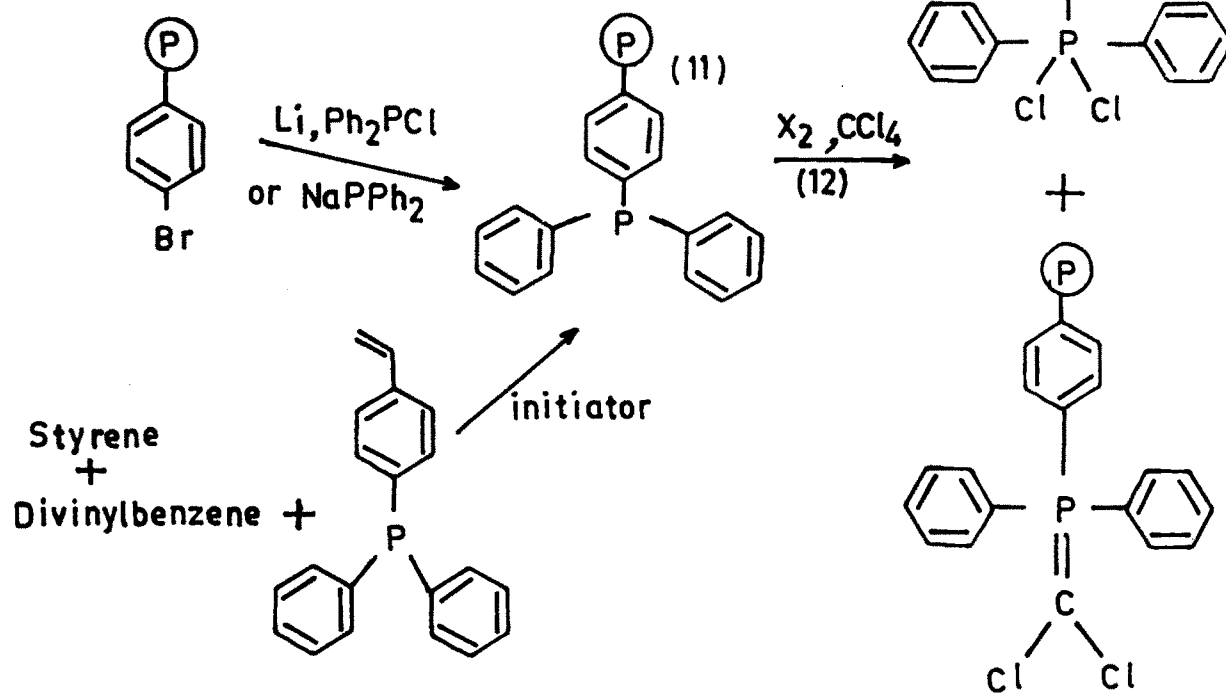
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(9)



(10)

Phosphine resins:—

4-diphenyl phosphinous isopropyl benzene (ca x 3) - a better analogue of the polymeric phosphine<sup>30</sup>.

The reactive groups in polymer supported reagents need not be covalently attached. Anion exchange resins containing reactive anions may also be used as reagents. An attractive feature here is that if macroporous resins are used, the reactions can be carried out in non-polar solvents such as hexane, benzene and dichloromethane. The resin, therefore, provides a means of making anions available for reaction in non-polar media and is an alternative to phase-transfer catalysed or crown ether catalysed reactions<sup>30,31</sup>. The resins can be re-used.

In view of our work on chemoselective reduction using the borohydride exchange resin (BER), a brief survey of reductions using polymer-supported reagents is given here. Polymer-supported borohydride has been prepared and used in ethanol to reduce benzaldehyde to benzyl alcohol<sup>32</sup>. The reaction was, however, much slower than that using sodium borohydride.

A few simple organic substrates in aqueous or ethanolic solution have been reduced by passage down columns of the titanous or chromous forms of an anion-exchange resin (see Table 1)<sup>33,34</sup>. Resins containing transition metal ions can be considered as redox resins and oxidations as well as reductions can almost certainly be carried out.

The most extensively studied reagent for effecting the conversion of aldehydes and ketones to alcohols is the polymer-





Table 1 : Reduction Using Polymer-Supported Ions

Substrate	Supported ion	Reaction conditions <sup>a</sup>		Yield (percent)	Reference
		Solvent	Temperature (°C)		
p-Nitroaniline	Ti <sup>3+</sup>	Ammonical ethanol	40	100	33
p-Benzoquinone	Ti <sup>3+</sup>	Water	40	90	33,34
1,4-Napthaquinone	Ti <sup>3+</sup>	Ethanol	60	89	34
Azobenzene	Ti <sup>3+</sup>	Ethanol	20	65	34
Furil	Ti <sup>3+</sup>	Ethanol	60	85	34
Benzil	Ti <sup>3+</sup>	Ethanol	60	97	34
Benzil	Cr <sup>2+</sup>	Ethanol	60	88	34
Benzoin	Cr <sup>2+</sup>	Ethanol	60	91	34
Triphenyltetra-azolium chloride	S <sub>2</sub> O <sub>4</sub> <sup>2-</sup>	Water	20	85	34

a - A solution of the substrate was passed down a column of the reagent.

