

SOME ASPECTS OF CATALYTIC ACTIVITY AND STEREOCHEMISTRY IN MACROMOLECULAR SYSTEMS

Francesco Ciardelli, Emo Chiellini, Carlo Carlini and Mauro
Aglietto

Istituto di Chimica Organica Industriale, University of Pisa
and Centro di Studio del C.N.R. per le Macromolecole Stereordi-
nate ed Otticamente Attive, Pisa, Italy.

INTRODUCTION

Natural catalysts display in general extremely high selectivity and stereo-
selectivity, their peculiar properties being due in the most cases to their
macromolecular nature. Indeed this allows the coexistence, in the same macro-
molecule, of active functional groups giving cooperative effects thanks to
their relative spatial disposition.

The geometry of the different groups is determined by the macromolecule
secondary structure and makes the catalyst specific only for substrates with
a stereochemical structure fitting well in the active sites. Nature has
provided a lot of examples of specific catalyst/substrate pairs and in several
cases it has been possible to rationalize the origin of such specificity(1).
On this basis several attempts have been made in order to prepare synthetic
macromolecular catalysts with comparable catalytic properties to natural
systems(2,3). While on one side a large number of new systems have been
developed showing reactivity much higher than monomeric analogs, very little
has been done as far as specificity and stereoselectivity are concerned(4).
A strong limitation arises from the difficulty to prepare systems with reacti-
ve groups and a well defined primary and secondary structure.
In the present paper we shall describe our approach to the problem based on
the following steps:

- a) Preparation of copolymers with chiral moieties providing a local or a macro-
molecular spatial order.
- b) Introduction in these polymeric matrices of potentially catalytic groups.
- c) Preliminary studies of the catalysis by the above systems in reactions in-
volving chiral or prochiral substrates.

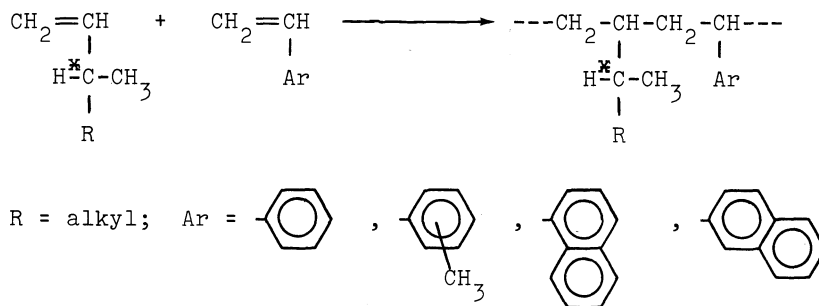
a) PREPARATION OF COPOLYMERS OF CHIRAL AND FUNCTIONAL MONOMERS AND THEIR STEREOCHEMISTRY

Copolymerization is a very convenient way to prepare a macromolecular system
the properties of which are determined by the characteristics of both co-
monomers. Accordingly copolymerization of an optically active monomer with a
comonomer bearing a reactive group should give an asymmetric perturbation of
the latter if the former monomer units are capable to induce a spatial order
in the whole macromolecule.

Copolymerization of vinylaromatic monomers, such as styrene, *o.*, *m.*, *p.* methyl-
styrene, 1- and 2-vinylnaphthalene, with optically active α -olefins in the
presence of isotactic specific Ziegler-Natta catalysts gives (Scheme 1) macro-
molecules where the aromatic group is imbedded in a stereordered secondary
structure(5).

In fact in the spectral region over 185 nm, where only electronic transitions
of the π -electron system of the aromatic chromophore are located, the co-
polymers show dichroic bands having markedly different features with respect
to low molecular weight models containing a single aromatic chromophore per
molecule. In particular in the region (270-245 nm) of the weak 1L_b electron

Scheme 1



ic transition of the aromatic chromophore, the copolymers show a dichroic band the intensity of which is much higher than for low molecular weight structural models(6,7). However a "conformational model", where the phenyl group is in the same spatial situation as in the polymer, has ellipticity of the same order of magnitude as the corresponding copolymer(8). Therefore the circular dichroism(CD) in this region is substantially due to the single aromatic group disposed in a definite stereochemical arrangement.

