CHAPTER 1

A REVIEW ON THE APPLICATION OF FUNCTIONALISED POLYMERS IN ORGANIC SYNTHESIS

INTRODUCTION :

The application of functionalized polymers as an attractive new technique for organic chemistry has received considerable interest since the first report on solid-phase peptide synthesis by Merrifield[1]. The advantages of functionalized polymers in general organic chemistry, for both preparative purpose and technological applications, have been described[2,3].

Polymer supported catalysts and reagents, greatly simplified many of the organic syntheses. Now the stage is reached that, polymers have application in almost all the fields of science.

POLYMER :

A polymer is a giant molecule built up of relatively small, chemically bonded, repeating units. Ordinary polymer generally consists of molecules of different molecular weights. The molecular weight of a polymer refers to a weight average.

The size of polymer molecule is expressed in terms of the average number of repeat units in the molecule and is called degree of polymerisation (DP). From the known DP and known molecular weight of the monomer (repeat unit), the average molecular weight of polymer is easily computed.

Average molecular weight = DP x molecular weight of monomer.

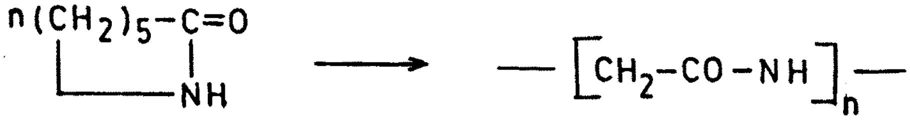
When only one type of monomer unit is present in polymer it is called a homopolymer; a polymer having two or more structural units is referred to as a copolymer. In "linear polymers" the monomer units are joined together in straight open chain fashion, whereas "cross linked polymers" have a three dimensional network.

PREPARATION OF SYNTHETIC POLYMERS :

Synthetic polymers are formed by the polymerisation of the monomers. Polymerisation processes are basically of two types : addition polymerisation or polycondensation and the polymers resulting are classified by their mode of formation as either "addition polymers or condensation polymer". For example polyethylene which is normally produced by addition polymerisation of monomer, ethylene.

$$n\,CH_2{=}CH_2 \longrightarrow -(CH_2-CH_2)_n$$

nylon-6 normally considered to be condensation polymer, is actually produced by addition polymerisation of caprolactam:



$$n\,(CH_2)_5-C{=}O \text{ (ring closed through NH)} \longrightarrow -\left[CH_2-CO-NH\right]_n-$$

Addition polymerisation proceed either by radical or by ionic mechanism and can be carried out either in bulk solution or in suspension or emulsion. Polycondensation proceed according to the method demanded by the reactive functional groups.

SYNTHESIS OF FUNCTIONALIZED POLYMERS :

There are two possible methods of preparing a functionalized polymer. The first method involves starting with a properly functionalized monomer and then polymerising it. The chief advantage of this method is that the resulting polymer is truely homogeneous and the degree of functionalization in such polymer is also fixed and high. Monomer instability and incompatible polymerization conditions tend to limit preparation by this route to relatively simple polymers.

The second and most frequently employed method involves first forming a polymeric carrier and subsequently introducing functional groups into the performed polymer structure. The degree of functionalization is easily controlled in this case but the distribution of the groups on the polymer matrix may not be uniform.

STRUCTURE AND PROPERTIES OF FUNCTIONALIZED POLYMERS :

Functionalized polymers are synthetic macromolecules. Functionalized polymeric supports must possess

1. a structure which permits adequate diffusion of reagents into the reactive sites, a phenomenon which depends on the extent of a swelling or solvation.

2. the effective pore size and pore volume.

3. the chemical and mechanical stability of the resins under conditions of a particular chemical reaction or reaction sequence.

These in turn depends on the degree of cross linking of the resin and the conditions employed during preparation of the resin.

Three main types of resins[4] can be identified : (a) microporous or gel type resins, (b) macroporous resins and (c) macroreticular resins.

Microporous species are prepared from a vinyl monomer and a difunctional vinyl monomer 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 good solvent a soft gel net work is formed with the generation of considerable porocity depending on the degree of the cross linking. Where the latter is $\leqslant 1\ \%$, 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 preparation by most reagents and yet retaining sufficient mechanical stability to provide ease of handling. Copolymer bead made by suspension polymerization of 90 % styrene and 2 % divinyl benzene isomers have found very wide applications as a result of these factors.

Macroporous resins are prepared 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 porocity[5]. Removal of 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 ~ 20 %. Materials of this type are not readily available from commercial sources.

Where the solvent employed during polymerization is good solvent for the monomer, but a precipitant for the polymer, the term macroreticular is generally employed to describe the product[6]. The latter is highly rigid porous material which retains its overall shape and volume when the participant 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 greater than 50 % divinyl benzene content are employed[7]. This enables such products to be subjected to high pressures ~ 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 the 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 can be subsequently washed away to create permanent voids[8].

POLYMERS AS AIDS IN ORGANIC SYNTHESIS,POLYMER SUPPORTED REAGENTS:

The credit for the systematic introduction of polymers as reagents for organic synthesis goes both to Merrifield (1963) and to Letsinger and Kornet (1963).

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).

$$ⓟ\text{—X} + \text{substrate} \longrightarrow ⓟ\text{—Y} + \text{Product} \;\cdots\cdots\cdots (1)$$

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

When a reagent is covalently bonded to a polymer, it acquires the physical properties of the latter. Consequently the functionalized polymer (if reasonably cross-linked) remains insoluble in common organic solvents. If the polymer is porous and swells in a suitable solvent, the functional groups anchored on it are easily available for chemical transformation. Covalent attachment of the functional groups to the polymer helps in "keeping track" of the transformed product in a chemical synthesis, resulting in simplification of the process.

The polymer mediated reactions basically classified into three main categories :

1. The first type includes the reactions in which the polymer acts as a carrier for the substrate. The product remains attached to the support while the biproducts, excess of reagents and solvents all remain in solution and can be removed by filtration. The synthesis may involve a single stage or it may be sequential synthesis of bipolymers, where the successive addition of monomers is carried out as a graft on the basic polymer chain. The last stage in such synthesis involves cleavage of the product from the polymer backbone.

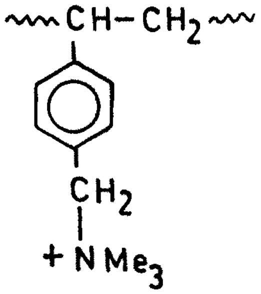
2. The second type includes reactions in which a polymer incorporating a conventional synthetic reagent e.g. a peracid, N-bromoimide, metal hydride, is reacted with a low molecular weight substrate which is transformed into the

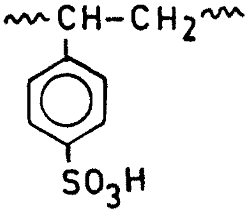
product. The excess of polymeric reagent and the spent polymer remain insoluble whereas the product goes into solution.

3. The third type includes reactions of polymeric reagents carrying catalytic groups. These reactions are not basically different from the reactions classified under 2. In this case the biproduct polymer is the same as functionalized polymer.