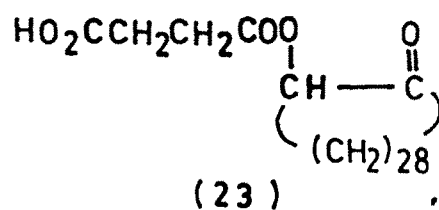
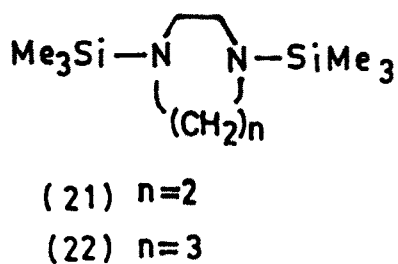
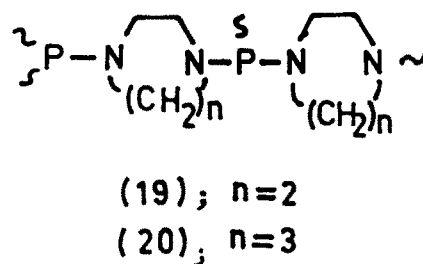
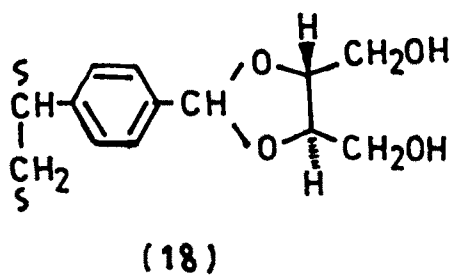
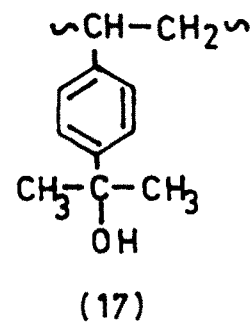
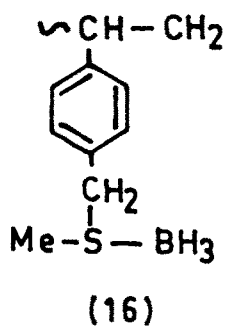
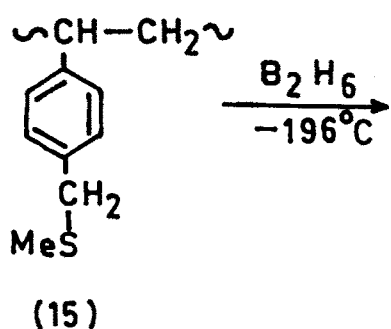
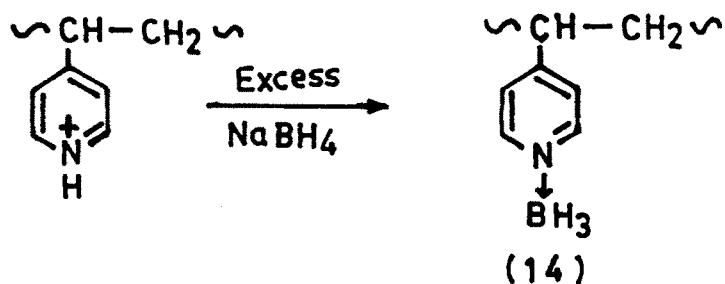
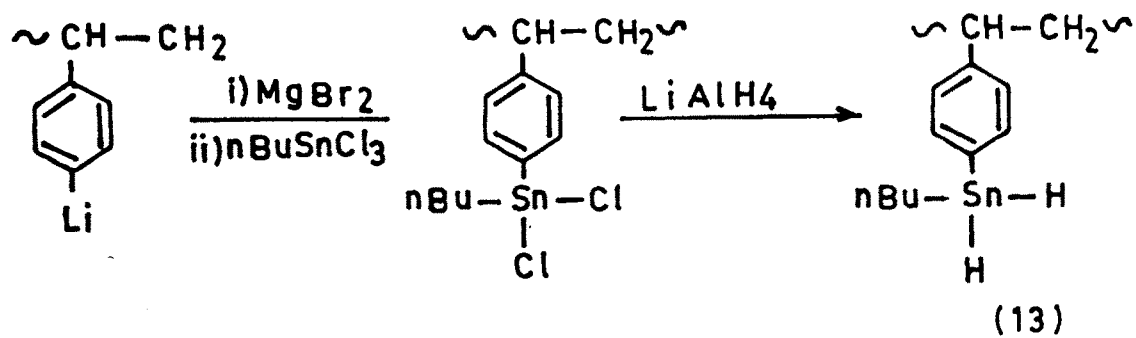
supported tin hydride (4.13). This was prepared from a cross-linked macroporous polystyrene via the reaction outlined in chart 4 as below :

An advantage of the reagent over non-polymeric tin hydrides is that it is odourless and non-toxic. When aldehydes and ketones were reduced with this reagent yields were generally good but long reaction times were required. (see Table 2). In this case attempts to regenerate the spent reagent were not very successful.

