

## REACTIONS ON AND WITH POLYMERS

Georg Manecke and Peter Reuter

Institut für Organische Chemie, Freie Universität Berlin  
Takustr. 3, D-1000 Berlin 33

**Abstract** - By some selected examples the application of polymers as supports, as reagents, and as catalysts are described. Special attention is given to novel trends in this field, with particular emphasis on results obtained in the authors' laboratory. The advantages of the presented polymers compared to their low molecular mass counterparts are demonstrated.

### INTRODUCTION

Since a long time chemical reactions of polymers are known. In most cases these reactions are carried out in order to modify the physical properties of the polymers. Since the first pioneering works the interest in polymers as reagents for organic synthesis grew rapidly. Indeed, polymers as reagents show in some cases great advantages over their low molecular mass analogues. One of the biggest advantages is the ease of separation of the polymer reagent, which in most cases is an insoluble crosslinked polymer. In some cases the polymer reagent can be used in great excess in order to give high yields of the desired product without any difficulties in the work up process. Reactive, toxic or malodorous compounds may be handled much safer and more comfortable when they are used in a polymeric form. This is of special interest when the low molecular mass compounds are sensitive to air, may be dangerous to handle because of their ability to explode or their toxicity. Especially in pharmaceutical chemistry where substances of high purity have to be produced - free from contaminations of the reagent - this method of preparing chemical compounds is a very useful approach. In some cases it is possible to work with polymer reagents in columns like with ion-exchangers. This is a useful concept for reactions which are to be carried out continuously.

Polymer reagents can be prepared in different ways. The reagent can be fixed to a given reactive polymer by polymeranalogous reaction(s) or they can be prepared by polymerization of a monomer reagent. As the physical and chemical properties of the polymer reagents often depend on the structure of the polymer matrix it can be seen that for every reaction with a polymer reagent a "tailor made polymer" can be prepared. Especially when for the reagent the physical properties such as mechanical strength, porosity or rigidity of the matrix are of importance it is favourable to prepare a polymer reagent by polymeranalogous reactions. In this case the preparation should be essentially free of side reactions. If a polymer reagent is prepared by polymerization or copolymerization of the monomers it may be necessary to study their polymerization parameters in order to get high yields and good physical properties of the desired polymer. Sometimes it is of great importance to overcome diffusion problems in polymer reagents and in such a case it might be necessary to prepare such reagents in a macroporous form. Even linear polymers, which may be soluble in the reaction medium can be used. In this case no problem of diffusion arises, but separation of the polymer reagent may be more difficult.

Polymer reagents may behave quite different compared with their low molecular mass analogues. They can act as reagents which simulate high concentration or high dilution behaviour of the reactive species. For the first case polymers with a low degree of crosslinking and a high percentage of reactive groups, in the latter polymers with a high degree of crosslinking and a low percentage of reactive groups are used.

As there are lots of reports on polymer reagents (1-12), catalysts (13-15), immobilized enzymes (16-18) and polymers for the Merrifield synthesis (19,20) we don't want to give another review on this topic. It is therefore the aim of this publication to show novel trends in the use of polymer reagents with particular emphasis on results obtained in our own laboratory.

Reactions on and with polymers can be classified according to three general reaction types:

a) polymers as carriers for substrates

A low molecular mass substrate is bound to a reactive polymer and reactions on the fixed substrate are carried out with low molecular mass reagents. Consecutively the bound substrate is split off from the carrier.

b) polymers as reagents

The polymer itself is the reagent for the transformation of a low molecular mass substrate and

c) polymer catalysts

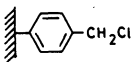
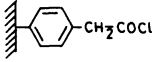
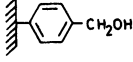
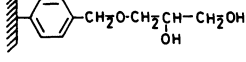
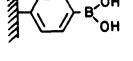
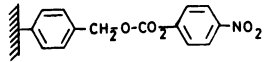
Catalytically active sites are attached to an insoluble polymer which in this way acts as a heterogenous catalyst.

Certainly not all types of reactive polymers fit this categorization but we will follow it in this article.

### POLYMERS AS CARRIERS FOR SUBSTRATES

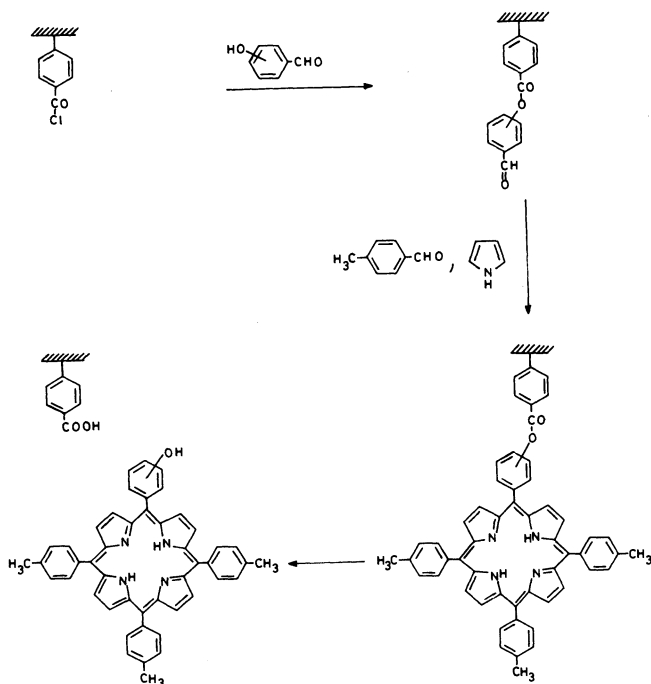
The best and longest known polymers which undergo this type of reaction are those which are employed in the solid phase synthesis of polypeptides (19,20), oligosaccharides (21) and oligonucleotides (22). Here the polymer acts as a protecting group for unsymmetrical substrates. Polymers that act as protecting group for different substrates can contain e.g. chloromethyl (19), acid chloride (23), hydroxymethyl (24), diol (25), boronic acid (26) or 4-nitrophenylcarbonate (27) groups.

#### polymers as protecting agents

reactive polymer	reaction type
	ester of N-protected aminoacids
	monoprotection of diols (C <sub>2</sub> - C <sub>10</sub> )
	monoprotection of diacidchlorides
	monoprotection of dialdehydes
	diol protection in carbohydrates
	monoprotection of diamines

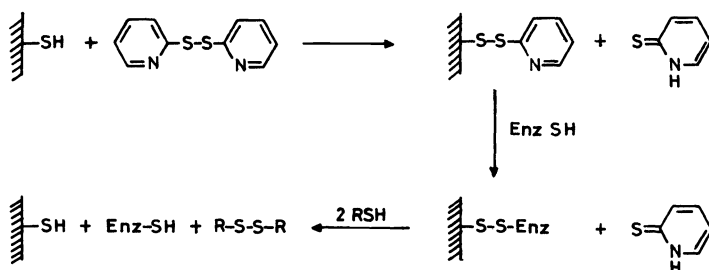
As seen from this figure not only unsymmetrical bifunctional or polyfunctional compounds can be monoprotected. It is also possible to monoprotect symmetrical dialdehydes (25) diacidchlorides (24), dialcohols (23) and diamines (27). The great value of using polymer supports in the monoprotection of symmetrical bifunctional compounds was demonstrated in the synthesis of insect sex attractants by Leznoff (28).

This principle is only a special case for the use of polymers for fishing out a minor component (the monoprotected product) out of a complex reaction mixture by a polymer reagent. The great advantages of this technique was clearly demonstrated by the synthesis of a threaded macrocycle (29). It was synthesized by binding first the macrocycle to a polymer support. The threading synthesis was then carried out several times and all other products of the reaction except the desired ones were washed away. This concept was also used in the synthesis of unsymmetrical tetraarylporphyrines (30) on a polymer support. The symmetrical products could be separated by simple filtration and washing.



