

Topographical nature of the polymer matrix and reactivity of attached functional groups: Effect of crosslink density on the efficiency of solid-phase hypochlorite oxidations[†]

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MS received 27 January 1989; revised 24 April 1989

Abstract. A series of crosslinked polystyrene-supported hypochlorite reagents with the reagent function in different microenvironments were prepared and their reactivities in oxidation and halogenation reactions on organic substrates were investigated. The reactivity of the hypochlorite reagent function was observed to be dependent on the topographical nature of the polymer matrix. The reactivity in these cases depends on the degree of crosslinking which affects the extent of functionalisation and also the mechanical integrity and stability of the polymer support. Hypochlorite reagents starting from 1%, 2%, 4% and 20% crosslinked polystyrenes were prepared and used for oxidation and halogenation reactions. The reactivity of the hypochlorite function is reduced considerably when the degree of crosslinking is increased. A decrease in the degree of functionalisation is also observed with increase in the degree of crosslinking.

Keywords. Solid phase organic reactions; polymeric reagents; polymeric hypochlorites; crosslink density.

1. Introduction

When the polymer-supported solid-phase strategy was developed, polymers were considered only as heterogenizing media for immobilizing low-molecular substrates, without having much influence in deciding the course and extent of the reactions (Hodge and Sherrington 1980; Mathur *et al* 1980; Akelah and Sherrington 1981). The whole macromolecule cannot be considered a single species, but it contains many functional entities depending on the number of attached reactive groups (Patchornik 1982). Thus, the binding of an active species to a polymer chain results in a new reagent with different structure, reactivity and selectivity. Apart from the effect of possible heterogenization, polymer attachment gives systems containing several active species per macromolecule which can behave differently from the low-molecular weight analogues, because of co-operative interactions (Kopolow *et al* 1971). The presence of other groups in the macromolecule can also be important for hydrophobic interactions with the substrate and for selectivity if groups with particular steric requirements are used (Pillai and Mutter 1982).

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[†]Taken in part from the PhD thesis *Polymeric analogues of t-butyl hypochlorites as solid-phase organic reagents*, by K Sreekumar, M.G. University, Kottayam, 1988

The topographical nature of the polymer matrix exerts a significant influence on the reactivity of the attached functional groups. Lloyd and Alfrey (1962) investigated the role of the topology of the gel network on chemical reactivity. The topography of a polymer matrix is determined by the chemical nature of the monomers, the molar percentage of crosslinks and the monomer dilution ratio. Among these factors, the role of the crosslinks is the most dominating. A knowledge of the dependence of the topographical nature of the polymer backbone on the reactivity of the attached functional groups requires a study of the effect of crosslink density on solid-phase polymer-supported reactions. Recently, we have developed a polystyrene-supported hypochlorite reagent for solid-phase oxidations and halogenations of organic substrates (Sreekumar and Pillai 1987). This polystyrene support system appeared to be amenable to structural variations for studying the effect of crosslink density, functional group capacity and effect of spacers (Sreekumar and Pillai 1989) on the reactivity of the attached functional groups. Thus, in this work, we report on the studies directed to correlate the effect of crosslink density on the extent of functionalisation reactions and the reactivity of the hypochlorite reagents in polymer-supported solid-phase reactions.

2. Results and discussion

Polystyrene-supported hypochlorite reagents (A to E) were prepared starting with 1%, 2%, 4% and 20% crosslinked styrene-divinylbenzene copolymer beads. Reagents having one and no spacer groups were prepared following the procedure reported earlier (Sreekumar and Pillai 1987). Hypochlorite reagents having three, four and five spacer-methylene groups have been prepared by a seven-step polymer-analogous reaction (Sreekumar and Pillai 1989).

In various polymer-analogous reactions, the effect of crosslink density on the extent of functional group conversions is observed to a great extent. This is most conspicuous in the case of the hypochlorite reagents in which the tertiary carbons bearing the hypochlorite function are attached directly to the polymer backbone. As the length of the spacer increases, the effect of increasing crosslinks in retarding the extent of functional group conversions diminishes gradually. Even with the hypochlorite reagent having a five-methylene spacer, the reactivity of the functional group is considerably reduced as the degree of crosslinking increases. This effect is

