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SYNTHESIS OF LINEAR POLY(1-BENZYLTRIMETHYLENEIMINE) BY THE HOFMANN REACTION OF POLY(1-CYANOETHYLTRIMETHYLENEIMINE) QUATERNIZED WITH BENZYLBROMIDE

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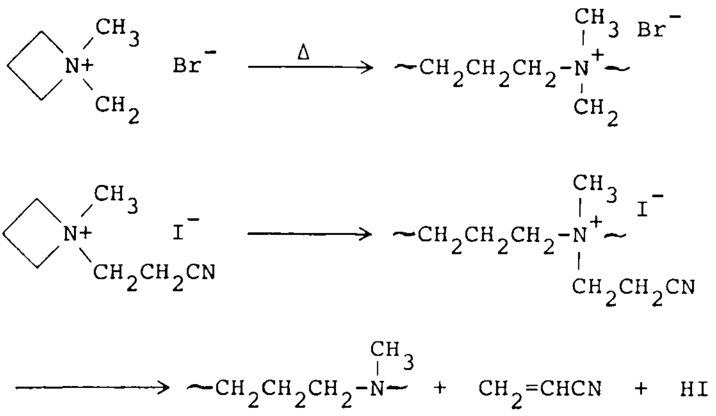
ABSTRACT

The synthesis of a linear polymer having a tertiary amino group in a part of the main chain has been attempted by several methods. However, it was difficult for the linear polyamine to form because of the complicated reaction of the amino group. In the polymerization of weakly basic cyclic amines, e.g., 1-cyanoethylazetidine or 1-cyanoethylaziridine, high molecular weight polymers, poly-1-cyanoethyltrimethyleneimine (poly-CET) and poly-1-cyanoethylethyleneimine (poly-CEE), were obtained. An attempt was made to convert poly-CET and poly-CEE into poly(1-benzylalkyleneimine)s (poly-BET and poly-BEE). Linear poly-BET was prepared by the alkylation of poly-CET (MW about 6000) with benzylbromide, followed by the elimination of the cyanoethyl group of polymer by heating. The poly-BET obtained was a white, greasy substance with a molecular weight of about 5000; its structure was determined by NMR spectroscopy. The cyanoethyl groups were replaced completely by benzyl groups. However, poly-BEE with a complete exchange to benzyl group was not obtained from poly-CEE due to the remaining cyanoethyl groups. Residual cyanoethyl groups replaced about 40% of the amino groups in poly-CEE.

