

## Polymer Supported Alkoxides: Synthesis and Reactivity

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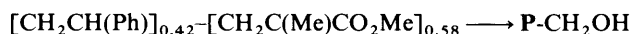
The preparation of a new type of ionomer, polymeric alkoxides, is described. Dimethyl sulphoxide (DMSO) is the most convenient solvent for a study of their reactivity. Comparison of these polymeric bases with low molecular weight alkoxides was achieved by a study of the regio- and the stereo-selectivity of 2-bromo-octane elimination, and of the  $E_2/S_N2$  competition from 2-*p*-methoxyphenyl-1-tosyloxypropane. The results show that the polymeric backbone does not induce any steric hindrance and that the basicity of the alkoxides is lowered by fixation on a polymer support.

A number of moisture-sensitive basic reagents frequently used in organic synthesis may be protected by being bound onto a polymer. The moisture-sensitive function is thus embedded in a hydrophobic environment and protected from hydrolysis;<sup>1</sup> the reusable reagent is easy to separate from the products in solution. Patchornick has described such systems, namely trityl-lithium<sup>2</sup> and lithium di-isopropylamide<sup>3</sup> supported on a Merrified resin. We have now prepared primary, secondary, and tertiary alkoxides bound on linear or crosslinked polymers. Because of the steric hindrance arising from the macromolecular backbone, we thought that these polymeric bases might behave differently from their low molecular weight analogues.

*Preparation of the Polymeric Alkoxides.*—A number of factors govern the reactivity of the products. (1) Where the OH function lies near the polymer backbone, the steric influence of the polymer is likely to be highest. (2) The close proximity of several OH groups may hinder the total ionization, because of repulsive forces between two or more ionized functions; thus the loading capacity in OH groups (number of OH groups in equiv. by gram) must not be too high.<sup>4</sup>

We chose to work with copolymers of styrene and a vinyl alcohol precursor. Styrene-vinyl acetate polymer is commercially available. From styrene-methyl vinyl ketone and styrene-methyl methacrylate, linear polymers were obtained by radical copolymerization, and crosslinked resins by suspension copolymerization with divinylbenzene (DVB). These were then converted into alcohols by subsequent hydrolysis or reduction, respectively.

The primary alcohol was obtained by reduction of the styrene-methacrylate copolymer with sodium bis(2-methoxyethoxy)aluminium hydride (Red-Al) in toluene. Treating the linear polymer with  $\text{LiAlH}_4$  led to gel formation with some ester function remaining, as the i.r. spectrum showed. With Red-Al the linear polymer is 100% reduced, and a 10% DVB crosslinked polymer *ca.* 50%: throughout **P** stands for polymer.



The styrene-vinyl acetate copolymer was quantitatively hydrolysed by alcoholic potassium hydroxide in toluene to give the secondary alcohol.



For the tertiary alcohol, the styrene-methyl vinyl ketone copolymer was treated with 2 equiv. of  $\text{MeMgBr}$  in toluene. The reaction was quantitative for the linear polymer, and seems incomplete with the resin.



The ionization was performed using a strong base, such as potassium *t*-butoxide or lithium hexamethylsilylamide, in tetrahydrofuran (THF). As previously reported for the ionization of poly(*p*-hydroxystyrene),<sup>5</sup> the linear polymer precipitated rapidly when a small amount of base was added. Thus, the alkoxides bound on linear or crosslinked chains can be easily separated from the solution by simple filtration. They were carefully washed with THF and THF-pentane before drying.

The loading capacity in OH groups was determined from the oxygen content given by microanalysis. Assuming total ionization of these groups led to the theoretical values for the alkoxide functions. The experimental values were obtained by quenching the basic centres with aqueous HCl and subsequent titration of the acid in excess. The difference between the theoretical and the experimental values is the result of incomplete ionization (Table 1). Various ionizations and titrations showed no appreciable differences according to loading.

