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The first direct formation of an organolithium reagent on a soluble polymer by chlorine–lithium exchange: functionalised linear polystyrene

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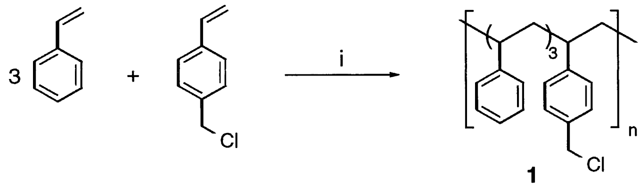
Abstract—The lithiation of a soluble chloromethylated polystyrene **1** (prepared by AIBN-induced copolymerisation of styrene and 4-chloromethylstyrene in 3:1 molar ratio) with an excess of lithium powder and a catalytic amount (10%) of DTBB, and reaction with different electrophiles leads, after hydrolysis, to the expected functionalised polymers **2**–**8**. © 2001 Elsevier Science Ltd. All rights reserved.

Functionalised polymers have been widely used in different processes such as liquid- and solid-phase synthesis, for supporting several reagents or as protecting groups, as well as the base for chromatographic phases and in catalytic processes.[1] Much of the current research on this topic uses insoluble polymer resins (cross-linked resins) in the so-called solid-phase reactions, which have the following advantages: (a) isolation and purification of the reaction products can be easily achived by simple filtration; (b) once the polymer is recuperated, its regeneration and reuse is generally an easy operation; and (c) this technique is particularly interesting for unstable intermediates and toxic or bad-smelling molecules.[2] However, the insoluble nature of these resins complicates the characterisation of the products linked to the polymeric material. In order to overcome this deficiency, a series of soluble polymers has been developed, the common property of all of them being their linear character.[3] On the other hand, a general way to introduce functionality into a cross-linked or a linear polymer would be its metallation and further reaction with electrophilic reagents. To the best of our knowledge, this reaction has only been carried out on cross-linked polymers using activated magnesium[4] or calcium[5] and chloromethylpolystyrene (Merrifield resin[6]). In the case of the corresponding lithiated insoluble polymers the direct lithiation of the same chlorinated materials fails under a variety of conditions due to coupling processes, which increase the degree of cross-linking of the resin.[7] For these reasons, two alternatives through a sulphur–lithium[7] or tin–lithium[8] exchange have been described to generate the expected lithiomethyl resin. Only one example of bromine–lithium exchange has been reported using an excess of *n*-butyllithium but having the bromine atom directly attached to the aromatic ring in the starting polystyrene.[1a] In this communication we describe for the first time the lithiation of a soluble chloromethyl-containing polymer using a 4,4′-di-*tert*-butylbiphenyl (DTBB)-catalysed lithiation[9–11] using or not using Barbier-type[12] reaction conditions.

The starting soluble polymer was prepared according to the reported procedure[13] by refluxing styrene and 4-chloromethylstyrene (3:1 molar ratio) for 40 h in benzene and using 1,1′-azobis(isobutyronitrile) (AIBN) as the radical initiator. After precipitation with cold methanol, the expected polymer **1** was obtained in ca. 30% yield. The product is soluble in typical organic solvents, such as chloroform, dichloromethane, ethyl acetate, benzene, THF or DMF, and insoluble in methanol or water (Scheme 1).[14,15]



Scheme 1. *Reagents and conditions*: (i) AIBN (cat.), PhH reflux, 40 h.

Keywords: chlorine–lithium exchange; functionalised soluble polystyrenes; DTBB-catalysed lithiation.

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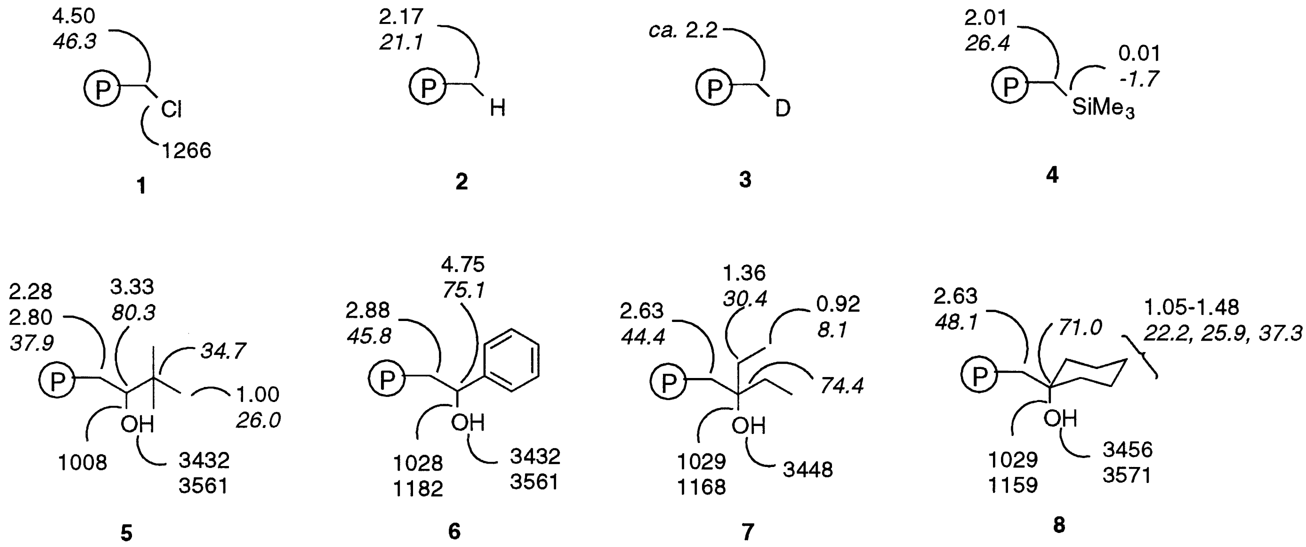

Figure 1. Compounds **1**–**8** prepared.