Hallensleben has investigated the use of the polymer-supported borane complex (4.14) prepared as shown below, to reduce aldehydes and ketones<sup>35</sup>. When the linear version of (4.14) was used in dry benzene as a reducing agent, moderate yields of alcohols were obtained.

A cross-linked version of (4.14) was prepared and used as a reagent in columns, the substrate in benzene being passed down the column at 70°C. Since the initial reaction product was a boron ester, the column could be washed free of starting material before decomposition of the ester by acid. The results are shown in Table 3.

A somewhat similar reagent has been described in a recent patent<sup>36</sup>. Thus, the cross-linked polymer (4.15) was treated with excess of borane to give polymer (4.16), an odourless easily handled polymeric version of  $\text{Me}_2\text{S}:\text{BH}_3$ . Polymer (4.15) was used to reduce acetophenone quantitatively.



CHART—4

Table 2 : Reduction of Aldehydes and ketones using polymeric Tin Hydride (13)<sup>a</sup>

Substrate	Reaction time (h)	Yield (percent)	Substrate	Reaction time (h)	Yield (percent)
Acetophenone	45	92	Benzophenone	44	54
t-Butyl methyl ketone	41	92	4-Phenyl cyclohexanone	42	61
Benzaldehyde	40	91	4-Phenyl cyclohexanone	4 <sup>b</sup>	750
Heptanol	38				

a - Unless indicated otherwise, reactions were carried out using 3 molar equivalents of reagent in toluene under reflux. At the end of the reaction period the tin alkoxide was hydrolysed with HCl.

b - Reaction carried out in THF at r.t. in the presence of 5 mol percent of PtCl<sub>4</sub>.

Table 3 : Reduction of Aldehyde and ketones by polymer (4.14)

Substrate	Reaction time (h)	Yield (percent)	
		Linear polymer <sup>a</sup>	Cross-linked polymer <sup>b</sup>
Benzaldehyde	4.0	14	19
p-Nitrobenzaldehyde	0.5	74	-
p-Chlorobenzaldehyde	1.5	51	66
Cyclopentanone	2.5	40	42
Benzophenone	2.5	12	14

a - Reaction carried out in benzene under reflux.

b - Reaction carried out using a column technique with benzene at 70°C.

Another two types of polymer-supported alkoxyaluminium hydrides are used for reduction. The first was prepared by treating a cross-linked polymer containing the residues (4.17) with an excess of lithium aluminium hydride in ether<sup>37</sup>. This reagent could reduce cyclohexanone to cyclohexanol. The second alkoxyaluminium hydride was prepared by treating a cross-linked polymer containing the chiral diol residues (4.18) with lithium-aluminium hydride in ether<sup>38</sup>. This reagent was used to reduce the ketone group in prostaglandin.

Reduction of quinones to quinols can be achieved by using the polymer prepared by means of Friedel-Crafts reaction between 2-bromomethylantraquinone and cross-linked polystyrene, followed by sodium borohydride reduction.

The polymer supported tin hydride (4.13) has also been used to replace iodo and bromo groups by hydrogen<sup>39</sup>. The yields were generally high and removal of the resin at the end of the reaction period left an almost pure product.