The most common strongly basic anion exchange resins are cross linked polystyrenes containing quaternary ammonium groups (1). The desired anions may be bound to these polymer either by displacing a relatively weakly bound anion or by treating hydroxide form of the resin with the acid corresponding to the anion. The latter is usually the method of choice when the desired anion is only weakly bound. The order of affinities quoted for some strongly basic anion-exchange resins is as follows :

$I^- > C_6H_5O^- > Br^- > CN^- > NO_2^- > Cl^- > IO_3^- > CH_3COO^- > OH^- > F^-$


(1)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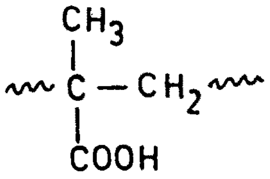

(3)

The common cation exchange resin contains either benzene sulphonic acid groups (2) or aliphatic carboxylic acid groups (3). The desired cation may be bound to these either by treating the acid form of resin with appropriate metal hydroxide or by displacing weakly bound cation. The order of affinities quoted for some cation-exchange resins is as follows :

Strongly acidic : $Ni^{2+} > Cu^{2+} > Co^{2+} > Mn^{2+} > Ag^{+} > Na^{+} > H^{+}$
Weakly acidic : $H^{+} \gg Ag^{+} > Na^{+}$

ANION EXCHANGE IN ORGANIC SYNTHESIS :

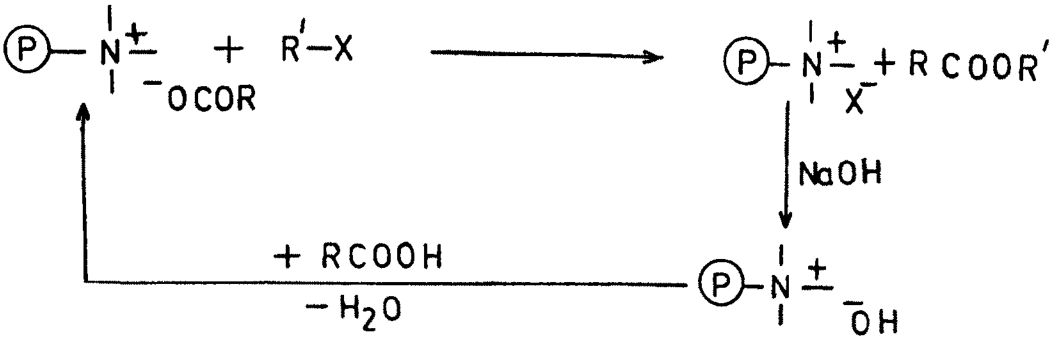
The anion exchangers are extremely important from view of synthetic point. The anion exchangers can actually be considered as potential substituents of tetraalkyl ammonium salts, the catalysts usually employed in the phase transfer technique. It has to be pointed out however, that ion exchangers can also be thoroughly dried for instance by azeotropic distillation, this feature providing two main advantages over traditional phase transfer catalysis.

The high degree of dehydration of the anions linked to the resin on the one hand avoid undesired hydrolytic side reactions and on the other hand tremendously increase their nucleophilicity, especially in the case of small anions such as fluorine one. Furthermore the ease of removal of resin from the reaction mixture permits the use of a substantial excess of the reagent, thereby enhancing the reaction rates and yields. Finally, the choice of the solvent is seldom critical, mostly being determined by the desired reaction temperature: protic solvents such as alcohols even water has been used in case of highly reactive species. Thus commercially available ion exchange resin can often be used instead of expensive and time consuming building of a specific macromolecular backbone.

Concerning the strcture of the polymeric support, better results were obtained using so called macroreticular resins which are characterised by good mechanical properties and by large pores more accessible to organic molecules.

Reactions were generally performed in batch, stirring the functionalized resin with the reagent in suitable solvent. Sometimes the product can be obtained simply by passing a solution of the substrate down a column packed with a polymeric reagent. This technique provides opportunity of a continuous process. In most of the cases, the resin can be generated by washing with appropriate reagent solution.

Preparation of esters from carboxylic acids and alkyl halides[9] according to the following scheme has been described.

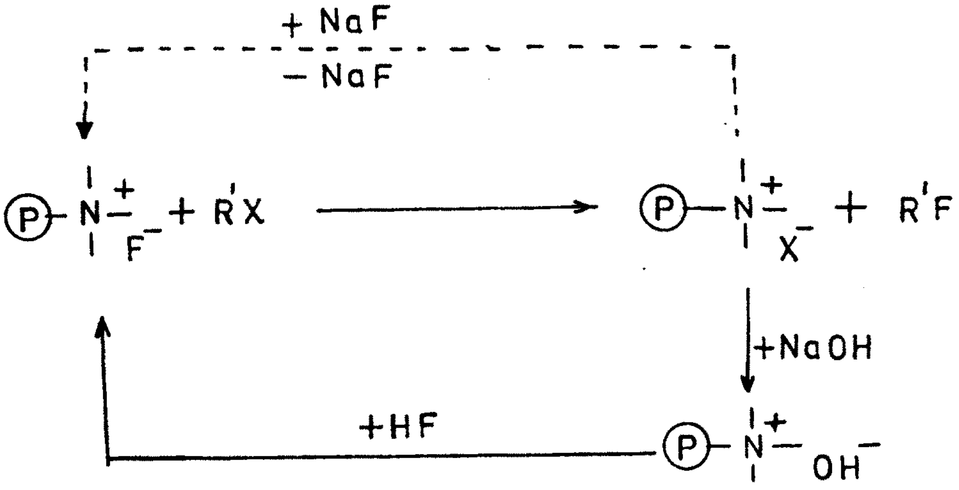


The results are collected in Table 1.

Table 1 - Esters from resin bound carboxylate anions and alkyl halides

Acid	Halide	% Yield
C_6H_5COOH	CH_3I	90
	i-C_3H_7Br	60
	C_2H_5-O_2CCH_2Br	99
	$C_6H_5CH_2Cl$	79
	CH_3O Tos	91
C-$C_6H_{11}COOH$	CH_3I	76
	i-C_3H_7Br	28
C_6H_5CH=$CHCOOH$	CH_3I	97
	i-C_3H_7Br	59
n-$C_{11}H_{23}COOH$	CH_3I	93
	i-C_3H_7Br	52

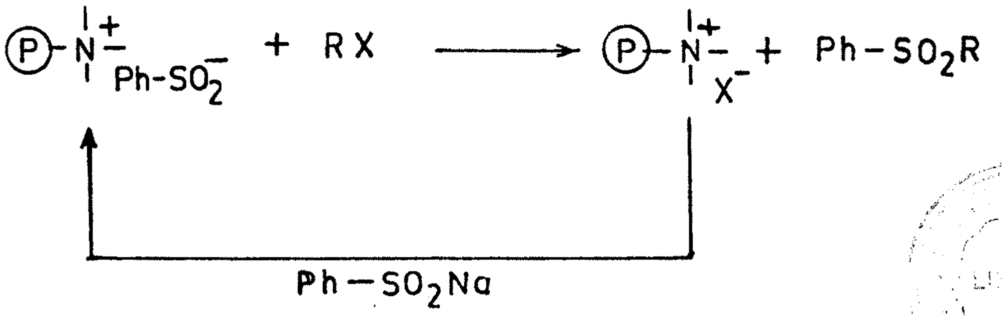
Similarly all the possible halogen/halogen interchange have been performed[10] by reaction of alkyl halides with a suitable form of the resin. The most interesting result from a synthetic point of view, has been, the preparation of alkyl fluorides.



