Bromination and Lithiation: Two Important Steps in the Functionalization of Polystyrene Resins

M. Jean Farrall and Jean M. J. Fréchet*

Department of Chemistry, University of Ottawa, Ottawa, Ontario, K1N 6N5, Canada

Received June 21, 1976

Reactions used for the bromination and lithiation of cross-linked polystyrene resins have been explored. In the presence of bromine and catalytic amounts of a thallium(III) salt, polystyrene resins are smoothly brominated and give homogeneous reactive resins with a highly reproducible degree of functionalization. These resins can be lithiated easily by reaction with an excess of *n*-butyllithium in benzene. Other swelling agents such as tetrahydrofuran gave incomplete removal of the bromine. The direct lithiation of polystyrene with *n*-butyllithium and tetramethylethylenediamine gave lithiated polymers containing approximately 2 mequiv of functional group per gram, while direct lithiation in the presence of triethylenediamine gave lower degrees of functionalization. The lithiated resins were used to prepare polymers containing carboxylic acid, thiol, sulfide, boronic acid, amide, silyl chloride, phosphine, alkl bromide, aldehyde, alcohol, or trityl functional groups for applications in polymer-assisted syntheses.

Functionalized resins have found numerous applications[1,2] recently as supports in solid-phase synthesis,[3] reagents[4] or protecting groups[5,6] in organic synthesis, and supports for chromatography or catalysis.[2,7] The reactions which are used in the functionalization of insoluble resins are similar to those carried out on soluble materials, but are usually more difficult to control and evaluate owing to the insolubility of the resins, which makes the reaction heterogeneous and often prevents the simple characterization of the products by the usual methods of analysis.

A large number of the functional resins which have been prepared to date were synthesized by chemical modification of cross-linked polystyrene. When functional groups are to be introduced by modification of a preformed polymer, the purity of the starting material must be ascertained[8] since minute amounts of surface impurities remaining from the emulsion polymerization reaction may prevent the introduction of certain types of functional groups. This is particularly true with solvent-swellable cross-linked polystyrene beads which are much more sensitive to surface impurities than highly cross-linked macroreticular resins since the latter contain pores of well-defined size and accessibility. It should be emphasized, however, that the washed solvent-swellable resins are usually more reactive and often give better yields than their macroreticular counterparts.[5,9] In addition, since the degree of functionalization of a resin prepared via several successive reactions is usually wholly dependent on the control of the first functionalization reaction, it is important to design these reactions in such a way that they are easily reproducible and yield reactive polymers with easily replaceable functional groups.

A review of the literature shows that two versatile types of functional resins are those in which some of the aromatic rings are halogenated or metalated, yet the procedures commonly used in the halogenation or metalation of polystyrene resins are often described incompletely or are impractical, difficult to control, and sometimes even yield unreactive resins. In other cases, the metalation reactions are incomplete and leave behind other functional groups which may prove troublesome in further reactions or in the characterization of the polymers.

Halogenation of Polystyrene Resins. The method used most often in the bromination of insoluble polystyrene resins was developed by Heitz and Michels[10] and involves the reaction of polystyrene with bromine in the presence of ferric chloride as catalyst. This procedure gave resins containing from 2.2 to 3.9 mequiv of bromine per gram. The reaction has, however, been reported to give unreproducible results[11] and often yields a colored resin of low quality and lacking homogeneity.[12] In addition, we have observed that in a number of cases the polymer is less reactive than that prepared by other methods. A second procedure, first described by Camps et al.,[11] uses the reaction of a stoichiometric amount of thallium acetate with the resin followed by bromination to produce a polymer containing about 1 mequiv of bromine per gram. This procedure was also used by Weinshenker et al.[12,13] to prepare polymers containing up to 4 mequiv of bromine per gram. The major drawbacks of this procedure are that a large amount of costly thallic acetate is used in the reaction (e.g., 100 g of thallic acetate sesquihydrate for 50 g of cross-linked polystyrene[13]) and that an extensive washing procedure is required to remove the considerable amount of sparingly soluble thallium salts generated by the reaction. However, this method affords a polymer which is visually cleaner than that obtained in the ferric chloride catalyzed bromination, and the reaction is presumed to occur at the para position of the aromatic rings of the polystyrene.

We have reinvestigated the bromination of cross-linked polystyrene with the aim of obtaining a reliable procedure for the preparation of a clean and homogeneous polymer with a predictable degree of substitution of the aromatic rings.

A number of catalysts, solvents, and reaction conditions were studied for the bromination of cross-linked polystyrene. As can be seen in Table I, the ferric chloride catalyzed bromination of polystyrene gave reasonably consistent results when the reaction was carried out in refluxing carbon tetrachloride for short periods of time in the dark. The degree of substitution could be controlled by varying the amount of bromine used in the reaction. High degrees of functionalization were obtained by using a slight excess of bromine, but under the reaction conditions, polybromination was not observed. We also studied the bromination of 1% cross-linked polystyrene in the presence of thallic acetate. Our results indicate that the thallic acetate is not required in stoichiometric amount but that very small amounts of the reagent are sufficient to catalyze the reaction. Once again the reactions were carried out in carbon tetrachloride with a short refluxing period in the dark. The polymers obtained were almost colorless and had a cleaner appearance than those obtained by the ferric chloride method; in addition, the reaction seemed to proceed more easily than with ferric chloride as a smooth disappearance of the bromide was observed to occur rapidly at reflux temperature. As can be seen in Table I, the degree of functionalization obtained in each reaction was found to be independent of the amount of thallic acetate used and was only a function of the amount of bromide. Thus the reaction was easily performed

