Articles

Phase-Transfer-Catalyzed Chlorination of Poly(*p*-methylstyrene)

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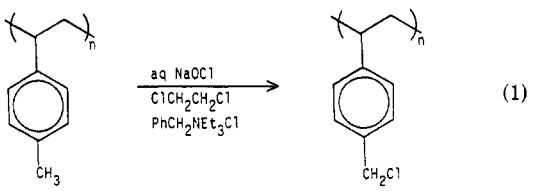
ABSTRACT: Chlorination of the methyl groups of poly(*p*-methylstyrene) with aqueous sodium hypochlorite (laundry or swimming pool bleach) and phase-transfer catalyst such as benzyltriethylammonium chloride provides chloromethyl-substituted polystyrenes. Conversions of up to 20% of methyl to chloromethyl groups were achieved with no detectable formation of dichloromethyl groups. Conversions of up to 61% of methyl to chloromethyl groups occurred with ≤4.4% concomitant formation of dichloromethyl groups. The method has been applied to soluble, 1% cross-linked, and 20% cross-linked poly(*p*-methylstyrene).

Introduction

Chloromethylated polystyrenes are key intermediates in the preparation of anion-exchange resins,[1] supports for solid-phase peptide synthesis,[2] and supports for polymeric reagents and catalysts.[3] The currently available methods for preparation of chloromethyl-substituted polystyrenes have severe limitations. Lewis acid catalyzed chloromethylation is most often performed with the carcinogenic chloromethyl methyl ether and its unavoidable contaminant, the far more potent carcinogen bis(chloromethyl)ether.[4] Methods are available to generate chloromethyl methyl ether *in situ*,[5] and alternative less volatile chloromethyl ethers of unknown toxicity have been used to lessen the hazard.[6] The other major route to chloromethyl-substituted polystyrenes is copolymerization of (chloromethyl)styrenes, available as a 70/30 meta/para mixture at a high price.[7] We report here a third method, phase-transfer-catalyzed chlorination of poly(*p*-methylstyrene) with commercial aqueous sodium hypochlorite bleach solutions (eq 1). Previously, Hamilton and co-workers[8] selectively monochlorinated toluene with hypochlorite and a phase-transfer catalyst.



(1)

Results

p-Methylstyrene was homopolymerized and copolymerized in suspension with divinylbenzene to a 1% cross-linked gel and to a 20% cross-linked macroporous resin by methods identical with those used for cross-linked polystyrenes.[7] The polymer was dissolved or swollen in a halogenated solvent and treated with an excess of either laundry bleach (3.5% sodium hypochlorite) or swimming pool bleach (9.4% sodium hypochlorite) and a phase-transfer catalyst. For quick analysis of the degree of chlorination, the peak areas due to the unreacted methyl carbons at 21.1 ppm, the chloromethyl carbons at 46.1 ppm, and the dichloromethyl carbons at 71.7 ppm were compared in 75-MHz ^{13}C NMR spectra. Selected samples were subjected to combustion analysis for chlorine. The results are shown in Table I. For comparison, a conventional reagent for free radical chlorination, sulfuryl chloride, was tried also.[9] Results are shown in Table II.

All of the higher conversion reactions incorporate chlorine into the polymers at locations not detected by ^{13}C NMR spectral analysis. The spectra were analyzed thoroughly for the presence of signals of other carbon functional groups that might be expected, but no signals were found in the regions of 96 ppm ($ArCCl_3$), 173 ppm ($ArCO_2H$), 192 ppm (ArCHO), 54 ppm (–CHCl– in backbone), or 68 ppm(–C(Ar)Cl– in backbone). Because of much higher reactivity of aliphatic than of aromatic hydrogen atoms in free radical substitution and because acid-catalyzed electrophilic aromatic substitution seems unlikely in aqueous sodium hypochlorite at pH 8.5, we presume that excess chlorination has occurred on the polymer backbone. However, aromatic chlorination would be indetectable by ^{13}C NMR, because the chlorinated carbon signals would be hidden by the protonated aromatic carbon signals at 126–129 ppm.

Infrared spectra of the polymers were analyzed for the bands that could be attributed to backbone C–Cl bonds,[9] but none could be found.

Discussion

The ^{13}C NMR analyses in Table I support the following conclusions:

1. Methyl groups of soluble, 1% cross-linked gel, and 20% cross-linked macroporous poly(*p*-methylstyrene) all can be chlorinated.