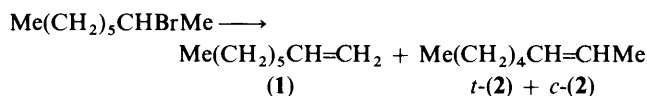
The ionized polymers are soluble or swell only in polar or high donor-number solvents such as dimethylformamide, dimethyl sulphoxide (DMSO), and triglyme. When these bases are neutralized, the polymers are again soluble or swell in tetrahydrofuran or toluene, which proves the reversibility of the ionization.

In an ionized copolymer the major component of which is a non-ionic backbone, ion-pairs are formed. Above a certain ion content these ion-pairs can coalesce into larger aggregates, which behave essentially like a crosslinked network.<sup>6,7</sup> A loading of  $1.5-2.5 \times 10^{-3}$  equiv./g in alkoxide functions is probably sufficient to allow this aggregate formation. The breaking of these associations can be effected by a very polar solvent such as DMSO which was chosen for this study.

The reactivity of these polymeric alkoxides was tested by two processes: (1) 2-bromo-octane elimination, and (2)  $E_2/S_N2$  competition reactions with 2-*p*-methoxyphenyl-1-tosyloxypropane. The results so obtained were compared with those obtained under similar conditions for low molecular weight analogues.

### Results and Discussion

*Reactivity of the Polymeric Alkoxides.*—(1) *Regio- and Stereo-selectivity of 2-Bromo-octane Elimination.*—It is well known that



the orientation of elimination depends on a number of widely studied factors.<sup>8</sup> In the present work we were only concerned with the influence of the base and the solvent.

We verified that during the reaction there was no isomerization between the various alkenes. (i) The results confirmed that

**Table 1.** Loading in alkoxide function

Polymer	Theoretical value (equiv./g)	Experimental value (equiv./g)
P-CH <sub>2</sub> OK Linear	5.5 × 10 <sup>-3</sup>	4.1 × 10 <sup>-3</sup>
10% DVB	2.4 × 10 <sup>-3</sup>	1.5 × 10 <sup>-3</sup>
P-OK Linear	2.8 × 10 <sup>-3</sup>	2.4 × 10 <sup>-3</sup>
P-C(Me) <sub>2</sub> OK Linear	2.8 × 10 <sup>-3</sup>	2.5 × 10 <sup>-3</sup>
5% DVB	2.8 × 10 <sup>-3</sup>	1.5 × 10 <sup>-3</sup>
10% DVB	3.8 × 10 <sup>-3</sup>	2 × 10 <sup>-3</sup>

**Table 2.** Regio- and stereo-selectivity of the 2-bromo-octane elimination, in DMSO at 20 °C, in the presence of polymeric or low molecular weight alkoxides

Base	% (1)*	% <i>t</i> -(2)*	% <i>c</i> -(2)*	<i>t</i> -(2): <i>c</i> -(2)
MeOK	25.5	61	13.5	82:18
Bu <sup>t</sup> OK	37	48	15	76:24
KOH	28	62.5	9.5	87:13
MeSOCH <sub>2</sub> K	28	64	8	89:11
P-CH <sub>2</sub> OK	27.5	60	12.5	83:17
P-OK	25	61	14	81:19
P-C(CH <sub>3</sub> ) <sub>2</sub> OK	32	56	12	82:18
linear				
5% DVB	31.5	55	13.5	80:20
10% DVB	31.5	55.5	14	80:20

