

Lithiation of crosslinked polymers prepared using 2-vinylthiophen: application to the preparation of polymer-supported reagents

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Copolymers of 2-vinylthiophen and divinylbenzene and of 2-vinylthiophen, styrene, and divinylbenzene were prepared by benzoyl peroxide-initiated suspension polymerizations. The polymers were lithiated using *n*-butyllithium, and the lithiated materials reacted further to give polymers containing carboxylic acid, triarylphosphine or aldehyde functional groups. The lithiation reactions were complex and the percentage of the thienyl residues that reacted depended critically on the proportions of 2-vinylthiophen and styrene used in the preparation of the polymers and on the solvent used in the lithiation reaction. The results strongly suggest that the extent of lithiation was limited by the diffusion of the metallating agent into the crosslinked polymer. The polymers containing triarylphosphine substituents, used in conjunction with bromine or with tetrabromomethane, were effective reagents for the conversion of alcohols into alkyl bromides.

(Keywords: poly(vinylthiophen); lithiation; polymer-supported reactions)

INTRODUCTION

Polymer-supported organic reagents are often prepared by the chemical modification of a preformed crosslinked polymer¹⁻³. Polystyrene is commonly used as a support because it is readily available and in general it can be chemically modified fairly easily. Lithiation of polystyrenes is particularly important because the products react smoothly with a wide range of electrophiles. Polystyrene can be lithiated directly using *n*-butyllithium in the presence of tetramethylethylenediamine but at best only *c.* 20% of the phenyl groups are lithiated⁴⁻⁶. Higher degrees of lithiation can be achieved by first brominating polystyrene and then carrying out a halogen-metal exchange¹, although multiple treatment with *n*-butyllithium may be required. Unfortunately, we have found these lithiation procedures tend to give erratic results and are wasteful of *n*-butyllithium. This has prompted us to investigate the lithiation of other polymers⁸⁻¹⁰. Polymers prepared using 2-vinylthiophen (2-VT) are of particular interest because *n*-butyllithium reacts with thiophene at the α -position much more readily than it does with benzene. In a previous paper⁸ we have reported the efficient lithiation of linear poly(2-vinylthiophen) and transformations of the product. We now wish to report lithiations of some cross-linked polymers prepared using 2-VT.

EXPERIMENTAL

Materials and spectra

Tetrahydrofuran (THF) was dried by distilling under nitrogen from calcium hydride and stored over molecular

sieves. Benzene and cyclohexane were dried over sodium wire. 2-VT was prepared as reported¹¹. Other materials were obtained commercially. Inhibitors were removed from the styrene and divinylbenzene (DVB) (the latter containing 55% isomers of divinylbenzene and 45% of isomers of ethylvinylbenzene by weight) by washing with 10% aqueous sodium hydroxide solution and distilling. Unless indicated otherwise, polymeric products were dried overnight in a vacuum oven (2 mm Hg) at 60°C. Infra-red spectra were recorded on a Nicolet MX-1 FTi.r. instrument for KBr discs. The degree of substitution (DS) of a given polymer is the percentage of aromatic residues, both thienyl and phenyl, which have undergone substitution. Elemental analyses were carried out by Butterworth Laboratories Ltd, Teddington, UK.

Preparation of polymers using 2-vinylthiophen

Copolymers were prepared by suspension polymerization using 2-VT, styrene, and DVB in various proportions, and benzoyl peroxide as the initiator (see Table 1). The proportion of thiophen residues in the copolymers were determined quantitatively by elemental analysis for sulphur. A qualitative estimate could be obtained by i.r. spectroscopy because polymers prepared using 2-VT showed characteristic absorptions at 847, 823, and 1448 cm⁻¹ which were not present in the spectrum of polystyrene. The following polymerization procedure is typical.

Preparation of polymer (IV) (see Table 1). The polymerization was carried out in a baffled glass reactor¹² fitted with a metal stirrer and flushed with nitrogen. A mixture of 2-VT (15.91 g, 0.145 mol; freshly prepared), styrene (5.02 g, 0.048 mol), commercial DVB (1.01 g, i.e. 0.004 mol divinylbenzenes) and benzoyl peroxide (0.21 g) was suspended in a solution of poly(vinyl alcohol) (1.0 g, $M_n = 100\,000$) in distilled water (200 ml) contained in the

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Table 1 Preparation of 2% crosslinked polymers using 2-vinylthiophen and functionalization of the products via lithiation