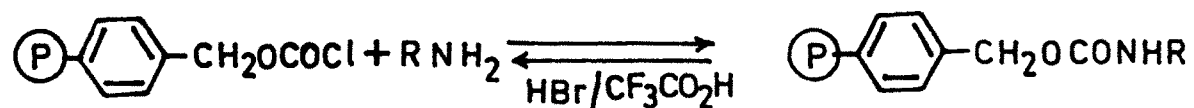
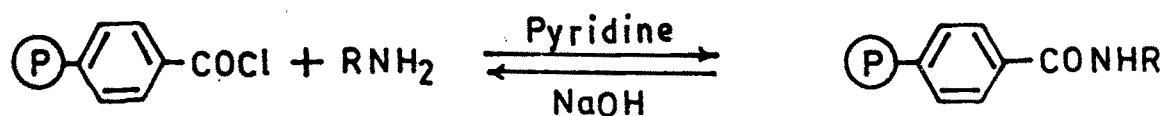
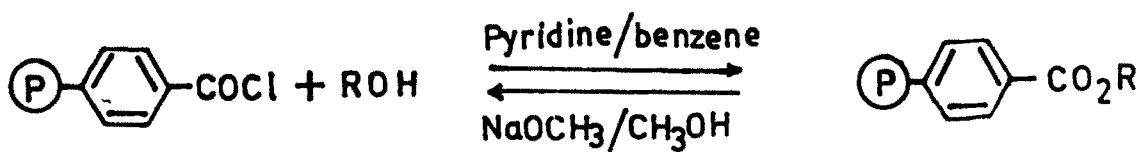
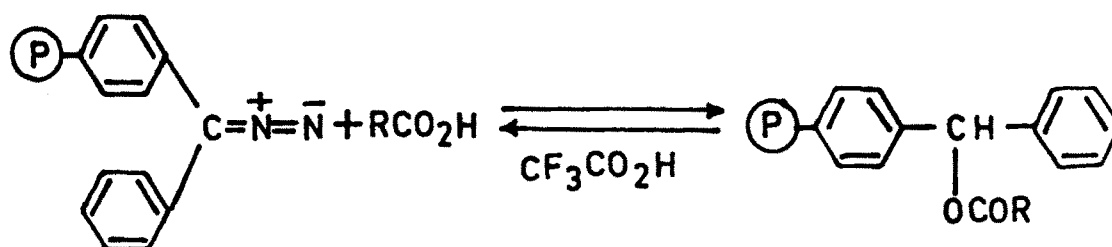
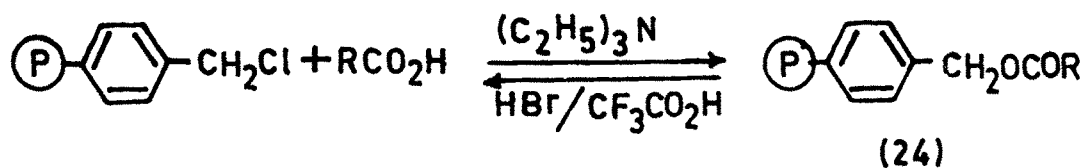
Patchornik attached lipoic acids via the carboxyl group to various hydrophilic polymers, then reduced the disulphide group with sodium borohydride<sup>40</sup>. The product was used to reduce disulphide bridge in peptides and proteins such as the oxidized forms of glutathione and cystine. Harpp and his coworkers prepared the insoluble polymers (4.19) and (4.20) with phosphorous trichloride and compounds (4.21) and (4.22) showed that they can be successfully used to effect desulphurization<sup>41</sup>.

### Reactions Using Polymer Supported Substrates :

The best known reactions of this type are those employed in the solid phase synthesis of polypeptides<sup>42</sup>, oligosaccharides<sup>43</sup> and oligonucleotides<sup>44</sup>. These reactions can be regarded as examples of the use of polymer supported protecting groups, and illustrate well the merits of such protecting groups, i.e. easy isolation of polymer supported product, possible use of excess reagent to obtain high yields of polymer supported products, automation of reaction procedures etc. Chart 5 shows some polymer supported protecting groups which have been utilised in the solid phase synthesis of natural polymers and which are suitable for the protection of acids, alcohols and amines. Two examples of their use in other areas will be considered.

The first illustrates the use of a polymer supported protecting group to assist in the isolation of a product formed in only trace amounts<sup>45</sup>. Thus, the acid (4.23) was attached to chloromethyl resin (5.24) and in the presence of the product 1,10-decanediol was reacted with trityl chloride.

At the time it reacted a very small amount of decane derivatives was threaded through the macrocycle and so became trapped on the resin. Other products were washed away and the tritylation reaction repeated 70 times to accumulate a workable amount of threaded macrocycle. The resin was then washed thoroughly and the 'hooplane' (6.25) released from the resin and purified.



CHART—5



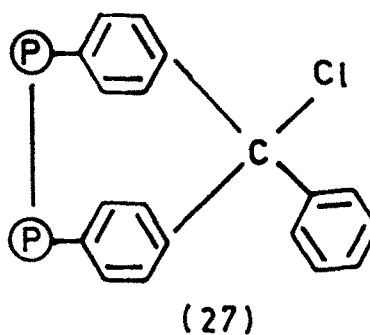
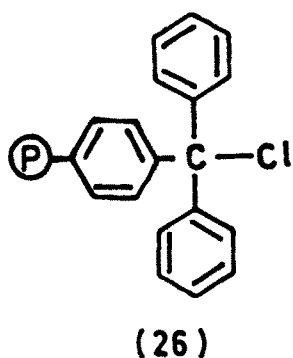
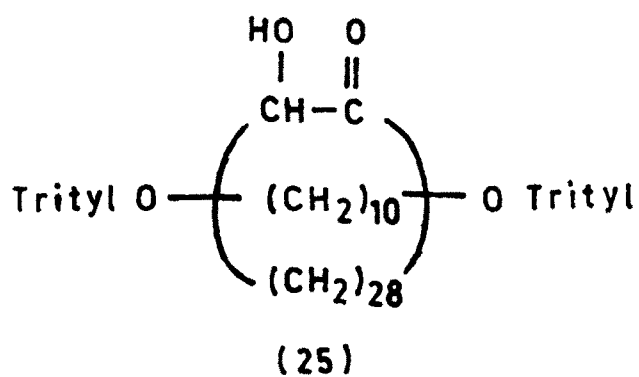
The polymer supported trityl chloride (6.26), prepared from 2 percent cross-linked polystyrene, was separately treated with butane-1,4-diol, heptane-1,7-diol and decane-1,10-diol in pyridine. After unattached diol had been washed away, the free hydroxyl groups were acetylated. The products were then cleaved from the resin. The yields of diol monoacetates were 50-60 percent. In each case 30-50 percent of the diol was recovered, indicating that both the hydroxyl functions of these molecules had reacted with the resin. In this particular case, using the resin facilitated isolation of diol monoacetate but did not give significantly different proportions of monoprotected and di-protected diol than might have been obtained using classical procedures.