Owing to the effectiveness of this system, extraordinarily mild reaction conditions may be employed and good yields can be obtained. The basicity of fluoride ion seems to be strongly exchanged by the polymeric support.

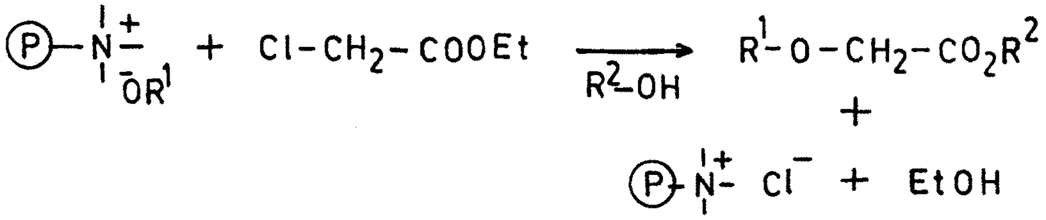
Secondary alkyl fluorides are prepared in substantial amounts starting from sulphonates, these substrate being less prone to the elimination reaction than the corresponding alkyl halides. On the other hand, quantitative alkene formation was observed with chlorocyclohexane. This feature however can be turned to advantage, and the 3 bromo-2,6,6 trimethyl-cyclohex-2-ene-1 carbaldehyde was for instance, prepared from the corresponding 2,3 dibromo saturated compound by means of fluoride form of the resin in refluxing toluene[11].

Phenyl sulphones were easily obtained[12] according to the following scheme :



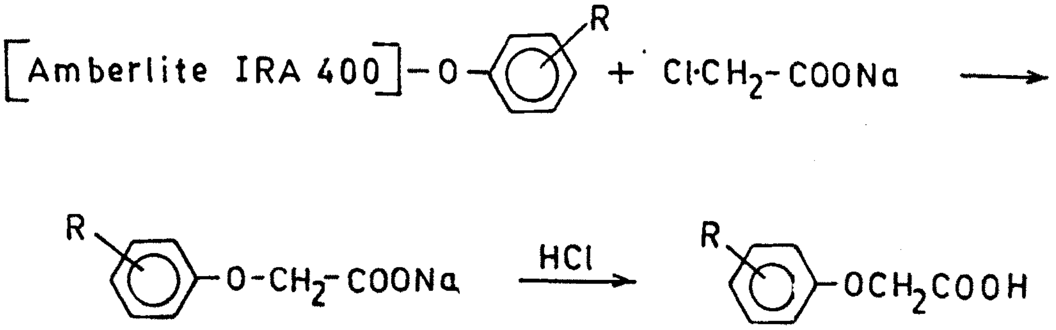
Mild conditions, fast reaction rates and high yields seem to make the above method an improvement over other existing procedures.

Aryloxyacetic esters were easily obtained[13] from the reaction of phenoxide anion held on Amberlite IRA-400 with ethyl chloroacetate in methanol or ethanol as

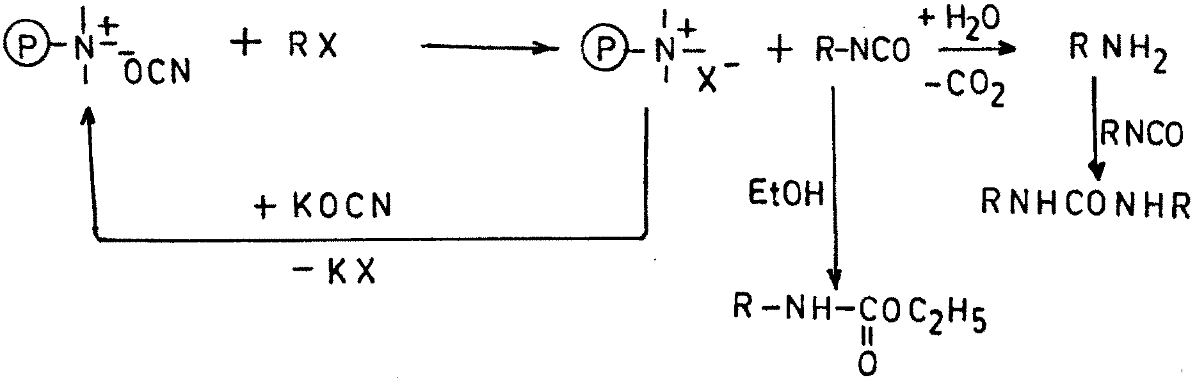


Interestingly trans esterification was observed when alcohols were used as solvents and the products were obtained in high yield and purity.

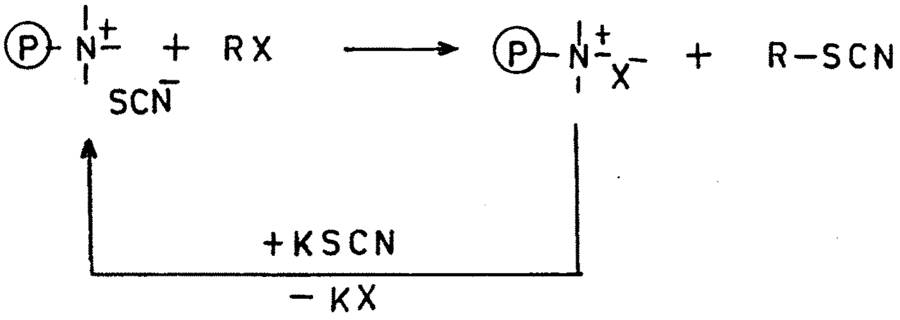
Phenoxides supported on Amberlite IRA-400 on reaction with sodium salt of chloroacetic acid gave corresponding aryloxy acetic acid in high yields. Nitrophenols, 4-hydroxy coumarin and p-hydroxyethylbenzoate gave excellent yields of the product[14]. The scheme is as below



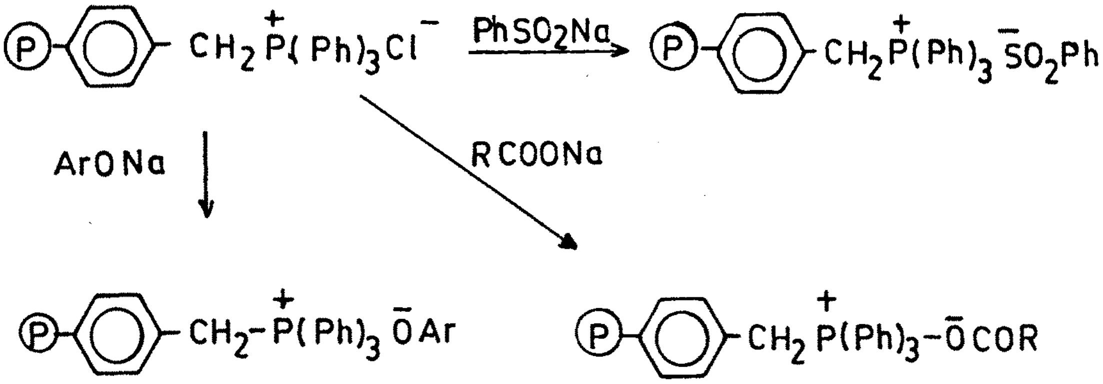
The aryloxy acetic acid of p-hydroxy ethyl benzoate prepared by above method was not possible to prepare by traditional method due to hydrolysis of ester group. Polymer supported cynate and thiocynate can be prepared by washing the resin in chloride form with aqueous solution of potassium salts of the two anions. The cynate resin resulted is somewhat unstable and undergoes decomposition on heating. Removal of water by azeotropic distillation was therefore not possible preventing the isolation of expected isocynates. The products obtained by treatment of the cynate resin with alkyl halides were identified as N,N'dialkylureas, arising from a hydrolytic reaction caused by previously formed isocynate by residual water present in the resin. Thoroughly washing the resin in ethanol and performing the reaction in the same solvent, N-substituted ethyl urathanes were prepared[15].