Entry number	Polymer number	Polymer preparation %2-VT		Lithiation Conditions ^c	%DS of functionalized polymers ^d Substituent group		
		In feed ^a	In polymer ^b		-CO ₂ H ^e	-P(C ₆ H ₅) ₂ ^f	-CHO ^g
1	(I)	12	23	A	11 (48)	14	13
				B	2 (9)		
				C	16 (69)		
				D	0		
2	(II)	25	41	A	22 (50)	32	33
				B	25 (61)		
				C	30 (73)		
				D	0		
3	(III)	50	65	A	34 (52)	43	40
				B	38 (58)		
				C	43 (66)		
				D	0		
4	(IV)	75	87	A	29 (33)	37	44
				B	15 (17)		
				C	48 (55)		
				D	0		
5	(V)	98	98	A	20 (20)	43	47
				B	3 (3)		
				C	56 (55)		
				D	0		
6	Polystyrene ^h	0	0	A	1		
				D	21		

^a Molar percentage of 2-vinylthiophen used to prepare polymer. The feed also contained 2% of divinylbenzenes. The rest was styrene

^b Percentage of vinylthiophen units in resulting polymer, determined by elemental analysis for sulphur

^c Lithiation conditions: A, in benzene at 20°C for 4.5 h; B, in THF at 20°C for 4.5 h; C, in benzene at 40°C for 2 h; D, in cyclohexane, various conditions

^d Overall degree of substitution, expressed as the percentage of rings (thienyl or phenyl) which have been substituted. Numbers in parentheses express the degree of substitution as the percentage of thienyl rings which have been substituted

^e DS determined by titration with alkali

^f DS determined by elemental analysis for phosphorus

^g DS determined by elemental analysis for nitrogen on the oxime derivative

^h Results reported for 2% cross-linked polystyrene^{3,7}, for comparison

reactor. The suspension was stirred at approximately 800 rpm. The temperature of the mixture was raised to 85°C and kept at this temperature for 15 h. The mixture was then allowed to cool, excess liquid was decanted off, and the polymer remaining was collected on a filter. The product was washed successively with water, methanol, and ether. The yield was 10.9 g, 51% w/w. Analysis gave: S = 25.56%, indicating that 87% of the units were derived from 2-VT.

Lithiations of polymers

The following procedure is typical.

Lithiation of polymer (I) (see Table 1). The polymer (0.40 g, equivalent to 3.8 mmol of monomer units) was suspended in dry benzene (10 ml), and a hexane solution of n-butyllithium (3.0 ml of 1.6 M solution, 4.8 mmol) was added via a septum cap using a syringe. The mixture was stirred for 2 h at 40°C and then a further 2 h at room temperature. The mixture became deep red. The polymer was filtered off under nitrogen, and washed twice with cyclohexane (20 ml portions).

Attempted lithiations using THF or cyclohexane as solvents were carried out in a similar manner. During the attempted metallations in these solvents the resins frequently became very dark brown. Addition of TMEDA did not improve the yields of metallated products with either of these solvents.

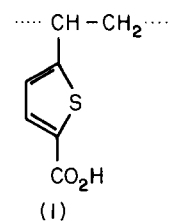
Reactions of lithiated polymers

Each of the lithiated polymers was reacted with carbon

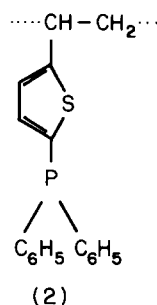
dioxide, diphenylchlorophosphine, and dimethylformamide (see Table 1). The following reactions are typical.

With carbon dioxide. The lithiated polymer prepared from 0.40 g of polymer (I) (see above and Table 1) was suspended in dry THF (10 ml), and then a slurry of dry ice in THF was added to the mixture. The deep red colour of the polymer faded. The mixture was stirred for 1 h, the temperature gradually rising to room temperature. The polymer was then filtered off, and successively washed twice with a mixture of THF-2M HCl (3:1, 15 ml), the contact time being 15 min for both washings, carbon tetrachloride (10 ml), acetone (10 ml), toluene (10 ml), and methanol (10 ml). The dried product (0.36 g) had ν_{\max} 3600–2600 cm⁻¹ (broad, carboxyl O–H group) and 1677 cm⁻¹ (carbonyl group).

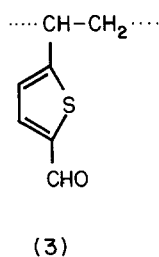
A sample of the above product was heated under reflux for 2 h with dioxan-water (15 ml) and excess standard sodium hydroxide, and then left stirring overnight at room temperature. Titration of this mixture with standard hydrochloric acid indicated the polymer contained 1.46 mequiv. of carboxylic acid groups formula (I)/g. This corresponds to a DS of 16%.