More successful results were, however, obtained using the polymer supported trityl chloride (6.27), also prepared from 2 percent cross-linked polystyrene. This resin is more rigid than (6.26) and the results are good.

### Polymer Supported Catalysts

Numerous transition metal complexes have been described in recent years, which are useful catalysts for hydrogenation, isomerisation, hydroformylation etc. Many of these catalysts have now been attached to resins<sup>46</sup>. This has the advantage that the valuable catalyst is easily removed from the reaction mixture and is available for re-use. One of the earliest of these polymer supported catalysts to be described was the polymer supported analogue of the hydrogenation catalyst  $K_2PdCl_4$ . This was prepared

by treating the hydroxide form of an anion exchange resin with this salt<sup>47</sup>. Most of the monomeric catalysts contain triphenylphosphine ligands and polymer supported analogues of these catalysts have generally been prepared by replacing one or more of these ligands with phosphine residues of resin (3.11). For example, when a suspension of the resin in toluene was stirred with  $(\text{Ph}_3\text{P})_3\text{RhCl}$ , the polymer supported hydrogenation catalyst (6.28) was obtained<sup>48</sup>. Reaction of the resin with  $(\text{Ph}_3\text{P})_2\text{Ni}(\text{CO})_2$  and with  $(\text{Ph}_3\text{P})_3\text{RhH}(\text{CO})$  similarly gave the cyclo-dimerisation catalyst (6.29) and hydroformylation catalyst (6.30) respectively. Some reactions using these catalysts are given in chart 7. In the hydroformylation of pent-1-ene, catalyst (6.30) produced a substantially higher ratio of hexan-1-al to 2-formylpentane than the corresponding homogeneous catalyst, especially when the resin had a high phosphine content and the ratio of phosphine to rhodium was high. The reasons for this are not clear. Often the polymer supported catalysts are somewhat less active than their soluble counterparts, probably because the substrates need to diffuse into the resins. The diffusion problem can be avoided by using a linear polymer<sup>48</sup> though the catalyst is not as easily recovered or by attaching the catalyst only to the surface of a resin or other suitable material<sup>49</sup>, through the catalyst will probably have a lower activity per unit weight. Polymer supported catalysts are not always less active, however the catalyst obtained by treating the polymer supported titanocene derivative (6.31) with n-butyl lithium is ca 70 times more active as a hydrogenation catalyst than the non-supported analogue, probably because the active groups



Polymer supported catalysts :