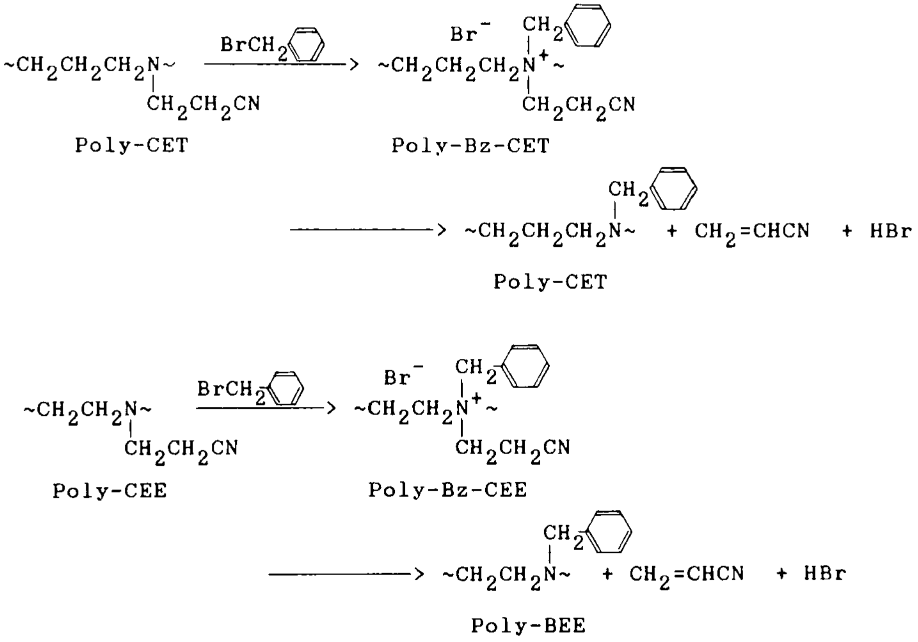
INTRODUCTION

Poly(tertiary amine)s have many potentially useful applications in the pharmacological and biomedical fields. The synthesis of a linear polymer which has a tertiary amino group as a part of the main chain has been attempted in a number of ways, such as the ring-opening polymerization of cyclic amines [1] and the polycondensation of aklanediamine and dihaloalkane [2]. However, the synthesis of linear poly(tertiary amine)s by those methods is not easy because of the complicated reaction of the amino groups [3], except for linear polyethyleneimine which is obtained by special polymerization techniques such as the $LiAlH_4$ reduction of linear poly(*N*-acetylethyleneimine) [4] and the hydrolysis of poly(*N*-2-tetrahydropyranylaziridine) [5]. On the other hand, the ring-opening polymerization of 1-substituted aziridine has been reported, and the effect of the substituent on nitrogen was very interesting. For example, in the polymerization of the lower basic monomer, e.g., 1-cyanoethylaziridine, a high molecular weight polymer was produced, while a high molecular weight linear polymer could not be obtained from the basic monomers 1-benzylaziridine and 1-phenethylaziridine which are more basic and have bulky groups on nitrogen [6].

On the other hand, the ring-opening polymerization of quaternary cyclic ammonium salts such as 1-methyl-1-benzylazetidinium iodide formed an ionene-type polymer [7]. For example, the bulk polymerization of 1-methyl-1-benzylazetidinium iodide was carried out by heating them to their melting points, and linear poly(1-benzyl-1-methylazetidinum iodide) was formed. In this polymerization of 1-methyl-1-cyanoethylazetidinium iodide, the elimination of the cyanoethyl groups was observed during the polymerization as a side reaction, giving the structure of poly(1-methylazetidine) [7] (Scheme 1). Consequently, it should be possible to obtain linear poly(tertiary amine)s if the cyanoethyl groups of poly(quaternary ammonium salts)s can be removed by some nucleophilic reagents. Therefore, an attempt was made to convert poly(1-cyanoethylalkyleneimine)s (poly-CEA) into poly(1-benzylalkyleneimine)s (poly-BEA) by the alkylation of poly(1-cyanoethylalkyleneimine)s (poly-CEA) with benzylbromide, followed by β-elimination of cyanoethyl groups with nucleophilic reagents (Scheme 2).



SCHEME 1.



SCHEME 2.

EXPERIMENTAL

Materials

Poly-CET and poly-CEE as parent polymers were synthesized by the ring-opening polymerization of 1-cyanoethylazetidine [7] and 1-cyanoethylaziridine, respectively. Benzylbromide and ethanolamine were commercial reagents which were dried and then purified by distillation.

Procedure

A quaternization of a polymer having the cyanoethyl group was carried out as follows: benzylbromide was added to the polymer solution and then the reaction mixture was refluxed for the required time. The reaction mixture was removed from the solvent *in vacuo,* and the polymer obtained was washed with dried ether several times, followed by vacuum drying to constant weight.

The quaternized polymer was refluxed in a solvent containing alkali or in freshly distilled ethanolamine for several hours. The reaction mixture was diluted with water, followed by extraction with chloroform, which gave the desired poly(tertiary amine) as a viscous material. On the other hand, polymer precipitated in acetonitrile was washed with 1 *N* NaOH, and then dissolved in chloroform. The chloroform solution was washed with 1 *N* NaOH, and concentrated under reduced pressure. The polymer obtained was washed with dried ether, followed by vacuum drying to constant weight.

RESULTS AND DISCUSSION

The synthesis of poly(1-benzylazetidine) (poly-BET) was carried out by conversion of cyanoethyl groups into benzyl groups on poly(1-cyanoethylazetidine) (poly-CET). Poly-CET was obtained by the ring-opening polymerization of 1-cyanoethylazetidine with 3-hydroxy-1-propane sulfonic acid sultone as initiator [8]. Its molecular weight was about 6000 determined in chloroform solution by the vapor pressure method ($\eta_{sp}/C = 8.86$, $C = 0.5$ g/100 mL HCOOH at 30°C).