With diphenylchlorophosphine. The lithiated polymer prepared from polymer (III) by method C (see Table 1, footnote c) (0.54 g, 5.1 mmol of monomer units) was suspended in dry THF (10 ml) under nitrogen, and diphenylchlorophosphine (3.6 g, 16.5 mmol) was added. The temperature rose to about 45°C initially. The mixture was stirred for 2 h at room temperature, during which time the dark red colour of the resin gradually faded. The polymer was filtered off, and washed successively with 10 ml portions of benzene, THF, ether, water, and methanol. Analysis of the dried polymer (0.68 g) gave P = 6.03%, indicating the presence of residues of formulae (2) and a DS of 32%.



With *N,N*-dimethylformamide (DMF). DMF (4.0 g) was added to a suspension in THF (10 ml) of the lithiated resin prepared from polymer (V) by method C (0.47 g, 4.3 mmol of monomer units) under nitrogen. The mixture was stirred for 2 h at room temperature. The polymer was filtered off and washed with 10 ml portions of THF-water (2:1), THF-2M HCl (3:1), water, THF, and methanol. The dried product (0.42 g) had ν_{\max} 1667 cm^{-1} (carbonyl group) consistent with the presence of residues of formula (3).



To estimate the content of formyl groups a sample of this product (0.10 g) was heated under reflux with hydroxylamine hydrochloride (0.19 g) in pyridine (3 ml) for 4 h. The product was filtered off and washed with pyridine, THF-water (2:1), THF, benzene, and methanol. The dried product (0.08 g) had ν_{\max} 3238 cm^{-1} (O-H) but showed no carbonyl absorption at 1667 cm^{-1} . Analysis gave N = 5.06%, indicating a DS of 47%.

Conversion of alcohols into bromoalkanes using a polymer-supported triarylphosphine

The following are typical of the reactions summarized in Table 2.

Using bromine. Bromine (0.23 g, 1.44 mmol) in chloroform (1.5 ml) was added to a vigorously stirred mixture of 1-octanol (0.18 g, 1.39 mmol) and supported phosphine (see Table 1, entry 5C) (1.25 g, 2.80 mmol of phosphine) in chloroform (10 ml) at room temperature, under nitrogen. The mixture was heated under reflux for 3 h. After

Table 2 Conversion of alcohols to bromoalkanes using polymer-supported phosphine reagents

Alcohol	Yield of bromoalkane (%)	
1-Octanol	96 ^a	56 ^{b,c}
2-Octanol	66 ^a	57 ^{b,c}

^a By reaction with bromine in chloroform at 61°C for 3 h

^b By reaction in tetrabromomethane at 21°C for 5 h

^c Yields obtained using reagent prepared from polystyrene were 98% for both alcohols¹⁴

cooling, the resin was removed by filtration and the filtrate analysed by g.l.c. (using an SE-30 column at an oven temperature of 130°C, and 2-methylnaphthalene as an internal standard). The yield of 1-bromooctane, was 96%. The recovered polymer had ν_{\max} 1120 cm^{-1} , indicating the presence of the phosphine oxide residues.

Using tetrabromomethane. This was carried out as described above, but using octan-2-ol (90 mg, 0.67 mmol) and carbon tetrabromide (220 mg, 0.67 mmol) in place of bromine. For the g.l.c. analyses, naphthalene was used as the internal standard. The yield was 57%.

Solvent absorption properties of polymers

A weighed sample of polymer (0.50 g) was placed in a weighed glass tube fitted with a sintered glass filter. Solvent (2 ml) was added, and the sample left for 30 min. Excess solvent was then removed by centrifugation (10 min), and the tube plus sample reweighed. The amount of solvent absorbed per g was calculated. The results are summarized in Figure 2.

RESULTS AND DISCUSSION

Polymer preparations

2-VT was synthesized as reported from thiophen and acetaldehyde¹¹. Using the 2-VT and DVB together with, in most cases, styrene, five 2% cross-linked polymers were prepared by suspension polymerization with benzoyl peroxide as the initiator (see Table 1). The i.r. spectra of the products were consistent with those of the previously-described 2-VT linear polymers, which had also been characterized by their ¹H n.m.r. and ¹³C n.m.r. spectra⁸, and linear polystyrene. Elemental analyses indicated that the copolymers had a higher thiophen content than the original feed (see Table 1). This was expected from the reported reactivity ratios of the two monomers¹³.