Table I. Bromination of 1% Cross-Linked Polystyrene[a]

Expt	Catalyst	Molar ratio catalyst/PS	Molar ratio bromine/PS	mequiv bromine per gram	Degree of functionalization
1	$FeCl_3$	1:77	1.12:1	4.97	0.85
2	$FeCl_3$	1:61	1.12:1	5.32	0.96
3	$FeCl_3$	1:37.5	0.39:1	2.87	0.39
4	$Tl(OAc)_3$	1:9.6	0.42:1	2.89	0.39
5	$Tl(OAc)_3$	1:50	0.41:1	2.66	0.35
6	$Tl(OAc)_3$	1:105	0.21:1	1.76	0.21
7	$Tl(OAc)_3$	1:62	0.44:1	3.10	0.43
8	$TlCl_3$	1:58	1.25:1	6.05[b]	>1
9	$TlCl_3$	1:68	1.16:1	5.16	0.91
10	$TlCl_3$	1:78	0.4:1	2.95	0.40
11	$TlCl_3$	1:61	0.43:1	3.15	0.43
12	Tl salt[c]		0.48:1	3.19	0.44

[a] Typical reaction conditions were as follows: reaction in CCl_4 1 h at room temperature followed by 1.75 h at reflux. [b] Reaction at reflux temperature for 24 h. [c] Thallium salt recovered from expt 4.

Table II. Carboxylation of Lithiated Polystyrene

			Product	
Starting resin Br, mequiv/g	Molar ratio BuLi/Br	Solvent	COOH, mequiv/g	Br, mequiv/g
2.89	4:1	THF	1.4	1.53
2.89	3:1	Cyclohexane	1.3	1.45
2.89	3:1	Benzene	2.9	0
2.78	2.4:1	Toluene	2.7	0

with small amounts of thallic acetate and yielded polymers with desirable physical aspect and easily controlled degree of substitution.

To ascertain whether other thallium(III) salts were also useful catalysts in this bromination, the reaction was attempted using catalytic amounts of thallic chloride, and, in every case, the reaction gave results comprable to those obtained for thallic acetate. In one instance we observed the introduction of more than one bromine atom per aromatic ring, but this result was only obtained in a reaction involving an excess of bromine and a 24-h reaction period at reflux temperature.

Excellent results were also obtained when a small amount of an unknown thallium salt recovered after a previous bromination with thallium acetate was used as catalyst in a new bromination reaction. Other catalysts such as zinc chloride in tetrahydrofuran or stannic chloride in carbon tetrachloride gave polymers with very low degrees of functionalization and would therefore only be suitable for applications involving the introduction of small numbers of functional groups. An interesting result was obtained when the bromination reaction was carried out in acetic acid: the reaction mixture containing the cross-linked polymer became gradually homogeneous as the polymer dissolved. Cleavage of the polymer chains was extensive as evidenced by the low viscosity ($[\eta] = 0.115$, 30 °C, toluene) of the brominated polymer after 1 day of reaction. This depolymerization was, however, only observed when acetic acid was used in conjunction with the catalyst.

The iodination of cross-linked polystyrene proved to be more difficult and we observed that the degree of functionalization depended on the amount of thallic trifluoroacetate used. Thus, unlike the bromination reaction in which the thallium salt acted as a catalyst, a stoichiometric amount of thallic trifluoroacetate was required to effect the iodination.

Lithiation of Cross-Linked Polystyrene. Two main reaction routes have been studied for the lithiation of soluble polystyrene. The first one, developed by Braun,[14] involved the reaction of a solution of halogenated polystyrene with an excess of *n*-butyllithium. The reaction was usually carried out on substrates obtained by polymerization of *p*-iodostyrene. The second route, developed by Chalk,[15] involved the direct lithiation of a solution of polystyrene by reaction with a 1:1 complex of *n*-butyllithium and *N,N,N′,N′*-tetramethylethylenediamine. This reaction was studied further by Evans et al.,[16] who showed that both meta and para lithiation occurred with a meta–para ratio of 2:1.

A number of workers have used the first route and prepared cross-linked polystyryllithium intermediates by the two-step bromination–lithiation procedure.[11–13] We have also used this reaction route in a number of preparations and have found that the outcome of the reaction varied considerably depending on the type of polymer used, its degree of bromination, and the solvent used for the lithiation. Thus, brominated macroreticular resins were found to react completely with *n*-butyllithium in tetrahydrofuran,[17] even when the starting resin contained a large proportion of brominated aromatic rings. In contrast, the lithiation of 1% cross-linked resins in THF gave varying results depending on the degree of functionalization. In the case of brominated polymers containing approximately 1–1.5 mequiv of bromine per gram, we obtained almost complete removal of the bromine in one reaction with *n*-butyllithium, while more highly substituted polymers required several successive treatments with this reagent. For example, a polymer containing 3 mequiv of bromine per gram, when allowed to react with excess *n*-butyllithium in THF and quenched with methanol, yielded a product which still contained 1.9 mequiv Br/g. A second treatment under the same reaction conditions reduced the bromine content to 0.6 mequiv/g, and a third treatment resulted in complete removal of the bromine from the polymer. In contrast to this behavior, a single treatment with *n*-butyllithium in benzene was sufficient to effect complete removal of the bromine from a 1% cross-linked polymer containing 3 mequiv of bromine per gram. These results were confirmed by a second study in which the 1% cross-linked polymer was brominated, then allowed to react with an excess of *n*-butyllithium, and the resulting product quenched by addition of a slurry of dry ice in tetrahydrofuran. The results of this study, shown in Table II, indicate clearly that the lithiation reaction is incomplete in tetrahydrofuran or cyclohexane but occurs quantitatively in benzene or toluene. The difference in behavior for the lithiation in cyclohexane vs. benzene or toluene can be explained easily if one considers the swelling properties of these solvents. In benzene or toluene, the 1% cross-linked resin is fully swollen and allows easy penetration of the reagent while in cyclohexane the resin is only partially swollen and therefore a number of reactive sites are located in pores which are inaccessible to the reagent.