A white, powdery polymer was first precipitated by the alkylation of poly-CET with benzylbromide; it was presumed to be poly(1-benzyl-1-cyanoethylazetidinium bromide) (poly-Bz-CET). The precipitated polymer was heated in alkaline solution or in ethanolamine at its boiling point and produced poly(tertiary amine) (poly-BET) through β-elimina-

TABLE 1. Synthesis of Poly-BET from Poly-CET. Exchange Reaction of Cyanoethyl Groups and Benzyl Groups on the Polymer Chain

		Benzylation			Decyanoethylation					
Run	B/P[a]	Solvent,[b] mL	Temperature, °C	Time, h	Nu[c]	Temperature, °C	Time, h	Yield, %	η_{sp}/C[d]	bz[e]
1	1	Ac	80	12	$NaHCO_3$	80	5	89	0.60	70
2	1	Ac	60	12	NaOH	60	5	84	0.65	67
3	2	Ac	60	12	NaOH	60	5	80	0.60	100
4	2	Ac[f]	80	48	ETAM[g]		5	78	0.72	100[h]
5	2	Ac	80	60	Washed with 1 *N* NaOH			89	1.31	100
6	2	$CHCl_3$	60	60	Washed with 1 *N* NaOH			84	1.48	89
					Synthesis of Poly-BEE from Poly-CEE					
7	2	Ac	80	60	Washed with1 *N* NaOH			53	0.19	53

[a] Mole ratio of polymer and benzylbromide. Polymer: 0.01 mol.

[b] Solvent Ac: Acetonitrile.

[c] NaOH, $NaHCO_3$ [0.02 mol in MeOH (6 mL) and H_2O(4 mL)].

[d] $C = 0.5$ g/100 mL HCOOH at 30°C.

[e] Ratio of benzyl groups in polymer.

[f] Acetonitrile, 30 mL.

[g] In refluxing ethanolamine, 15 mL.

[h] NMR spectrum are shown in Fig. 1.

tion of the cyanoethyl group from poly-Bz-CET. The results obtained are summarized in Table 1.

In the synthesis of poly-BET, the best results were obtained by a 100% molar excess of benzylbromide in acetonitrile at 60°C, followed by refluxing in excess ethanolamine for 5 h at about 150°C (Run 4 in Table 1). The exchange reaction to change cyanoethyl groups into benzyl groups proceeded completely under these condition and produced poly-BET. However, complete quaternization of poly-CET could not be attained when an equimolar amount of benzylbromide for the tertiary amino group was used.

Poly-BET was obtained as a white, greasy polymer with a molecular weight of about 5000 (GPC, polystyrene standard in THF, Fig. 1). Ethanolamine is an effective dealkylating reagent for low molecular weight quaternary ammonium salts [9]. The NMR and IR spectra of the poly-BET obtained and those of the parent polymer (poly-CET) together with the peak assignments, are given Figs. 2 and 3.

The NMR spectrum of poly-BET from poly-CET agreed very closely with that of poly-BET obtained by the ring-opening polymerization of 1-benzylazetidine [10]. The NMR spectrum of poly-BET consists of four absorptions, one due to phenyl protons (δ 7.19, 5H), one from the methylene proton attached to the phenyl group (δ 3.44, 2H), one from the methylene proton adjacent to the tertiary amino group ($-N-CH_2-$, δ 2.31, 4H), and the last one from the methylene proton in the center of trimethylene group ($-CH_2-$, δ 1.53, 2H).

For this kind of polymer reaction, the occurrence of main chain scis-

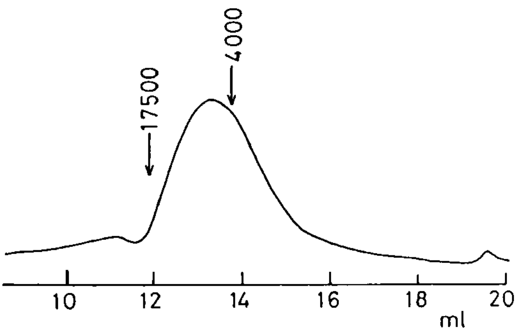


FIG. 1. GPC curve of poly-BET obtained from poly-CET. Standard sample, polystyrene; column, Shimazu SE-100; solvent, THF.