Lithiations and reactions of lithiated polymers

The five polymers were lithiated under various conditions (see Table 1, footnote c) using a commercial solution of *n*-butyllithium in hexane. In each case the extent of metallation was estimated by reacting the lithiated polymer with carbon dioxide (during which the red colour of the lithiated polymer was lost) to give polymers with residues of formula (1) followed by titrations of the carboxyl groups. In some cases chlorodiphenylphosphine and *N,N*-dimethylformamide were also used as electrophiles. With these electrophiles the overall reaction yields to give residues of formulas (2) and (3) were respectively estimated by phosphorus analyses, and by conversion of the formyl groups into oxime groups followed by nitrogen analyses. The DS values achieved with all three electrophiles were of the same order, but

those obtained with carbon dioxide were generally a little higher than those obtained with the other two.

It is clear from the results, summarized in Table 1, that the reaction of the thiophen-containing crosslinked polymers with *n*-butyllithium and/or the subsequent reaction with carbon dioxide is complex. This is in contrast to the situation with linear poly(vinyl-2-thiophen) where the same reaction sequence leads to an essentially quantitative introduction of the carboxyl group⁸.

Initially THF was used as the solvent for the lithiations because this solvent had given excellent results in the lithiation of linear poly(2-vinylthiophen)⁵. However, with the present crosslinked polymers use of THF gave modest to poor results (see Table 1). In the direct lithiation of polystyrene the use of THF also gave poor results⁴⁻⁶. With cyclohexane no lithiation was observed for any polymer, even though cyclohexane has been used with some success in the direct lithiation of polystyrenes⁴⁻⁷. The presence of tetramethylethylenediamine did not improve the yields with either solvent. Much better results were obtained with benzene as the solvent, but the DS values obtained were critically dependent on the copolymer composition.

The results obtained with THF or benzene as the reaction solvent for the overall introduction of carboxyl groups are summarized in Figure 1. Several features are noteworthy. First, the DS values obtained never exceeded the percentage of thiophen residues in the polymers, thus suggesting that, as expected, these are the only residues

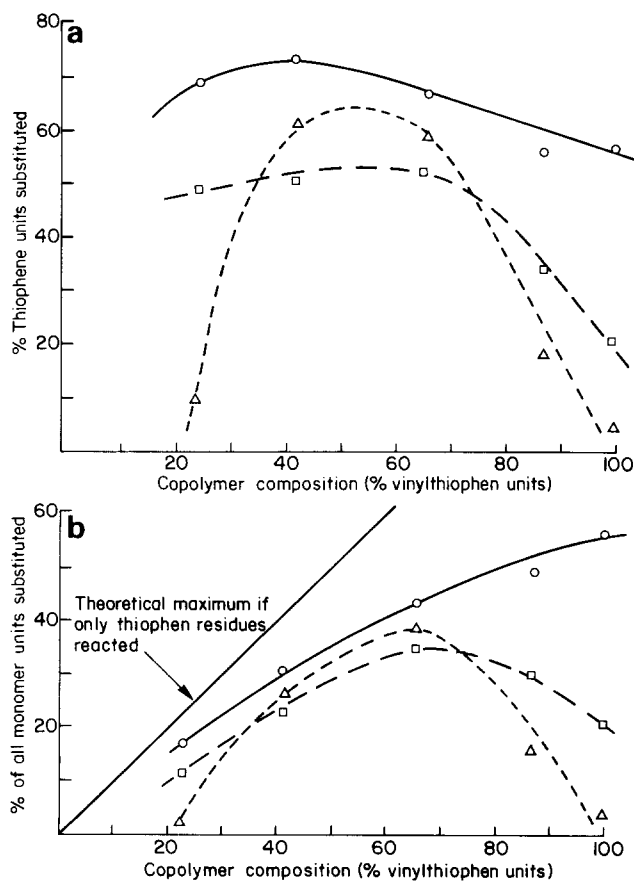


Figure 1 Degree of lithiation as a function of copolymer composition. (a), DS expressed as percentage thiophene groups substituted; (b), DS expressed as percentage of all aromatic groups substituted. \circ , In benzene at 40°; \square , in benzene at 20°; \triangle , in THF at 20°