\* Number of mol for 100 mol of (1) + *t*-(2) + *c*-(2)

the effective base is the polymer-bound reagent and not KOH or *dimethyl K<sup>+</sup>*, which could arise as the result of the action of either residual water in the polymer or DMSO on the polymeric alkoxides, respectively (Table 2). Thus, KOH and *dimethyl K<sup>+</sup>* lead to a higher *t*-(2):*c*-(2) ratio than any supported bases. (ii) With the polymeric alkoxides, the oct-1-ene proportion is 25% for primary and secondary alkoxides and 30% for tertiary. Crosslinking has no influence. (iii) With MeOK and Bu<sup>t</sup>OK in the same solvent, the oct-1-ene proportion increases from 25 to 37%. A medium such as Bu<sup>t</sup>OK/Bu<sup>t</sup>OH, yields 70% of (1).<sup>8</sup>

Previous studies on the selectivity of elimination showed that in solvents of low polarity or at high concentrations of base, a high proportion of (1) and a small *t*-(2):*c*-(2) ratio were obtained. In contrast, in polar solvents there is an increase in the amount of alk-2-ene and a decrease in the *t*-(2):*c*-(2) ratio.<sup>9a,b</sup> These results were attributed to a displacement of the association equilibrium from aggregates towards free ions. The low proportion of oct-1-ene observed with all the polymeric alkoxides shows that the active species are not aggregated.

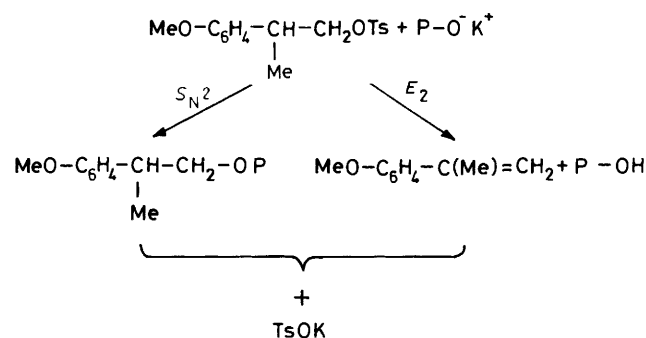
In a polar solvent such as DMSO an increase in the strength of the base gives rise to more of the terminal alkene, but does not affect the *t*-(2):*c*-(2) ratio.<sup>10</sup> Moreover, the bulkier the base the lower the *t*-(2):*c*-(2) ratio, the amount of 1-alkene being unaffected.<sup>11</sup> As the *t*-(2):*c*-(2) ratio is unchanged between the polymeric alkoxides, the small variation in the amount of (1) can be attributed to the strength of the base. Primary and secondary polymeric alkoxides behave like MeOK, while the tertiary one should be less basic and bulky than Bu<sup>t</sup>OK (Table 2). The polymer backbone induces no steric hindrance.

***E*<sub>2</sub>/*S*<sub>N</sub>2 Competition.**—Attack of base on 2-*p*-methoxyphenyl-1-tosyloxypropane can give rise to two products by the following competing processes.<sup>12</sup> The *E*<sub>2</sub> process is favoured in polar solvents with the most basic nucleophiles.<sup>13</sup>

The results reported in Table 3 confirm that the macromolecular backbone and crosslinking have no noticeable influence. We chose another small molecule, potassium isobutoxide, to compare with P-CH<sub>2</sub>OK. While MeOK mimics only the pendant group, Me<sub>2</sub>CHCH<sub>2</sub>OK takes into account

**Table 3.** Elimination product yields in the *E*<sub>2</sub>/*S*<sub>N</sub>2 competition, for the reaction of *p*-MeOC<sub>6</sub>H<sub>4</sub>CH(Me)CH<sub>2</sub>OTs with polymeric or low molecular weight alkoxides in DMSO

Base	<i>E</i> <sub>2</sub> (mol %)
P-CH <sub>2</sub> OK Linear or with 10% DVB	75
P-C(Me) <sub>2</sub> OK linear or crosslinked	95
MeOK	75
(Me) <sub>2</sub> CHCH <sub>2</sub> OK	95
Bu <sup>t</sup> OK	95



the macromolecular chain. Thus, Me<sub>2</sub>CHCH<sub>2</sub>OK gives only elimination, while MeOK as P-CH<sub>2</sub>OK gives a *E*<sub>2</sub>/*S*<sub>N</sub>2 ratio of 75:25. This observation in addition to the observed levelling effect of polymeric alkoxides in the previous reaction, leads to the conclusion that the ionic pendant group seems to obtrude from the apolar backbone, probably because it is well solvated by DMSO, and the matrix is released.

