Functionalization of Polystyrene. 1. Alkylation with Substituted Benzyl Halide and Benzyl Alcohol Compounds

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Received February 3, 1978

The alkylation of several macroreticular type polystyrenes with substituted benzyl chloride (**2a–e, 4c, 5,** and **7b**) and benzyl alcohol compounds (**4a** and **7a**) was investigated under various reaction conditions in order to obtain functionalized polymers. In parallel, the alkylation of toluene as a model compound was studied. It was found that the alkylation depends on the following factors: (1) catalyst concentration—higher than 0.18 M concentrations of $AlCl_3$ in nitrobenzene are enough to secure high conversion yields; (2) the molar ratio between catalyst and alkylating agent, which is dependent on the metal-binding ability of the substituents on the alkylating compound. With weak ligands, such as phenols, only catalytic amounts of catalysts were used. With strong ligands, hydroxycarbonyls, amines, and hydroxyamines, excess over equimolar amounts had to be applied. With benzyl alcohol derivatives, equimolar ratios were applied to convert the alcohol into the chloride. Of the polymers studied, XE-305, a 4% divinylbenzene–styrene copolymer, could be functionalized under controlled conditions to any desired degree of functionality, by the right choice of the ratio polymer–alkylating agent–catalyst. Exhaustive alkylations were achieved by an impregnation method which employed high local concentration under the reaction conditions. Highly cross-linked polymers, XAD-2 and XAD-4, were harder to alkylate, and only a limited degree of functionalization was achieved.

Introduction

Insoluble polymers are drawing attention in all fields of research where recycle of reagent, catalyst, or ligand is essential and where facile separation between reactants and products is required. Major advances in applying polymeric reagents have been made in peptide synthesis,[1] organic synthesis,[2,3,4] catalysis,[5] and metal ion coordination.[6–8] Generally, success relied on the right choice of both functional group and polymeric matrix.

Polystyrene, because of its commercial availability in gel, macroreticular,[9] expanded,[10] or isoporous[11] form, is the polymer of choice for most applications. However, the number of synthetic reactions used in the functionalization of this polymer is restricted to chlorosulfonation, chloromethylation, halogenation, acylation, lithiation, nitration, and a few others.[12] Recently, we have shown that highly efficient acyl-transfer agents for peptide synthesis could be prepared by alkylation of polystyrene with chloromethylaryl compounds. 4-Hydroxy-3-nitrobenzylated polystyrene (**2b**)[13] and polystyrene-bound 1-hydroxybenztriazole[14] are now routinely used in this department; 4-hydroxy-3-nitrobenzylated polystyrene and poly(triphenylmethyllithium) prepared by this method were used in various interpolymeric reactions.[15–17]

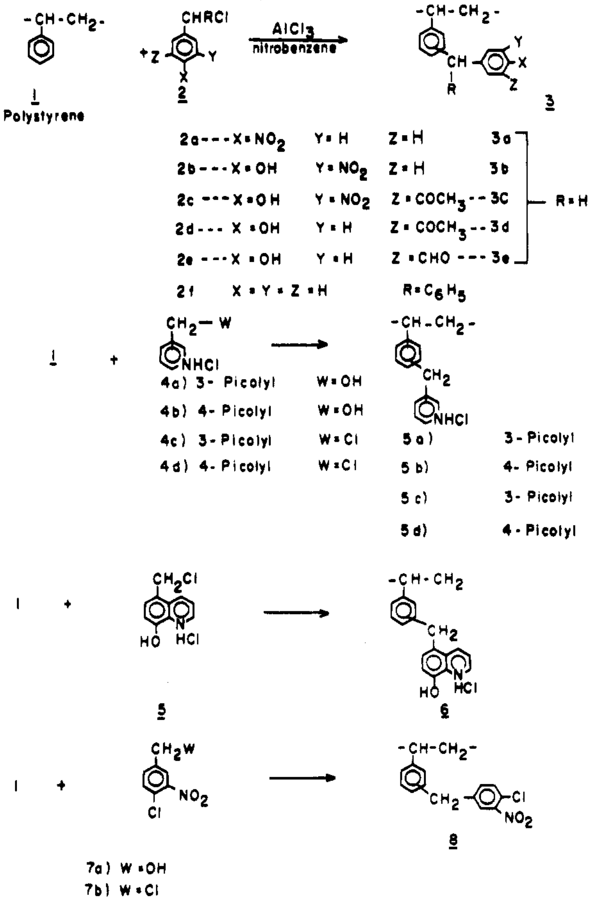
In this paper we have made a systematic study of the alkylation of polystyrene and of a model compound, toluene, under a variety of reaction conditions, with the intention of learning about the factors which might allow the facile preparation of desired functionalized polystyrenes.

Results and Discussion

The alkylation[18] of polystyrene of the macroreticular type, XE-305, with chloromethylaryl derivatives (**2**) was investigated in nitrobenzene (N) using aluminum chloride (A) as catalyst (see Scheme I).

First the generation of the benzylcarbonium ions derived from several chloromethylphenol derivatives (**2b–e**) and 5-chloromethyl-8-hydroxyquinoline (**5**) was investigated using three catalysts, aluminum chloride, boron trifluoride, and zinc chloride, as 1 M solutions in nitrobenzene at 25 °C. The ratio of the benzylic hydrogens assigned to the benzylcarbonium ions at 4.0–4.3 ppm and benzylic hydrogens assigned to starting materials at 4.6–5.25 ppm was measured in the reaction mixture after 24 h (see Table I); this ratio served to determine the degree of formation of carbonium ions.