Table III. Direct Lithiation of Cross-Linked Polystyrene[a]

Solvent	Polystyrene, mequiv	Amine used (mmol)	n-BuLi mmol	Reaction conditions	Ⓟ-COOH, mequiv/g
Cyclohexane	27	TMEDA (25)	34	65°C, 4.5 h	2.0
Cyclohexane	25	TMEDA (25)	27	70°C, 1.5 h	1.4
Cyclohexane	25	TMEDA (56)	30	67°C, 4 h	2.0
Heptane	26	TMEDA (25)	27	68°C, 3 h	1.52
Benzene	26	TMEDA (25)	27	70°C, 3.5 h	0.15
Tetrahydrofuran	24	TMEDA (25)	35	75°C, 3 h	0
Cyclohexane	30	TEDA (24)	25	65°C, 3 h	0.4
Cyclohexane	19	TEDA (18)	18	70°C, 4 h	0.6
Cyclohexane	24	TEDA (22)	32	70°C, 24 h	1.1

[a] TMEDA = tetramethylethylenediamine; TEDA = triethylenediamine.

This explanation does not hold true for a comparison of the lithiation reaction in tetrahydrofuran vs. benzene or toluene since all three solvents have excellent swelling properties. It is more likely that in the more polar solvent, tetrahydrofuran, ionic repulsions limit the accessibility of the reagent thus causing the reaction to stop once a fraction of the functional groups have reacted with n-butyllithium.

The direct lithiation of 2% cross-linked polystyrene by reaction with a 1:1 complex of n-butyllithium and N,N,N',N'-tetramethylethylenediamine was recently reported by Fyles and Leznoff.[19] The resulting lithiated polymer, after quenching with carbon dioxide, yielded a carboxylated resin containing 0.6–0.9 mequiv of functional group per gram.[19] Better results were obtained with a macroreticular polymer, which after lithiation and quenching with carbon dioxide, gave resins containing from 1.1 to 1.5 mequiv of functional group per gram. This one-step lithiation reaction is advantageous for applications in which the position of the functional group on the aromatic ring is unimportant since, as was mentioned earlier, the lithiation occurs on both meta and para positions.[16] We have investigated the direct lithiation with the aim of improving the degree of functionalization since, in a number of applications, it might be desirable to obtain more highly functionalized resins. Our procedure involved the reaction of an amine–n-butyllithium complex with the resin at 65–70 °C in a nonpolar solvent. The minimum degree of functionalization of the lithiated resins was estimated by acid–base titration of the carboxylic acid resin obtained by rapid quenching of the lithiated resin with carbon dioxide. As can be seen in Table III, best results were obtained with tetramethylethylenediamine (TMEDA) in a nonpolar hydrocarbon solvent such as cyclohexane or heptane.

An increase in the molar ratio TMEDA-n-BuLi from 0.7:1 to 1.9:1 did not change the degree of functionalization while shorter reaction times decreased it noticeably. Other solvents such as benzene or tetrahydrofuran were unsuitable for the reaction. In another series of experiments, triethylenediamine was used instead of TMEDA but the reaction was more sluggish and longer reaction times were required to achieve a degree of functionalization greater than 1 mequiv per gram.

In our experiments with TMEDA-n-butyllithium we observed that the degree of functionalization of 2 mequiv per gram, which is obtained readily under the conditions shown in Table III, seemed to be the maximum which could be obtained after carboxylation. This functionalization corresponds to the introduction of carboxyl groups on 23% of the aromatic rings of the polystyrene resins. Presumably this is due to the fact that the solvents chosen for the reaction are unable to swell the resin and thus the penetration of the relatively bulky TMEDA–butyllithium complex in the pores of the resin is severely limited and only the most accessible sites can be functionalized. It must be remembered, however, that the actual percentage of aromatic rings which are lithiated is probably higher than 23% since the carboxylation reaction which is used for the measurement of the degree of functionalization is not quantitative.

A comparison of the bromination–lithiation vs. direct lithiation procedure would therefore indicate that the two-step lithiation is probably the method of choice if control of the position of lithiation and of the degree of functionalization is desired, since predictable results can be obtained in the bromination over a very broad range of degrees of functionalization; in addition, since the resin is fully swollen during the bromination, a more even distribution of the functional groups can be expected.