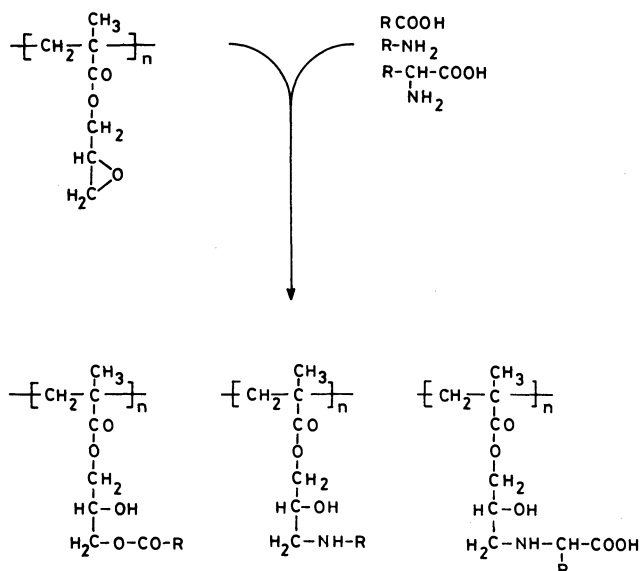
In all of these cases - where a polymer is used for the protection of functional groups - after completion of the required number of reactions on the solid phase the product is obtained by cleaving it off and filtering from the polymer matrix.

A novel approach for the reversible binding of substrates to a polymer matrix was found in the following disulphide groups containing agarose (31). This can be used for the reversible binding of thiol group containing substrates by thiol disulphide exchange.

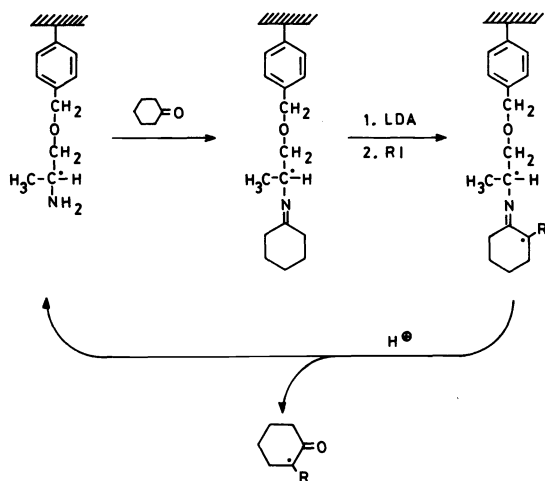


EnzSH = thiol group containing enzyme  
RSH = low molecular mass thiol

Enzymes containing thiol groups could be reversibly immobilized, and proteins containing thiol groups separated from those without thiol groups by simple filtration. The advantage of this reversible binding of reactive groups to a polymer lies in the ability of splitting off the reagent from the polymer in the case that it has lost its activity and regenerate the polymer reagent by reacting it with dipyridyldisulphide. Most of the polymers which are used as supports are derivatives of styrene divinylbenzene copolymers. Usually they are employed in bead form. The bead form is preferred, because of its flow properties in columns. Recently other monomers like glycidylmethacrylate could be polymerized in a macroreticular bead form (32). These polymers could be used for the binding of several substrates like carboxylic acids, amines and amino-acids.



Asymmetric synthesis of 2-alkyl-cyclohexanones are known in the literature (33). This synthesis yielded enantiomers of high optical purity. Leznoff (34) was able to transfer this reaction of low molecular mass reagents to a polymer support with the advantage that the expensive chiral reagent was regenerable and could be reused after a completed reaction cycle with only slight decrease in activity. Remarkable 95 % of optical yield and 80 % of chemical yield were observed.

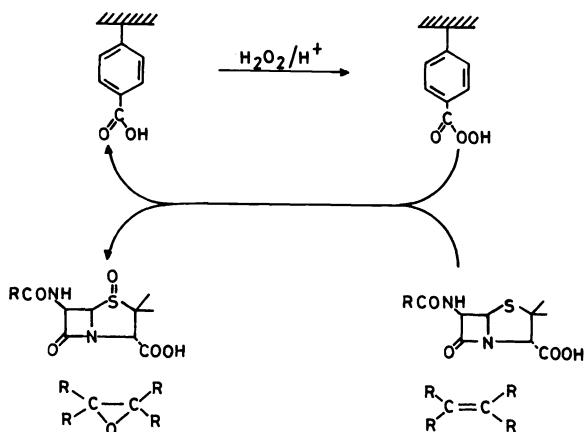


LDA=Lithiumdiisopropylamide

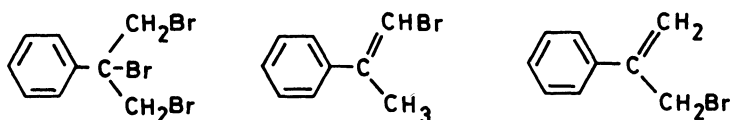
#### POLYMERS AS REAGENTS

Polymers of this type are for example the polymers for oxidation or halogenation, the polymer Wittig reagents and polymer group transfer reagents.

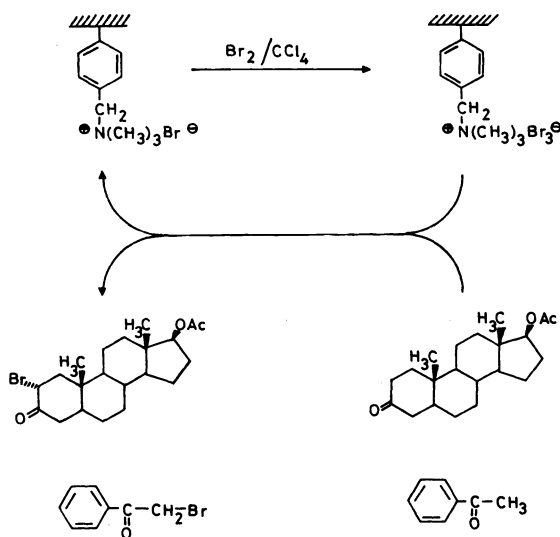
Polymer peracids are able to epoxidize olefines in high yields (35). They can be recon-verted into the peracid form. The advantage of the polymer in comparison to low molecular mass peracids is the fact that the by-product of this reaction - the organic acid - is remaining attached to the polymer. The epoxid is obtained by simple filtration and following evaporation of the solvent. A novel approach for the oxidation with polymer peracids was found in the oxidation of penicillines to the corresponding sulfoxides (36).



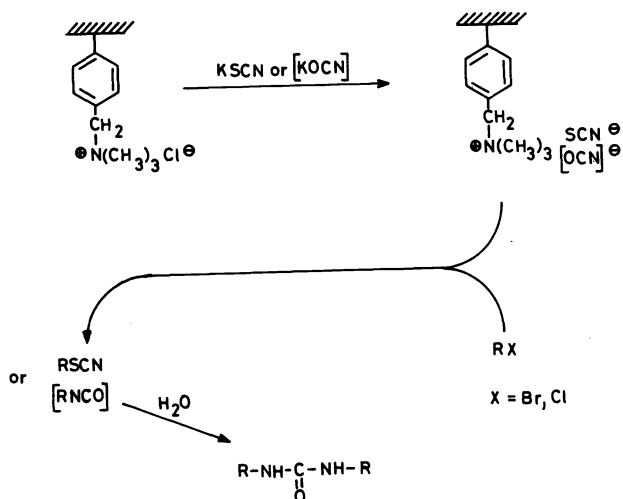
Several polymer reagents were used for halogenation or oxidation of various substrates. Polymer bromo- or chloro-succinimide (37, 38) reacted quite different compared with the low molecular mass analogues. E.g. bromination of cumene gives the three following bromides.