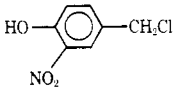
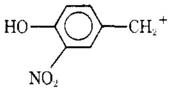
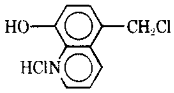
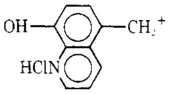
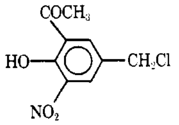
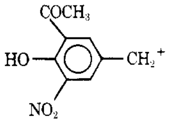
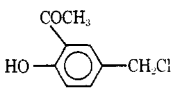
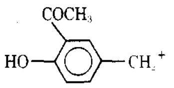
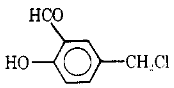
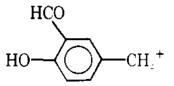
Scheme I. Alkylation of Polystyrene with Substituted Benzyl Chloride and Benzyl Alcohol Compounds



The reaction mixture was then poured on concentrated HCl, to regenerate the starting halide, and again the ratio of the benzylic hydrogens assigned to the self-alkylation products (having same chemical shift as the benzyl carbonium ion signals) and the starting material was measured. This ratio gives the degree of self-alkylation and oligomerization reactions (see Table I). In the case of 2-acetyl-4-chloromethylphenol (**2d**) and 4-chloromethyl-2-formylphenol (**2e**), polymeric products precipitated out of solution, and the degree of self-alkylation could not be measured.

0022-3263/78/1943-3151$01.00/0

Table I. Control Experiments for Autoalkylation and Polymerization

compd	$ArCH_2Cl$, ppm	Catalyst (1 M)	reaction mixture[a]			conditions		product[c]
			$ArCH_2^+$ carbonium ion	$ArCH_2^+$, ppm[b]	intensity ratio $ArCH_2Cl/ArCH_2^+$	temp, °C	time, h	
 **2b**	4.60	$AlCl_3$		4.2	0.1	25	24	starting compound
 **5**	5.25	$AlCl_3$		4.3	0.1	25	24	starting compound
		BF_3		4.5	0	70	24	90% self-alkylated product
		$ZnCl_2$			0			starting compound
 **2c**	4.90	$AlCl_3$		4.3	0.1			
		BF_3		4.3	0.05	70	24	starting compound
		$ZnCl_2$		4.3	0.2			
 **2d**	4.60	$AlCl_3$			>100	25	24	insoluble polymer
		BF_3		3.98	2.4	70	24	50% self-alkylated product (no reaction at 25 °C)
		$ZnCl_2$		4	>100	70	24	100% condensation[d]
 **2e**	4.65	$AlCl_3$			100	25	24	insoluble polymer
		BF_3		4.0	0.5	70	24	40% self-alkylated (no reaction at 25 °C)
		$ZnCl_2$		4.0	1.43	70	24	70% self-alkylated (no reaction at 25 °C)

[a] 24 h at 25 °C in nitrobenzene. [b] The carbonium ions are characterized by a broad absorption band of 30–60 Hz. [c] Condensation products have the same chemical shifts as carbonium ions. [d] Condensation products are soluble in reaction media.

Table II. Alkylation of Toluene[a]

compd	$ArCH_2Cl$, ppm	catalyst[b]	$ArCH_2C_6H_4CH_3$		$ArCH_2Ar$		$ArCH_2Cl$ unreacted %
			ppm	% yield	ppm	% yield	
2b	4.6	$AlCl_3$	4.2	100	4.2	0	0
5	5.25	$AlCl_3$	4.3	90	4.3	0	10
		BF_3		40		0	60
		$ZnCl_2$		0		0	100
2c	4.90	$AlCl_3$	4.3	100	4.3	0	0
		BF_3		20		0	80
		$ZnCl_2$		75		0	25
2d	4.6	$AlCl_3$	4.0	85	4.0	15	0
		BF_3		70		10	10
		$ZnCl_2$		80		20	0
2e	4.65	$AlCl_3$	4.0	90	4.0	10	0
		BF_3		90		10	0
		$ZnCl_2$		80		20	0

[a] 1 M concentration of all the components in nitrobenzene. [b] $AlCl_3$, 24 h at 25 °C; BF_3 and $ZnCl_2$, 24 h at 70 °C.

Examining Table I it is clear that 4-chloromethyl-2-nitrophenol (**2b**), 5-chloromethyl-8-hydroxyquinoline (**5**), and 2-acetyl-4-chloromethyl-6-nitrophenol (**2c**) are perfectly stable, but form, with aluminum chloride as catalyst, sufficient amount of reactive carbonium ions. 2-Acetyl-4-chloromethylphenol (**2d**) and 4-chloromethyl-2-formylphenol (**2e**) are turned completely into the corresponding carbonium ions in the presence of aluminum chloride and produce unwanted side products. However, their activity can be moderated by the use of boron trifluoride or zinc chloride.

Next, the alkylation of toluene, representing a polystyrene analogue, was studied with compounds **2b**, **2c**, **2d**, **2e**, and **5** in nitrobenzene (see Table II) containing 1 M concentration of aluminum chloride, boron trifluoride, or zinc chloride.

Aluminum chloride was found to be an effective catalyst with all the phenols studied, and quantitative alkylations were achieved at 25 °C. For the other two catalysts 70 °C was needed for efficient conversions. From the percent of unreacted chloromethyl compound, the order of reactivity of the various chloromethylphenols is as follows: 4-chloromethyl-2-formylphenol > 2-acetyl-4-chloromethylphenol > 4-chloromethyl-2-nitrophenol > 2-acetyl-4-chloromethyl-6-nitrophenol > 5-chloromethyl-8-hydroxyquinoline.

The amount of self-alkylation products, determined by the ratio of the intensities of the CH_3 to CH_2 protons in the NMR spectra, before and after workup (see Experimental Section), is low. Only in the case of **2d** and **2e** were 10–20% amounts detected independent of the catalyst used.