## Experimental

**Preparation of Primary Polymeric Alcohol.**—(a) *Linear polymer of styrene-methyl methacrylate.*<sup>14</sup> The copolymerization of styrene (106 ml, 1 mol) and of methyl methacrylate (76 ml, 0.66 mol) initiated by azoisobutyronitrile (AIBN) (364 mg, 2.2 mmol) was carried out in acetonitrile (182 ml) at 70 °C under an argon atmosphere. After 4 h of vigorous stirring, the solution was concentrated, and the polymer was precipitated in methanol. It was purified by dissolution in DMF and precipitation in methanol; *v*<sub>max</sub>(neat) 1730 cm<sup>-1</sup> (CO) [Found: C, 73.65; H, 8.1; O, 18.25. Calc. for (C<sub>8</sub>H<sub>8</sub>)<sub>0.42</sub>(C<sub>5</sub>H<sub>8</sub>O<sub>2</sub>)<sub>0.58</sub>: C, 74.04; H, 7.87; O, 18.09%]; ester, equiv. g<sup>-1</sup>, 5.7 × 10<sup>-3</sup>.

(b) *Suspension polymerization.*<sup>15</sup> Divinylbenzene (FLUKA) is a technical product containing ethylvinylbenzene (50%). It was used without distillation. The DVB content in the polymer was expressed as percentage (w/w) of the total mixture of monomers. The polymerization was carried out in saturated aqueous NaCl containing sodium lignosulphate (0.1%), calcium chloride (2.5%), and carboxymethylcellulose (1%). The volume of the suspension was adjusted so that the ratio of the organic layer to the aqueous one was equal to 0.8. The monomers and the AIBN initiator (2 or 3% of the weight of monomers) were dissolved in benzyl alcohol (50% of the weight of this organic layer).

In a typical experiment, a three-necked flask equipped with a mechanical stirrer was charged with an aqueous suspension (55 ml) which was stirred for 15 min at 50 °C. Then, the organic layer containing methyl methacrylate (0.1 mol), styrene (0.067 mol), DVB mixture (0.033 mol), AIBN (470 mg), and benzyl alcohol (20 ml), was added all at one time. The temperature was raised to 70 °C and the mixture was stirred for 8 h. After cooling,

the beads were poured off into water-acetone (50:50, v/v). They were filtered off and washed successively with water, methanol, THF, and pentane {Found: C, 77.3; H, 8.0; O, 14.3. Calc. for  $(C_{10}H_{10})_1 [(C_8H_8)_{2.82} (C_5H_8O_2)_{2.92}]_2$ : C, 77.81; H, 7.83; O, 14.36%}; ester, equiv.  $g^{-1}$ ,  $4.49 \times 10^{-3}$ .

(c) *Reduction of the ester function.* (i) *Linear polymer:* Red-Al (2 mol equiv.) in 3.5M toluene was introduced through a syringe via a rubber septum into a stirred solution of polymer (2 g) in toluene (100 ml). After being stirred for 4 h under reflux, and cooling, the mixture was hydrolysed with 6M-HCl-THF (50:50 v/v). The organic layer was then separated and toluene was evaporated. Purification was achieved by several dissolutions in THF and precipitations in acidic medium and in water [Found: C, 79.85; H, 9.3; O, 11.0. Calc. for  $(C_8H_8)_{0.42} (C_4H_8O)_{0.58}$ : C, 79.77; H, 9.36; O, 10.86%]. OH equiv.  $g^{-1}$ ,  $6.9 \times 10^{-3}$ .