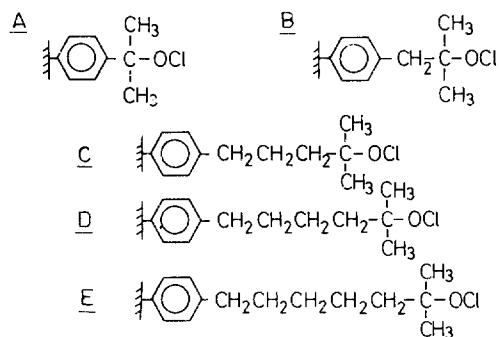


Chart 1.

noticed markedly in the final capacity of the hypochlorite resins. Similar effects of increasing reactivity with increase in separation of the active function from the polymer matrix is observed in the case of phase-transfer catalysts (Brown and Jenkins 1976; Molinari *et al* 1977), immobilized enzymes (Porath *et al* 1975) and affinity chromatography (Miller *et al* 1971; Steers *et al* 1971).

2.1 Functionalisation reactions for the preparation of hypochlorite reagents: influence of crosslink density

In the preparation of the hypochlorite reagent with no spacer groups to separate the hypochlorite function from the polymer backbone, the extent of functional group conversions during the reaction sequence is dependent on the degree of crosslinking. The functional group capacity of each resin is maximum with the 1% crosslinked sample. It gradually decreases as the degree of crosslinking increases to 2%, 4% and 20%. With the 20% crosslinked resin the degree of functionalisation is almost negligible. Similar observations were made in the preparation of the reagents with different spacers. The results are presented in tables 1–5.

2.2 Effect of crosslink density on oxidation reactions with hypochlorite reagents

When hypochlorite reagents prepared from differently crosslinked polystyrenes are used for the oxidation of alcohols to carbonyl compounds, it is observed that the reagents prepared from 1% crosslinked polystyrenes are most efficient in terms of

Table 1. Effect of crosslink density on the extent of functionalisation reactions for the preparation of hypochlorite resin (structure A) (with no spacer).

Crosslink density (%)	Capacity (meq/g)		
	Acetyl resin	<i>t</i> -Alcohol resin	Hypochlorite resin
1	9.312	6.71	1.72
2	6.12	4.02	1.43
4	3.12	1.81	1.128
20	1.24	0.97	0.87

Table 2. Effect of crosslink density on the extent of functionalisation reactions for the preparation of hypochlorite resin (structure B) (with one spacer).

Crosslink density (%)	Capacity (meq/g)		
	2-Oxopropyl resin	<i>t</i> -Alcohol resin	Hypochlorite resin
1	4.17	3.71	2.51
2	3.87	3.01	2.33
4	2.92	1.9	1.14
20	1.11	1.12	0.91

Table 3. Effect of crosslink density on the extent of functionalisation reactions for the preparation of hypochlorite resin (with three spacers) (structure C).

Cross-link density (%)	Capacity (meq/g)						
	β -Keto propionic acid resin	Butyric acid resin	Butyryl chloride resin	Butyryl malonate resin	2-Oxopentyl resin	<i>t</i> -Alcohol resin	Hypochlorite resin
1	4.4	4.34	4.4	3.78	3.21	3.01	2.99
2	4.08	3.97	3.97	3.67	3.11	2.92	2.81
4	3.15	2.98	2.77	2.71	2.28	2.61	2.14
20	2.01	1.92	1.72	1.61	1.21	1.31	0.92

reaction period and yield of the product. Oxidation of benzyl alcohol to benzaldehyde was taken as the model reaction for studying these effects. The amount of benzaldehyde formed after a fixed time interval was measured spectrophotometrically at 470 nm (Lappin and Clark 1951). In the present study the measurements were taken after 22 h. The dependence of the capacities of the hypochlorite resins **A** to **E** and the variation of their reactivities towards oxidation of benzyl alcohol as a function of crosslink density are depicted in figures 1 and 2, respectively.

From this observation of the diminution of the reaction rate with the increase in the degree of crosslinking, it can be assumed that the reactivity of the hypochlorite function attached to the polymeric network is highly dependent on the variables of gel preparation (Morawetz 1975). It might be expected that groups placed close to crosslinks might be less accessible to reagents in the continuous phase. This leads to non-equivalence of the reactive groups attached to the polymer network. For an effective reaction to occur, the functional groups should be accessible to the reagents in the continuous phase. In the case of crosslinked polymers, they being insoluble, this can be achieved in the presence of good solvents, which can swell the polymer network, the network is expanded considerably and the functional groups are exposed to the continuous phase (Kun and Kunin 1968). As the degree of crosslinking increases, the ability of the solvents to penetrate into the three-dimensional polymer network decreases, and the movements of the reagents within such an interior may be diffusion controlled (Ford 1984; Warshawsky 1979).