In the region of the strong allowed ${}^1\text{B}$ transition(190- 200 nm) of the aromatic group the copolymer shows in its CD-spectrum a typical couplet which is absent in all models. By contrast the conformational model has in this region only one CD band of the same order of magnitude as the copolymer. The absence of the splitting in compounds with only one aromatic chromophore per molecule clearly indicates that it is originated by intramolecular interactions among aromatic groups assembled in similar chiral environment. Indeed a mutual geometrical disposition of a single chirality is necessary to give rise to a CD-couplet(6,7). A detailed picture of this geometry has been obtained by performing CD calculations using equations derived from DeVoe theory(9). Excellent agreement between experimental and calculated CD spectra were obtained(10,11) only assuming that the aromatic units were disposed along a single screw sense helical chain, the basic parameters being the same as for the corresponding homopolymer helices in the crystalline state. The predominance of a single screw sense was determined by the chirality of the α -olefin. A situation of this type is represented in Figure with an (S)- α -olefin which preferentially induces a left handed helix(12).

In this situation the aromatic group electronic transitions become optically active, their chiroptical properties being determined by the helical conformation of the macromolecule rather than by the local asymmetry of the asymmetric carbon atoms, more or less closely attached to the group itself.

Being the asymmetric perturbing effect of conformational origin, it will be observed until the conformation survives, as occurs in the crystalline state and in the solution if the macromolecules are unperturbed. The use of very good solvents and high temperature can markedly reduce the extent of the stereoregular conformation and then the asymmetric perturbation of the reactive groups.

Similar effects, even if in a less remarkable extent, are observed in the case of non highly stereoregular copolymers. If one looks to the chiroptical properties of random and alternating copolymers of styrene with (-)-menthyl acrylate obtained as shown in the Scheme 2, observes that in both cases a CD band at 262 nm, due to the induced optical activity in benzene chromophore, is present(13). In the obtained alternating copolymer, where the average distance between phenyl and asymmetric carbon atoms of the menthyl groups is shorter(Scheme 2), the ellipticity of the above CD-band is lower than in the random copolymers having rather high content of menthyl acrylate units. This result can be accounted for a cooperative asymmetric effect among chiral units in block sections.

In this type of copolymers the lower and at present unknown stereoregularity does not allow to define a possible ordered secondary structure of the macromolecule. However these polymers are very interesting for the great potential-

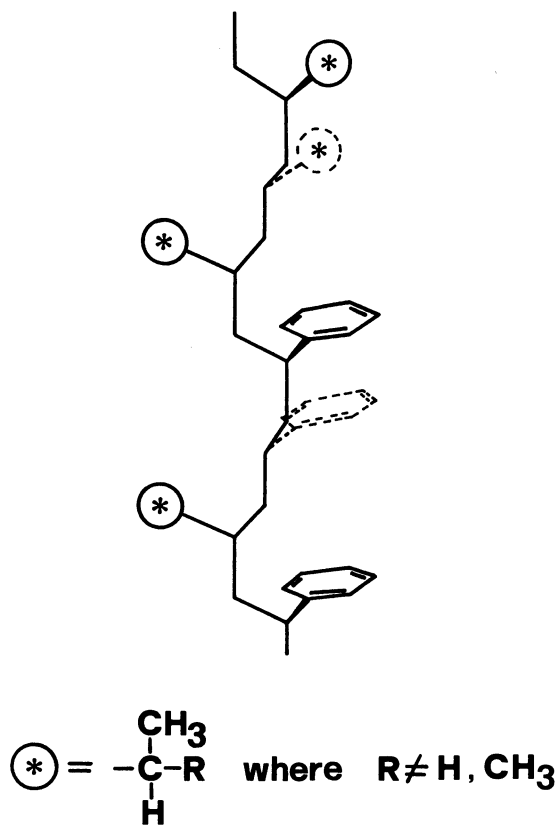
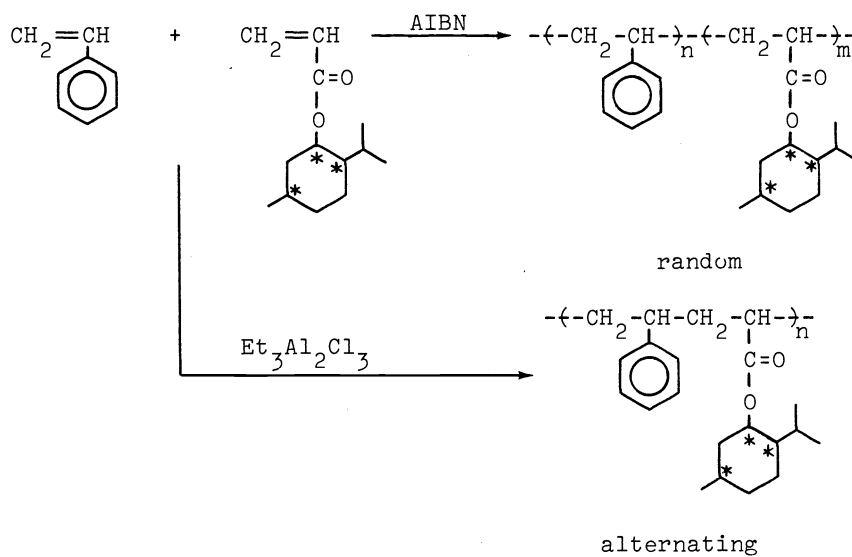