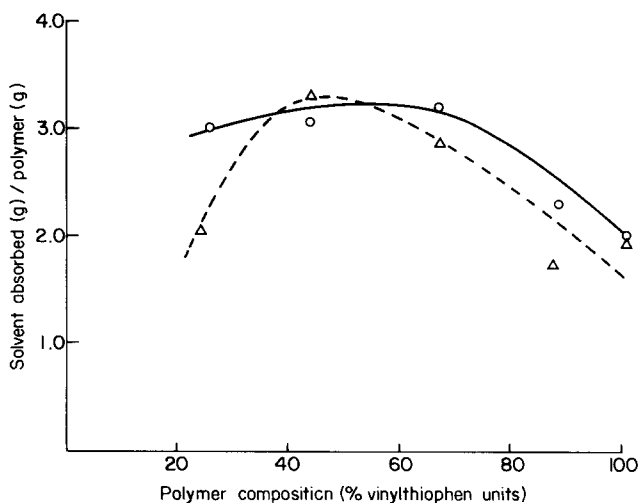


Figure 2 Solvent absorption as a function of polymer composition. \circ , Benzene; \triangle , THF

to be lithiated under the present reaction conditions. Second, that in THF at 20°C and in benzene at 20°C the fraction of thiophen residues carboxylated is lower with polymers containing either a low or a high percentage of thiophen residues than it is for polymers of intermediate composition. Third, the superior results obtained with benzene at 40°C rather than 20°C indicate that diffusion effects are important. Moreover, as the carboxylation steps were carried out under identical conditions, the results indicate that it is the lithiation step rather than the carboxylation step that is mainly, if not entirely, responsible for the less-than-quantitative overall reaction yields. Fourth, the best DS (56%) was obtained for the crosslinked polymer prepared from only 2-VT and DVB. Fifth, the highest fraction of thiophene residues that reacted was obtained with copolymer (II) in which 73% reacted.

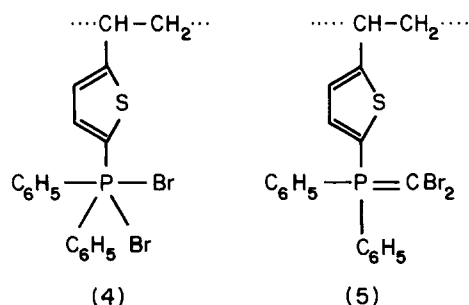
Thus, although it is not absolutely clear, it is almost certain that the results obtained with the crosslinked polymer differ from those obtained with the linear polymer because with the former the extent of lithiation is limited by the diffusion of the metallating agent into the crosslinked polymers and the various polymers do not all swell in the reaction solvents and absorb the reagents equally well. Consistent with this it was found (Figure 2) that the absorption of THF and of benzene by the initial crosslinked polymers showed a similar bell-shaped dependence on the composition of the polymers as did most of the lithiations. Furthermore this effect, as with the lithiations, was more pronounced with THF than with benzene.

Brominations using polymer-supported phosphines

As noted previously many functionalized crosslinked polymers have been used as organic reagents¹⁻³. Thus, polymers with triphenylphosphine residues have been used to convert alcohols into bromides¹⁴. It was, therefore, of interest to see if the present supported triarylphosphines could be used similarly.

Two types of reactions were examined. In one, a phosphine-containing polymer was reacted with bromine to give a polymer containing triarylphosphine dibromide residues of formula (4), which were then reacted with octan-1- or -2-ol. In the second, the phosphine residues

of formula (2) were reacted with carbon tetrabromide to generate a polymer with triarylphosphine dibromide residues of formula (4) and ylid residues of formula (5). This polymer was reacted with the same alcohols. The results, summarized in Table 2, indicate that whilst the octyl bromides are formed in lower yields than when crosslinked polystyrenes with phosphine residues are used¹⁴, the bromination reactions proceeded in good to excellent yields.



CONCLUSIONS

Various 2% crosslinked polymers prepared from 2-VT, DVB, and, in all but one case, styrene were lithiated more readily than 2% crosslinked polystyrene and without the use of tetramethylethylenediamine or a large excess of n-butyllithium. The lithiation appears to take place preferentially in the thiophen rings. However, the extent of lithiation is crucially dependent on the polymer composition and the choice of reaction conditions. It is almost certainly limited by diffusion of the metallating agent into the crosslinked polymer. The best result was obtained with a polymer prepared only from 2-VT (98%) and DVB (2%). When this polymer was lithiated for 4 h

using n-butyllithium in benzene at 40°C it reacted to give a DS of 56%. The lithiated polymers were reacted with carbon dioxide, diphenylchlorophosphine, and N,N-dimethylformamide to give, respectively, polymers with residues of formulas (1), (2), and (3). The polymers with phosphine residues of formula (2) were used, in combination with bromine or tetrabromomethane, to convert alcohols to bromides in good to excellent yields.

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