Ethylbenzene gave on chlorination with polymeric chlorosuccinimide only ring substitution. This different behaviour was explained by the polarity of the matrix. An easy to obtain and cheap bromination reagent was found in the use of anion exchange resins for  $\alpha$ -bromination of ketones. With this resin even steroidal ketones could be brominated in high yields (39).



Anion exchange resins could also be used in the synthesis of  $N,N'$ -dialkylureas, thiocyanates as well as  $N$ -alkylurethanes from halides by nucleophilic substitution (40). The ureas were formed from the intermediately obtained isocyanates because water could not be removed quantitatively from the resin. In ethanol as solvent ethylurethanes were formed.

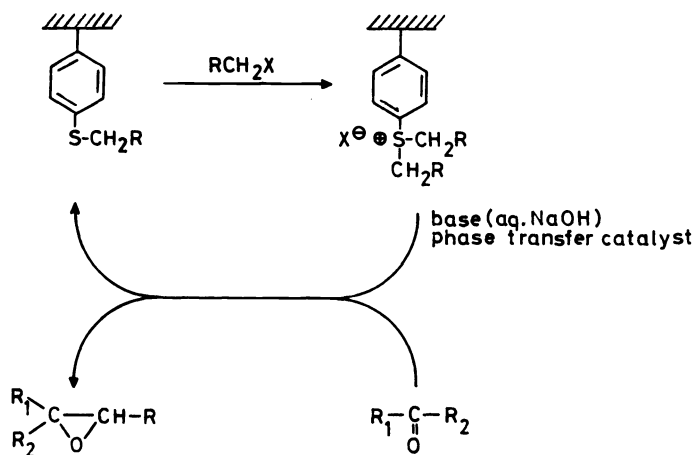


Halogenated nylons could be used in the oxidation of various substrates (41, 42). In this case linear polymers were used. The halogenated nylons are soluble in different organic solvents. In the course of the reaction the nylons precipitate by forming hydrogen bonds.

Manecke and Stärk (43) used polymer-bound N-bromo-benzophenone-imine in allylic and aromatic side chain brominations. These polymers showed good mechanical and chemical properties and could be used several times with only slight loss of activity.

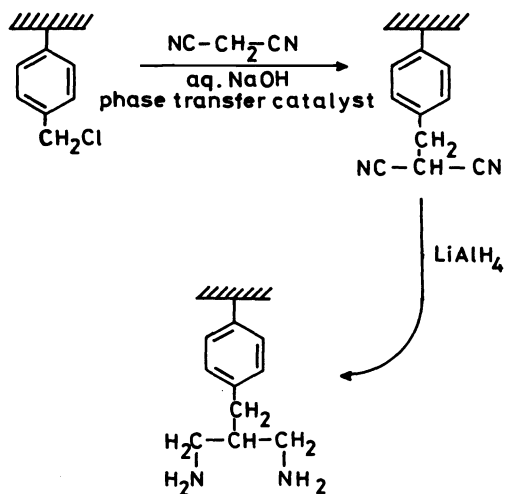
Polymer N-chlorobenzotriazole was used by Manecke and Wunsch (44) in the oxidation or chlorination of various substrates.

Another mild oxidation reagent is the polymer thioanisole-chlorine (45). With this polymer, alcohols can be oxidized to aldehydes. In addition to the other advantages of polymer reagents, this polymer - in contrast to the low molecular mass analogue - is odourless. Polymer thioethers could also be used in the synthesis of epoxides from ketones (46). The polymer thioether was converted to a sulfonium salt by reaction with an alkylfluoro-sulphonate. From the sulfonium salt polymer ylides were prepared under phase transfer catalytic conditions. Other conditions for the elimination gave a great decrease in activity of the polymer reagent after each regeneration step.

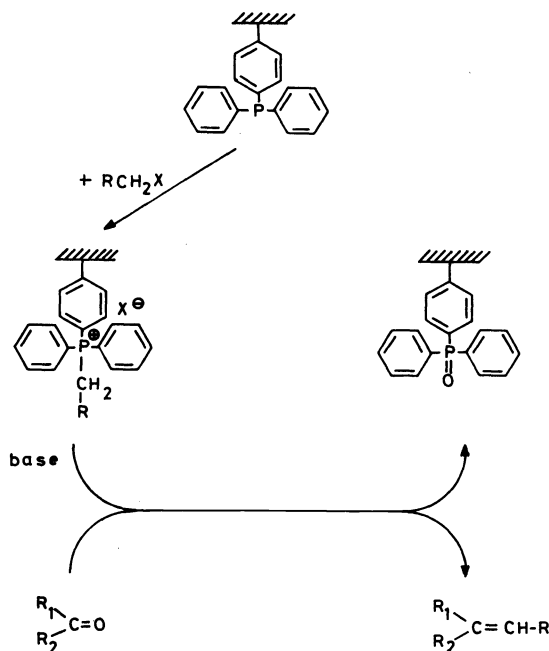


After reaction of the polymer ylide with a ketone high yields of epoxides were obtained and the polymer could be regenerated and reused several times without loss of activity.

The advantage of using milder reaction conditions for the derivatisation of polymers was demonstrated in the preparation of polymer bound dinitriles and diamines. Under phase transfer catalytic reaction conditions (47) they could be obtained in quantitative yields. Under normal conditions only 30 % of the functional groups were converted.

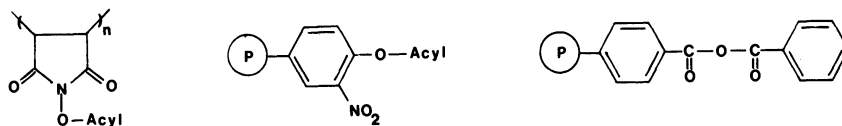


Polymer selenium compounds avoid the difficulties which arise from the use of toxic and malodorous low molecular mass substances (48, 49). Polymeric triphenylphosphine is a reagent which can be used for several reactions. In the presence of carbon tetrachloride it can be used for halogenations (50). Alcohols can be transformed to chlorides, acids to acid-chlorides (50), acids and amines to amides (51), primary amines yield nitriles and secondary amines give iminoylchlorides (52). The polymer showed a faster rate of reaction compared with the low molecular mass analogue. On the other hand polymeric triphenylphosphine can be used for Wittig reactions (53). The yields in this reaction are comparable with those in solution. The stereoselectivity of this reaction depends on the cation of the base used for the elimination. If Lithium bases are used for the generation of the ylide normally transolefines are obtained. In the case of polymeric Wittig reagents  $\text{Li}^+$  ions can be excluded by filtration and washing of the polymer (54). Thus, it was possible to get cis-olefines in high yields. The possibility to keep the by-product of this reaction the triphenylphosphinoyl attached to the polymer is another advantage of this polymer reagent.

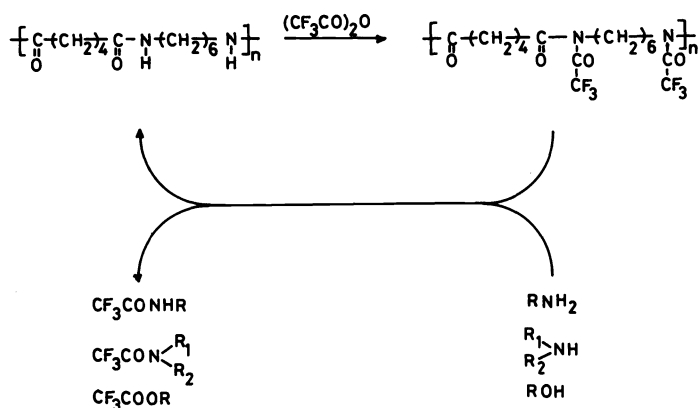


If the reaction is carried out in solution the triphenylphosphineoxide is sometimes difficult to be removed.

Lots of investigations were made in the field of polymer acylating reagents. Acyloxysuccinimide polymers (55), polymers of acyloxynitrostyrene (56) and mixed anhydrides of poly-4-vinylbenzoic acid (57) have been used in acylating reactions.