Thiocynates were similarly obtained in good yields by treating primary or secondary alkyl bromides in hydrocarbon under reflux. Concerning the regioselectivity of the alkylation of the bidentate thiocynate ion, exclusive sulpher attack has been observed in anology with the reaction in solution[15a].

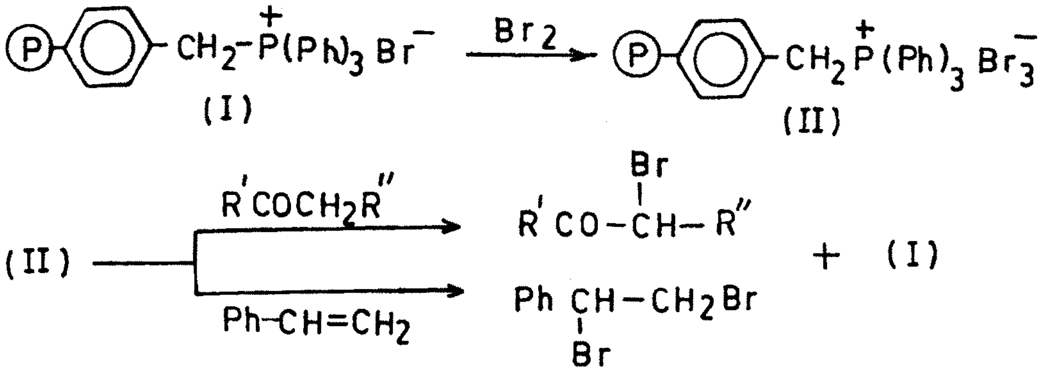


Insoluble polymer bound nucleophilic reagents derived from poly (vinyl benzyltriphenylphosphonium chloride) have been prepared by treatment with the sodium salt of carboxylic acids, benzenesulphinic acid and phenols. These reagents were used for the synthesis of carboxylic acid esters, sulphones and C/O-alkylation of phenols by reaction with alkyl halides[15b].

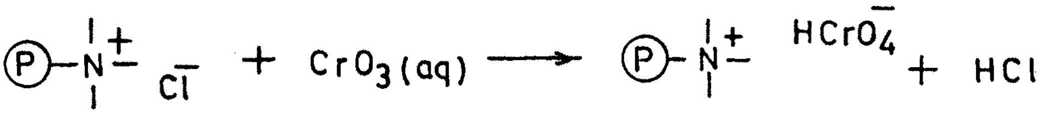


In addition to the ease and simplicity of the method and regeneration of the polymeric biproduct, the polymeric reagent seems to increase nucleophilicity of the anions. The reaction is fast and the yields are more than other traditional methods.

Insoluble poly(vinylbenzyltriphenylphosphonium perbromide) was prepared by the chemical modification of 2 % crosslinked poly(p-bromomethylstyrene) with triphenyl phosphine followed by treatment of polymeric salt with bromine. This is selective brominating agent of alkenes and carbonyl compounds. In addition to the excellent yields of brominated products and ease and simplicity of the method, the resulting polymeric biproduct would be simply regenerated to give the reagent without loss of activity[20]. The scheme is as below



The anion exchange resins were bound to be useful in preparation of a number of different reagents e.g. washing the resin, in the chloride form with an aqueous solution of chromic acid, a chromate form of resin was readily obtained.

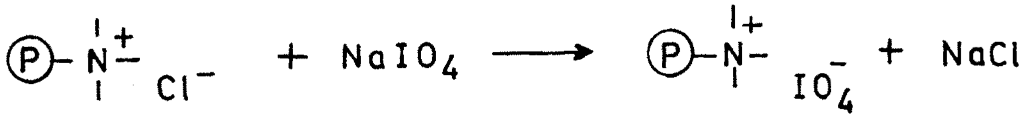


Iodometric titration of the chromate displaced from the resin by reaction with aqueous 1 N KOH overnight, proved that a 1:1 exchange between chloride and chromate anion took place. This reagent is remarkably effective in oxidising primary and secondary alcohols to aldehydes and ketones[16]. The solvents are hexane, benzene, chloroform or tetrahydrofuran.

Although oxidation is relatively slow the oxidation is very clean and no traces of acids or other biproducts were detected in reaction mixture.

The enhanced nucleophilicity of supported chromate ion provides an attractive route to carbonyl compounds starting from allylic and benzillic halides[17]. The latter are probably converted by the resin, in refluxing benzene, to chromate esters which spontaniously decompose to aldehydes and ketones. Also the use of resin in this case circumvents the low solubility of chromate ion in organic solvents.

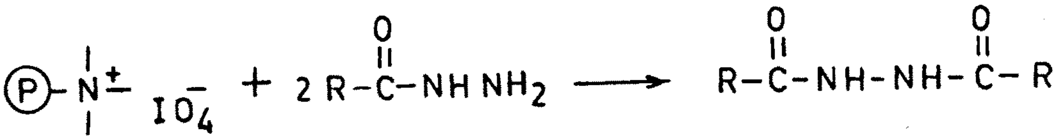
Treatment of chloride form of resin with aqueous sodium periodate followed by drying affords polymer supported periodate. This reagent in methylene chloride or chloroform smoothly oxidizes catechols and quincls under unhydrous conditions to o- and p-quinones respectively[18].



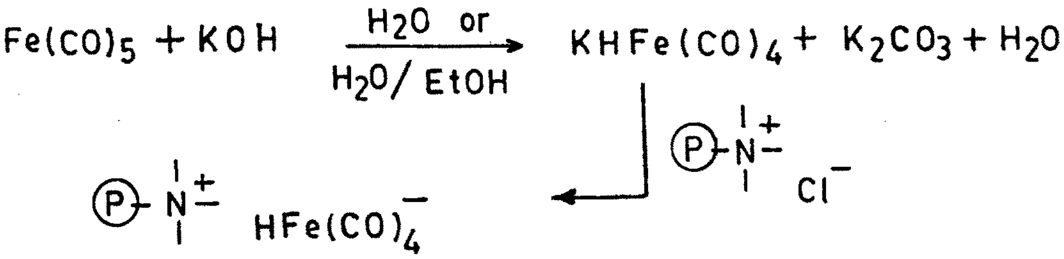
$$\text{Ⓟ}-\overset{|\,+}{\underset{|}{N}}-\ Cl^- + NaIO_4 \longrightarrow \text{Ⓟ}-\overset{|\,+}{\underset{|}{N}}-\ IO_4^- + NaCl$$

Polymer supported periodate also oxidises sulphides[18] in methanol or water as solvent or as part of the solvent giving sulphoxides.