Dry polymer **1** was lithiated in THF at −78°C under DTBB catalysis (10% molar) using an excess of lithium powder (ca. 1:10 molar ratio) for 2 h. The subsequent hydrolysis with water or deuterium oxide yielded the expected compounds **2**[15,16] and **3**,[15,17], respectively (Table 1, entries 1 and 2 and Fig. 1). When other electrophiles, such as chlorotrimethylsilane or carbonyl compounds, were used, the best results were obtained under Barbier-type conditions, that is carrying out the reaction in the presence of the electrophile, and performing the final hydrolysis with cold methanol. Thus, functionalised polymers **4**–**8** were isolated (Table 1, entries 3–7 and Fig. 1).[19] Either for the two-step or for the Barbier process, a chlorine–lithium exchange occurred prior to the reaction with the electrophile, so the corresponding benzylic organolithium intermediate is probably involved in the reaction. In Fig. 1, some structurally characteristic selected spectroscopic data are included for compounds **2**–**8**.[20]

Table 1. Preparation of functionalised polymers **2**–**8**

Entry	Electrophile	Product[a]	
		No.	Yield (%)[b]
1	H_2O	**2**	≈100
2	D_2O	**3**	≈100[c]
3	Me_3SiCl	**4**	≈100
4	Bu^tCHO	**5**	75[d]
5	PhCHO	**6**	74[d]
6	Et_2CO	**7**	48[d]
7	$(CH_2)_5CO$	**8**	58[d]

[a] In all cases the conversion was total, checked by disappearance of the C–Cl band at 1266 cm^{-1} in the IR spectra, after hydrolysis. For characterisation of compounds **2**–**4**, see Refs. 16–18.

[b] Isolated yield based on the starting polymer **1**.

[c] No Me signal was observed in both ^1H and ^{13}C NMR spectra.

[d] 300 MHz ^1H NMR yield from the isolated reaction product, which contains in all cases variable amounts (25–40%, from ^1H NMR) of polymer **2**.

In summary, effective lithiation of a soluble chloromethylated polymer has been achieved using lithium and DTBB in a catalytic amount as the electron-transfer agent. The reaction of the lithiated polymer with different electrophiles afforded functionalised polymers.

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14. Apart from the spectroscopic data for polymer **1** included in Fig. 1, this starting material was characterised by microanalysis [found: C, 83.3; H, 7.0. $C_{33}H_{33}Cl{\cdot}1/2H_2O$ (corresponding to $3{\times}PhCHCH_2{+}ClCH_2C_6H_4CHCH_2$) requires C, 83.61; H, 7.23%] and HRMS (EI)[15] [Found: 104.0629 (47%); $C_8H_8^+$ requires 104.0626. 117.0706 (100%); $C_9H_9{}^+$ requires 117.0704. 152.0400 (13%); $C_9H_9Cl^+$ requires 152.0393]
15. For HRMS analysis of this type of polymers see Ref. 5. A Finnigan MAT95S spectrometer was used for the corresponding measurements in this study (see Refs. 14, 16 and 17).
16. Characterisation of polymer **2** (see also Fig. 1 for some spectroscopic data) was performed by microanalysis [found: C, 90.3; H, 7.8. $C_{33}H_{34}{\cdot}1/2H_2O$ (corresponding to $3{\times}PhCHCH_2{+}MeC_6H_4CHCH_2$) requires C, 90.16; H, 8.0] and HRMS (EI)[15] [Found: 104.0608 (1%); $C_8H_8^+$ requires 104.0626. 118.0761 (3%); $C_9H_{10}{}^+$ requires 118.0782].
17. Characterisation of polymer **3** (see also Fig. 1 for some spectroscopic data) was performed by ^2H NMR [$\delta_D = 2.97$, referred to the $CDCl_3$ signal ($\delta_D = 7.14$)] and HRMS (EI)[15] [found: 92.0615 (9%); $C_7H_6D^+$ requires 92.0610. 105.0708 (1%); $C_8H_7D^+$ requires 105.0689. 117.0700 (63%); $C_9H_9{}^+$ requires 117.0704].
18. Characterisation of polymer **4** (see also Fig. 1 for some spectroscopic data) was performed by microanalysis [found: C, 82.5; H, 8.6. $C_{36}H_{42}Si{\cdot}H_2O$ (corresponding to $3{\times}PhCHCH_2{+}Me_3SiC_6H_4CHCH_2$) requires C, 83.02; H, 8.5]
19. *General procedure for the preparation of compounds* **2**–**8**: To a dark green suspension of lithium powder (ca. 75 mg, 10 mmol) and DTBB (15 mg, 0.05 mmol) in THF (5 mL) was slowly added (ca. 2 h) a solution of the polymer **1** (230 mg, 0.5 mmol) and the electrophile (2.5 mmol) in THF (10 mL) at −78°C under argon. After stirring for 2 additional hours at the same temperature, the resulting mixture was hydrolysed with methanol (10 mL) and the resulting precipitate was filtered, washed with water (3× 15 mL), methanol (3×15 mL) and dried (0.1 Torr) to give compounds **4**–**8**. For compounds **2** and **3**, after the lithiation step water (1 mL) or deuterium oxide (0.5 mL) were, respectively added and the mixture worked up as above described.
20. Spectroscopic data given in Fig. 1 were obtained as follows: NMR in a Bruker AC-300 spectrometer using $CDCl_3$ as solvent, given in ppm respect to TMS and in italics for the ^{13}C signals. IR in a Nicolet 400 D-FT apparatus in KBr, given in cm^{-1}.