Table III. Alkylation of XE-305[a] with 4-Chloromethylnitrobenzene

					product						
						$ArCH_2$ incorporation			% conversion[d,e]		
							mmol/g of polymer		$ArCH_2Cl$ ↓		
$ArCH_2Cl$, mmol	A/N, mL[b]	N, mL[c]	temp, °C	time, h	wt, g	mmol[e]	e	f	$ArCH_2$-Ⓟ	D.F.	obsd
5	10	0	70	72	2.61	4.47	1.71	1.67	89.6	0.23	all solvent absorbed
8	10	0	70	72	2.98	7.26	2.42	2.28	90.1	0.38	all solvent absorbed
16	10	0	70	72	3.77	13.00	3.4	3.08	81.3	0.6	all solvent absorbed
3	30	0	70	72	2.31	2.30	1.0		76.0	0.12	
8	30	0	70	72	2.87	6.40	2.23		80.0	0.33	
8	1	9	70	72	2.83	6.10	2.15	1.9	76.2	0.32	all solvent absorbed
8	1	19	70	72	2.28	2.05	0.90	1.04	25.6	0.11	
8	1	29	70	72	2.10	0.73	0.35	0.49	9.1	0.04	
8	1	39	70	72	2.00	0	0	0	0	0	
16	30	0	70	72	3.41	10.36	3.04	2.55	64.7	0.54	
8	1	9	70	24	2.60	4.41	1.69	2.68	55.1	0.23	g

[a] 2 g of XE-305. [b] A/N = 1.8 M aluminum chloride in nitrobenzene. [c] N = nitrobenzene. [d] Equivalent weight of XE-305 = 104 (uncorr). [e] By weight increase. [f] From nitrogen analysis. [g] Impregnation, method B.

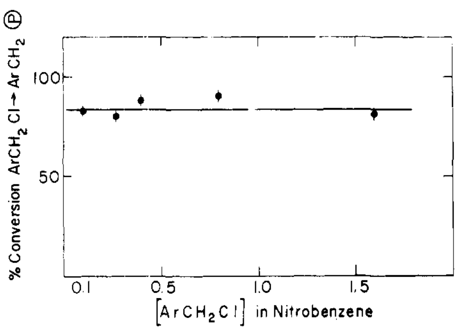


Figure 1. Percent conversion dependency on 4-chloromethylnitrobenzene concentration in 1.8 M $AlCl_3$ in nitrobenzene.

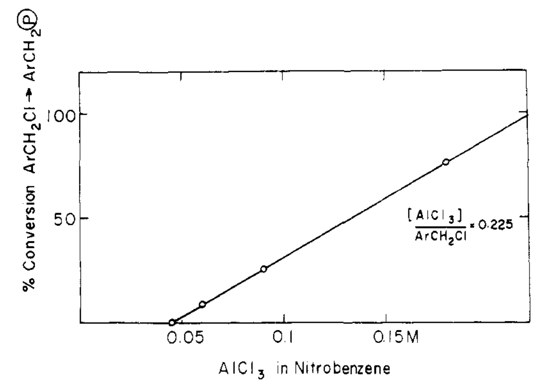


Figure 2. Percent conversion dependency of 4-chloromethylnitrobenzene on $AlCl_3$ concentration.

The alkylation[18] of macroreticular polystyrene XE-305[19,20] was investigated under various reaction conditions, with substituted benzyl halides of the following types: (I) not incorporating any metal-chelating ligands (**2a**, **2f**, **7b**); (II) incorporating only weak metal-chelating ligand, such as phenolic OH groups (**2b**); and (III) incorporating strong metal-chelating ligands such as carbonyl (**2c**, **2d**, and **2e**) or amine (**4c** and **5**).

Although preparative alkylations (see Experimental Section) were carried out successfully even at 25 °C for shorter periods, comparative alkylations were conducted mostly at 60–70 °C for 72 h for the purpose of obtaining comparative results of conversion degrees at equilibrium conditions.

Alkylation with Nonchelating Ligands. 4-Chloromethylnitrobenzene seemed an appropriate model to study the dependency of product formation on both substrate and catalyst concentration, since this compound forms a stable carbonium ion, free from side reactions or ion association effects throughout the range of concentration studied.

The dependence of $ArCH_2Cl$ conversion to $ArCH_2$-Ⓟ (Ⓟ representing the polystyrene matrix, Ar the substituted aryl moiety) on $ArCH_2Cl$ concentration is shown in Figure 1. With 0.18–1.8 M aluminum chloride the conversion factor is independent of the $ArCH_2Cl$ concentration. The same degree of conversion is achieved throughout the range of 0.1–1.8 M $ArCH_2Cl$ concentration. In <0.18 M aluminum chloride solutions, the conversion is directly proportional to the catalyst concentration (Figure 2), implying that for maximum conversions higher than 0.18 M concentration of catalyst must be used.

Alkylation with Weak Metal-Chelating Ligands. Similarly to 4-chloromethylnitrobenzene (**2a**), which needs only a catalytic amount of aluminum chloride, 4-chloromethylnitrophenol (**2b**) and 4-chloromethyl-2-nitrochlorobenzene (**7b**) complex with aluminum chloride very weakly and require only a catalytic amount of aluminum chloride (see Table IV).

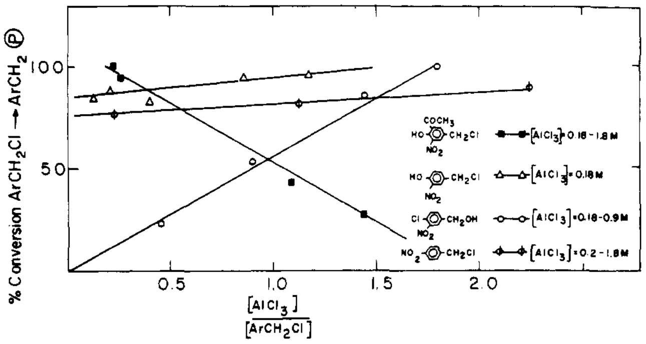
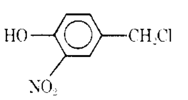
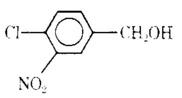
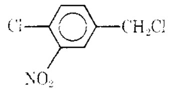


Figure 3. Percent conversion dependency on the ratio $AlCl_3$/$ArCH_2Cl$.