To test the reactivity of the polystyryllithium resin and explore its application to the preparation of polystyrene resins containing various functional groups, a number of reactions were studied (Schemes I and II). In all cases the lithiated resins were prepared in situ from their brominated precursor since this procedure allowed the calculation of a functional group yield for every reaction. The results of these reactions are shown in Table IV. In most cases the functional yield could be estimated either by direct titration[18] for resin II, or by elemental analysis for sulfur, boron, nitrogen, silicon, phosphorus, or bromine for resins III–IX. As can be seen in Scheme

Scheme I

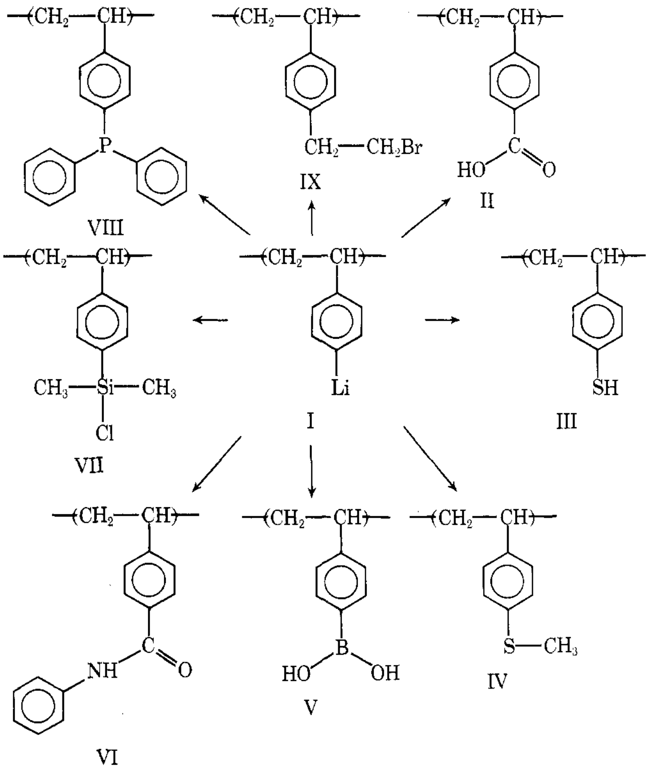
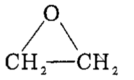
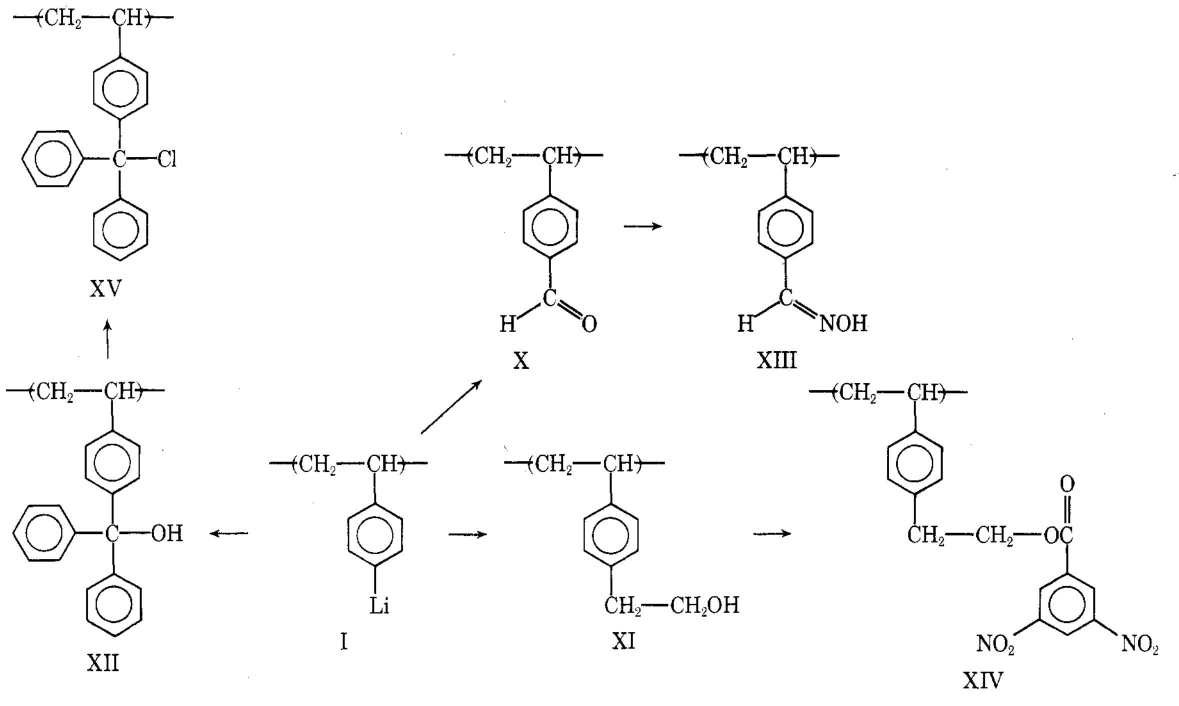


Table IV. Reactions of Lithiated Resin I[a]

Precursor Ⓟ-Br		Product				
mequiv/g	Degree of functionalization	Reagent	Structure	mequiv/g	Degree of functionalization	Functional yield, %
2.89	0.39	CO_2	II Ⓟ-COOH	2.9	0.35	90
2.8	0.37	S_8	III Ⓟ-SH	3.9[b]	*d*	*d*
3.1	0.43	CH_3SSCH_3	IV Ⓟ-SCH_3	2.6	0.31	72
2.89	0.39	$B(OCH_3)_3$	V Ⓟ-$B(OH)_2$	3.15	0.38	97
2.89	0.39	$C_6H_5N{=}C{=}O$	VI Ⓟ-$CONHC_6H_5$	2.2	0.31	80
3.1	0.43	$Si(CH_3)_2Cl_2$	VII Ⓟ-$Si(CH_3)_2Cl$	2.2	0.28	65
2.8	0.37	$ClP(C_6H_5)_2$	VIII Ⓟ-$P(C_6H_5)_2$	1.92	0.31	84
1.76	0.21	$BrCH_2CH_2Br$	IX Ⓟ-CH_2CH_2Br	1.13	0.14	67
2.8	0.37	$(CH_3)_2NCHO$	X Ⓟ-CHO	2.3[c]	0.26	70
2.89	0.39	 $CH_2—CH_2$ (O)	XI Ⓟ-CH_2CH_2OH	2.8[c]	0.33	85
2.8	0.37	$C_6H_5COC_6H_5$	XII Ⓟ-$C(C_6H_5)_2OH$	1.4[c]	0.20	54