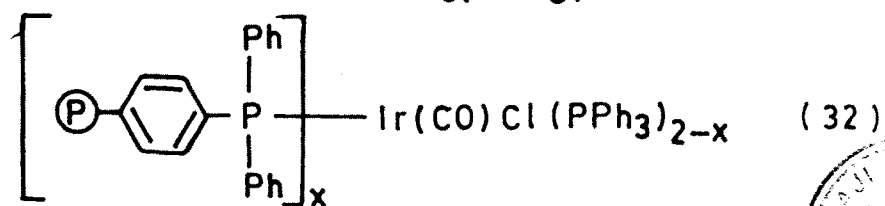
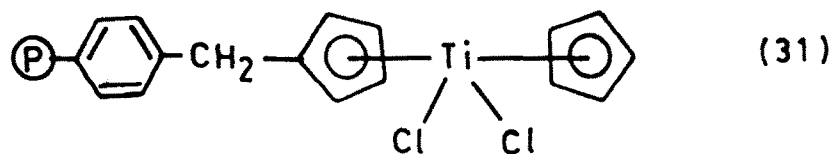
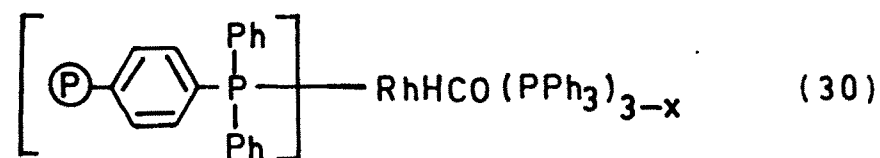
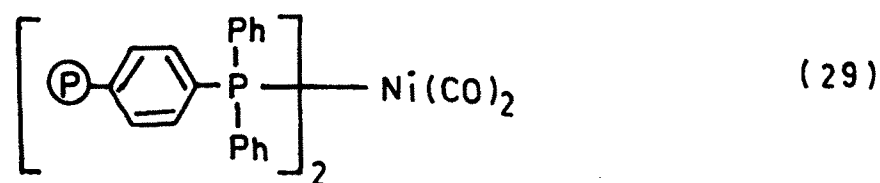
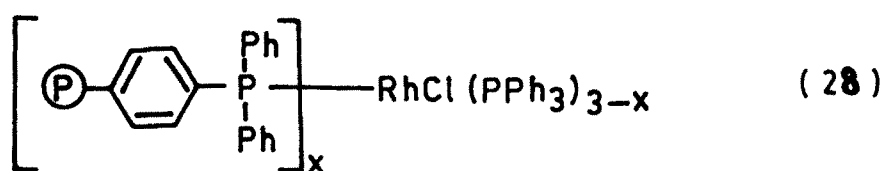
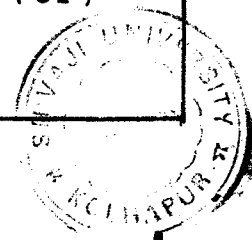
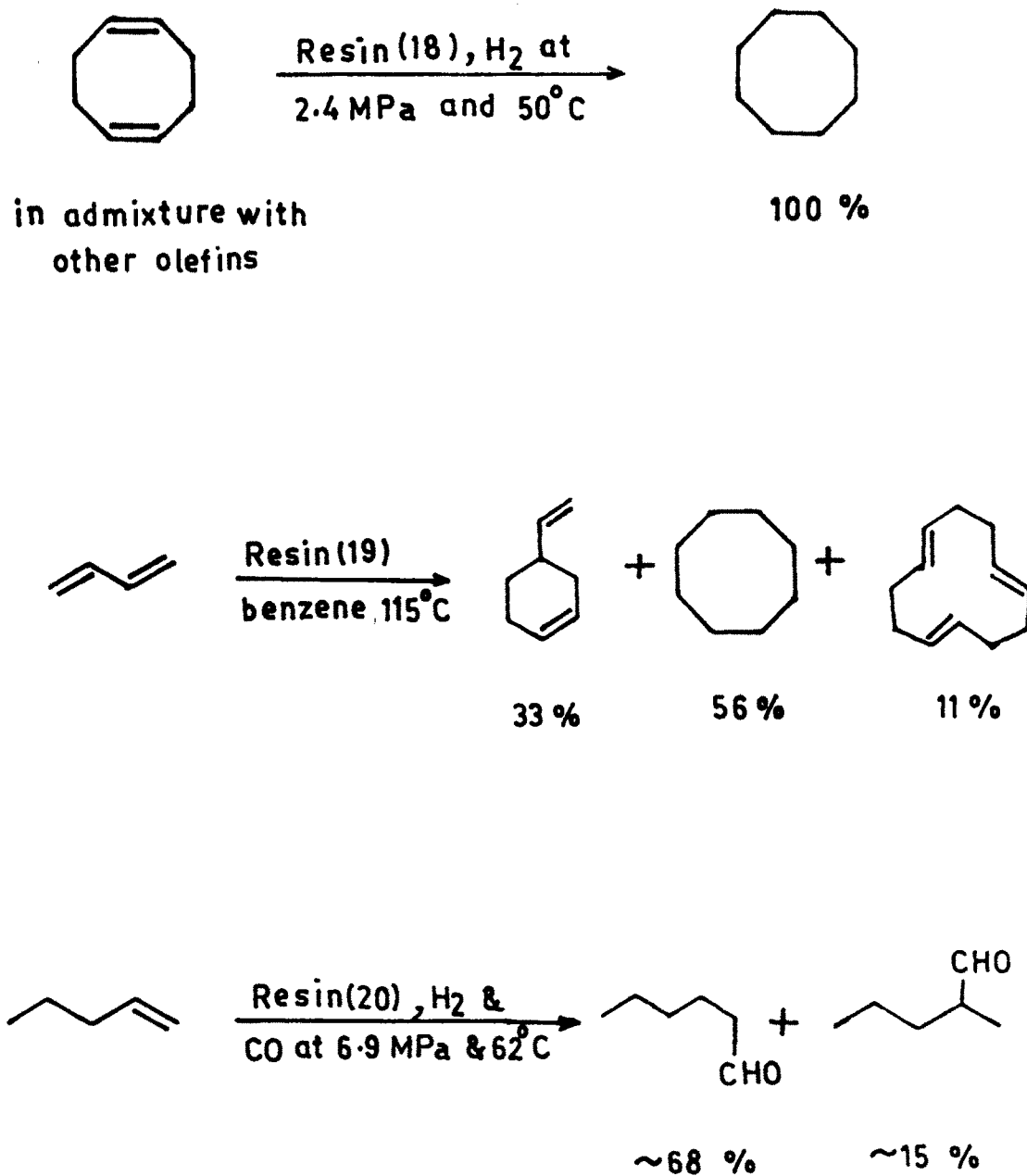


CHART-6





CHART—7

are well spaced on a 20 percent cross-linked resin, and dimerisation leading to inactive products occurs less readily than in solution. Another example is the polymer supported catalyst (6.32). This has been used to catalyse the hydrogenation of cyclo-octa-1,4-diene to cyclo-octene and cyclo-octane. The activity of the catalyst increases as the ratio of phosphine to iridium decreases, and if the ratio is less than 5:1 the catalyst is substantially more active (ca x 200) than the corresponding homogeneous catalyst. It is suggested that the greater activity arises because the restricted mobility of the polymer supported phosphine ligands makes them less efficient than monomeric phosphine at intercepting the reactive co-ordinatively unsaturated iridium intermediates.