The conversion factor (see Figure 3) for **2a** and **2b** is practically independent of the ratio $AlCl_3/ArCH_2Cl$ and this is expected for other monovalent-type ligands as **7b**.

The Alkylation with Strong Metal-Chelating Ligands. Type III substrates, incorporating strong metal-chelating ligands as hydroxy or carbonyl (**2c**, **2d**, or **2e**, see Table V) or amine (**4a**, **4b**, or **5**, see Table VI) bind an equivalent amount of $AlCl_3$ by chelation, and therefore reduce the effective catalyst concentration, leading to lower conversion figures. As demonstrated in Figure 3, 4-chloromethylnitrobenzene (**2a**)

Table IV. Alkylation of XE-305 with Weak Metal-Chelating Ligands[a]

compd	mmol	AlCl$_3$, mmol	N, mL	wt, g	ArCH$_2$ incorporation			% conversion ArCH$_2$Cl ↓ ArCH$_2$–Ⓟ	D.F.	notes
					mmol[b]	mmol/g of polymer [b]	mmol/g of polymer [c]			
 **2b**	1.54	1.8	10	2.23	1.51	0.68	0.7	98.05	0.08	
	2.10	1.8	10	2.30	1.97	0.85	0.9	93.8	0.10	
	4.20	0.72	10	2.47	3.09	1.25	1.1	73.5	0.16	
	4.20	1.8	10	2.53	3.48	1.38	1.17	83.1	0.18	
	4.20	3.6	10	2.58	3.81	1.49	1.27	90.7	0.20	
	4.20	1.8	10	2.55	3.60	1.42	1.33	85.9	0.19	
	8.4	1.8	10	3.14	7.50	2.39	2.14	89.3	0.39	
	12.6	1.8	10	3.60	10.5	2.92	2.70	83.3	0.55	
	12.6	1.8	10	2.06	0.39	0.19	0.23	3.1	0.02	at 25 °C
	20.0	10.8	10	4.80	18.42	3.85	3.2	92.1	0.965	after procedure B
 **7a**	4	1.8	10	2.15	0.88	0.41	0.25[d]	22.0	0.05	
	4	3.6	10	2.36	2.11	0.89	0.81[d]	52.7	0.11	
	4	5.8	10	2.60	3.52	1.36	1.33[d]	88.0	0.18	
	4	9.0	10	2.60	3.52	1.36	1.32[d]	88.0	0.18	
	2	3.6	10	2.36	2.11	0.90	0.67[d]	105.5	0.11	
	4	7.2	10	2.70	4.10	1.53	1.33[d]	102.5	0.21	
	6	10.8	10	2.96	5.63	1.90	1.70[d]	94.7	0.29	
	8	14.4	10	3.26	7.39	2.28	2.18[d]	93.8	0.39	
	6	14.4	10	3.00	5.9	1.97	1.77[d]	98.3	0.31	
 **7b**	20	1.6	13.4	4.23	13.08	3.09		65.4	0.68	

[a] 2 g of XE-305 at 70 °C for 72 h. [b] By weight increase. [c] By %N analysis. [d] By %Cl analysis.

Table V. Alkylation of XE-305 with Strong Metal-Chelating Ligands[a]

compd	mmol	A/N,[b] mL	N,[c] mL	temp, °C	time, h	wt, g	ArCH$_2$ incorporation			% conversion[d] ArCH$_2$Cl ↓ ArCH$_2$–Ⓟ	D.F.	Oxime mmol/g	notes
							mmol[d]	mmol/g of polymer [d]	mmol/g of polymer [e]				
2c	10	8	12	25	24	2.5	2.57	1.03		25.7	0.13		
	13	12	8	60	48	3.2	6.18	1.93		47.5	0.32		
	20	12	0	60	72	3.7	8.76	2.37		43.8	0.46	1.07	
	7	1	9	70	72	3.3	6.70	2.03	1.36	95.6	0.35		16 mL SnCl$_4$
	8	1	9	70	72	3.6	8.25	2.29	1.67	100	0.43		0.5 mL SnCl$_4$
	8	0	5	70	72	3.2	6.18	1.93	1.59	77.2	0.32		0.5 mL SnCl$_4$ B method
2d	20	0.03	10	60	72	2.1	0.67	0.32		3.3	0.03		
	10	7.5	92.5	60	24	2.4	2.68	1.12	1.15	26.8	0.14		ArCH$_2$Cl added dropwise for 24 h
	8.6	6	0	25	72	2.62	4.16	1.59		48.3	0.22	1.32	
	8	5	0	70	24	2.4	2.68	1.12		33.5	0.14	1.01	B method
2e	8	6	0	70	3	2.9	6.66	2.30		83.2	0.34	1.56	B method

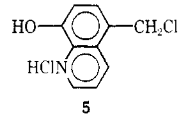
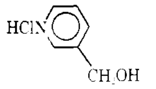
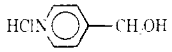
[a] 2 g of polymer. [b] 1.8 M aluminum chloride in nitrobenzene. [c] Nitrobenzene. [d] From weight increase. [e] From nitrogen analysis.

and 4-chloromethyl-2-nitrophenol (**2b**) [type I substrates] bind to XE-305 independently of the AlCl$_3$ to ArCH$_2$Cl ratio. 2-Acetyl-4-chloromethyl-6-nitrophenol (**2c**) is strongly dependent on this ratio. High conversion of type III ligands are obtained only when an equivalent amount of a strong complexing agent, such as SnCl$_4$, is added and the AlCl$_3$ is then able to catalyze. The fact that conversion yields are even lower at AlCl$_3$/ArCH$_2$ ratios of higher than unity is due to the deactivation of the partially-substituted polymer by the complexation of its functional hydroxycarbonyl groups with the excess aluminum chloride (see Tables V and VI).