[a] Reactions performed using 1% cross-linked brominated polystyrene using *n*-butyllithium in benzene for the lithiation. [b] 3.9 mequiv of S per gram. The resin contains S–S bonds in addition to S–H bonds. [c] Calculated from the elemental analysis of a derivative; see Scheme II. [d] See ref 20.

Scheme II



II, the estimation of the yields for resins X, XI, XII was done by the preparation of derivatives XIII, XIV, and XV for which reliable elemental analyses for nitrogen or chlorine could be carried out. The yields quoted for X–XII should be taken as minimum yields since an additional step was required for the analysis. In all cases no attempts were made to optimize the yields.

We are presently studying polymeric reagents and protecting groups derived from resins III–VII.

Experimental Section

The resins used in this research were a solvent-swellable 1% divinylbenzene–styrene copolymer, Bio-Beads SX 1, purchased from Bio-Rad Laboratories, and a macroreticular resin, Amberlite XE-305, purchased from British Drug House. Tetrahydrofuran (THF) used in the experiments below was purified by distillation from lithium aluminum hydride. Benzene, cyclohexane, and toluene were dried over calcium hydride. All other chemicals were reagent grade and used without further purification unless specified. All the lithiation reactions and the reactions involving lithiated resin intermediates were carried out under inert atmosphere in a specially designed flask fitted with a coarse porosity fritted glass filter. This one-piece reaction vessel allowed the addition or removal of solvents and excess reagents or by-products, the washing of the resin, etc., without transfer or exposure to the atmosphere. Infrared spectra were recorded on Perkin-Elmer 457 or Beckman IR-20 A spectrophotometers using potassium bromide pellets. Elemental analyses were performed by Chemalytics Inc., Galbraith Laboratories, or in this laboratory (halogen analyses only) using a Parr peroxide bomb with 200–300-mg samples of the halogenated resins.

Washing of Cross-Linked Polystyrene Resins. The resins used were washed routinely to remove surface impurities.[8] The following solutions were used at 60–80 °C with, in each case, a contact time of 30–60 min with the resin: 1 N NaOH, 1 N HCl, 2 N NaOH–dioxane (1:2), 2 N HCl–dioxane (1:2), H_2O, dimethylformamide. The resins were then washed at room temperature with the following: 2 N HCl in methanol, H_2O, methanol, methanol–dichloromethane (1:3), methanol–dichloromethane (1:10). The resins were then dried under reduced pressure at 50–70 °C. In general the washing was accompanied by a loss of weight of up to 10%.

Bromination of Cross-Linked Polystyrene Resins. A. Partial Bromination of 1% Cross-Linked Polystyrene Beads. To a suspension of 20 g of washed resin in 300 ml of carbon tetrachloride was added 1.18 g of thallic acetate. The reaction mixture was stirred in the dark for 30 min, then 13.6 g of bromine in 20 ml of carbon tetrachloride was added slowly. After stirring for 1 h at room temperature in the dark, the mixture was heated to reflux for 1.5 h. The reaction mixture, which had lost all the coloration due to free bromine, was collected on filter and washed with carbon tetrachloride, acetone, acetone–water (2:1), acetone, benzene, and methanol. After drying under vacuum, 26.3 g of resin containing 3.10 mequiv of bromine per gram was obtained (24.8% Br). Thus the resin obtained in this preparation had functional groups on 43% of the aromatic rings (theory 44%). Similar reaction conditions were used in bromination reactions with thallic chloride or ferric chloride as catalysts. The results of the bromination reactions are shown in Table I. In one instance (expt 4, Table I), the spent thallium salt was recovered after the reaction and used as catalyst (0.1 g for 2 g of resin) in the bromination of a fresh sample of polystyrene (expt 12, Table I). The reaction carried out as described above gave a very homogeneous, almost colorless, brominated resin containing 3.19 mequiv Br/g. In all cases the resins obtained from the thallium salt catalyzed reaction were visually cleaner than those obtained from the ferric chloride catalyzed reactions.

B. Bromination of a Macroreticular Resin with an Excess of Bromine. One hundred grams of dry Amberlite XE-305 resin was suspended in 1 l. of dry carbon tetrachloride and 1 g of anhydrous ferric chloride was added. The reaction mixture was stirred in the dark while a solution of 60 ml of bromine in 250 ml of carbon tetrachloride was added slowly. The reaction mixture was then stirred overnight at room temperature. The resulting mixture, which still contained free bromine, was filtered and the resin washed repeatedly with acetone until all the bromine coloration had disappeared. Further washings were made with dioxane–water (2:1) and butanone. After drying in vacuo at 60 °C the cream-colored polymer weighed 145.1 g and contained 3.93 mequiv of bromine per gram. The resin obtained by this procedure was, however, not very homogeneous.

A duplicate experiment carried out under the same reaction conditions yielded a colored product containing 3.3 mequiv of bromine per gram.