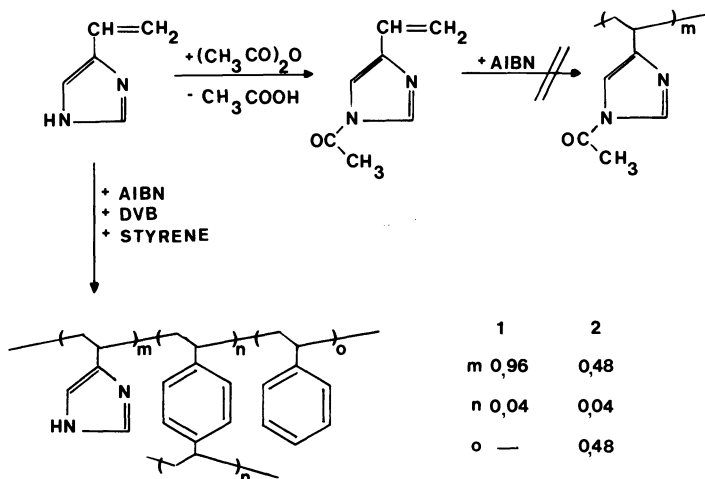


N-trifluoroacetylonylons and N-trifluoroacetyl-polyurethanes were investigated by R.C. Schulz et al. (58) and showed to be good and selective acylating reagents for the acylation of amines and alcohols. As in the case of the halogenated nylons the N-acylated products are also soluble in certain solvents and precipitate in the course of the reaction.

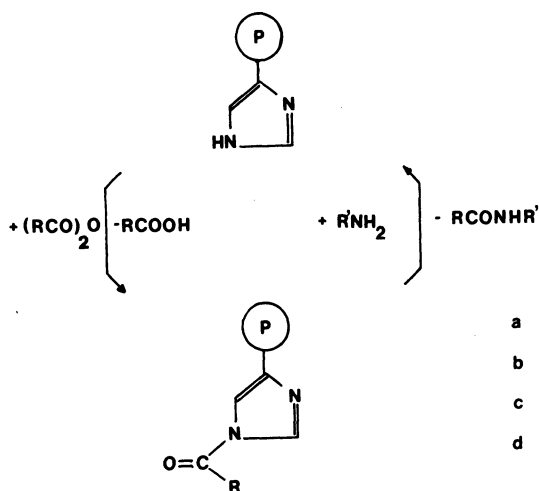


The selective acylation of only one enantiomer of racemic amines can be carried out if an optically active nylon is used for the reaction.

We have found that polymer N-acylated imidazoles are very good and selective acylating reagents (60). The following picture shows the preparation of 4(5)-vinylimidazol-polymers and their reaction with several acid anhydrides to yield the reactive polymers.



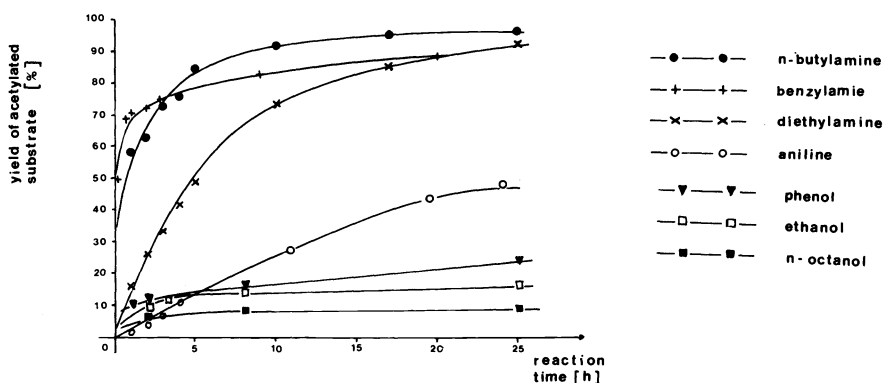




- a R: CH<sub>3</sub>-
- b C<sub>2</sub>H<sub>5</sub>-
- c C<sub>6</sub>H<sub>5</sub>-
- d CF<sub>3</sub>-

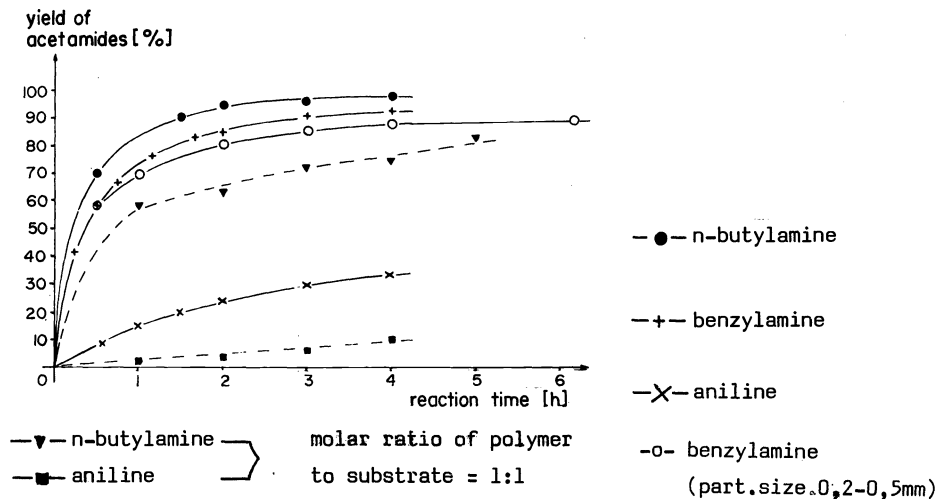
The polymers were used for the acylation of amines and alcohols. A graduated reactivity was found for the reaction with these compounds according to the nucleophilicity of the substrate.

Reaction of different amines and alcohols with 1-acetyl-4-vinylimidazole-divinylbenzene copolymer in dioxane at room temperature (molar ratio polymer : substrate = 1 : 1)



The reactivity of the polymers in respect to the low molecular mass substrates decreases in the order aliphatic amine, aromatic amine, phenol, aliphatic alcohol. The rate of reaction was faster and the conversions were higher when a 2:1 excess of the polymeric reagent was used or the particle size was reduced.

Reaction of different amines with 1-acetyl-4-vinyl-imidazole-divinylbenzene copolymer at a molar ratio of polymer : substrate = 2:1 in dioxane at room temp.



As seen from the following table amines were acetylated after 3 hours of reaction time in high yields.

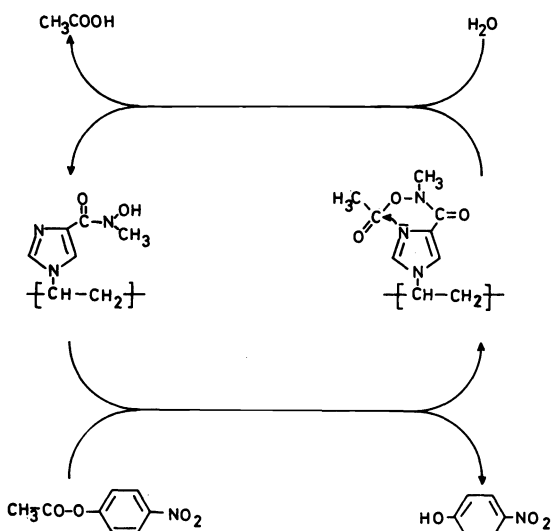
Reaction of 1-acyl-4-vinylimidazole polymers with different  
amino-group containing compounds

amine	molar ratio polymer:substrate	solvent	reaction time hrs.	yield %
<b>1-acetyl-4-vinylimidazole 4 % divinylbenzene copolymer</b>				
hydrazine H <sub>2</sub> O	1:1	dioxane	3	70
t-butylamine	1:1	dioxane	4	32
hydroxylamine HCl	1:1	dioxane	1	75
benzylamine	2:1	dioxane	3	92
ethanolamine	1:1	dioxane	2	73
ethanolamine	2:1	dioxane	2	86
cyclohexylamine	2:1	dioxane	3	97
aniline	2:1	dioxane	3	14
<b>1-propionyl-4-vinylimidazole 4 % divinylbenzene copolymer</b>				
benzylamine	2:1	dioxane	3	98
<b>1-benzoyl-4-vinylimidazole 4 % divinylbenzene copolymer</b>				
benzylamine	2:1	dioxane	3	84
<b>1-acetyl-4-vinylimidazole styrene 1:1 copolymer 4 % crosslinked</b>				
4-ethylaniline	2:1	benzene	3	98
aniline	2:1	benzene	3	97
t-butylamine	2:1	benzene	3	63
<b>1-trifluoroacetyl-4-vinylimidazole styrene 1:1 copolymer 4 % crosslinked</b>				
benzylamine	2:1	benzene	3	100
glycineethylester	2:1	benzene	3	90
alaninemethylester	2:1	benzene	3	87
aniline	2:1	dioxane	3	96

