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A Convenient Preparation of Benzylamino and Benzylhydrazino Polystyrene

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SUMMARY

Amino and hydrazino polystyrene have been prepared by a new and efficient procedure from chloromethylpolystyrene.

INTRODUCTION

Aminomethylpolystyrene prepared from chloromethylstyrene cross-linked with < 4% divinylbenzene has been widely used as support - 1) in solid phase peptide synthesis (MERRIFIELD 1969 ; MITCHELL et al. 1976 ; SARIN et al. 1980 ; SPARROW 1976 ; STEWARD and YOUNG 1969) - 2) and more recently in several general organic reactions (SKORNA et al. 1978). Polymeric supports have also found application as trapping agents for some short-lived intermediates during a reaction (REBEK et al. 1974 ; 1975 ; 1979). In particular, (TAM et al. 1980) have shown that it is possible to reattach an intermediate cleaved from a multidetachable resin.

The present report describes an efficient method for the formation of polymeric benzylamine and benzylhydrazine by a novel chemical modification of the chloromethyl group bound to the polymer.

Polymeric benzylamine has previously been prepared from chloromethylresin either by reaction with an excess of ammonia (RICH 1975) or via GABRIEL synthesis (MITCHELL 1976 ; SPARROW 1976 WEINSHENKER 1972). These methods, however generally give poorly fonctionalized resins (< 1 meq/g).

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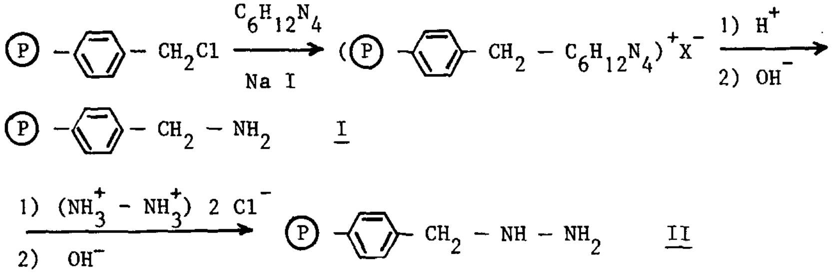
AMINATION OF CHLOROMETHYLATED COPOLYMERS

Primary amines can be conveniently prepared by the DELEPINE reaction (DELEPINE 1895) of an alkylhalide with hexamine. The original procedure has been improved (GALAT 1939) by use of dimethylformamide as solvent and addition of sodium iodide. This procedure has not however been seen applied to polymeric substrates.

SCHEME I



EXPERIMENTAL

The displacement of chloride ion from commercial chloromethylpolystyrene (1.6 meq Cl/g resin) was accomplished by shaking the resin with a solution of hexamethylene tetramine in anhydrous DMF in the presence of sodium iodide at 140°C for 15 hours. The resultant aminomethylpolystyrene resin I was then poured into water, stirred for 30 minutes, filtered and washed with a 3 N solution of hydrochloric acid for 24 hours. Filtration, followed by treatment with a dilute solution of sodium hydroxide (10%, 24h) gave the desired resin which was filtered, successively washed several times with water and methanol and dried *in vacuo* at 70°C.

RESULTS AND DISCUSSION

Resin I contained 1.59 meq N/g resin. The characteristic I.R. bands (Nujol ^{R}) was observed at 3 350 cm^{-1} (ν N-H) ; 1 670 cm^{-1} (δ N-H) ; 1 600 cm^{-1} (ν c=c). 94% of chloride sites were transformed.

HYDRAZINATION OF CHLOROMETHYLATED COPOLYMERS

Hydrazine itself has not been directly grafted although EMERSON et al. (1979) have prepared sulfonylhydrazine resins in order to form sulfonylhydrazone derivatives.

The alkylation of a hydrogen donnor by an alkyl halide is catalysed by the formation of a hydrogen bond between the fluoride anion and the electron acceptor, CLARK (1977). The use of KF as catalyst is therefore an attractive and efficient way to prepare hydrazinopolymers (cf Table I).

EXPERIMENTAL

An heterogeneous mixture containing hydrazine dihydrochloride, chloromethylresin, KF and D.M.F., was smoothly stirred at 140°C for 15 hours. The resin was washed with slighty alkaline aqueous solution and then with water to pH 7. The polymer was washed with methanol several times and dried *in vacuo* at 70°C overnight to a constant weight. I.R. bands (Nujol ^{R}) : 3 350 cm^{-1} (ν N-H) ; 1 665 cm^{-1} (δ N-H) ; 1 600 cm^{-1} (ν c=c). The best results show 82% of chloride sites transformation.

A few examples of various solvents used in the two reactions are given in Table I. Anhydrous conditions are necessary for the nucleophilic substitution in order to minemize competitive hydrolysis. Thus, use of aqueous ammonia, super nucleophilic guanidine or hydrazine hydrate leads to inefficient reactions.

Thus, the high transformation of chloride ion sites and the experimently convenient procedure offer significant advantages over previous methods for the preparation of amino and hydrazino resins.

TABLE I

Preparation of I and II resins

Amination of chloromethylpolystyrene resin[a]

Run	Reagent[b]	Catalyst[c]	Solvent[d]	Time	Temperature	Substitution[e] N meq/g	Cl meq/g
1	$C_6H_{12}N_4$	I Na	dry C_2H_5OH	15h	70°	1.28	0.29
2	-	I Na	D.M.F.	15h	100°	1.34	0.14
3	-	I Na	dry C_2H_5OH	2 months	r.t.	1.58	0.02
4	-	none	D.M.F.	15h	100°	0.63	0.28
5	-	P.T.(triton B)	Na OH	2 days	r.t.	0.03	
6	-	I Na	dry D.M.F.	15h	140°	1.59	0.10
hydrazination of chloromethylpolystyrene resin[a]							
7	N_2H_4 , $2H_2O$	KF	D.M.F.	13h	100°	2.06	trace
8	N_2H_4 , 2ClH		Pyridine	8h	85°	1.24	0.58
9	-	KF	D.M.F.	15h	100°	2.24	0.05
10	-	KF	D.M.F.	2 months	r.t.	1.10	0.45
11	-	P.T.(triton B)	Na OH	2 days	r.t.	trace	
12	-	KF	dry D.M.F.	15h	140°	3.01	0.28

a) 2% cross-linked divinylbenzene-styrene copolymer (Merck). Chloride content 1.6 meq Cl/g resin.

b) 60 m mol/g resin for 1-6 reactions ; 100 m mol/g resin for 7-12 reactions.

c) 6 m mol/g resin for 1, 2, 3, 6 ; 14 m mol/g resin for 4, 7, 9, 10, 12.

d) 15 ml/g resin.

e) Determined by elemental nitrogen analysis.

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