Lithiation of 1% Cross-Linked Brominated Resin. A. In Tetrahydrofuran Followed by Methanol Quenching. A brominated resin (2.45 g) (3 mequiv Br/g) was swollen in 30 ml of dry THF and 4 ml of 2.5 M *n*-BuLi in hexane was added. After 1.5 h at room temperature the liquid phase was removed and 30 ml of dry THF was added followed by 4.5 ml of 2.5 M *n*-BuLi in hexane. The reaction mixture was stirred and heated to 65–70 °C for 1.5 h. After removal of the liquid phase, a new 30-ml portion of dry THF was added followed by 3 ml of methanol. The brown coloration of the polymer disappeared instantly. After filtration, the polymer was washed with THF, methanol, THF–water (2:1), water, THF–water (2:1), THF, and finally methanol. After drying, 2.23 g of polymer was obtained. Elemental analysis for bromine revealed that the polymer still contained 1.95 mequiv of Br/g. The above reaction sequence was repeated using 1.81 g of the polymer recovered above (1.95 mequiv Br/g) and two successive additions of 2.5 M *n*-BuLi (3 ml at room temperature, and 3.5 ml at 65–70 °C). After quenching with methanol and washing as above, 1.61 g of a resin containing 0.68 mequiv Br/g was obtained. After a third treatment with two successive portions of *n*-BuLi (2 ml at room temperature, then 3 ml at 65–70 °C) followed by quenching with methanol and washing, the resin was found to have lost all its bromine.

B. In Tetrahydrofuran Followed by Quenching with Carbon Dioxide. A stirred suspension of 1.73 g of brominated resin (2.89 mequiv/g) in 20 ml of dry THF was treated with 5 ml of 1.6 M *n*-BuLi in hexane for 1.5 h at room temperature. The liquid phase was removed and 20 ml of dry THF was added followed by 3 ml of 1.6 M *n*-BuLi; after 1 h of stirring at room temperature the liquid phase was again removed and a third portion of 20 ml of dry THF and 4 ml of 1.4 M *t*-BuLi were added. After 1 h of stirring at room temperature, the liquid phase was removed, the resin was washed twice with dry THF, and a slurry of powdered dry ice in dry THF was added. After washing twice with THF–2 N HCl (3:1) the resin was washed further as described above in A, then dried to yield 1.59 g of a resin which still contained 1.53 mequiv of Br/g. In addition, acid–base titration of the resin[18] showed that it contained 1.4 mequiv of –COOH group per gram.

C. In Cyclohexane Followed by Quenching with Carbon Dioxide. The lithiation was carried out by heating a suspension of 2.04 g of brominated resin (2.89 mequiv/g) in 20 ml of cyclohexane with 10 ml of 1.6 M *n*-BuLi in hexane at 68 °C for 3 h. After quenching with solid carbon dioxide in THF, washing and drying, 1.92 g of a resin containing 1.45 mequiv Br/g and 1.3 mequiv –COOH/g was obtained.

D. In Benzene or Toluene Followed by Quenching with Carbon Dioxide. The lithiation was carried out using 2.04 g of brominated resin (2.89 mequiv/g) swollen in 30 ml of dry benzene by adding 10 ml of 1.6 M *n*-BuLi and stirring the suspension at 60 °C for 3 h. After quenching with powdered carbon dioxide in THF, washing, and drying, 1.86 g of a polymer containing 2.9 mequiv of –COOH per gram was obtained. The infrared spectrum of the polymer included very broad hydroxyl and carbonyl absorptions. Similar results were obtained using toluene as solvent (see Table II).

Direct Lithiation of Cross-Linked Polystyrene Resin. Washed polystyrene (2.8 g, 27 mequiv) was suspended in 20 ml of dry cyclohexane containing 4 ml (25 mmol) of tetramethylethylenediamine (TMEDA) and 13.5 ml of 2.5 M *n*-BuLi were added to the stirred mixture. The reaction mixture turned red gradually during 4.5 h of heating at 65 °C. After the liquid phase was removed, the resin was rinsed twice with dry cyclohexane to yield the desired lithiated resin.

The lithiated resin prepared above was quenched by addition of a slurry of dry ice in tetrahydrofuran. After washing as described above and drying, the resin contained 1.99 mequiv of –COOH per gram.

Similar reactions were carried out under different reaction conditions with TMEDA or triethylenediamine. The reaction conditions and results of these experiments are summarized in Table III.

Applications of Lithiated Resin I to the Preparation of Selected Functional Polymers. All the reactions shown in Schemes I and II were carried out on a lithiated resin prepared by reaction of a 1% cross-linked solvent-swellable brominated resin using an excess of *n*-BuLi in benzene (65 °C, 2.5 h). After cooling and removal of the liquid phase, the lithiated resin was washed two or three times with dry benzene. After addition of enough dry THF or benzene to fully swell the resin, an excess of the required reagent was added as described below.

Preparation of Polymeric Thiol III Ⓟ-SH. Resin I was prepared from 3.14 g of brominated polystyrene (2.8 mequiv/g). The resin was suspended in 35 ml of dry THF and 3.31 g of sulfur was added. The reaction mixture turned dark red instantly, then became brown as heat was evolved. After 1 h at room temperature, 30 ml of 3 N HCl was added and the stirring was continued for 30 min. After filtration, the resin was washed repeatedly with THF–water (3:1), THF, CCl_4, CS_2, ether, ethanol, water, THF–water (2:1), THF, and finally methanol. After drying, 3.0 g of resin III were obtained.