2. Chloromethyl contents suitable for use of the 1% cross-linked gel resin for solid-phase peptide synthesis and for most polymer-supported reagents and catalysts can be achieved with no detectable dichloromethyl groups by reaction with 3.5% sodium hypochlorite (laundry bleach) at room temperature. Up to 20% conversion to chloromethyl groups with no dichloromethyl groups was attained (run 33).

3. The relative activities of the phase-transfer catalysts are $PhCH_2NEt_3Cl$ > n-Bu_4NHSO_4 > n-Bu_4NBr (runs 26, 28, 29, 43, and 44).

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Table I
Reactions of Poly(p-methylstyrene)[a] with NaOCl Solutions

run	solvent[b] (mL)	% OCl^- (mL)	PTC[c] (mmol)	T, °C	time, h	mequiv of Cl/g NMR[d]	mequiv of Cl/g Cl anal.	yield,[d] % CH_2Cl	yield,[d] % $CHCl_2$
25[e]	C (100)	3.5 (400)	TBAHS (4.3)	25	2	0.95	f	11.7	0
26	C (100)	3.5 (400)	TBAHS (4.1)	25	6.4	0.72	f	8.9	0
27	C (100)	3.5 (400)	TBAHS (8.3)	25	6.5	1.53	f	19.4	0
28	C (100)	3.5 (400)	TBAB (4.2)	25	6.5	0.28	f	3.4	0
29	C (100)	3.5 (400)	BTAC (4.2)	25	6.5	0.87	f	10.8	0
35	C (100)	3.5 (400)	BTAC (4.2)	25	13	1.22	1.11	15.3	0
33	C (100)	3.5 (400)	BTAC (4.2)	25	23.2	1.58	f	20.2	0
34	C (100)	3.5 (400)	BTAC (4.2)	25	47	2.33	f	25.1	2.7
37	C (100)	3.5 (400)	BTAC (8.3)	25	16.1	1.86	1.59	21.9	1.0
43	DCE (100)	3.5 (400)	BTAC (8.4)	68	17	3.95	4.79	47.3	3.8
44	DCE (100)	3.5 (400)	TBAHS (8.4)	68	17	2.24	f	27.2	1.0
41	DCP (100)	3.5 (400)	BTAC (8.4)	80	16	3.03	f	38.7	1.0
47	DCE (100)	9.4 (400)	BTAC (8.4)	55	8	6.28	7.91	72.9	11.8
48	DCE (30)	9.4 (200)	BTAC (2.1)	23	5	3.27	3.87	41.0	1.7
49	DCE (33)	9.4 (200)	BTAC (2.2)	23	16.2	4.83	6.28	60.8	4.4
51[g]	DCE (16)	9.4 (200)	BTAC (1.5)	23	25	f	4.99	f	f

[a] 5 g of 1% divinylbenzene cross-linked poly(p-methylstyrene), 8.31 mequiv/g. [b] C = $CHCl_3$; DCE = $ClCH_2CH_2Cl$; DCP = $CH_3CHClCH_2Cl$. [c] TBAHS = n-Bu_4NHSO_4; TBAB = n-Bu_4NBr; BTAC = $PhCH_2NEt_3Cl$. [d] Calculated from the peak heights and line widths of the methyl, chloromethyl, and dichloromethyl peaks in the ^{13}C NMR spectra of the product using the triangulation method; corrections for residual backbone methylene carbon of the polymer as well as NOE effects were applied. [e] 5 g of linear poly(p-methylstyrene). [f] Not determined. [g] 5 g of 20% divinylbenzene cross-linked, macroporous poly(p-methylstyrene), 5.52 mequiv/g; the diluent during polymerization was 4-methyl-2-pentanol.[7]

Table II
Chlorination of Poly(p-methylstyrene) with SO_2Cl_2 and AIBN at 60 °C in Benzene

time, h	mequiv of Cl/g NMR	mequiv of Cl/g Cl anal.	yield, % CH_2Cl	yield, % $CHCl_2$
0.4	2.97	2.76	36.8	1.6
2.5	5.7	7.13	72.1	6.7

4. With 3.5% sodium hypochlorite (laundry bleach) and 1,2-dichloroethane as swelling solvent for the 1% cross-linked gel polymer, the maximum degree of chlorination was attained at 68 °C with 47% of the methyl groups converted to chloromethyl and 4% converted to dichloromethyl groups (run 43). Use of 1,2-dichloropropane as swelling solvent at 80 °C gave lower conversion (run 41).