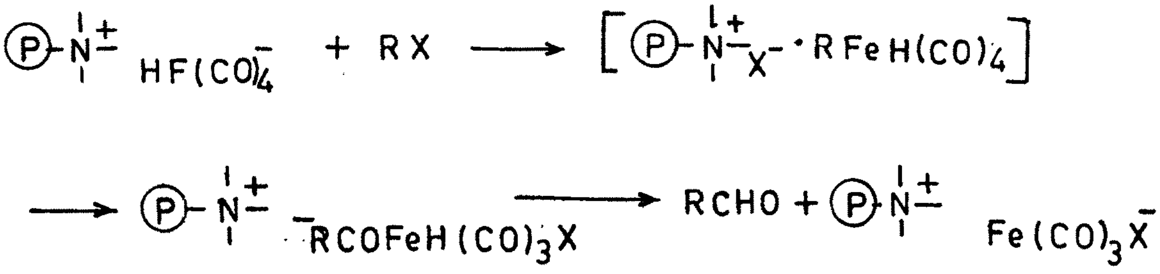
Recently, the oxidation of acid hydrazides is carried out by polymer supported periodate in methanol or ethanol as solvent, giving good yields of diacyl hydrazines[19]. Oxidation is fast, clean and no traces of biproducts were detected in reaction mixture.



Iron tetracarbonylferrate monohydride anion $FeH(CO)_4^-$ described by Colmann[21] may be quickly exchanged, by a column technique, with a chloride ion of the resin[22].

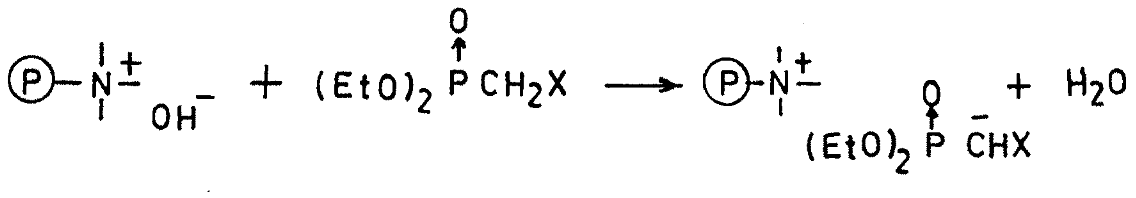


This reagent prepared immediately before use, is capable of converting primary alkyl bromides to the homologus aldehydes in THF under reflux for four hrs. The choice of the solvent is critical.



The same reagent described above also behaves as a practical reducing agent which is helpful in converting aromatic nitro compounds to amines[23], α-bromocarbonyl compounds to the corresponding halogenated compounds and 1,2 dibromoderivatives to olefins.

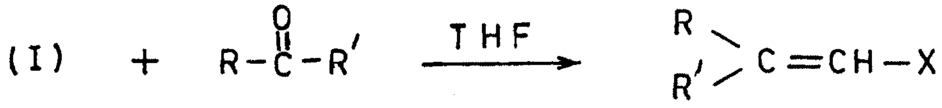
Phosphonates, substituted with electron withdrawing groups (-CN or-COOMe) have been supported[24], owing to the high acidity of the α-C-H bonds, as



X = -CN , -COOR

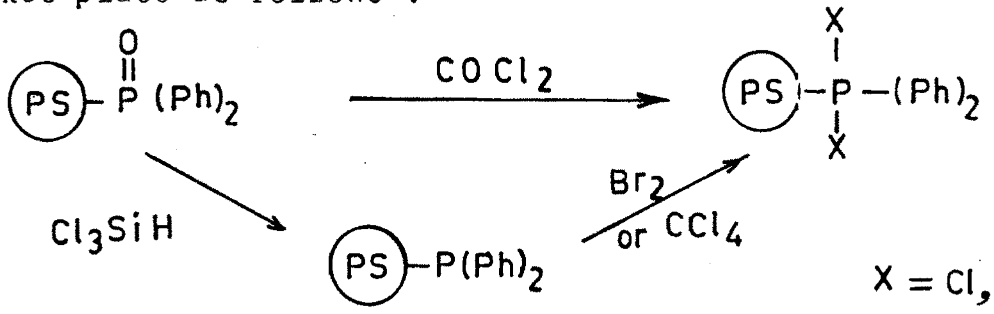
(I)

The treatment of carbonyl compounds with the polymer-bound Witting-Horner reagent in various solvents for 1-2 hrs. give olefins in high yields, at room temperature.



$$(I) + R-\overset{O}{\overset{\|}{C}}-R' \xrightarrow{THF} \begin{matrix} R \\ R' \end{matrix}\!\!>C=CH-X$$

The polymeric phosphines have been used as their dihalides and are efficient reagents for the cleavage of ethers[25] and for the conversion of carboxylic acids, alcohols and primary amides in to corresponding acid chlorides, alkyl halides and nitriles respectively. The dihalide formation takes place as follows :



X = Cl, Br

The recovered polymeric phosphene oxide is readily converted to the polymeric phosphine dihalide for reuse[26].

Polymer supported borohydride have been prepared and used in ethanol to reduce benzaldehyde to benzyl alcohol[27].

The reaction was however much slower than that using sodium borohydride.

Recently the selective reduction of α,β unsaturated carbonyl compounds was carried out by using polymer supported borohydride, corresponding unsaturated alcohols were obtained in high yields[28]. Also the reaction may be performed in aprotic solvents without significant change in yields.

POLYMER SUPPORTED REAGENTS : COVALENTLY ATTACHED :

Several polymer supported N-haloamides have been used to oxidise alcohols. Some of the work was that of Okawara et al.[29] They prepared the linear polymer (1.1) of maleimide, the linear copolymer of styrene and maleimide (1.2) and their derivatives. Each polymer was converted to the corresponding N-bromoamide by treatment with bromine in aqueous sodium hydroxide.

On treatment of nylon-66 (1.3a) with butyl hypochlorite, chlorine oxide in carbon tetrachloride or aqueous hypochlorous acid[30]. The reagent (1.3b) is soluble in benzene but the spent reagent is not. Primary alcohols yield mainly the esters, these are probably formed by the way of hemiacetal.

The polymer supported analogue of coreys reaction[31] has been studied by Crosby et al. using polymer (1.4) in place of thioanisole[32]. The main advantage of using the polymer are

(i) ease of work up, (ii) polymer is odourless, (iii) polymer can be reused. The oxidation takes place as shown in (1.4).

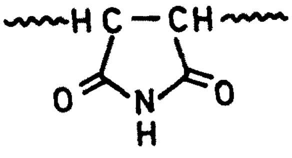
The Wittig reaction is widely used for the synthesis of olefins and research group of Castells[33-35], Heitz[36-37], Hodge[38-39] and McKindey[40] have investigated the corresponding polymer supported reaction. The reactions involved are shown in Chart 2. One attraction of the polymer-supported version is that removal of the polymer at the end of reaction removes all the phosphorus containing species. In the convensional Wittig reaction separation of the olefin from triphenyl phosphine oxide which is formed often requires careful chromatography. This is particularly undesirable if the products are labile or if reaction has been carried out on a small scale.