The infrared spectrum of the resin included a –SH absorption at 2560 cm^{-1}.

Anal. S, 12.6 (3.9 mequiv/g); Br, none. This result indicates that S–S bonds as well as SH bonds must be present in the polymer.[20]

Preparation of Polymeric Sulfide IV Ⓟ-SCH_3. The lithiated resin was prepared from 10 g of brominated polystyrene (3.1 mequiv/g). The resin was suspended in 100 ml of dry THF and 11 ml of methyl disulfide was added with stirring. After 15 min at room temperature and 30 min at 65 °C, the resin was collected on a filter and washed successively with THF, ether, THF–water (2:1), water, THF, benzene, and finally methanol. After drying 8.64 g of resin IV was obtained.

Anal. S, 8.33 (2.6 mequiv/g); Br, none.

A similar resin has been prepared on macrocreticular Amberlite XE-305 by other workers.[13]

Preparation of Polymeric Boronic Acid V Ⓟ-$B(OH)_2$. Resin I was prepared from 15 g of brominated polystyrene (2.78 mequiv/g). The resin was suspended in 150 ml of dry THF and 18 ml of trimethyl borate was added. After stirring at room temperature overnight, the liquid phase was removed and the resin washed with THF. After addition of 140 ml of dioxane, 12 ml of water, and 36 ml of HCl, the mixture was heated to 60 °C with stirring for 1.5 h. The resin was then collected on a filter and washed repeatedly with dioxane–water (3:1), dioxane, acetone, and finally methanol. The dry resin weighed 12.96 g and its infrared spectrum included a large hydroxyl absorption.

Anal. B, 3.4 (3.15 mequiv/g).

A similar resin has been prepared in our laboratory[6] using Amberlite XE-305.

Preparation of Polymeric Amide VI Ⓟ-$CONHC_6H_5$. The lithiated resin was prepared from 1.91 g of brominated polystyrene (2.89 mequiv/g). The resin was swollen in 20 ml of dry benzene and 3 ml of phenyl isocyanate was added. After 15 min of stirring at room temperature, the mixture was stirred at 65 °C for 30 min. The resin was collected on a filter and washed successively with ethanol, THF, water, THF–water (2:1), THF, ether, and finally methanol. After drying, 2.13 g of VI was obtained. The infrared spectrum of VI showed a large carbonyl absorption at 1650 cm^{-1} and NH peaks at 3380 and 3300 cm^{-1}.

Anal. N, 3.04 (2.2 mequiv/g); Br, none.

Preparation of Silylated Polymer VII Ⓟ-$Si(CH_3)_2Cl$. Resin I was prepared from 2.46 g of brominated polystyrene (3.1 mequiv/g). The resin was suspended in 35 ml of dry benzene and 4 ml of dichlorodimethylsilane was added. After 45 min at room temperature, the polymer was collected on a filter and washed repeatedly with dry benzene to yield VII. Resin VII could be used directly without further purification (removal of lithium chloride). For analytical purposes the chloride was hydrolyzed to the corresponding silanol by addition of water in pyridine. After washing with pyridine, THF, THF–water (3:1), water, THF, benzene, and finally ether, the resin was dried under vacuum to yield 2.45 g of a resin which exhibited large hydroxyl absorptions at 3600 and 3380 cm^{-1}, and bands at 1250 (Si–C), 820 (Si–OH), 770 cm^{-1} (Si–C).

Anal. Si, 6.16 (2.2 mequiv/g).

Preparation of Polymeric Phosphine VIII Ⓟ-$P(C_6H_5)_2$. The lithiated resin was prepared from 2.49 g of brominated polystyrene (2.8 mequiv/g). The resin was suspended in 30 ml of dry THF and 5 ml of chlorodiphenylphosphine was added. After 1.75 h at room temperature the resin was collected on a filter and washed as above for IV. After drying the resin weighed 2.87 g.

Anal. P, 5.96 (1.92 mequiv/g); Br, none.

A polymer prepared by other workers[11] via a similar reaction sequence contained 0.7 mequiv P/g.

Preparation of Polymeric Bromide IX Ⓟ-CH_2CH_2Br. Resin I was prepared from 2.30 g of brominated polystyrene (1.76 mequiv/g). Resin I was added to a solution of 7 ml of 1,2-dibromoethane in 40 ml of dry benzene and the mixture was stirred at room temperature for 2.5 h. After filtration the resin was washed as described above for IV. After drying, 2.19 g of IX was obtained.

Anal. Br, 9.04 (1.13 mequiv/g).

Preparation of Polymeric Aldehyde X Ⓟ-CHO and Its Oxime XIII. Resin I was prepared from 2.6 g of brominated polystyrene (2.8 mequiv/g). The resin was suspended in 35 ml of dry THF and 5 ml of *N,N*-dimethylformamide was added with stirring. After 1.75 h at room temperature, the resin was collected on a filter and washed with THF–water (2:1), THF–water–HCl (8:2:1), water, THF–water (2:1), THF, and finally methanol. After drying, the resin weighed 2.25 g. The ir spectrum of X included absorptions at 2720 ad 1690 cm^{-1}.

For analytical purposes, the oxime XIII was prepared by reaction of 0.79 g of X with 1 g of hydroxylamine hydrochloride in 10 ml of pyridine. After 4 h at 90 °C, the resin was washed successively with pyridine, water, THF–water (2:1), THF, benzene, dichloromethane, and methanol. After drying, 0.8 g of resin XIII was obtained. The ir spectrum of XIII showed a large hydroxyl absorption at 3350 cm^{-1} and no residual carbonyl absorption.