Ethanolamine an unsymmetrical bifunctional substrate could be selectively N-acetylated even when a molar ratio of 2:1 for polymer to substrate was used. The swellability of the matrix has a pronounced effect on the yields of acetamides. A copolymer of 1-acetyl-4-vinylimidazole with 4 mol% divinylbenzene gives in dioxane only 14 % of acetanilide after 3 hours of reaction, while 1:1 copolymer with styrene using the same amount of crosslinking agent yields in benzene 97 % of acetanilide after the same time of reaction. This is a good example for the optimization of a polymer reagent by changing the polymer composition. Trifluoroacetylation with this polymer gave higher yields of the trifluoroacetamides due to the higher reactivity of the trifluoroacetyl group. Also trifluoroacetyl amides of  $\alpha$ -amino acid esters could be obtained in high yields. After the reaction the polymers could be regenerated by repeated reaction with acid anhydrides. They showed after 20 reaction cycles no decrease in activity.

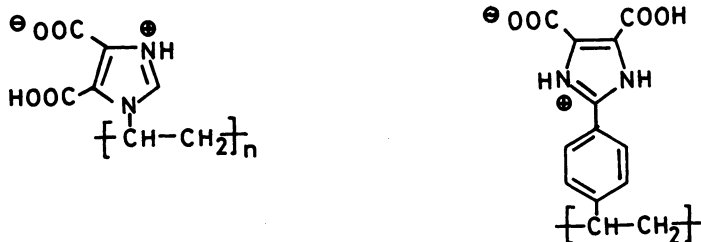
#### POLYMER CATALYSTS

Polymers containing imidazole groups are not only of interest as reagents but also as catalysts (61). It is known that imidazoles and hydroxamic acids are catalysts for saponifications of active esters. While for imidazole the acylation of the imidazole is the rate limiting factor for the saponification, for hydroxamic acids the deacylation of the acylhydroxamic acids is the rate determining factor. Kunitake and Okahata (62) prepared polymers which contained these two different nucleophiles in a copolymer to enhance the esterolytic activity of the polymer by the cooperative effect of these two compounds. Indeed they found with these polymer catalysts a much higher reaction rate for the esterolysis in comparison to polymer catalysts with only hydroxamic acid or imidazole groups. We prepared polymers of the N-vinylimidazol-4-carboxylic acid and investigated their catalytic activity in esterolytic reactions (63).

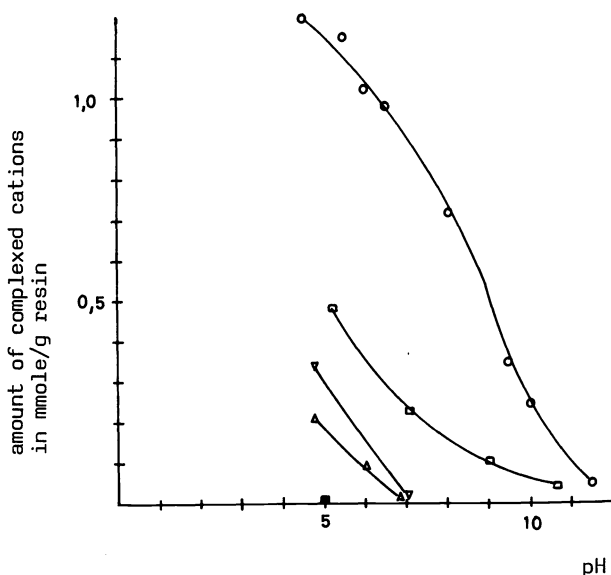


These polymers contain the two nucleophiles in only one monomer unit. The activity of the polymers was higher than for imidazole and benzylhydroxamic acid alone. Yet the increase in activity was not very pronounced. This may be because of the low pKa value of the imidazole function. To prepare more active bifunctional catalysts it may be necessary to use a monomer hydroxamic acid derivative in which the hydroxamic acid group is not conjugated with the imidazole group.

Polymer imidazole derivatives are also of interest in the specific binding of metal cations. Therefore we prepared polymer imidazolecarboxylic acids with an excellent selectivity for mercury ions (64, 65).



pH-dependence of the metal-cation complexation of poly(N-vinylimidazol-biscarboxylic acid) in the presence of EDTA

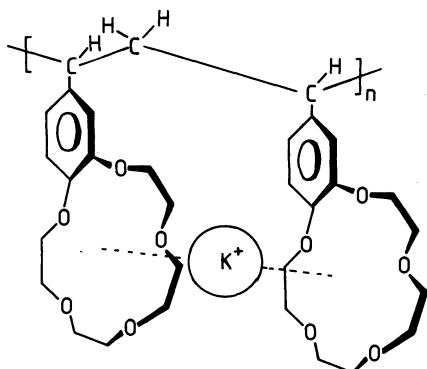


○ = Hg<sup>2+</sup>; □ = Cu<sup>2+</sup>; ▽ = Cd<sup>2+</sup>; △ = Zn<sup>2+</sup>; ■ = Pb<sup>2+</sup>  
 conc. Mt<sup>2+</sup> = 10<sup>-2</sup> mole/l  
 conc. EDTA = 1,5 · 10<sup>-2</sup> mole/l

With these polymers it was possible to complex Hg<sup>2+</sup>-ions even in the presence of EDTA. Separations of mercury and lead and mercury and cadmium ions were possible. From 20 % NaCl-solution a 32 ppm amount of Hg<sup>2+</sup>-ions could be removed up to 90 %. This is of special interest for the removal of toxic mercury ions from waste waters. The polymers were easily regenerated by hydrochloric acid.

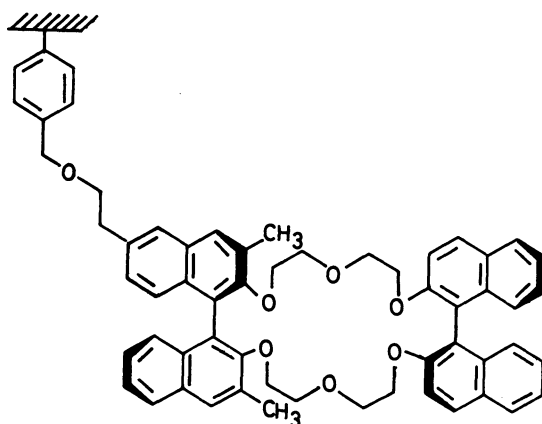
Selective ion exchangers for the transition metals are known since a long time. For the selective complexation of alkali and alkaline earth metal cations polymers of crown ethers, cryptands and podands can be used. Polymer crown ethers have been prepared by different authors (66-70). Smid et al. (67) demonstrated that the polymers showed the same selectivity in the complexation of alkali and alkaline earth metal cations as the low molecular mass compounds but the polymers were more effective in extracting the metal picrates from an aqueous solution. The polymers were dissolved in chloroform.