The introduction of any functional group into a resin will inevitably remove some of the original pore-volume; when a long reaction sequence of several steps is attempted for the construction of a large structural unit, a corresponding fall of efficiency of the extent of functional group conversions has been reported (Gubitosa *et al* 1977). Thus in the synthesis of the hypochlorite reagents with spacers of different lengths by multistep reaction sequences, even though the introduction of the first functional group on the polystyrene of differing crosslink densities was not so difficult, the decrease in extent of conversion was most marked in the last step of each reaction sequence, i.e. the conversion of the *t*-alcohol resin to the hypochlorite resin. The capacity of the hypochlorite resin was seriously affected by the changing degree of crosslinking which changes the local polarity of the crosslinked polymer system. In the absence of the crosslinks the local polarity is averaged over the life time of the

Table 4. Effect of crosslink density on the extent of functionalisation reactions for the preparation of hypochlorite resins (structure D) (with four spacers).

Crosslink density (%)	Capacity (meq/g)						
	γ -Keto butyric acid resin	Pentanoic acid resin	Pentanoyl chloride resin	Pentanoyl malonate resin	2-Oxoheptyl resin	<i>t</i> -Alcohol resin	Hypochlorite resin
1	4.22	4.07	4	3.9	3.6	3.41	3.01
2	3.86	3.82	3.86	3.79	3.2	3.11	2.92
4	3.17	2.9	2.81	2.8	2.35	2.81	2.64
20	1.72	1.67	1.69	1.62	1.27	1.24	1.25

Table 5. Effect of crosslink density on the extent of functionalisation reactions for the preparation of hypochlorite resins (with five spacers) (structure E).

Crosslink density (%)	Capacity (meq/g)						
	δ -Keto pentanoic acid resin	Hexanoic acid resin	Hexanoyl chloride resin	Hexanoyl malonate resin	2-Oxoheptyl resin	<i>t</i> -Alcohol resin	Hypochlorite resin
1	4.77	4.33	4.21	4.17	4.08	3.78	3.21
2	4.2	4.02	4.07	3.52	3.42	3.48	3.02
4	3.28	2.89	2.98	2.92	2.61	3.01	2.62
20	1.81	1.64	1.66	1.57	1.52	1.41	1.41

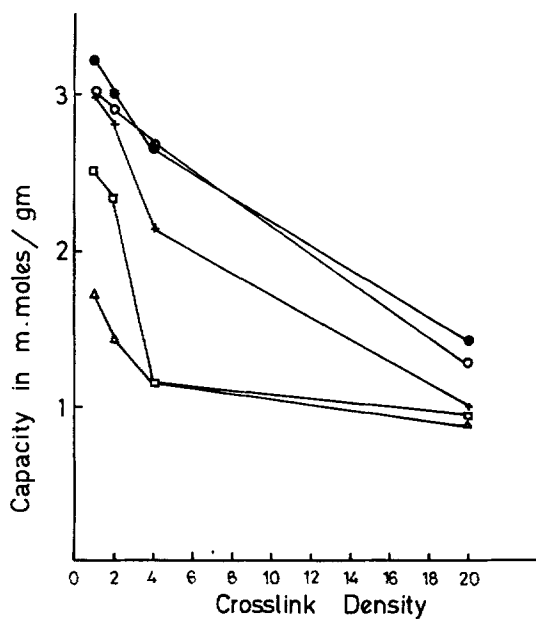


Figure 1. Effect of crosslink density on the capacity of the hypochlorite function [$n = 0(\Delta)$, $1(\square)$, $3(+)$, $4(\circ)$, $5(\bullet)$].

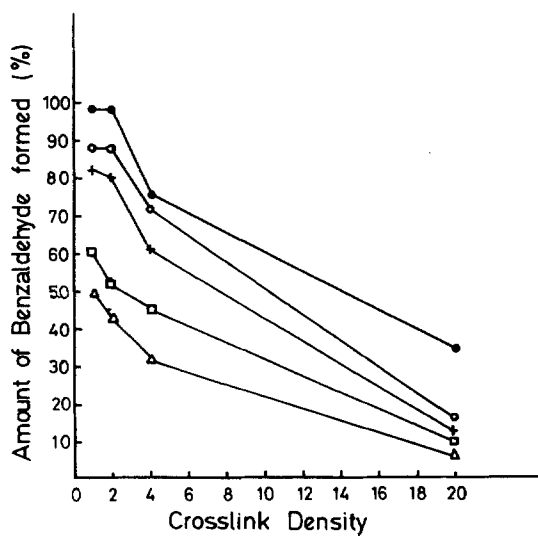


Figure 2. Effect of crosslink density on the reactivity of hypochlorite oxidising reagents (symbols have the same meaning as in figure 1).

reaction by microbrownian motions, but this is impossible in the case of crosslinked polymer networks (Regen and Lee 1974).