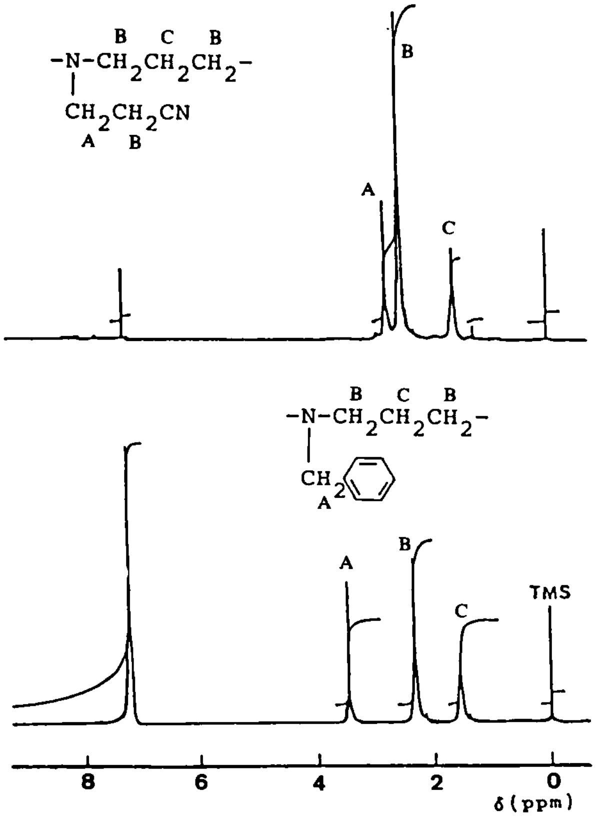


FIG. 2. NMR spectra of poly-CET and poly-BET obtained from poly-CET (in $CDCl_3$).

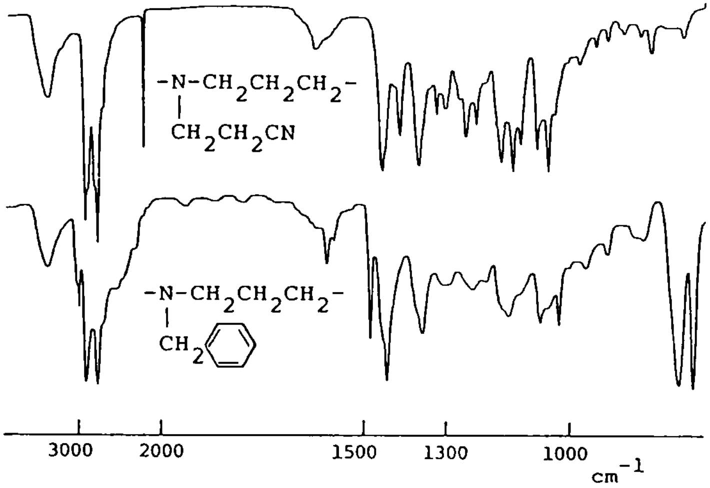


FIG. 3. IR spectra of poly-CET and poly-BET obtained from poly-CET (KBr disk).

sion is predictable. However, the molecular weight of the poly-BET obtained was only slightly affected by the dealkylation.

The polymer poly Bz-CET precipitated during the quaternization of poly-CET with benzylbromide in acetonitrile was confirmed by its NMR spectrum (Fig. 4). However, contrary to our expectations, the NMR spectrum obtained was assigned to poly(1-benzyltrimethyleneiminum)-hydrobromide and then to the NMR spectrum of poly-BET with the addition of NaOH powder in NMR sample tubing (Fig. 4).

From the above description, it is believed that β-elimination of acrylonitrile from the quaternized polymer may occur in the refluxing acetonitrile. In the reaction of poly-CET and benzylbromide at 60°C in DMSO-d_6, the formation of acrylonitrile was directly monitored by using an