Polymer supported phase-transfer catalysts including ammonium and phosphonium salts, crown ethers and cryptands have been prepared and shown to be active in the reactions of n-octyl halides with potassium iodide and potassium cyanide, the generation of dichlorocarbene from sodium hydroxide and chloroform, and the benzylation of  $\beta$ -naphthol<sup>50</sup>.

Alluminium trichloride is reported to form a stable complex with polystyrene resins<sup>51</sup>. In the dry (unswollen) state the chloride is, in effect, encapsulated in polystyrene and is protected from moisture. In the presence of the reaction solvent, the resin swells and the chloride becomes available for reaction. The complex catalyses ether and ester formation<sup>51</sup>.

### Organic Synthesis on Polymeric Carriers

There are a number of areas where polymer molecules have been employed as a convenient support upon which to carry out a synthesis. Completion of the latter is followed by cleavage of the product from the support. In principle, the synthesis can be a very complex one involving many steps, and quite clearly a resin support offers a convenient method of isolating and purifying the product at all stages of the synthesis. The same carrier principle has also been used in a asymmetric synthesis, in some cyclization and related reactions, and also in the detection of reaction intermediates.

In asymmetric synthesis technique an optically active compound or functional group is attached to a macromolecular support or the optically active polymer is used as an asymmetric reagent or catalyst. Most applications have used the latter approach, but in principle, in order to achieve the significant induction, at some stage in the reaction the substrate must become intimately associated with, or specifically bound to; the optically active center. At this point the polymer acts effectively as an asymmetric carrier species. Synthesis of atrolactic acid using 1,2-o-cyclohexylidene- $\alpha$ -D-xylofuranose bound to a polymeric tri-tylchloride polymer is done<sup>52</sup>. A polymer-supported optically active primary alkoxy amine has been used in a similar role in the synthesis of chiral 2-alkylcyclohexanones<sup>53</sup>. There are many more examples of polymer-supported optically active metal complexes and chiral bases being employed in asymmetric induction, and also more recently chiral phase-transfer catalysts.

In conventional cyclization reactions a high dilution technique is used in order to promote intramolecular reaction. When a rigid polymer support is used, the concentration of molecule to be cyclized on the polymer can be made higher than normally used in solution. This has reduced the synthetic problems encountered in the preparation of macrocyclic compounds such as cyclic peptides<sup>54,55,56</sup> and threaded macrocydes<sup>57</sup>. Dieckmann<sup>58</sup> and other cyclization<sup>59,60</sup> have also been improved by this approach.

Among the various advantages associated with functionalized insoluble polymers, the possibility of maintaining mutual separation of reactive functional groups bound to the same polymer support is particularly attractive, and exploitation of this has been described earlier. This technique involves the generation of a reaction intermediate from an insoluble polymeric precursor and its trapping by a second solid-phase reagent. The isolation and detection of an adduct provide positive evidence for the liberated free reactive intermediate<sup>61,62</sup>.

### Polymer-bound Formulations<sup>63</sup>

Polymer-bioactive formulations have become increasingly used especially in areas outside pharmacology. The principle of controlled release from these formulations is that a bond to the polymer undergoes fission to release the agent at a designed rate. Polymers that have been used include synthetic and naturally occurring preparations as indicated in chart 8(a). There are two approaches : the first includes polymerisation of a monomer containing covalently

linked agent, it can also involve copolymerisation with any inert comonomer, the second to an existing polymer.

The ready availability of waste cellulosic type materials such as bark, saw-dust or kraft-lignin has led to investigation of their potential use as a matrix for herbicides used extensively in agriculture and forestry. These materials have the advantage of not only being biodegradable but also contributing to the humus content of the soil. The herbicide 2,4-D (8.33) is water soluble at neutral and higher pHs so it can readily leach out of the soil. By attaching the herbicide to lignin or to a cellulose byproduct, an ester is produced that slowly releases the herbicide on hydrolysis, chart 8(b). This type of controlled release system has also been employed with other matrices such as synthetic polymers.

Compounding formulations are those in which an agent is used with a 'filler' that is usually a polymer. Release of the agent from the compounded material is by three main processes; (i) diffusion-dissolution where the agent, which is soluble and then escapes; (ii) when the agent is insoluble in the elastomer and is held mechanically, water may diffuse into the filler matrix and leach out the agent; (iii) the agent is released following slow dissolution of the matrix in the solvent, usually water.

Probably the best known examples of controlled release technology are in marine antifouling. Classical antifouling paint coatings contain a mixture of rosin and cuprous oxide among other ingredients. The rosin slowly dissolves by virtue of its acidic group and releases the copper salts by an exfoliation process.