Figure. Spatial disposition of side chains along a left-handed 3_1 helical chain.

Scheme 2

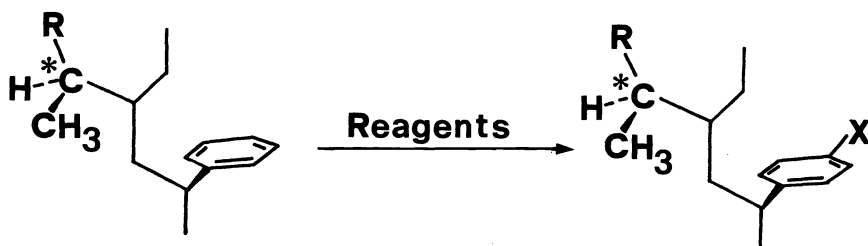


lity and simplicity of radical initiated copolymerization.

b) INTRODUCTION OF REACTIVE GROUPS IN THE CHIRAL COPOLYMERS

In the case of stereoregular copolymers obtained from vinylaromatic monomers with chiral α -olefins, reactive groups are better introduced by chemical reactions on the hydrocarbon copolymer. Indeed, direct copolymerization of chiral α -olefins with functional monomers in the presence of Ziegler-Natta catalysts is possible only in very few cases and gives polymers of non completely definite stereochemistry(14). On the other side, electrophilic substitutions at the *para*-position of the phenyl ring are possible and have been shown to take place without modifying stereochemistry of the copolymer(14,15). In this way several functional copolymers have been obtained where the functional group is imbedded in an optically active macromolecular matrix having high conformational homogeneity. The groups introduced in the *para*-position of the phenyl ring were:halo, chloromethyl, diphenylphosphino, diphenylphosphinomethyl, and alkyl ammonio-methyl chloride(Scheme 3)

Scheme 3



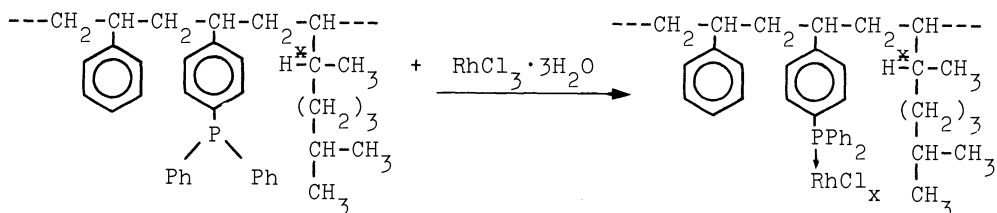
| Reagents | X |
|--|--|
| I_2/HIO_4 | I |
| $FeCl_3/Br_2$ | Br |
| $CH_3OCH_2Cl/ZnCl_2$ | CH_2Cl |
| $\left. \begin{array}{l} 1) I_2/HIO_4 \\ 2) Li(n.C_4H_9) \\ 3) ClP(C_6H_5)_2 \end{array} \right\}$ | $P(C_6H_5)_2$ |
| $\left. \begin{array}{l} 1) CH_3OCH_2Cl/ZnCl_2 \\ 2) LiP(C_6H_5)_2 \end{array} \right\}$ | $CH_2P(C_6H_5)_2$ |
| $\left. \begin{array}{l} 1) CH_3OCH_2Cl/ZnCl_2 \\ 2) N(CH_3)_3 \end{array} \right\}$ | $CH_2\overset{\oplus}{N}(CH_3)_3 Cl^-$ |