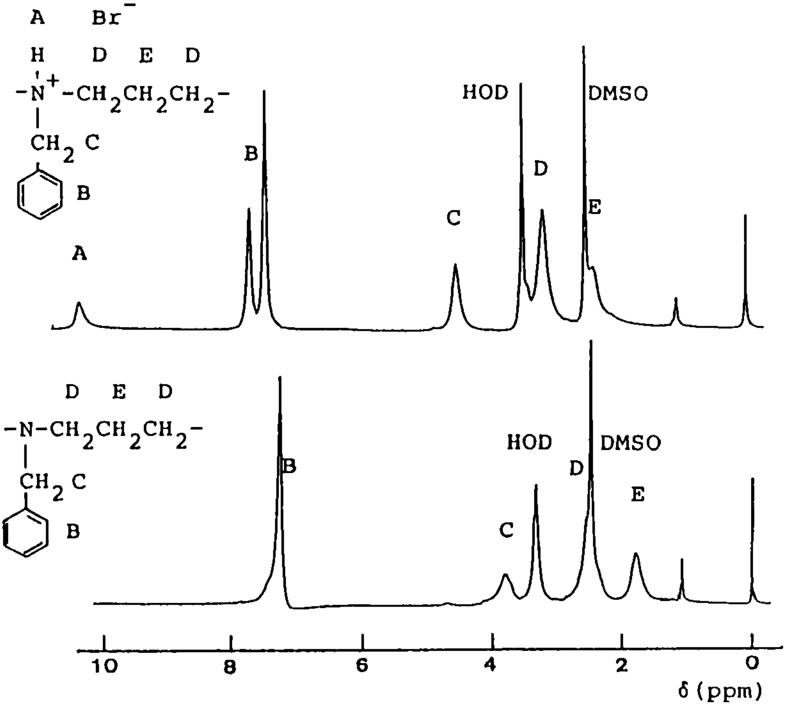


FIG. 4. (A) NMR spectrum of the polymer precipated in course of the reaction of poly-CET and benzylbromide, poly(1-benzyltrimethyleneiminum)hydrobromide (in DMSO-d_6). (B) NMR spectrum of polymer neutralized by addition of NaOH, poly-BET (in DMSO-d_6).

NMR spectrometer. Figure 5 shows the NMR spectrum of the reaction mixture after 6 h, and NMR peaks due to acrylonitrile are observed.

Thus, the direct synthesis of poly-BET from poly-CET with benzyl bromide was carried out by heating in refluxing acetonitrile for 60 h (Run 5 in Table 1). The polymer precipitated in acetonitrile was washed with 1 *N* NaOH and extracted with chloroform. The NMR spectrum of the polymer obtained coincided with the poly-BET obtained by Run 3 in Table 1.

Decyanoethylation of poly(quaternary ammonium salt)s also occurred readily with a weak base, such as sodium carbonate, or by heating without any base.

The synthesis of poly(1-benzylaziridine) (poly-BEE) was carried out in a similarly manner. The result obtained is shown in Table 1 (Run 6).

In this reaction, the conversion of poly(1-cyanoethylaziridine) (poly-CEE) into poly-BEE was not easy, and it produced poly-BEE as a white, viscous substance having a low reduced viscosity. The overall yield of poly-BEE decreased too. The conversion of cyanoethyl groups into benzyl groups with benzylbromide was stopped at about 55% of the tertiary amino groups on Poly-CEE. This was estimated by the NMR spectrum

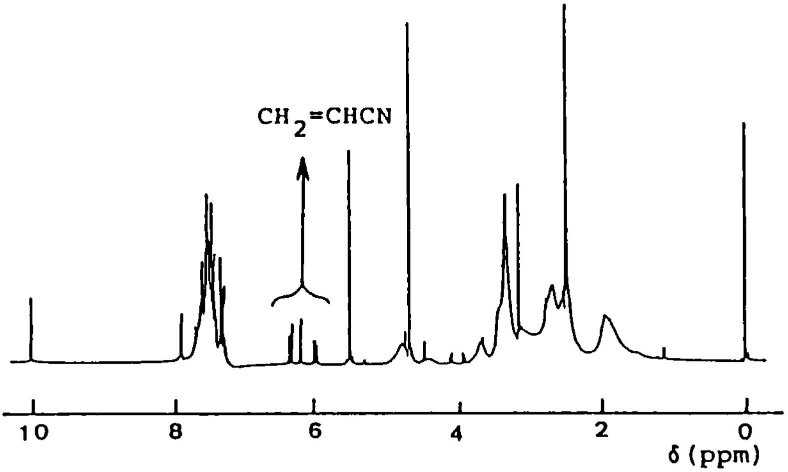


FIG. 5. NMR spectrum of the reaction mixture of poly-CET and benzylbromide at 60°C for 6 h in NMR sample tube (in DMSO-d_6). There is elimination of acrylonitrile in the reaction system.

of the Poly-BEE obtained (Fig. 6). An infrared spectrum of the poly-BEE obtained indicated a peak at 2240 cm^{-1} based on the remaining cyanoethyl groups in the polymer, and a low molecular weight oligomar was produced as a by-product [yield 53%, $\eta_{sp}/C = 0.01$).

