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George B. Butler^a; Seok H. Hong^a

^a Center for Macromolecular Science & Engineering and Department of Chemistry, University of Florida, Gainesville, Florida

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PREPARATION OF WATER-SOLUBLE POLYMERS VIA THE MANNICH REACTION

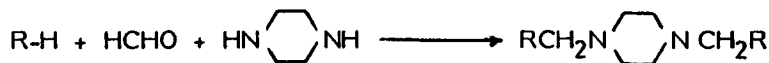
GEORGE B. BUTLER and SEOK H. HONG

Center for Macromolecular Science & Engineering
and Department of Chemistry
University of Florida
Gainesville, Florida 32611

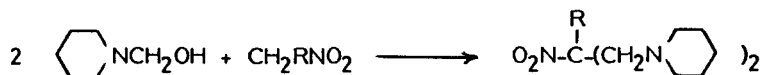
INTRODUCTION

The Mannich reaction, defined as the condensation of ammonia or a primary or secondary amine with formaldehyde and a compound containing at least one hydrogen atom of pronounced activity, was first shown to yield polymers from suitably selected reactants as early as 1946 [1]. Surprisingly, very few further attempts to utilize this interesting reaction in polymer formation have been reported in the literature.

The choice of the amine used in the reaction is important. It is known that primary amines can react at both amine H-atoms, and therefore it is difficult to obtain secondary Mannich bases free from tertiary derivatives [2]. The use of secondary bifunctional amines such as piperazine leads to symmetric Mannich bases in which both of the amino groups have reacted. Attempts to restrict the reaction to only one amine function or hydrolysis of the Mannich products obtained from piperazines invariably leads to the formation of disubstituted piperazines [3]:



Henry was the first to show that Mannich-type reactions will occur with nitroalkanes [4, 5]. He established that *N*-hydroxymethylpiperidine condenses with nitromethane and nitroethane to yield, respectively, 2-nitro-1,3-dipiperidinopropane and 2-methyl-2-nitro-1,3-dipiperidinopropane.



Later, Senkus successfully carried out reactions using monoalkylamines and nitroalkanes such as 1- and 2-nitropropane and 2-nitrobutane [6].

Johnson extended the work of Senkus to various aliphatic secondary amines [7]. He also carried out these reactions by two different methods: (A) reaction of the amines, formaldehyde, and nitroparaffin; and (B) reaction of the amine with the nitroalcohol or nitrodiol. Although the same end products resulted in either case, the latter reaction was slower.

It was the objective of this research to utilize the Mannich reaction between formaldehyde, selected amines, and the nitroparaffins as the active hydrogen compounds to synthesize amine-containing and/or quaternary ammonium-containing polymers. Nitroethane, as well as 1-nitropropane, was utilized as the active hydrogen compound.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are reported uncorrected. Pressures are expressed in torr (mmHg). Elemental analyses were performed by either Atlantic Microlabs, Inc., Atlanta, Georgia, or Department of Chemistry, University of Florida, Gainesville, Florida.

Proton nuclear magnetic resonance (NMR) spectra (60 MHz) were recorded on a Varian EM360L instrument. Carbon-13 NMR (25 MHz) and 100 MHz proton NMR spectra were recorded on a Jeol-JNM-FX-100 spectrometer. Chemical shifts are expressed in parts per million (ppm) on the δ scale downfield from tetramethylsilane (TMS) or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) unless otherwise indicated.

Infrared (IR) spectra were recorded on a Perkin-Elmer 281 spectrophotometer. Absorbances are expressed in wavenumbers (cm^{-1}) using the 1601 cm^{-1} line as standard. Solid samples were run as a KBr pellet; liquid samples were analyzed neat, as a thin film between NaCl plates. Absorption bands are assigned the classifications weak (w), medium (m), strong (s), broad (br), and shoulder (sh).

Molecular weights of polymers were determined by vapor-pressure osmometry (VPO) on a WESCAN Model 233 molecular weight apparatus. Benzil was used as a calibration standard. Intrinsic viscosities were measured with an Ubbelohde dilution viscometer.

Synthesis of *N,N*-Dimethyl-*N',N'*-bis(2-methyl-2-nitro-1-propyl)-1,3-propanediamine

Procedure A. To a solution of *N,N*-dimethyl-1,3-propanediamine (DMPA) (5.109 g, 0.050 mol) in 20 mL 1,4-dioxane was added formalin solution (8.303 g, 37 wt% aqueous, 0.100 mol). A catalytic amount (~0.1 g) of hydrochloric acid was added and the mixture stirred. Then 2-nitropropane (9.091 g, 0.102 mol) was added and stirring was continued for 50 h at 60°C. The reaction mixture was cooled, neutralized with 1 g NaOH, and extracted three times with 30 mL methylene chloride. The combined organic phase was dried over MgSO₄ overnight, filtered, and evaporated to yield a yellow oil (7.55 g, 49.7%).

Procedure B. To a solution of 2-nitropropane (4.546 g, 0.061 mol) in 20 mL 1,4-dioxane at 0.5°C (in an external ice bath) was added formalin solution (4.015 g, 37 wt% aqueous, 0.0495 mol) and potassium carbonate (0.235 g). The ice bath was removed, and the mixture was stirred at room temperature for 45 h. Then *N,N*-dimethyl-1,3-propanediamine (2.555 g, 0.025 mol) in 10 mL 1,4-dioxane was added. The reaction mixture was brought to reflux and extracted three times with 40 mL ether. The combined organic phase was dried over MgSO₄ overnight, filtered, and evaporated to yield a yellow oil (1.87 g, 24.6%).