5. The 9.4% sodium hypochlorite (swimming pool bleach) is far more active than the 3.5% sodium hypochlorite (laundry bleach). A 73% conversion to chloromethyl groups with 12% dichloromethyl groups was obtained at 55 °C (run 47), and a 61% conversion to chloromethyl groups with 4% dichloromethyl groups was obtained at room temperature (run 49). A 41% conversion to chloromethyl groups was obtained with <2% dichloromethyl groups (run 48).

Chlorination has little effect on the swelling of the 1% cross-linked polymers in chloroform and does not render the soluble poly(p-methylstyrene) insoluble. These results indicate no appreciable secondary cross-linking of the polymer. In contrast, the chloromethylation of polystyrene proceeds with significant secondary cross-linking.[1]

Sulfuryl chloride and phase-transfer-catalyzed sodium hypochlorite reactions both introduce some chlorine at undetermined sites at conversion to CH_2Cl higher than 20%. A previous report[9] of much higher degrees of free radical chlorination using sulfuryl chloride or *tert*-butyl hypochlorite provided infrared spectral evidence for chlorination on the backbone. Although we suspect the excess chlorine reported in Tables I and II is on the polymer backbone, we could not detect it. Probably the backbone-chlorinated ^{13}C nuclei give severely broadened indetectable NMR peaks due to low rotational mobility about C–C bonds.

Conclusions

Chlorination of poly(p-methylstyrene) with commercial laundry or swimming pool bleach solutions and a phase-transfer catalyst provides a much safer alternative to chloromethylation of polystyrene with chloromethyl methyl ether for preparation of functional derivatives of polystyrene.

Experimental Section

The polymers were prepared from p-methylstyrene (Mobil Chemical Co. PMSA25 monomer) and 55–60% active divinylbenzene (Polysciences) by suspension polymerization.[7] Monomers were freshly distilled under vacuum. The percent cross-linking reported is weight percent of active divinylbenzene. The 20% cross-linked macroporous polymer was prepared with 35 wt % 4-methyl-2-pentanol in the monomer phase. Swelling ratios were determined by volume as swollen volume in $CDCl_3$/dry volume with a precision of ±0.2.

Elemental analyses were performed by Galbraith Laboratories (Knoxville, TN). Infrared spectra were recorded with KBr disks on a Perkin-Elmer Model 681 spectrophotometer. ^{13}C NMR spectra of polymer gels swollen in $CDCl_3$ were run at 75.43 MHz on a Varian XL-300 spectrometer at 24 °C using 16-mm-o.d. tubes, 8 K data points, a 38-μs 90° pulse width, a 5-s delay between acquisitions, 100–1400 acquisitions per spectrum, and an exponential line broadening factor of 4 Hz. Peak areas were measured by triangulation with correction of the base line of the chloromethyl peak for the underlying backbone methylene carbon resonances. Analyses were performed with full ^1H decoupling, and peak areas were corrected for nuclear Overhauser enhancement factors. The NOE's were independently determined to be 1.674 and 1.816 (peak area with full ^1H decoupling/peak area with ^1H decoupling only during data acquisition) for the methyl and chloromethyl carbon peaks in a 1% cross-linked gel polymer.

The sodium hypochlorite solutions were laundry bleach (Clorox) and swimming pool bleach (10% hypochlorite solution, Mid-American Chemical, Inc., Oklahoma City, OK). By iodometric titration[10] they contained 3.5 wt % (0.51 M) and 9.4 wt % (1.47 M) sodium hypochlorite. The phase-transfer catalysts and reagent grade solvents were used as received from Aldrich Chemical Co. (PTC, $ClCH_2CHClCH_3$), Fisher Scientific ($CHCl_3$), and Eastman ($ClCH_2CH_2Cl$).