The low reactivity of the tertiary amino groups on poly-CEE for

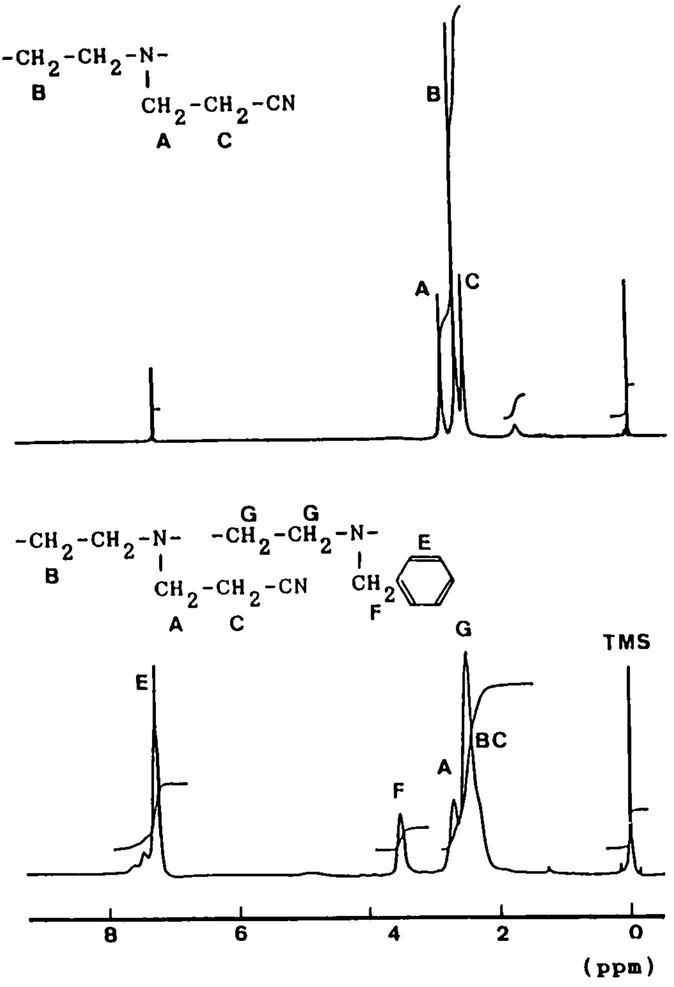


FIG. 6. NMR spectra of poly-CEE and poly-BEE obtained from poly-CEE (in $CDCl_3$).

TABLE 2. Solubilities of Polymers[a]

	H_2O	CH_3OH	DMSO	DMF	CH_3CN	$CHCL_3$	THF
Poly-CET	−	−	+	+	+	+	−
Poly-BET	−	−	+	+	−	+	+
Poly-CEE	−	−	+	+	+	+	−
Poly-BEE	−	−	+	+	−	+	+

[a] + = soluble, − = insoluble.

benzylbromide is explained by the neighboring group effect of the ethyleneimminium salt, which differs remarkably from that of poly-CET. The quaternized reaction of poly(*N*-*t*-buthylethyleneimine) with methyltriflorosulfonate has been reported [11]. The decrease in the overall yield and the reduced viscosity of poly-BEE were probably due to degradation of the partially quaternized polymer formed by the reaction with benzylbromide. The solubilities of the polymers obtained are given in Table 2.

CONCLUSIONS

Linear poly-BET was prepared by benzylation of poly-CET with benzylbromide, followed by elimination of the cyanoethyl groups of the polymer by heating. The cyanoethyl groups of poly-CET were replaced completely by benzyl groups. This method is to be expected for the synthesis of the linear poly(trimethyleneimine) having arbitrary functional group on the nitrogen atom.

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