In the case of poly(vinylbenzo-15-crown-5) and potassium picrate the ratio of salt to crown units reached a maximum of 0.5 indicating the formation of a 2:1 complex on the polymer matrix, while with poly(vinylbenzo-18-crown-6) a 1:1 complex formation was observed (67).

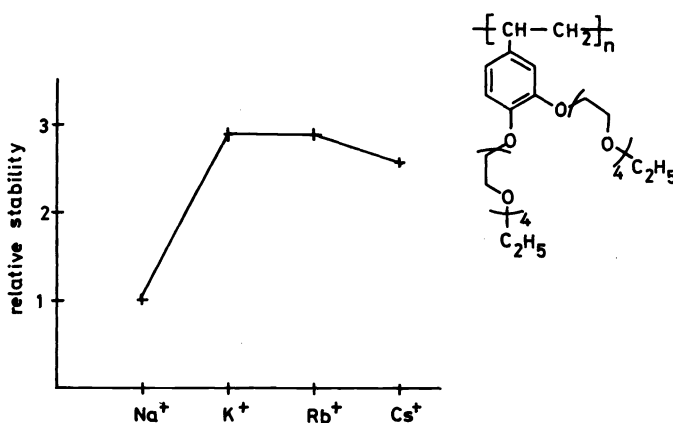


Blasius et al. (71) prepared various polymer crown ethers and cryptands. With these polymers it was possible to separate the different alkali metal cations or to invert the anion or cation of alkali salts on a packed column.

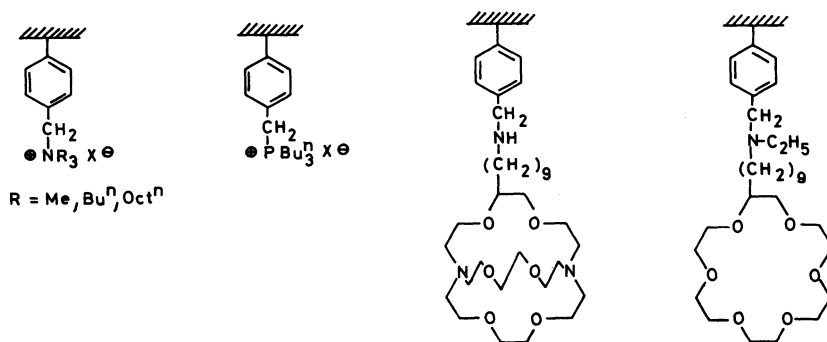
Cram et al. (72) prepared an optically active crown ether, which was bound to a polymer matrix. With this polymer a total optical resolution of racemic  $\alpha$ -amino acid and  $\alpha$ -amino acid estersalts was possible on a packed column.



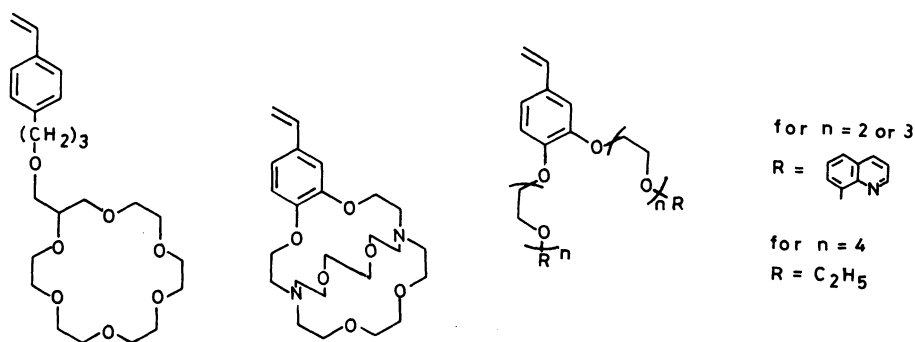
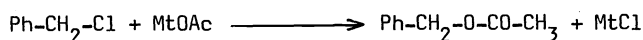
Polymer crown ethers and cryptands show according to the size of the molecular cavity a peak selectivity for the different cations; this means that the cation that fits the dimensions of the macrocycle best is complexed favorably. We found that polymer podands (open chain crown ethers) show in contrast a plateau selectivity, meaning that a wider range of cation sizes are complexed equally well. Here the polymers behaved just like their low molecular mass counterparts (73). The cation with the smaller ionic radius ( $\text{Na}^+$ ) was complexed weakly while the larger cations ( $\text{K}^+$ ,  $\text{Rb}^+$  and  $\text{Cs}^+$ ) were complexed stronger with no pronounced selectivity for one of these cations. These results were obtained with the following polymer podand (74).



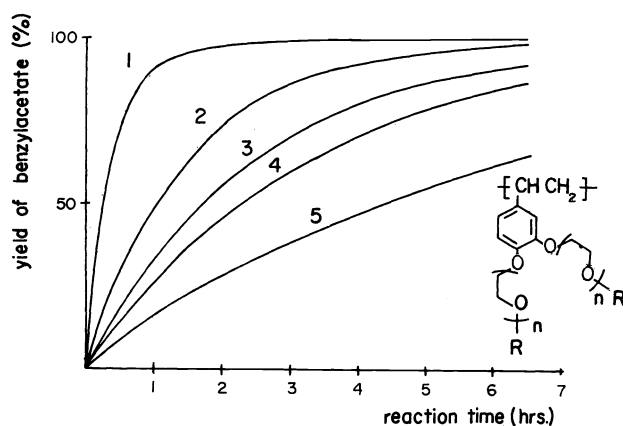
The polymer neutral alkali metal complexing agents are not only of interest because of their unique complexing properties. They also can be used for phase transfer catalyzed reactions. Though a lot of reports deal with the catalytic activity of low molecular mass crown ethers, cryptands and podands only very little is known about the phase transfer activity of polymers of these substances (75). Montanari et al. (75) prepared polymers containing ammonium, phosphonium, crown and cryptand groups attached to a polymer backbone. He showed that of these compounds the polymer cryptands were the most efficient catalysts in liquid/liquid phase transfer nucleophilic substitution of octylbromide with  $\text{CN}^-$  and  $\text{I}^-$  anions.



We prepared different polymer crown ethers (76), cryptands (77) and podands (78) from the following monomers and investigated the polymers in respect to their catalytic activity in the solid/liquid nucleophilic substitution of benzylchloride with acetate ions.



reaction of benzylchloride with potassium acetate in acetonitrile (refluxing temperature) in the presence of podand catalysts

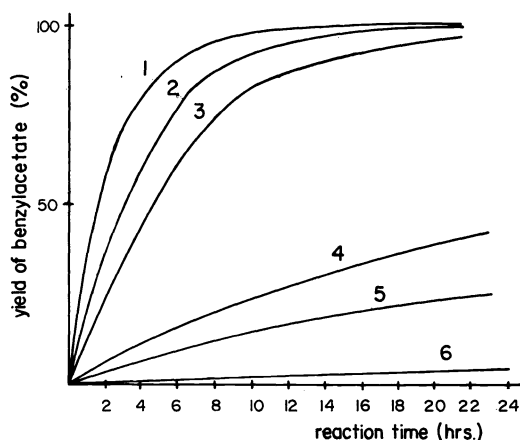
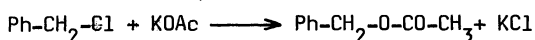


- 1 = 18-crown-6
- 2 = linear polymer podand with n = 3 and R = quinolinyl
- 3 = linear polymer podand with n = 3 and R = quinolinyl copolymer with 85 mole% styrene
- 4 = linear polymer podand with n = 4 and R = ethyl
- 5 = blank reaction

In acetonitrile as solvent the polymer podands were less active compared to their low molecular mass counterparts. There was found a pronounced effect of the different counter cations of the acetate ion. Thus, lithium and sodium acetate showed no or only very little conversion towards the desired ester while potassium acetate gave high yields in this reaction. Polymers containing different length of the oligoethyleneglycolether chain and different end groups showed a great dependence on these parameters of molecular design. Thus it was demonstrated that quinolinyl end groups are important for better catalytic activity compared to ethyl end groups. The superiority of quinolinyl end groups was found by Vögtle et al. (79) for low molecular mass podands. There was also found an optimal length of the oligoether chain for the investigated reaction. Though this effect is not very pronounced it is stated that an optimized polymer for the reaction of benzylchloride with potassium acetate can be designed. The polymer podands showed a quite different behavior when more unpolar solvents than acetonitrile were used. In these solvents the polymers catalyzed the esterification better than their low molecular mass analogues, but the yields in these solvents were not as high as in acetonitrile.