Chlorination of 1% Cross-Linked Poly(p-methylstyrene). (A) With 3.5% NaOCl (Run 37). In a 1-L round-bottom flask fitted with a mechanical stirrer having a Teflon blade 1 cm above

the bottom of the flask, 5.00 g of the polymer (8.31 mequiv/g) was swollen in 100 mL of chloroform under an argon atmosphere, and 400 mL of Clorox bleach (3.5% NaOCl solution, neutralized to pH 8.47 with concentrated HCl) was added to the flask. After addition of 1.899 g (8.34 mmol) of benzyltriethylammonium chloride, the reaction mixture was stirred at 210 rpm at 25 °C under argon for 16.1 h. The reaction mixture was filtered. The beads were washed with methanol three times, water three times, dichloromethane followed by 3/2 dichloromethane/methanol, methanol, and water five times, and methanol three times. The beads were dried at 50 °C under vacuum to give 5.091 g of chlorinated poly(*p*-methylstyrene).

(B) With 9.4% NaOCl (Run 49). The preceding method was modified to use just enough 1,2-dichloroethane (33 mL) to swell 5.00 g of the 1% cross-linked polymer. The rest of the procedure was identical with procedure A except 200 mL of the 9.4% NaOCl solution (swimming pool bleach) and 0.491 g (2.156 mmol) of benzyltriethylammonium chloride were used.

(C) With SO_2Cl_2. To 5.00 g of 1% DVB cross-linked poly(*p*-methylstyrene) (8.31 mequiv/g) were added 50 mL of benzene and 70 mg of AIBN (azobis(isobutyronitrile)). The mixture was stirred at room temperature under argon for 15 min and warmed to 60 °C. A solution of 104 mg of AIBN and 5.2 mL of SO_2Cl_2 (Eastman Organic Chemicals) in 5 mL of benzene was added over a period of 1 h. The reaction mixture was stirred for another 1.5 h and cooled to room temperature. Cold methanol was added with stirring. The mixture was filtered and the beads were washed with methanol three times, dichloromethane twice, and methanol three times and dried at 68 °C under vacuum for 15 h.

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Registry No. NaOCl, 7681-52-9; 4-$H_3CC_6H_4CH{=}CH_2$ (homopolymer), 24936-41-2; (4-$H_3CC_6H_4CH{=}CH_2$)·$H_2CHC_6H_4CH{=}CH_2$) (copolymer), 39419-87-9; $PhCH_2NEt_3Cl$, 56-37-1; Bu_4NHSO_4, 32503-27-8; Bu_4NBr, 1643-19-2; SO_2Cl_2, 7791-25-5.

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Synthesis and Reversible Photochromism of Azo Aromatic Poly(L-lysine)

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ABSTRACT: Poly(L-lysine) containing 95–97 mol % azo aromatic side chains was synthesized by two different procedures. The photochemical properties of the azo polypeptide poly[N^{ϵ}-(phenylazobenzoyl)-L-lysine] was investigated by absorption and circular dichroism spectroscopy in hexafluoro-2-propanol. The photochromism of the dichroic band in the visible wavelength region was found to be completely reversible as a function of irradiation time at different wavelengths and of the dark adaptation time due to the trans–cis photoisomerization of the azo aromatic moieties. The negative dichroic bands at 340 nm and below 240 nm showed decreases in their ellipticities for up to 4 h upon irradiation at 360 nm. Temperature has little effect on the rate of the photochromism. Cationic poly(L-lysines) with azo aromatic moieties may have promise as photoresponsive systems.

Introduction

Photochromic polypeptides represent interesting systems because of their relevance to the molecular mechanism of photoregulation in biological processes.[1,2] Neutral polypeptides containing photoisomerizable azo aromatic chromophores were first investigated by Goodman et al.[3-7] More recently, two groups have studied the light-induced reversible conformational properties of anionic photochromic polyaspartates and polyglutamates containing azobenzene residues.[8-13] Although Atreyi et al.[14] reported a conformational study of cationic poly(L-lysine) containing azo aromatic groups, a photochemical approach has not yet been examined. In this article I describe the synthesis and reversible photochromic properties of poly[N^{ϵ}-(phenylazobenzoyl)-L-lysine] (PPABLL).

From a different point of view, the main features of the optical activities arise from the dipole–dipole coupling of the chromophores. Theoretical calculations of optical rotatory power have shown that the intensity of the Cotton effect is inversely proportional to the square of the interchromophoric distance and is changed by the dihedral angle between the two transition moments.[15-17] We have investigated how the interchromophoric distance affects the intensity of circular dichroism (CD) using cationic sequential polypeptides.[18,19] Since the distance between azo chromophores is fixed in PPABLL, the transition dipole moment vectors and/or the dihedral angle between the chromophores is expected to change due to the

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