The Alkylation with Benzyl Alcohols. In the alkylations with 4-chloro-3-nitrobenzyl alcohol (**7a**) and 3-picolyl alcohol (**4a**) (see Table VI) aluminum chloride is consumed to convert the alcohol to the chloride, and a linear relationship is obtained (see Figure 3). For **7a**, a ratio of AlCl$_3$/ArCH$_2$OH = 1.5 is required to obtain the ordinary conversion factors (>80%) for monovalent ligands **2a** and **2b**, in comparison to 4-chloro-3-nitrobenzyl chloride (**7b**) where a ratio of AlCl$_3$/ArCH$_2$Cl = 0.18 is enough (see Table IV). Practically, benzyl alcohol compounds can be used for alkylation, but excess AlCl$_3$ is to be supplied.

Alkylation of Other Polymers. Besides low cross-linked XE-305 polymer and 2% divinylbenzene–styrene copolymer,[13] highly cross-linked polystyrenes of the polymeric adsorbant type, XAD-2 and XAD-4,[21] were alkylated (see Table VII). Figure 4 shows distinctly the effect of high cross-linkage on polymer reactivity. Whereas macroreticular XE-305 (containing approximately 4% divinylbenzene) and gel-type 2% divinylbenzene copolymer alkylate to high conversions

Table VI. Alkylation of XE-305 with Nitrogen Ligands[a]

compd	mmol	A/N, mL	N, mL	temp, °C	time, h	wt, g	$ArCH_2$ incorporation mmol[d]	mmol/g of polymer d	mmol/g of polymer e	% conversion[e] $ArCH_2Cl$ ↓ $ArCH_2$–Ⓟ	D.F.	notes
 **5**	1	1	0	70	48	2.1	0.52	0.25	0.17	51	0.03	
	2	2	0	70	48	2.15	0.77	0.36	0.49	38.5	0.04	
	4	4	0	70	48	2.4	2.11	0.88	0.96	52.7	0.11	
	6	6	0	70	48	2.5	2.57	1.03	1.08	42.8	0.13	
	6	6	0	70	72	3.1	5.65	1.82	1.28	94.2	0.30	B method
	8	5	20	25	72	2.8	4.11	1.47		51.3	0.22	
 **4a**	11	30	0	80	72	2.6	4.70	1.80		42.7	0.24	f
 **4b**	22	30	0	80	72	2.0	0	0		0		f

[a] 2 g of XE-305. [b] 1.8 M aluminum chloride in nitrobenzene. [c] Nitrobenzene. [d] From weight increase. [e] From nitrogen analysis.

Table VII. Alkylations of Various Macroreticular Polymers with 4-Chloromethyl-2-nitrophenol (2b)[a]

Ⓟ	**2b**, mmol	A/N,[b] mL	N,[c] mL	temp, °C	time, h	wt, g	$ArCH_2$ incorporation mmol[d]	mmol/g of polymer d	mmol/g of polymer e	% conversion[d] $ArCH_2Cl$ ↓ $ArCH_2$–Ⓟ	D.F.
XAD-2	2	1	11	65	48	2.18	1.18	0.54	0.41	59	0.06
	4	1	11	65	48	2.18	1.18	0.54	0.48	29.5	0.06
	8	1	11	65	48	2.25	1.64	0.73	0.48	20.5	0.09
	20	1	11	65	48	2.30	1.97	0.86	0.53	9.8	0.10
XAD-4	2	1	11	65	48	2.18	1.18	0.54	0.69	59	0.06
	4	1	11	65	48	2.22	1.44	0.65	0.88	36	0.08
	8	1	11	65	48	2.26	1.71	0.75	0.92	21.4	0.10
XE-305	2.1	1	10	70	72	2.30	1.97	0.85	0.9	93.8	0.10
	4.2	1	10	70	72	2.53	3.49	1.38	1.17	83.1	0.18
	8.4	1	10	70	72	3.14	7.50	2.39	2.14	89.3	0.39

[a] 2 g of polymer. [b] 1.8 M aluminum chloride in nitrobenzene. [c] Nitrobenzene. [d] From weight increase. [e] From nitrogen analysis.

(80–90%) independently of the $AlCl_2/ArCH_2Cl$ ratio at $AlCl_3$ concentration of higher than 0.18 M, the highly cross-linked XAD-2 and XAD-4, containing apparently 25–40% of divinylbenzene,[21] are linearly dependent on this ratio.

Finally, out of the two experimental methods applied, the impregnation method usually offered higher conversion degrees and yields. This is simply because of the high local concentration of both aryl chloride and catalyst achieved under reaction conditions. However, special proximity effects were observed and are under further investigation.

In conclusion, we have shown that polystyrene may be functionalized by alkylation under typical Friedel–Crafts conditions with a variety of substituted halomethyl- or hydroxymethylphenol derivatives. The alkylation may be carried out under controlled conditions to yield various functional polymers containing calculated and varying concentrations of functional groups. But under exhaustive conditions, using a stoichiometric excess of alkylating compound and under high local concentrations (impregnation method B), high binding of up to 4 mmol of functional group per gram of polymer are obtained.

Experimental Section

Polymers. Amberlites XE-305, XAD-1, XAD-2, and XAD-4 were obtained by courtesy of Rohm and Haas, U.S.A. The polymers were washed with 1 N HCl, H_2O, 1 N NaOH, DMF, methanol, and finally with ether, then dried at 80 °C for 24 h. No nitrogen or chlorine could be detected in polymer samples after this washing procedure.