Polymer crown ethers and cryptands catalyzed the reaction of potassium acetate with benzylchloride far better than the polymer podands due to the higher anion activation by these compounds. As seen from the following graph the polymer cryptands are far better catalysts compared to the polymer crown ethers.

nucleophilic substitution of benzylchloride with potassium acetate in acetonitrile at room temperature.



- 1 = cryptand 222
- 2 = polymer cryptand (particle size 0,05-0,1 mm Ø)
- 3 = polymer cryptand (particle size 0,1-0,2 mm Ø)
- 4 = polymer crown ether (10 % crosslinked)
- 5 = polymer crown ether (20 % crosslinked)
- 6 = blank reaction

The decrease in catalytic activity of the polymer cryptands compared with a low molecular mass counterpart was not very high. Copolymers of the cryptand with a polar comonomer (N-vinylpyrrolidone) or an unpolar comonomer (styrene) showed no effect on the catalytic activity of the copolymers. With polymer crown ethers a distinct effect of the degree of crosslinking on the activity was observed, while with polymer cryptands no such effect could be observed. With polymer cryptands only the reduction of the particle size gave a rate enhancement for the catalysis.

As there are lots of other reactions which can be carried out with polymer crown ethers, cryptands and podands these polymers seem to be a promising approach for further investigations in the field of polymer catalysts. The low molecular mass compounds are very expensive, often difficult to remove from the reaction mixture and are toxic. Therefore these neutral alkalimetal cation complexing agents are of great value if they can be handled in a polymer form, where all the disadvantages of the low molecular mass compounds are excluded.

Biological catalysts - the enzymes - can be handled just like polymer catalysts, when they are bound to a polymer matrix (16-18). Lots of reactive polymers have been prepared in order to bind the enzymes under mild physiological conditions to a given polymer. In addition to other carriers we have recently extensively investigated different kinds of poly(vinyl alcohol) products in the form of crosslinked gel particles, tubes with an interior surface coating of poly(vinyl alcohol) and poly(vinyl alcohol) containing synthetic pulp. Reactive groups like diazonium (80), isothiocyanato (80), benzoquinone (81), N-substituted maleinimide (82) or activated disulphides with 2-thiopyridine groups (80) have been introduced into these polymers. Activation of the polymers was also carried out with glutardialdehyde (83), bromocyan (84) and 2,4,6-trichloro-s-triazin (85). Different hydrolases, oxidoreductases and a transferase (hexokinase) which was coimmobilized with glucose-6-phosphate-dehydrogenase were bound to the reactive carriers. The properties of the immobilized enzymes were investigated. For example crosslinked gels of poly(vinyl alcohol) containing 1,4 mmole of diazonium groups allowed to bind up to 400 mg trypsin per gram of carrier, depending on the coupling conditions. 1 g of synthetic pulp activated by different reactions was able to bind up to 50 mg of enzyme. The immobilized enzymes were characterized with regard to their activities. Best results were obtained with immobilized hydrolases. In this case retained activities of up to 30 % were observed.

#### CONCLUSIONS

There are lots of other interesting reactions carried out with polymers as supports, as reagents or as catalysts which could not be described because of the limited space. These include polymers for condensation (86), polymer redox resins (87, 88), polymer metal containing catalysts (14), cyclisation reactions on polymers (89, 90) and so on. As other reviews deal with these topics, we don't want to add a further report. It was shown that polymers as supports, reagents or catalysts offer some great advantages over low molecular mass compounds. These advantages were demonstrated. However it must clearly be seen that there are also some disadvantages. The preparation of a polymer reagent is often a difficult and high cost procedure. In most cases reactions on polymers cannot be monitored by normal analytical methods, as the exact composition of the polymers after each reaction step often cannot be exactly determined. Therefore the multistep synthesis of a polymer reagent is often troublesome. There is also a limitation in multistep synthesis on polymer supports when the particular reactions cannot be carried out in quantitative yields. This is a difficulty in the usual Merrifield synthesis of large polypeptides. Because of diffusion problems sometimes polymer reagents do react much slower than their low molecular mass analogues. This is another disadvantage of the polymer reagents. Due to the high cost of polymer reagents, they should be regenerable quantitatively and reactions carried out with them should yield highly sophisticated products. We feel however that the advantages of many of the polymer reagents outweigh their disadvantages and that a broader field of applications will be found in the future.

#### REFERENCES

- 1) C.G. Overberger and K.N. Sannes, Angew.Chem.Int.Ed., **13**, 99 (1972)
- 2) A. Patchornik and M.A. Kraus, in Encyclopedia of Polymer Science and Technology, N.M. Bikales, Ed., Wiley, New York, 1976, Suppl. 1, p. 486
- 3) C.C. Leznoff, Chem.Soc.Rev., **3**, 65 (1974)
- 4) N.K. Mathur and R.E. Williams, J.Macromol.Sci.-Rev.Macromol.Chem. **C15** (1), 117 (1976)
- 5) P. Hodge, Chem.Br., **14**, 237 (1978)
- 6) C.C. Leznoff, Acc. Chem.Res., **11**, 327 (1978)
- 7) M. Kraus and A. Patchornik, CHEMTECH, Feb. 1979, 118
- 8) N.M. Weinshenker and G. Crosby, Ann.Rep.Med.Chem., **11**, 281 (1976)
- 9) W. Heitz, Adv. in Polym.Sci., **23**, 1 (1977)
- 10) D.C. Neckers, J.Chem. Educ., **52**, 695 (1975)
- 11) J.I. Crowley and H. Rapoport, Acc.Chem.Res., **9**, 135 (1976)
- 12) G. Manecke and P. Reuter, J.Polym.Sci. Polymer Symposium **62**, 227 (1978)
- 13) G. Manecke and W. Storck, Angew.Chem., **90**, 691 (1978)
- 14) E. Tsuchida and H. Nishide, Adv. in Polym.Sci., **24**, 1 (1977)
- 15) C.U. Pittman and G.O. Evans, CHEMTECH, Sept. 1973, 560
- 16) O. Zaborsky, Immobilized Enzymes, CRC Press Cleveland, 1973
- 17) "Enzymology" Vol. 1, "Immobilized Enzymes, Antigenes, Antibodies and Peptides", H.H. Weetall, ed., Dekker, New York 1975
- 18) L. Goldstein and G. Manecke in "Applied Biochemistry and Bioengineering", Vol. 1, L.B. Wingard, Jr., E. Katchalski-Kazir and L. Goldstein, eds., p. 23, Academic Press, New York, 1976
- 19) R.B. Merrifield, J.Am.Chem.Soc., **85**, 2149 (1963)
- 20) R.B. Merrifield, Science, **150**, 178 (1965)