While functional groups present in the monomer can interact with organometallic catalysts, such as Ziegler-Natta catalytic systems, modifying their activity and stereospecificity(16,17), radical initiation can be used to prepare chiral polymer reagents. Accordingly Overberger and Cho(18) prepared an optically active catalyst by radical copolymerization of 4(5)-vinylimidazole with (S)-2,5-dimethyl-1-hepten-3-one, which however did not display any chiral discrimination during esterolysis of nitrophenol esters of chiral carboxylic acids. In the same way (-)menthyl acrylate or -methacrylate can be copolymerized with 4-vinylpyridine or 4(5)-vinylimidazole to obtain polymeric catalysts for esterolytic reactions(19) in polyphase conditions.

c) SOME CATALYTIC USES OF CHIRAL COPOLYMERS

The phosphenated optically active styrene/olefin copolymers described in the previous section have been used as ligands for Rh(I) and Ru(II) complexes to be employed in catalytic transformations of racemic or prochiral olefins(20). Very small but definite asymmetric induction was observed in general, the best result having been obtained with a complex from $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ and a phosphenated polymeric ligand containing (-)(R)-3,7-dimethyl-1-octene, styrene and *p*.diphenylphosphino-styrene units in 49:33:18 ratio. In this complex the metal containing units have probably the structure shown below(Scheme 4).

Scheme 4

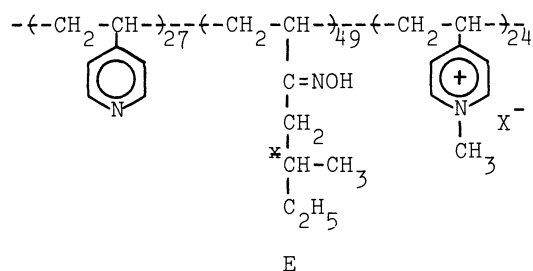


This complex is active for heterogeneous hydrosilylation of ketones and gives, from acetophenone, 1-phenylethanol with 2.5% optical purity and the same absolute configuration as the optically active 3,7-dimethyl-1-octene used to prepare the catalyst(20).

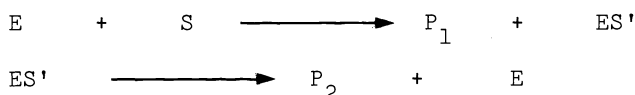
If we compare these systems with low molecular weight analogs even the relatively small asymmetric effect should markedly surprise(21) as the distance between asymmetric carbon atoms of a single configuration and reactive sites is far too large, seven or more carbon atoms. It must be also taken into account that all sites are not in the same asymmetric conditions and what we observe is only an average value. Moreover the pairs polymer/substrate examined up to now might not be the most convenient ones for evidencing asymmetric catalysis. In fact hydrocarbon systems have been in general used where no strong polar effect exists and a "double binding" to the catalytic sites is not possible. Even in the case of low molecular weight chiral phosphine/rhodium complexes considerable effects are observed only with substrates containing heteroatoms and polar groups(21). The problem is however not so simple, a certain responsibility being probably to be found in the structure of the polymeric catalyst itself. This is particularly true with reactions which do not require a cooperative assistance by other functional groups in the macromolecule which could give rise to a more complex intermediate state with more restricted steric requirements.