(ii) *10% DVB polymer:* The same experiment was performed on polymer (2 g) swelled in toluene (100 ml). After hydrolysis the polymer was filtered off and washed in a fritted funnel with acidic solution, water, THF, methanol, and pentane {Found: C, 80.0; H, 8.75; O, 11.25. Calc. for  $(C_{10}H_{10})_1 [(C_8H_8)_{2.82} (C_4H_8O)_{2.92}]_2$ : C, 82.82; H, 8.96; O, 8.22%}. The oxygen content is higher in the experimental analysis than in the theoretical one. The extent of the reduction could be obtained from the experimental oxygen content and the amount of ester (equiv.  $g^{-1}$ ) in the starting polymer; this led to a value of 54% reduction. The composition of the polymer would be:  $(C_{10}H_{10})_1 [(C_8H_8)_{2.82} (C_5H_8O_2)_{1.34} (C_4H_8O)_{1.58}]_2$ . OH equiv.  $g^{-1}$ ,  $2.6 \times 10^{-3}$ .

*Preparation of Tertiary Polymeric Alcohol.*—(a) *Linear copolymer of styrene-methyl vinyl ketone.*<sup>16</sup> The copolymerization of styrene (64 ml, 0.56 mol) and ketone (20 ml, 0.25 mol), initiated by AIBN (400 mg), was performed in toluene (320 ml) for 6 h at 70 °C. The solution was concentrated and the polymer was precipitated in pentane, dissolved in THF, and reprecipitated in methanol. [Found: C, 85.4; H, 8.15; O, 6.45. Calc. for  $(C_8H_8)_{0.63} (C_4H_6O)_{0.37}$ : C, 85.58; H, 7.94; O, 6.47%]; ketone, equiv.  $g^{-1}$ ,  $4.02 \times 10^{-3}$ .

(b) *Crosslinked polymers.* (i) *5% DVB:* The polymerization was carried out with the ketone (0.1 mol), styrene (0.21 mol), and DVB (0.025 mol) in the presence of isobutyl alcohol (0.17 mol) (30% of the weight of the organic layer) and AIBN (400 mg) {Found: C, 85.95; H, 8.25; O, 5.75. Calc. for  $(C_{10}H_{10})_1 [(C_8H_8)_{5.16} (C_4H_6O)_{3.2}]_2$ : C, 86.24; H, 8.01; O, 5.74%}. Ketone, equiv.  $g^{-1}$ ,  $3.59 \times 10^{-3}$ . (ii) *10% DVB:* Ketone (0.1 mol), styrene (0.114 mol), DVB (0.036 mol), benzylalcohol (50% of the weight of the organic layer), AIBN (470 mg) [Found: C, 84.2; H, 8.4; O, 7.15. Calc. for  $(C_{10}H_{10})_1 (C_8H_8)_{3.67} (C_4H_6O)_{2.91}$ : C, 84.92; H, 7.97; O, 7.16%]. Ketone, equiv.  $g^{-1}$ ,  $4.46 \times 10^{-3}$ .