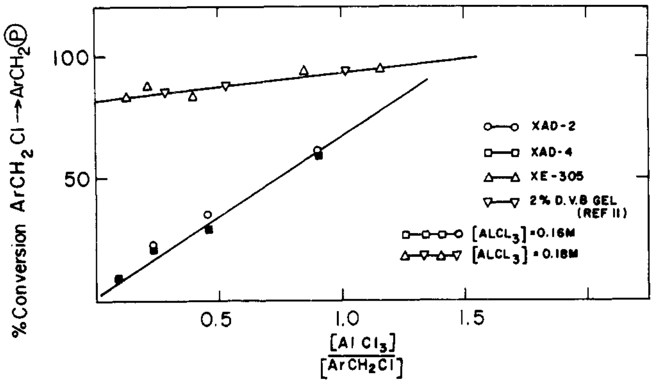


Figure 4. Alkylation of various polymers with 4-chloromethyl-2-nitrophenol.

Substituted 4-chloromethylphenols: 4-nitrobenzyl chloride (Puris) (**2a**), Fluka, mp 71–72.5 °C; 4-chloromethyl-2-nitrophenol[22] (**2b**), mp 72–74 °C; 2-acetyl-4-chloromethyl-6-nitrophenol (**2c**), mp 142–144 °C; 2-acetyl-4-chloromethylphenol[22] (**2d**), mp 73–75 °C; 4-chloromethyl-2-formylphenol[22] (**2e**), mp 84–85 °C; 3-picolyl chloride hydrochloride (**4c**), Aldrich, mp 147–150 °C; 4-picolyl chloride hydrochloride (**4d**), Aldrich, mp 160–163 °C; 5-chloromethyl-8-hydroxyquinoline hydrochloride[23] (**5**), mp 225 °C dec; 4-chloro-3-nitrobenzyl alcohol (**7a**), 98%, Aldrich, mp 62–64 °C.

Aluminum Chloride in Nitrobenzene (1.8 M) (A/N Solution). Aluminum chloride (243 g) from a freshly opened ampule was dissolved in 1 L of nitrobenzene (A.R. grade) which was standing over calcium chloride in an Erlenmeyer flask fitted with a calcium chloride drying tube.

2-Acetyl-4-chloromethyl-6-nitrophenol (2c). (A) Nitric Acid Solution A. Nitric acid (65%, 3.2 mL) was added dropwise to 6.40 mL of acetic anhydride stirred magnetically and cooled to 0–4 °C.

(B) The nitric acid solution A was added dropwise during 1 h to a solution of 6 g of 2-acetyl-4-chloromethylphenol and 6 mL of acetic anhydride in 20 mL of chloroform, cooled to 0–4 °C. The reaction mixture was left to stand for 1 h and the yellow crystalline product was filtered and washed with hexane. The final product is colorless, weighing 7.2 g: mp 142–144 °C; NMR ($CDCl_3$) δ 8.28 (d, 1 H), 8.12 (d, 1 H), 4.61 (s, 2 H), 2.75 (s, 3 H). Anal. Calcd for $C_9H_8NO_4Cl$: N, 6.10; Cl, 15.46. Found: N, 6.30; Cl, 15.17.

Control Experiments and Catalyst Selection (Table I). 4-Chloromethyl-2-formylphenol (**2e**), 2-acetyl-4-chloromethylphenol (**2d**), 2-acetyl-4-chloromethyl-6-nitrophenol (**2c**), and 5-chloromethyl-8-hydroxyquinoline (**5**) (5 mmol of each) were placed in 5 mL of 1 M solutions of aluminum chloride, boron trifluoride, and zinc chloride in nitrobenzene for 24 h at 25 and 70 °C. NMR spectra of **2c, 2d, 2e,** and **5** in nitrobenzene, as well as of the reaction mixtures after 24 h, were taken. The reaction samples were poured on 10 mL of 32% HCl, extracted with 2 × 25 mL of $CHCl_3$, and dried over Na_2SO_4, and the $CHCl_3$ was removed by evaporation under vacuum. NMR spectra of the samples were taken again in the nitrobenzene solvent. The ratio between the carbonium ion and condensation product was then calculated from the corresponding NMR signals.

Alkylation of Toluene in Nitrobenzene with 2b, 2c, 2d, 2e, and 5 (Table II). Solutions of the compounds **2b, 2c, 2d, 2e,** and **5** (1 M) in nitrobenzene containing equimolar amounts of toluene were prepared. NMR spectra of these solutions were taken to assure a CH_3/CH_2 ratio of 3:2. Equimolar amounts of catalyst were added and the reaction was allowed to proceed at 25 (with $AlCl_3$ as catalyst) or 70 °C (BF_3, $ZnCl_2$) for 24 h. The reaction mixtures were poured on 32% HCl, extracted with 2 × 25 mL of $CHCl_3$, dried over Na_2SO_4, and filtered, and the $CHCl_3$ and any excess toluene were removed by distillation under vacuum. The NMR spectrum of the remaining nitrobenzene solution was taken. The ratio of the alkylation product to the self-condensation products was calculated from the equations:

$$Y_{AP} = \frac{2}{3}\frac{I_{CH_3}}{I_{CH_2}} \times 100$$

$$Y_{CP} = \frac{I_{CH_2} - \frac{2}{3} I_{CH_3}}{I_{CH_2}} \times 100$$

where Y_{AP} = yield of alkylation product on toluene, Y_{CP} = yield of self-condensation products, I_{CH_3} = CH_3 signal intensity, and I_{CH_2} = CH_2 signal intensity.

The Alkylation of 4-Chloromethylphenol Compounds. General Procedure A (Tables III–VII). Dry XE-305 (2 g) was added to a measured volume of 1.8 M aluminum chloride in nitrobenzene (A/N solution) in a Erlenmeyer flask with a $CaCl_2$ drying tube. When necessary, nitrobenzene was added to dilute the catalyst concentration. After the addition of the alkylating compound, which dissolved readily in this reaction mixture, the reaction was allowed to proceed in a temperature-controlled oil bath without stirring for the specified time. The mixture was then poured on methanol, filtered, and washed thoroughly with hot CH_3OH/HCl (1:1), and then with CH_3OH, $CHCl_3$, and finally with ether. It was then dried at 60–80 °C for 24 h and weighed. A sample was submitted for elementary analysis. This washing procedure was tested on blank samples containing polymer, aryl chloride compound, and nitrobenzene, or polymer, $AlCl_3$, and nitrobenzene, and reproducbility was found to be satisfactory (±1%). In comparison, nitrogen or chlorine analysis showed reproducibility of not better than ±3%, due to the difficulty of weighing accurately electrostatically charged finely crushed polymer particles.