A first approach in this direction is supplied by copolymers to be used as catalysts for esterolytic reactions. The radically initiated copolymerization of 4-vinylpyridine(4VP) with (+)(S)-3-methyl-1-hepten-3-one(2MBVK) gave a copolymer where also 4VP units are in a dissymmetric environment. In fact the optical rotation of the copolymer is positive, that is opposite in sign to that of the homopolymer from 2MBVK, and non linearly dependent on composition, suggesting that 4VP units in the copolymer have positive optical rotation increasing in absolute value up to 70-80% of 2MBVK units. This conclusion was confirmed by CD spectra, showing a dichroic band at about 257 nm, where the lowest energy absorption band of pyridine ring is located and where the poly(2MBVK) does not show dichroic bands(22).

Partial methylation with dimethylsulfate followed by reaction with an excess of hydroxylamine hydrochloride gave the water soluble polymeric catalyst shown below:



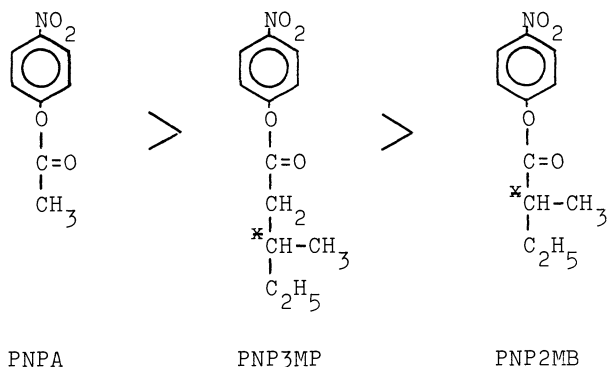
Type E polymers are active in the two steps esterolysis of activated *p*.nitrophenol esters(S) according to the following Scheme:



the second step being assisted by pyridine units(23).

Thus one could expect a possible double asymmetric effect in the hydrolysis of *p*.nitrophenol esters with chiral acids both in the first step [formation of the N-acyl derivative(ES')] and phenolate anion(P₁)] and in the second one [deacylation assisted by pyridine units to give the₁acyloxy anion(P₂)] .

Unfortunately in this copolymer the oxime showed a $pK_a=11.4$, thus requiring a pH of about 10 for an appreciable dissociation. At this pH the buffer becomes comparable in esterolysis to the catalyst itself. It was only possible to investigate the first reaction step(acylation) under pseudo first order conditions with 10/1 catalyst excess with respect to the substrate. In this step the polymer catalyst shows a remarkable steric effect on esterolysis, the relative reaction rate decreasing in that order:



The catalyst is also able to discriminate between the two antipodes of PNP2MB even if the reaction rate of the S antipode is only about 15% higher than for the R antipode. The chiral discrimination is no longer observable for PNP3MP where the chiral center is farther from the reaction site of the substrate. Clearly the chiral discrimination is here probably due only to a local effect as asymmetric chiral center and nucleophile are very close situated in the side chain of vinyl ketone units, the assistance role of the macromolecular structure consisting only in keeping the system in solution.

FINAL REMARKS

This paper points out that copolymerization can be an extremely useful, simple and economic way to obtain systems where two different monomers with distinct properties give rise to mutual cooperative effects at the stereochemical level. Indeed the way of inducing optical activity in non chiral chromophoric or functional monomers by copolymerization is now a well estab-

lished method. However quantitative aspects are still far to be completely solved, the average induced chirality being markedly affected by stereoregularity, composition and units distribution for each comonomers pair. This may be a limitation when using these systems as polymeric reagents or catalysts. In fact the relative structural heterogeneity can be reflected in chemical reactivity and it can occur that the less stereospecific sites are at the same time the most reactive, thus depressing stereoselectivity. This could explain the low chiral discrimination or asymmetric induction in general observed. The solution of the above problems can however be reached by overtaking some synthetic aspects. At present it seems that a substantial improvement can be achieved by introducing a very limited amount of reactive groups in a highly stereoregular matrix. Induced chirality in the isolated chromophores has been indeed recently shown to increase with decreasing its content(24). Alternating copolymer structure can offer a second way to avoid composition and distribution problems, but in this case a high stereoregularity has not been obtained yet(25).

Finally multifunctional catalysis and polymer/substrate binding can suggest a way to improve steric requirements of active sites. This approach is even more complex than the previous one from the synthetic viewpoint, even if the preliminary results described in this paper(22) can give an indication about the possibility of designing chiral polymer systems capable of a multistep catalysis.

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