- 21) J.M.J. Fréchet and C. Schuerch, J.Am.Chem.Soc., 94, 604 (1972); R.D. Guthrie, A.D. Jenkins and J. Stenliecek, J.Chem.Soc. (C), 1971, 2690
- 22) H. Koster and F. Cramer, Annalen, 1974, 946
- 23) C.C. Leznoff and J.Y. Wong, Can.J.Chem., 50, 2892 (1972); 51, 3756 (1973)
- 24) C.C. Leznoff and J.M. Goldwasser, Tetrahedron Lett., 1875 (1977)
- 25) C.C. Leznoff and W. Sywanyk, J.Org.Chem., 41, 3203 (1977)
- 26) J.M.J. Fréchet, L.J. Nuyens and E. Seymour, J.Am.Chem.Soc., 101, 432 (1979)
- 27) C.C. Leznoff and D.M. Dixit, J.Chem.Soc., Chem.Comm., 1977, 798
- 28) T.M. Fyles, C.L. Leznoff and J. Weatherston, Can.J.Chem., 55, 4135 (1977)
- 29) I.T. Harrison and S. Harrison, J.Am.Chem.Soc., 89, 5723 (1967)
- 30) C.C. Leznoff and P.J. Svirskaya, Angew.Chem., 90, 1001 (1978)
- 31) J. Carlsson, Hindustan Antibiotics Bulletin, 20, (3-4), 105 (1978)
- 32) F. Svec, J. Hradil, J. Coupek and J. Kálal, Angew.Macromol.Chem., 48, 135 (1975)
- 33) J.K. Whitesell and M.A. Whitesell, J.Org.Chem., 42, 377 (1977)
- 34) P.M. Worster, C.R. McArthur and C.C. Leznoff, Angew.Chem., 91, 255 (1979)
- 35) C.R. Harrison and P. Hodge, J.Chem.Soc., Perkin I, 1976, 605
- 36) C.R. Harrison and P. Hodge, J.Chem.Soc., Perkin I, 1976, 2252
- 37) C. Yaroslavsky, A. Patchornik and E. Katchalski, Tetrahedron Lett., 3629 (1976)
- 38) C. Yaroslavski and E. Katchalski, Tetrahedron Lett., 5173 (1972)
- 39) S. Cacci, L. Caglioti and E. Cernia, Synthesis, 1979, 64
- 40) G. Cainelli, F. Manescalchi and M. Panunzio, Synthesis, 1979, 141
- 41) H. Schuttenberg and R.C. Schulz, Angew.Makromol.Chem., 18, 175 (1971)
- 42) H. Schuttenberg, G. Klump, U. Kaczmar, S.R. Turner and R.C. Schulz, Polym.Prepr., Am.Chem.Soc. Div.Polym.Chem., 13, 866 (1972)
- 43) G. Manecke and M. Stärk, Makromol.Chem., 176, 285 (1975)
- 44) G. Manecke, E. Ehrenthal, W. Finck and F. Wunsch, Isr.J.Chem., 17, (4) in press
- 45) G.A. Crosby, N.M. Weinshenker and H.S.Uh, J.Am.Chem.Soc., 97, 2232 (1975)
- 46) M.J. Farrell, T. Durst and J.M.J. Fréchet, Tetrahedron Lett., 1979, 203
- 47) J.M.J. Fréchet, M. de Smet and M.J. Farrell, Tetrahedron Lett., 1979, 137
- 48) R. Michels, M. Kato and W. Heitz, Makromol.Chem., 177, 2311 (1976)
- 49) M. Kato, R. Michels and W. Heitz, J.Polym.Sci., Polym.Lett., 14, 413 (1976)
- 50) C.R. Harrison and P. Hodge, J.Chem.Soc., Chem.Comm., 1978, 813
- 51) P. Hodge and G. Richardson, J.Chem.Soc., Chem.Comm., 1975, 622
- 52) C.R. Harrison, P. Hodge and W.J. Rogers, Synthesis, 1977, 41
- 53) W. Heitz and R. Michels, Angew.Chem., 84, 296, (1972)
- 54) W. Heitz and R. Michels, Liebigs Ann.Chem., 1973, 227
- 55) M. Okawara, M. Akiyama and N. Narita, J.Polym.Sci., A-1, 7, 1299 (1969)
- 56) M. Fridkin, A. Patchornik and E. Katchalski, J.Am.Chem.Soc., 88, 3164 (1966)
- 57) M.B. Shambhu and G.A. Digenis, Tetrahedron Lett., 1973, 1627
- 58) R.C. Schulz and H. Schuttenberg, Angew.Chem., 88, 848 (1976)
- 59) R.C. Schulz, personal communication
- 60) G. Manecke and M. Stärk, to be published
- 61) C.G. Overberger, T.St. Pierre, N. Vorchheimer and S. Yaroslavsky, J.Am.Chem.Soc., 85, 3513 (1963)
- 62) T. Kunitake and Y. Okahata, Bioorg.Chem., 4, 136 (1975)
- 63) H. Nishide, W. Storck and G. Manecke, J.Molecular Catalysis, 6, 23 (1979)
- 64) G. Manecke and R. Schlegel, Makromol.Chem., 177, 3191 (1976)
- 65) G. Manecke and R. Schlegel, Makromol.Chem., 179, 19 (1978)
- 66) E. Shehori and J. Jagur-Grodzinski, J.appl.polym.Sci., 20, 773 (1976)
- 67) S. Kopolow, T.E. Hogen Esch and J. Smid, Macromolecules, 4, 359 (1971); 6, 133 (1973)
- 68) S. Bormann, J. Brossas, E. Franta and P. Gramein, Tetrahedron, 31, 2791 (1975)
- 69) M. Tomoi, O. Abe, M. Ikeda, K. Kihara and H. Kakinchi, Tetrahedron Lett., 33, 3031 (1978)
- 70) K. Kimura, H. Tamuru, T. Maeda and T. Shono, Polymer Bulletin, 1, 403 (1979)
- 71) E. Blasius, K.P. Janzen, W. Adrian, G. Klautke, R. Lorscheider, P.G. Maurer, B.v. Nguyen, T. Nguyen Tien, G. Scholten and J. Stockemer, Z. Anal.Chem., 284, 337 (1977)
- 72) G. Dotsevi, Y. Sogah and D.J. Cram, J.Am.Chem.Soc., 98, 3038 (1976)
- 73) J.M. Lehn in "Structure and Bonding", Vol. 16, J.D. Dunitz, P. Hemmerich, J.A. Ibers, C.K. Jørgensen, J.B. Neilands, D. Reinen and R.J.P. Williams eds., Springer, Berlin, Heidelberg, New York, 1973, p. 54
- 74) G. Manecke and P. Reuter, unpublished results
- 75) M. Cinouini, S. Colonna, H. Molinari, F. Montanari and P. Tundo, J.Chem.Soc., Chem. Commun., 1976, 394
- 76) G. Manecke and A. Krämer, to be published
- 77) G. Manecke and P. Reuter, to be published
- 78) K. Hiratani, P. Reuter and G. Manecke, J. Molecular Catalysis, 5, 241 (1979)
- 79) F. Vögtle and H. Sieger, Angew.Chem., 89, 410 (1977)
- 80) G. Manecke and H.-G. Vogt, Angew.Makromol.Chem., 78, 21 (1979)
- 81) G. Manecke and W. Beier, to be published
- 82) G. Manecke and H.J. Middeke, to be published

- 83) G. Manecke and H.-G. Vogt, J.Solid-Phase Biochem. in press
- 84) G. Manecke and H.-G. Vogt, to be published
- 85) G. Manecke and H.-G. Vogt, Makromol.Chem., 177, 725 (1976)
- 86) N.M. Weinshenker and C.M. Shen, Tetrahedron Lett., 1972, 3281; 3285
- 87) G. Manecke, Pure Appl.Chem., 38, 181 (1974)
- 88) H.G. Cassidy and K.A. Kun, "Oxidation-Reduction Polymers", Interscience, New York, 1965
- 89) J.I. Crowley and H. Rapoport, J.Am.Chem.Soc., 92, 6364 (1970)
- 90) A. Patchornik and M.A. Kraus, J.Am.Chem.Soc., 92, 7587 (1970)