These effects become more clear when parallel systems are considered. In the case of N-bromo-co-poly (acrylamide-methylene-bis-acrylamide), which was also used as an oxidising and halogenating reagent for organic substrates (George and Pillai 1988) an increase in the degree of crosslinking causes the rate of the reaction to increase, pass through a maximum and then decrease (George and Pillai 1989). The reactivity of the N-haloamide is maximum when the degree of crosslinking is 10%, at which point a better hydrophilic/hydrophobic balance is achieved. At very high degrees of crosslinking, the resin becomes very hydrophobic and it is found to swell very little in almost all solvents making the reactions difficult. Moreover, at very high degrees of crosslinking, the steric factors imposed by the polymer network adversely affect the reactivity considerably.

2.3 *Crosslink density, mechanical stability and reaction work-up*

The mechanical stability and integrity of the resin beads are important in the design of polymeric solid-phase reagents. These factors, characteristic of the network, are dependent on the crosslink ratio. In contact with a good solvent, lightly crosslinked resins are extremely fragile and even mechanical or magnetic stirring may cause considerable mechanical degradation and attrition of the support. Thus, in the preparation of the hypochlorite reagents having different spacer groupings from 1% crosslinked polystyrene, some mechanical loss due to powdering is noticed. In many of the steps of the reaction sequences, the work-up of the reaction mixture becomes difficult due to extensive swelling in the reaction solvents, the resin appears rubbery and assumes semi-solid form. But on washing with non-solvents, the gels collapse and the resins return to glassy bead form. The hypochlorite reagents prepared from 1%-crosslinked polystyrene lack mechanical integrity and stability and are not stable enough for recyclisation after the third cycle. Increased physical stability can be achieved with increased crosslinking, but there always exists a balance between the required mechanical properties and reactivity. Highly crosslinked resins are mechanically stable and rigid, but lack reactivity. From the analysis of the various reaction sequences carried out for the preparation of the hypochlorite reagents, it can be clearly seen that 2% crosslinked polystyrene possesses the required mechanical stability and reasonable chemical reactivity to work with. This is found to withstand the mechanical stress imposed by magnetic or overhead stirring. In terms of degree of functionalisation, 1% crosslinked resin possesses the maximum and 20% crosslinked resins possess the minimum loading capacity.

2.4 *Crosslinking, polarity and solvent effect*

The degree of crosslinking of the polymer support is important in deciding the net polarity of the polymeric reagent system. As the crosslink density originating from the divinylbenzene increases, the hydrophobicity of the polystyrene backbone attains prominence over the hypochlorite function in deciding the polarity of the system, even in the case of the reagent with the five-methylene spacer. An increase in the degree of crosslinking arising from the increased percentage of the divinyl monomer, which is highly hydrophobic, increases the hydrophobicity of the polymer matrix and that of the entire system. This adversely affects the efficiency of the polymeric reagent in effecting polar synthetic transformations.

3. Experimental procedure

The starting materials used were differently crosslinked styrene-divinylbenzene copolymer beads (Fluka, 200–400 mesh size). Functionalisation reactions leading to the formation of the hypochlorite resins were conducted according to the procedures reported earlier (Sreekumar and Pillai 1989). The alcohols used for oxidation were commercial samples purified by crystallisation or distillation. IR spectra were recorded on a Perkin-Elmer spectrophotometer.

3.1 Investigation of the efficiency of the oxidation reactions: Influence of crosslink density

Hypochlorite resins prepared from various crosslinked polystyrenes (1%, 2%, 4% or 20%) were shaken with the alcohol at room temperature for 22 h in chloroform solvent (20 ml). The resin to alcohol ratio taken was 2:1. After 22 h, the reaction mixture was filtered, washed with chloroform and the filtrate evaporated to get the oxidised product. The amount of carbonyl compound formed was determined by measuring the colour developed with 2,4-dinitrophenylhydrazine reagent at 470 nm.

Acknowledgement

The authors thank the Council of Scientific and Industrial Research for the award of a fellowship to KS.

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