(c) *Alkylation by MeMgBr.* MeMgBr solutions were prepared in ether and titrated. MeMgBr (0.032 mol) was introduced into anhydrous toluene (50 ml). The ether was distilled off under reduced pressure. After cooling at 0 °C, polymer [0.5 equiv., ca. 4 g of linear polymer dissolved in toluene (100 ml) or 4 g of crosslinked polymer swelled in toluene (50 ml)] was added dropwise with stirring. The mixture was then stirred for 4 h at room temperature and then hydrolysed with 6M-HCl-THF 50:50 (v/v). Work-up of the polymers was the same as previously described for the reduction of esters. Linear polymer [Found: C, 85.2; H, 9.1; O, 5.5. Calc. for  $(C_8H_8)_{0.63} (C_5H_{10}O)_{0.37}$ : C, 84.94; H, 8.98; O, 6.08%]; OH equiv.  $g^{-1}$ ,  $3.2 \times 10^{-3}$ ; 5% DVB polymer [Found: C, 85.1; H, 8.75; O, 5.05. Calc. for  $(C_{10}H_{10})_1 (C_8H_8)_{5.16} (C_5H_{10}O)_{3.2}$ : C, 85.74; H, 8.84; O, 5.42%]; OH equiv.  $g^{-1}$ ,  $3.15 \times 10^{-3}$ . 10% DVB polymer {Found: C, 84.1; H, 9.0; O, 6.05. Calc. for  $(C_{10}H_{10})_1 [(C_6H_8)_{3.67} (C_5H_{10}O)_{2.91}]_2$ : C, 84.20; H, 9.11; O, 6.69%}; OH equiv.  $g^{-1}$ ,  $3.8 \times 10^{-3}$ .

*Preparation of Secondary Polymeric Alcohol.*—The ethylene-vinyl acetate copolymer (POLYSCIENCES) contained vinyl acetate monomer (28%). Alcoholic KOH (2 M; 2 equiv.) was introduced dropwise into a heated solution of polymer (4 g) in toluene. This solution was stirred and heated for 8 h. After concentration and precipitation in pentane, the polymer was dissolved in hot DMSO-THF and precipitated in water. The neat i.r. spectrum of this polymer showed that the CO stretch had disappeared; OH equiv.  $g^{-1}$ :  $3.2 \times 10^{-3}$ .

*Polymer-bound Alkoxides.*—Bu<sup>t</sup>OK or  $[(Me)_3Si]_2NK$  (2 equiv.) dissolved in THF (*v* ml) were added dropwise with stirring on the polymer (2 g) dissolved or swelled in THF (75 – *v* ml) (*v* = 30–40 ml). The linear polymer precipitated readily. After 1 h, pentane (25 ml) was added in the case of the linear polymer. The polymers were then filtered off and washed carefully with THF-pentane or THF followed by pentane. Titration: HCl (0.02M; 20 ml) was added on polymeric alkoxides (100 mg). After being stirred for 0.5 h, the excess of acid was titrated by NaOH solution (0.05M).

*2-Bromo-octane Elimination.*—2-Bromo-octane (0.25 mmol) was added to a solution or a suspension of polymeric alkoxides (0.75 mmol) in DMSO (10 ml). This mixture was stirred under argon at room temperature. During the reaction, 1 or 2  $\mu$ l aliquots of the solution were regularly taken up and subjected to g.l.c. analysis on a SE<sub>30</sub> column (6 m long, at 75 °C). N<sub>2</sub> was used as gas carrier (2 kg cm<sup>2</sup>). The retention times were: octene (1), 18.8 mm; octene *t*-(2), 21.3 mm; octene *c*-(2), 23 mm. The proportions of the different isomers did not vary with time, or during repeated runs performed with the same base. The polymer could be recovered by pouring the mixture into an acidic medium, and could thus be re-used. In the case of low molecular weight analogues, alkoxide bases were prepared according to the procedures previously described by Bartsch and co-workers.<sup>17</sup>

*E<sub>2</sub>/S<sub>N</sub>2 Competition.*—2-*p*-Methoxyphenyl-1-tosyloxypropane (m.p. 34–35 °C)<sup>18</sup> and an authentic sample of 2-*p*-methoxyphenylpropene (m.p. 33 °C)<sup>19</sup> were prepared as described in the literature. The reaction was performed with the polymeric base (0.6 mmol) and the tosyloxypropane derivative (0.2 mmol) in DMSO (10 ml). The yield of the elimination reaction was determined by u.v. spectroscopy: 1 ml of the solution was diluted ( $\times 200$ ) in ethanol and the solution was examined at 257 nm. Styrene derivative:  $\lambda_{max}$ , 257 nm (log  $\epsilon$  4.187).

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