It is not merely possible to give account of all polymer supported covalently attached reagents. They are of numerous types and have wide application in oxidation, reduction, substitution, condensation, elimination reactions[41].

POLYMER SUPPORTED COMPLEXES :

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[42]. This has the advantage, that the valuable catalyst is easily removed from the reaction mixture and is available for reuse.

CHART-I



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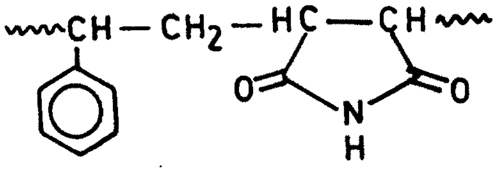

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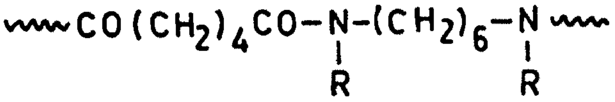
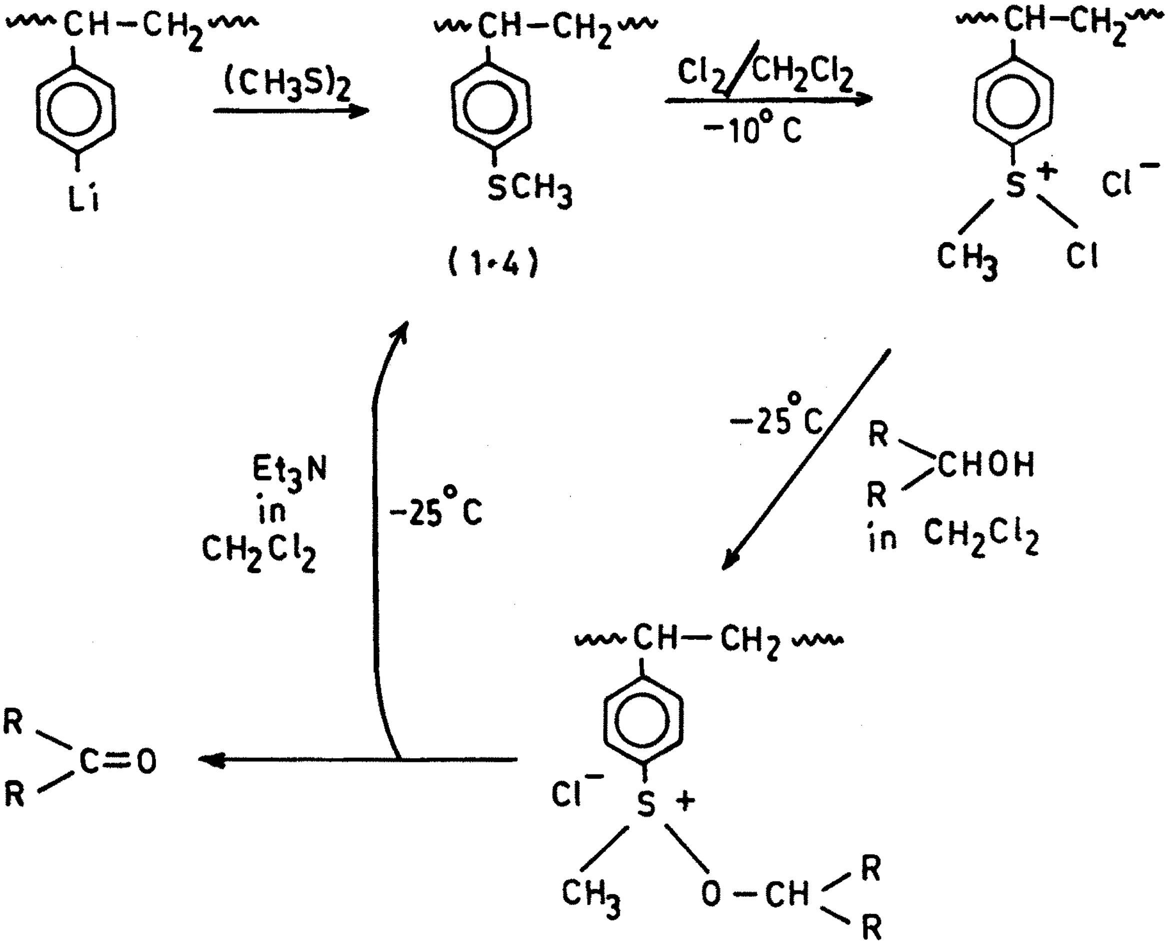


$$\sim CO(CH_2)_4CO-\underset{R}{N}-(CH_2)_6-\underset{R}{N}\sim$$

(1·3)