General Procedure B (Impregnation Method) (Tables III–VII). The 4-chloromethylphenol compound was dissolved in 5 mL of $CHCl_3$ and 2 g of dry XE-305 was added. The mixture was allowed to stand until all the solvent was swallowed by the polymer, usually 0.5 h. The excess solvent was then evaporated under vacuum at 40–50 °C. If the solubility of the 4-chloromethylphenol compound in $CHCl_3$ was low, as in the case of 5-chloromethyl-8-hydroxyquinoline, a fresh 5-mL solution was added and this procedure repeated until the desired amount was introduced into the polymer. The impregnated polymer was now reacted in A/N solution and worked up as described in procedure A.

Preparative Alkylations of XE-305. 4-Hydroxy-3-nitrobenzylated Polystyrene (3b) (after Procedure A). XE-305 (70 g) and 42 g (220 mmol) of 4-chloromethyl-2-nitrophenol were added to 300 mL of nitrobenzene, followed by 20 mL of 1.8 M aluminum chloride in nitrobenzene solution. The mixture kept without stirring at 65–70 °C for 48 h, with exclusion of moisture. The polymer worked up as described in procedure A to yield 104 g of product, representing 2.15 mmol of nitrophenol groups per gram of polymer, or a functionalization degree (D.F.) of 0.33.[24] The acetate derivative was prepared and titrated with 0.1 N benzylamine,[25] yielding 2.2 mmol/g of CH_3CO groups.

4-Hydroxy-3-nitrobenzylated Polystyrene (3b) (after Procedure B). XE-305 (10 g) was added to 50 mL of a solution of 18.7 g (100 mmol) of 4-chloromethyl-2-nitrophenol in 50 mL of CH_2Cl_2. The mixture was allowed to stand for 30 min to allow maximum swelling of the polymer and then the solvent was evaporated slowly. CH_2Cl_2 (50 mL) was added and this procedure repeated until all the 4-chloromethyl-2-nitrophenol was absorbed by the polymer. After drying at 50 °C under high vacuum for 18 h, 30 mL of 1.8 M aluminum chloride in nitrobenzene was added with swirling and shaking of the vessel. The polymer beads were wetted homogeneously, but all the catalyst solution was completely adsorbed by the polymer. The reaction was allowed to proceed in this dry state for 48 h at 65–70 °C and worked up as described in procedure A to yield 24 g of product representing 3.8 mmol of nitrophenol groups per gram of polymer (D.F. = 0.96). The acetate derivative was prepared and titrated with benzylamine, yielding 3.6 mmol/g of $COCH_3$ groups.

4-Chloro-3-nitrobenzylated Polystyrene (8) (after Procedure A). XE-305 (10 g) was reacted with 10 g (53 mmol) of 4-chloro-3-nitrobenzyl alcohol in 50 mL of nitrobenzene containing 10 g (76 mmol) of aluminum chloride for 3 days at 70 °C. The polymer was isolated as described in procedure A: 14.3 g of colorless polymer (1.77 mmol of chloronitrobenzene groups per gram of polymer) by weight (D.F. = 0.26) and 1.69 mmol/g by nitrogen analysis. The hydrazide was prepared by reflux with N_2H_4 in diglyme, yielding 1.4 mmol/g of $-NH_2NH_2$ groups according to %N analysis.

4-Chloro-3-nitrobenzylated Polystyrene (8) (after Procedure B).[26] XE-305 (18 g) was impregnated with 37 g (180 mmol) of 4-chloro-3-nitrobenzyl chloride and then reacted at 70 °C for 3 days in a solution of 2 g (15.3 mmol) of $AlCl_3$ in 120 mol of nitrobenzene. The polymer was isolated as described in procedure A: 38.1 g of product (3.1 mmol/g) (D.F. = 0.68). The hydrazide derivative was prepared, yielding 2.8 mmol/g of N_2H_4 by nitrogen analysis.

3-Acetyl-4-hydroxy-5-nitrobenzylated Polystyrene (3c) (after Procedure A). XE-305 (10 g) was reacted with 20 g (87 mmol) of 2-acetyl-4-chloromethyl-6-nitrophenol and 14 g (105 mmol) of aluminum chloride in 100 mL of nitrobenzene at 60 °C for 2 days, according to procedure A: 16 g of product, containing 1.94 mmol/g of hydroxy groups (D.F. = 0.32). The product has (2 mg/100 mg of KBr) a broad absorption at 3600 (OH bonded) and at 1660 cm^{-1} (CO). The oxime was prepared (see oxime preparations) and contains 1.47 mmol/g of ketoxime groups by %N analysis, showing a capacity of 0.3 mmol of Cu^{2+} per gram of polymer at pH 4: IR (2 mg/100 mg of KBr) 1620 cm^{-1} (C=N).

3-Acetyl-4-hydroxybenzylated Polystyrene (3d) (after Procedure B). XE-305 (20 g) was impregnated with 15.8 g (86 mmol) of 2-acetyl-4-chloromethylphenol and reacted at 25 °C for 3 days in 60 mL of 1.8 M aluminum chloride in nitrobenzene according to procedure B to yield 26.2 g of product **3d**, containing 1.6 mmol/g of hydroxy groups (D.F. = 0.22). The product has the following adsorption in the IR (2 mg/100 mg of KBr): 3610 (OH, bonded), 1650 cm^{-1} (CO).