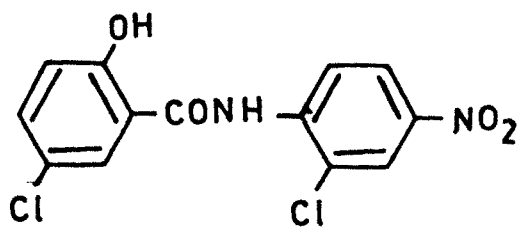
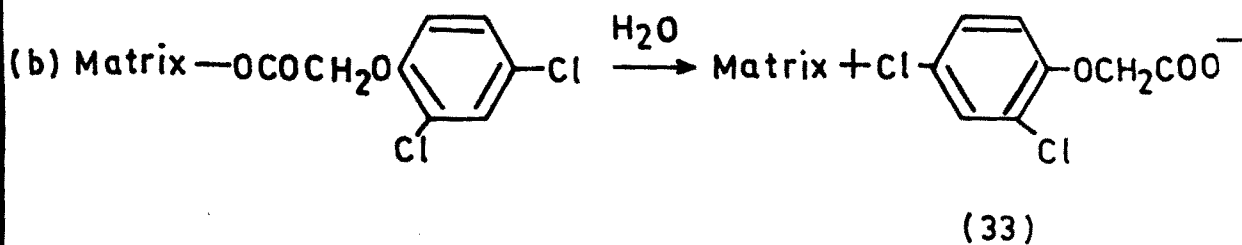
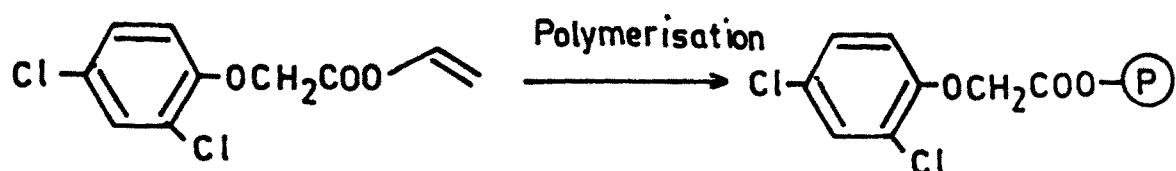
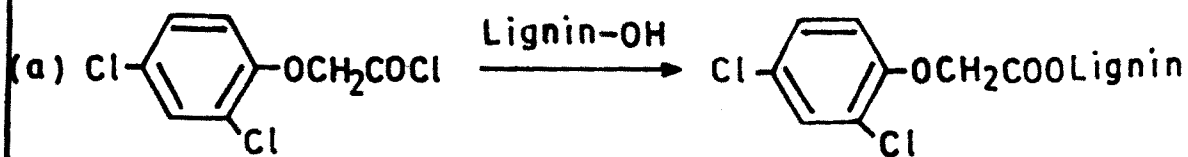
Some of the copper oxide forms a slime of basic copper carbonate that adheres strongly to the ship's hull from which the biologically effective cupric ion is slowly released.

Exfoliation is also the main release mechanism that operates with the modern trialkyltin-antifouling agents where rosin or synthetic acid resin is the compounding agent. Exfoliation is the basis of the new 'self polishing' antifouling paint systems where a tin acrylate copolymer undergoes slow hydrolysis at the surface. The carboxylate ion groups thus revealed (8.34) increase in number eventually resulting in the surface film of polymer chain being dissolved and washed away by the water flow. A new surface is thereby revealed and any rough patches are levelled out at the surface which is being continually renewed.

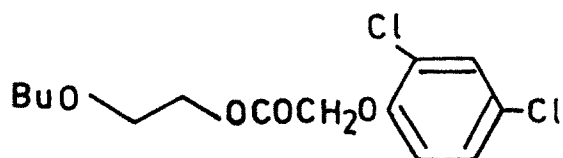
Diffusion dissolution is utilised in contact insecticide traps, the insecticide eg a pyrethroid is placed in a reservoir together with an insect attractant such as vanillin. The reservoir is placed between two plastic barriers and attached to a backing strip. The attractant and pesticide diffuse through the strip of plastic and the insect, attracted to the strip, is killed on contact with the pesticide. This method is clearly superior to the insecticide spray if the attractant is selective and only small amounts of agent are needed.

Water-borne pests require special treatment because of the diluting effect of the medium. Compounding of Bayluscide (8.33) in a neoprene support gives protection as a molluscicide against

Schistomiasis, the major snail-borne parasitic disease carried by water snails. An alternative method is to use a dripfeed into irrigation or drainage ditches. Aquatic weeds are also killed by compounding certain herbicides, surface weeds such as water hyacinth and duckweed, for example, are effectively controlled with butoxyethyl 2,4-D-(8.35), incorporated in to rubber and used with a flotation attachment. Bottom growing plants such as alligator weed are attacked by similar preparations except that the formulation has a sinker to keep the herbicide release at the bottom.



(34)



(35)

CHART — 8

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