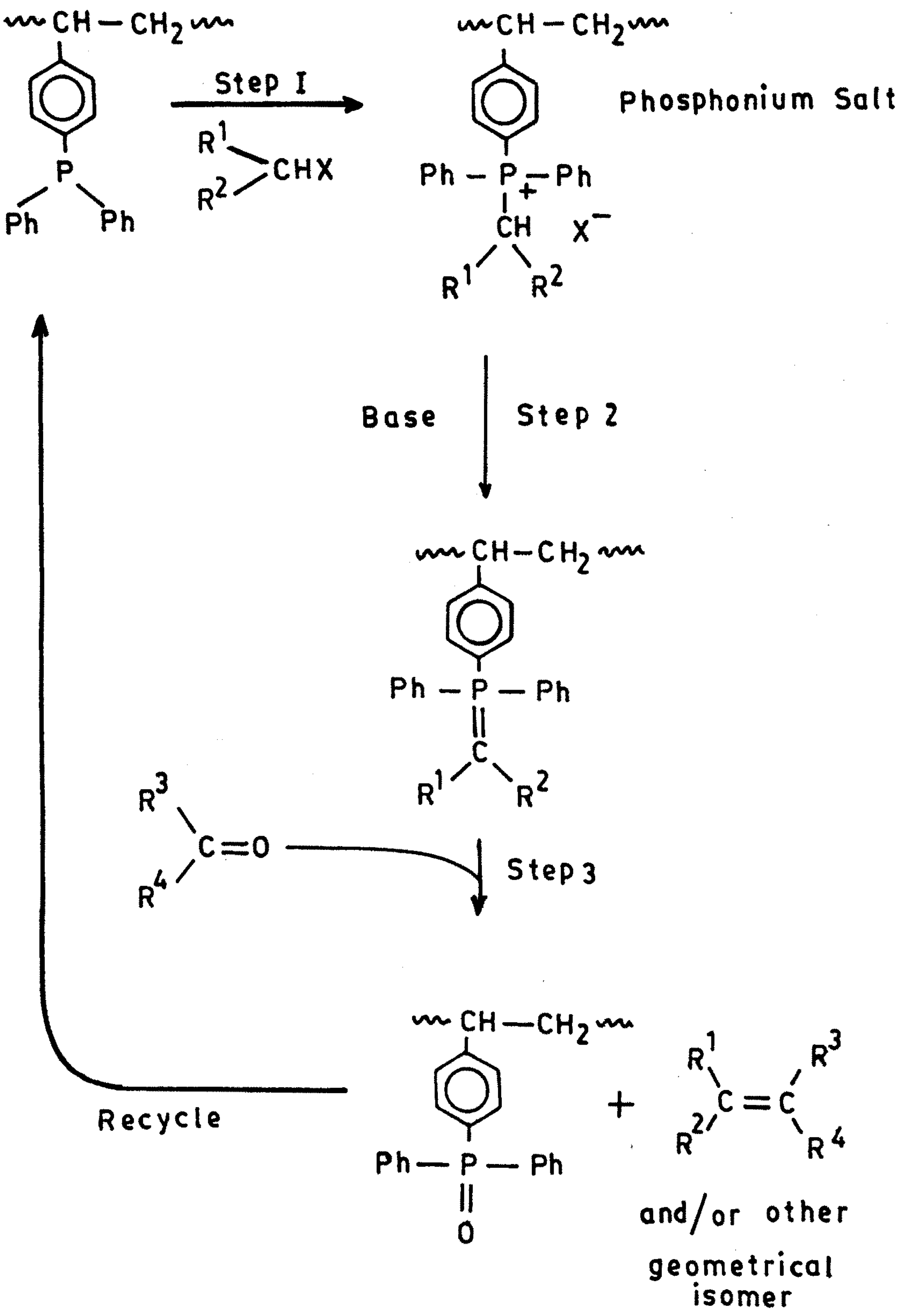
a ; R = H

b ; R = Cl



(1·4)

CHART-2


Step I
Phosphonium Salt
Base
Step 2
Step 3
Recycle
and/or other geometrical isomer

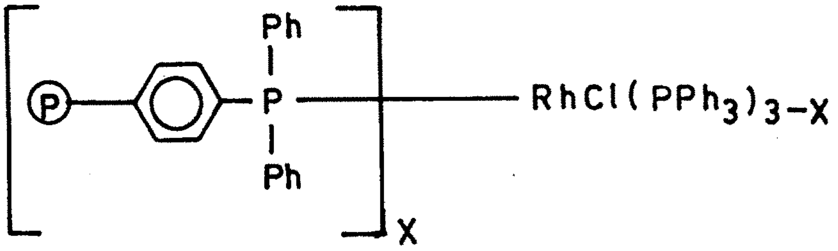
One of the earliest of these polymer supported catalysts to be described was the polymer supported analogue of the hydrogenation catalyst K_2PdCl_4. This was prepared by treating the hydroxide form of an anion exchange resin with this salt[43].

When suspension of phosphine resin in toluene was stirred with $(Ph_3P)_3RhCl$, the polymer supported hydrogenation catalyst (3.1) was obtained[35]. Reaction of the phosphine resin with $(Ph_3P)_2Ni(CO)_2$ and with $(Ph_3P)_3RhH(CO)$ similarly gave cyclodigermerisation catalyst (3.2) and hydroformylation catalyst (3.3) respectively.

Often the polymer supported catalysts are somewhat less reactive 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[44]. Polymer supported catalysts are not always less active. The catalyst obtained by treating the polymer supported titanocene derivative (3.4) is 70 times more active as a hydrogenation catalyst than the nonsupported analogue, probably because the active groups are well spaced on a 20 % cross-linked resin and dimerisation leading to the inactive products occurs less readily than that in solution.

Similarly iridium catalyst (3.5) can be obtained. This has been mainly used to catalyse hydrogenation of cyclic alkenes. The activity of the catalyst increases as the ratio of phosphine to iridium decreases. It is suggested that the

CHART-3



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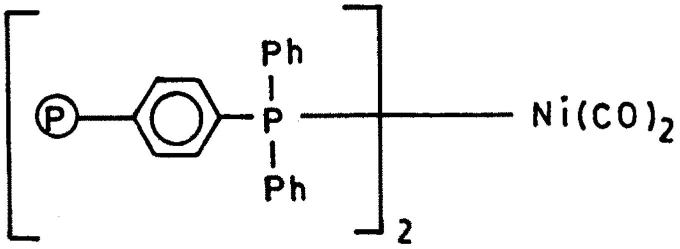

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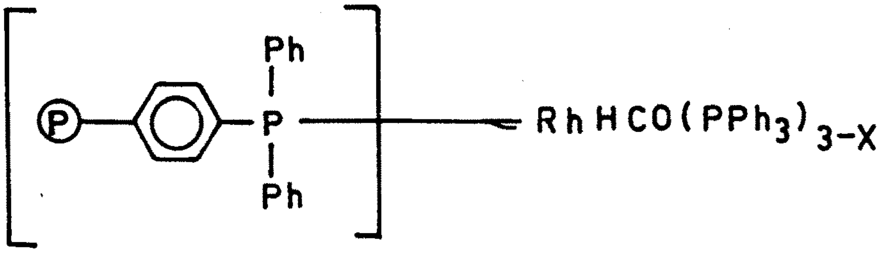

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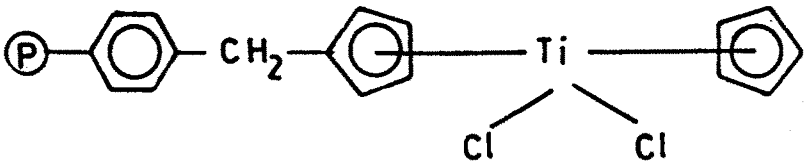

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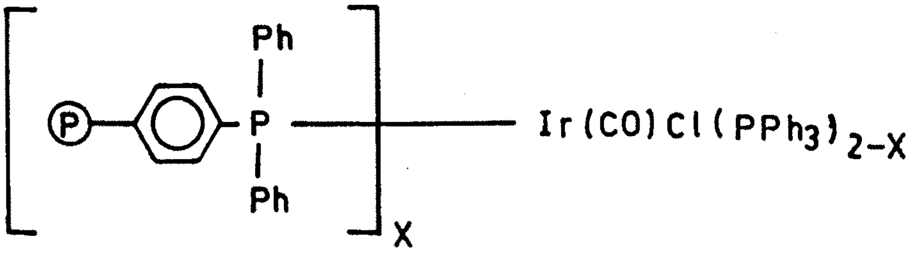

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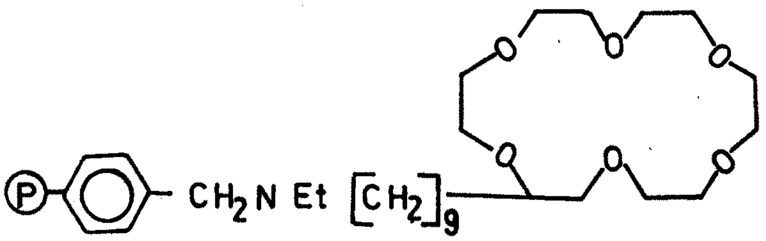


(6)

greater activity arises because the restricted mobility of polymer supported phosphine ligands makes them less efficient than monomeric phosphine at intercepting the reactive coordinatively unsaturated iridium intermediates.

Polymer supported phase transfer catalyst including ammonium and phosphorium salts, crown ethers (3.6) and cryptands have been prepared and shown to be active in reactions of n-octyl halides with potassium iodide and potassium cynide, the generation of dichlorocarbene from sodium hydroxide and chloroform and benzylation of β-naphthol[45-47].