The oxime was prepared as usual, yielding 1.32 mmol/g of ketoxime groups by %N analysis, showing a capacity of 0.08 mmol of Cu^{2+} per gram of polymer at pH 9.

3-Formyl-4-hydroxybenzylated Polystyrene (2e) (after Procedure B). XE-305 (20 g) was impregnated with 14 g (82 mmol) of 4-chloromethylsalicylaldehyde and reacted in 60 mL of 1.8 M aluminum chloride in nitrobenzene, according to procedure B, for 3 days at 70 °C to yield 29 g of product, containing 2.3 mmol/g of hydroxyl groups (D.F. = 0.35). The product has the following absorptions in the IR (2 mg/100 mg of KBr): 3600 (OH bonded), 1670 cm^{-1} (HC=O).

The oxime was prepared as usual, containing 1.6 mmol/g of aldoxime groups by %N analysis. The oxime has a capacity of 0.19 mmol/g for Cu^{2+} at pH 9.

Oximation Procedure. The polymer samples **3c, 3d,** and **3e** (10 g) were refluxed in 50 mL of a solution of 1 M $NH_2OH \cdot HCl$ + 1 N NEt_3 in methanol for 20 h. The polymers were filtered, washed with methanol, water, and methanol, and dried at 60–80 °C for 20 h.

Metal Complexation Experiments. The polymeric oximes derived from **3c, 3d, 3e** and polymer **6** (10 g) were swollen in 100 mL of

CH_2Cl_2, filtered, washed with CH_3OH to replace the CH_2Cl_2 then with H_2O to replace the CH_3OH, and then placed in 1.0-cm diameter columns. $CuSO_4$ solutions (100 mL of 0.1 N) adjusted with 1 N H_2SO_4 to pH 4 or with NH_4OH to pH 9 were passed at a 1 mL/min rate, and then followed by pH 4 water. The effluents were combined and analyzed. The polymer was eluted using 3 N H_2SO_4, and this solution was analyzed also. Good agreement was obtained for results by both methods; Cu^{2+} was determined using a Varian A-1000 atomic absorption spectrophotometer.

Registry No.—**2a**, 100-14-1; **2b**, 6694-75-3; **2c**, 66358-54-1; **2d**, 30787-43-0; **2e**, 23731-06-8; **4a**, 52761-08-7; **4b**, 62302-28-7; **4c**, 6959-48-4; **4d**, 1822-51-1; **5**, 4053-45-6; **7a**, 55912-20-4; **7b**, 57403-35-7; toluene, 108-88-3; divinylbenzene–styrene copolymer, 9003-70-7; Amberlite XE-305, 39464-91-0; Amberlite XAD-2, 9060-05-3; Amberlite XAD-4, 37380-42-0.

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Electrochemical and Mercury-Promoted Reduction of α,α'-Dibromophenylacetones in Acetic Acid[1]

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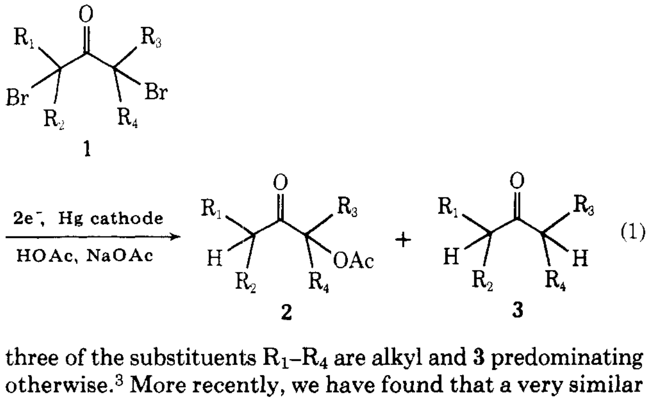
Received February 6, 1978

The factors governing the competition between formation of α-acetoxy ketones and the doubly dehalogenated ("parent") ketones in the electrochemical and chemical reduction of α,α'-dibromo ketones in acetic acid are explored in a series of dibromophenylacetones. The degree of substitution in the dibromo ketone has a major effect upon the competition. The mass spectra of starting ketones and product α-acetoxy ketones are discussed, and several characteristic features are observed.

We have previously described the conversion of a number of α,α'-dibromo ketones (**1**) to α-acetoxy ketones (**2**) by electrochemical reduction in acetic acid containing sodium acetate.[3] In general (neglecting small amounts of other products), the reaction generates a mixture of **2** and the corresponding "parent" ketone **3** (eq 1), with **2** predominating when at least three of the substituents R_1–R_4 are alkyl and **3** predominating otherwise.[3] More recently, we have found that a very similar conversion to that shown in eq 1 can be effected by allowing the dibromo ketone **1** to react with ultrasonically dispersed mercury in acetic acid.[4] Although similar products are formed in this chemical reduction, acetoxy ketones **2** are formed in higher relative amounts than in the electrochemical reduction. In the interests of exploring further the differences between the chemical and electrochemical versions of eq 1, and to test the hypothesis that the competition between **2** and **3** depends upon the relative ease of formation of an intermediate 2-oxyallyl cation[3,4] (see Discussion), we decided to carry out a study of the reduction, by both methods, of a series of α,α'-dibromophenylacetones (**4**–**10**) with differing degrees of α substitution. We report herein the results of that study, which are consistent with our original mechanistic hypothesis.[3,4]



Results

Synthesis of Ketones and Dibromo Ketones. Ketone **11** was commercially available; **12** was prepared by a straightforward route (phenylacetaldehyde plus isopropyl Grignard, and chromic acid oxidation of the resulting alcohol). Ketones **13**–**16** were all prepared by phase-transfer alkylation of the corresponding benzyl ketone, using a two-phase system consisting of aqueous sodium hydroxide and dichloromethane containing ketone, alkyl iodide, and tetrabutylammonium iodide according to the method of Brandstrom and Junggren.[5]

0022-3263/78/1943-3157$01.00/0