Anal. N, 3.1 (2.2 mequiv/g).

The minimum degree of functionalization of X could be calculated from this analysis and corresponds to 2.3 mequiv of aldehyde functional group per gram.

Preparation of Polymeric Alcohol XI Ⓟ-CH_2CH_2OH and Its 3,5-Dinitrobenzoate XIV. Resin I was prepared from 1.73 g of brominated polystyrene (2.89 mequiv/g). The resin was suspended in 25 ml of dry THF at −50 °C and 8 ml of condensed ethylene oxide was added. The mixture was allowed to reach room temperature gradually (1 h) and the resin was collected on a filter, then washed successively with THF–water (3:1) THF–water–HCl (8:2:1), water, THF, methanol, and finally ether. After drying, the resin weighed 1.49 g and exhibited a large hydroxyl absorption in the ir spectrum.

For analytical purposes the 3,5-dinitrobenzoate XIV was prepared by reaction of 0.46 g of XI with 0.63 g of 3,5-dinitrobenzoyl chloride in 10 ml of dry pyridine. After 1.5 h at 85 °C, the resin was filtered and washed as described above to yield 0.66 g of XIV. The ir spectrum XIV included a large carbonyl absorption at 1730 cm^{-1}.

Anal. N, 5.07 (3.62 mequiv N/g). The minimum degree of functionalization of XI could be calculated from this analysis and corresponds to 2.80 mequiv of $-CH_2CH_2OH$ functional group per gram.

Preparation of Polymeric Alcohol XII Ⓟ-$C(C_6H_5)_2OH$ and Its Chloride XV. Resin I was prepared from 13 g of brominated polystyrene (2.8 mequiv/g). The lithiated resin was suspended in 100 ml of dry THF and 11 g of benzophenone in 40 ml of THF was added. An exothermic reaction occurred immediately. After 2 h at room temperature the resin was collected on a filter and washed as described above for IV. After drying under vacuum 14.24 g of XII was obtained. The ir of XII included large hydroxyl absorptions at 3430 and 3580 cm^{-1}. The degree of functionalization calculated from the gain in weight of the resin corresponds to 1.6 mequiv of functional group per gram. This is confirmed by the analysis of chloride XV which contains 1.4 mequiv of chlorine per gram. The preparation of chloride XV has been described previously.[5]

Acknowledgments. Financial support of this work by the National Research Council of Canada in the form of a research grant and a postgraduate scholarship is gratefully acknowledged. The authors also wish to thank Ms. Elizabeth Seymour for data on the polymeric boronic acid and Ms. Lucy J. Nuyens for data on the polymeric alcohol XII.

Registry No.—Divinylbenzenestyrene copolymer, 9003-70-7; thallic acetate, 15843-14-8.

References and Notes

(1) A volume containing reprints of 62 important papers in this field has been published recently: E. C Blossey and D. C. Neckers, Ed., "Solid Phase Synthesis", Halsted Press, New York, N.Y., 1975.
(2) D. C. Neckers, *J. Chem. Educ.*, **52,** 695 (1975).
(3) R. B. Merrifield, *J. Am. Chem. Soc.*, **85,** 2149 (1963).
(4) C. C. Leznoff, *Chem. Soc. Rev.*, **3,** 65 (1974).
(5) J. M. J. Fréchet and L. J. Nuyens, *Can. J. Chem.*, **54,** 926 (1976).
(6) E. Seymour and J. M. J. Fréchet, *Tetrahedron. Lett.*, 1149 (1976).
(7) C. U. Pittman, *Chem. Technol.*, 560 (1973).
(8) H. M. Relles and R. W. Schluenz, *J. Am. Chem. Soc.*, **96,** 6469 (1974).
(9) J. M. J. Fréchet and K. E. Haque, *Macromolecules*, **8,** 130 (1975).
(10) W. Heitz and R. Michels, *Makromol. Chem.*, **148,** 9 (1971).
(11) F. Camps, J. Castells, M. J. Fernando, and J. Font, *Tetrahedron Lett.*, 1713 (1971); J. Moreto, J. Albaiges, and F. Camps, *An. Quim.*, **70,** 638 (1974).
(12) N. M. Weinshenker, G. A. Crosby, and J. Y. Wong, *J. Org. Chem.*, **40,** 1966 (1975).
(13) G. A. Crosby, N. M. Weinshenker, and H. S. Uh, *J. Am. Chem. Soc.*, **97,** 2232 (1975).
(14) D. Braun, *Makromol. Chem.*, **30,** 85 (1959).
(15) A. J. Chalk, *J. Polym. Sci., Part B,* **6,** 649 (1968).
(16) D. C. Evans, L. Phillips, J. A. Barrie, and M. H. George, *J. Polym. Sci., Polym. Chem. Ed.*, **12,** 199 (1974).
(17) To effect complete removal of all the bromine from the macroreticular resin in tetrahydrofuran, two or three additions of an excess of butyllithium were required with removal of the liquid phase before addition of a new portion of solvent and reagent.
(18) J. M. J. Fréchet and C. Schuerch, *J. Am. Chem. Soc.*, **93,** 492 (1971).
(19) T. M. Fyles and C. C. Leznoff, *Can. J. Chem.*, **54,** 935 (1976).
(20) **Note Added in Proof.** The S–S bonds were removed by reduction with $LiAlH_4$ in THF to yield the polymeric thiol (2.9 mequiv of sulfur per gram) with a degree of functionalization of 0.34 (91% yield).