ADVANTAGES AND DISADVANTAGES OF POLYMERIC REAGENTS :

Polymers and polymeric reagents are easily separable from low molecular weight compounds - with insoluble polymers, simple filtration or centrifugation may be used and with soluble polymers, ultrafiltration or selective precipitation. This, the most obvious advantage of polymeric reagents, has been their most widely used feature. This enables one for example, to use a large excess of either soluble or polymeric reagent in order to increase reaction rates and product yields. Excess starting material is easily separated from the product and may often be reused. Reaction side products are often easily removed. This feature makes the polymeric reagent usable in column or in batch process.

These reagents also often lack many inconvenient properties of corresponding low molecular weight reagents, such as lability, volatility, toxicity or odour.

The insolubility of cross-linked polymeric reagents also makes them inaccessible to each other. This allows the simultaneous use of several such reagents, leading sometimes to reaction not possible with the analogues soluble reactants.

Under proper conditions a polymer act as an immobilizing medium for the attached species. Reactions which in solution are possible only at extremely high dilution, may therefore be carried out at relatively high concentration on polymeric carriers. The polymeric backbone may be chosen or tailor make to provide a special microenvironment for reactions of the pendant reactive group. Thus special electronic or stearic conditions significantly different from those existing in bulk solution, may be created in the close vicinity of the reacting species.

Most of the reported chemical uses of polymeric reagents may be classified according to a few general types of processes. Such general classification is presented as in table below.

Table : General classification of processes utilizing polymeric reagents.

	Polymer property	Type of process or reagent
A.	Facile separation from low molecular weight compounds	1. Catalyst 2. Specific separation 3. Transfer agent 4. Carrier and blocking group
B.	Immobilization of attached species	1. High dilution 2. High concentration
C.	Microenvironmental effects	1. Utilizing polar effects 2. Utilizing stearic effects
D.	Mutual inaccessibility of polymeric reagents	1. Analysis 2. Synthesis

It should be pointed out, however, that this classification is by no means exhaustive or absolute. Some applications of polymeric reagents may properly fall into more than one of the reagent groups listed in Table above.

(A-1) A Polymeric catalyst may have an enzyme, an inorganic compound, or an organometallic compound as its active center[48-57]. Its reaction may be schematically represented as :

$$\textcircled{P}\text{-A} + \text{substrate} \longrightarrow \textcircled{P}\text{-A} + \text{product}$$

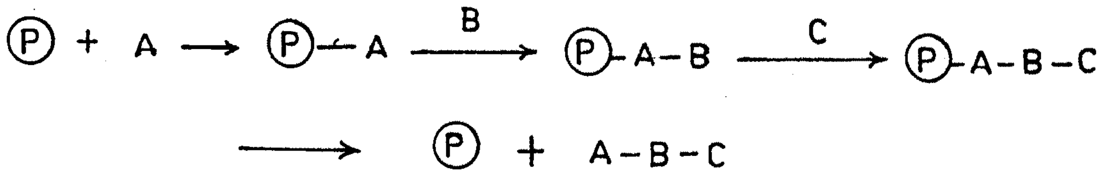
A = catalytic site.

Upon completion of the process the catalyst is easily removed from the product and may usually be reused without difficulty.

(A-2) In specific separation, polymer attached reagents are used to selectively bind one or a few species out of a complex mixture. Separation of polymer-bound compound from the mixture followed by release from the polymer constitutes a simple, highly efficient separation method in biochemistry, hydrometallurgy and analysis[58-64].

(A-3) Polymeric transfer agents react with low molecular weight reactants, transferring to them a functional moiety, thus yielding products which may often be obtained in pure form simply by filtering the polymer and removing the solvent. The use of several transfer polymers in series constitutes a 'chemical cascade' which may greatly simplify the multistep syntheses[65]. This is mainly useful in peptide syntheses.

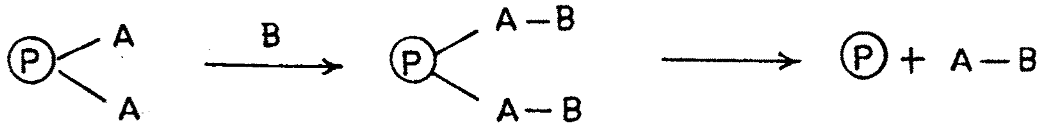
(A-4) When a polymer is used as a carrier or as a blocking group[66-69] in synthesis, it act either to make a chemical reagent easily separable in multistep syntheses or to block selectively certain functional groups in multi-functional compounds. Synthesis may be of one or more steps and products remain attached to the polymer. The final product is released from the polymer in a separate reaction.



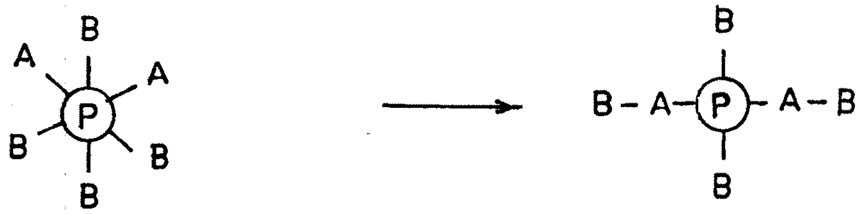
As a large excess of soluble reactant may be used in each step, very high yields of polymeric products are often obtained.

(B-1) The main use of the above mentioned processes is the ease of separating polymeric reagents from reaction mixtures. A different use of polymeric reagents relies on the fact that a rigid polymer retards (immobilizes) translational motion of the reactive species attached to it[70-71]. When diluted on the polymer these reactive species may participate in highly specific reactions without self-interactions associated with conventional reactions in solution.

Solution : A + B → A - A + A - B

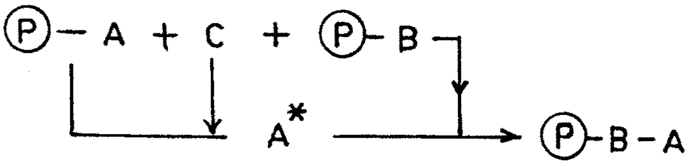


(B-2) On the other hand, when reactants are highly concentrated on the polymer, unusual kinetic and thermodynamic effects may be observed, due to spatial proximity imposed by polymer backbone



(C-1,2) Polymers may also be used to influence the outcome of chemical processes taking place in them by micro-environmental effects created by chemical and stearic structure of their backbone[72-73]. Thus the polarity of the polymer may influence the reactivity of functional group attached to it to a greater extent than the polarity of the solvent in which the polymer is dispersed. The specific stearic requirements of the channels and pores of a cross-linked polymer may impart size and strcture selectivity on reactions of substances attached to the polymer or diffusing into it.

(D-1) A recent use of polymer takes advantage of the fact that reactive group on different insoluble polymers are mutually inaccessible. One application of such reaction has been the detection of highly reactive, relatively short-lived reaction intermediates[74-75].



A* = short lived species.

The free existance of such species is proved by their formation on one insoluble polymer and their trapping on another.

(D-2) A multiplicity of polymers has also been used in syntheses involving two reagents simultaneously which are incompatible with each other in solution.

A highly active species A* is formed by reaction of a precursor A with polymer P - C. Immediately after its formation, the active species reacts with a second polymer yielding the products A - B.

There are some disadvantages, 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 case of regenerable and recyclable species this objection essentially disappears.

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