Procedure C. To an ice-cooled 250-mL round-bottomed flask containing 2-nitro-2-methylpropanol (11.91 g, 0.1 mol) in 25 mL THF was slowly added *N,N*-dimethyl-1,3-propanediamine (5.109 g, 0.050 mol) in 20 mL THF. A catalytic amount of triethylamine (1 mL) was added to this mixture. After the addition was complete, the solution was brought to reflux for 24 h. The solvent was evaporated under reduced pressure to yield a yellow oil (13.74 g, 90.5%).

Analysis. Calculated for C₁₃H₂₈N₄O₄: C, 51.31; H, 19.21; N, 18.42%. Found: C, 51.18; H, 9.13; N, 18.52%.

¹H NMR (CDCl₃, TMS): δ 1.55 (s, 12H), 2.15 (m, 2H), 2.19 (s, 6H), 2.6 (m, 4H), 3.08 (m, 4H).

¹³C NMR (CDCl₃, 77.0): δ 22.41, 24.22, 45.08, 52.68, 57.02, 63.89, 88.45.

IR (neat): 3350 (m, br), 2995 (s), 2950 (s), 2870 (s), 2830 (s), 2790 (s), 1540 (s), 1470 (s), 1400 (m), 1375 (s), 1350 (s), 1285 (m, br), 1200 (w), 1160 (m, sh), 1080 (m), 1040 (m), 1025 (m), 990 (w), 950 (w), 910 (w), 860 (s), 820 (m, sh), 750 (w, br), 650 (w) cm⁻¹.

Synthesis of Model Compounds with Chain-Stopping Reagents

General Procedure A. In a round-bottomed three-necked flask equipped with a Dean-Stark trap and a dropping funnel charged with fresh 1,4-dioxane was placed the mixture of the starting materials, i.e., amine component, formalin solution, and nitroalkane in 1,4-dioxane. A catalytic amount of sodium hydroxide was added, and the azeotropic mixture of 1,4-dioxane and water was distilled off with constant addition of fresh 1,4-dioxane. When the temperature of the outcoming vapor reached 100°C, the addition was stopped and the volume of the residual mixture was reduced to half of the original volume by continuous distillation. Petroleum ether was added to the reaction mixture and the upper layer was decanted. The resulting oil was crystallized from acetone or methanol.

General Procedure B. In a round-bottomed flask equipped with a condenser was placed the mixture of the methylol derivative of the nitroalkane and the amine in THF. A catalytic amount of triethylamine and 4 Å Molecular Sieves were added. The reaction mixture was refluxed for 10-15 h, cooled, and filtered. The filtrate was evaporated to yield a yellow oil which was crystallized from acetone or methanol.

Polymerization of (2) with *N,N'*-Dimethylethylenediamine

To a 100-mL round-bottomed flask equipped with a condenser was added a solution of (2) (8.665 g, 0.0641 mol) in 20 mL THF and *N,N'*-dimethylethylenediamine (DMEA) (5.653 g, 0.0641 mol). To this solution were added a catalytic amount of NEt_3 (1 mL) and 4 Å Molecular Sieves. The reaction mixture was refluxed for 20 h, cooled, and filtered. The filtrate was evaporated under reduced pressure to yield a brown, viscous oil (9.73 g, 81.0% yield).

Analysis. Calculated for $\text{C}_8\text{H}_{17}\text{N}_3\text{O}_2$: C, 51.33; H, 9.09; N, 22.45%. Found: C, 50.45; H, 9.02; N, 22.39%.

^1H NMR (CDCl_3 , TMS): δ 1.49 (s, 3H), 2.41 (s, 6H), 2.58 (s, 4H), 3.09 (m, 4H).

^{13}C NMR (CDCl_3 , 77.0): δ 24.46, 48.10, 60.53, 65.01, 90.70.

IR (neat): 3370 (m, br), 2980 (m), 2940 (m), 2870 (m), 2820 (m), 2800 (m), 2780 (m, sh), 1670 (m), 1645 (m), 1635 (m), 1535 (s), 1455 (s), 1395 (m), 1345 (m, sh), 1290 (m), 1270 (w), 1225 (w), 1165 (w), 1130 (w, br), 1085 (m), 1040 (m, sh), 955 (w), 945 (w), 855 (m), 830 (w) cm^{-1} .

Polymerization of (9) with DMEA

Procedure A. The following procedure was modified from the method reported by Angeloni and coworkers [8, 9]. In a 100-mL three-necked round-bottomed flask equipped with a stirrer, a condenser, and a gas inlet tube was placed a solution of (9) (8.057 g, 0.0426 mol) and DMEA (3.753 g, 0.0426 mol) in 70 mL 95% ethanol. Nitrogen gas was purged through the solution for 120 h at room temperature with constant stirring. During this period the color of the solution changed from yellow to dark brown. The solvent was evaporated under reduced pressure to afford a dark brown viscous oil (6.07 g, 76.2% yield) that was identical with the polymer obtained from (2) and DMEA.

Procedure B. Procedure A was modified as follows: (9) (7.408 g, 0.0391 mol) and DMEA (3.455 g, 0.0392 mol) were dissolved in 50 mL DMSO and placed in a 100-mL round-bottomed flask. Nitrogen gas was passed through the solution for 70 h at 70°C. Upon heating, the color of the solution changed slowly to dark brown. The solvent was removed by means of reduced pressure to yield a dark brown viscous oil (5.14 g, 70.2% yield) that was identical with the polymer obtained from Procedure A.

Reduction of Polymer

Procedure A. In a 1000-mL Erlenmeyer flask was placed a solution of sodium borohydride (5 g) in 250 mL methanol with stirring. A solution of polymer in chloroform was added dropwise after the addition of a catalytic amount of palladium on charcoal. When the bubbling had ceased, additional NaBH_4 was added. This process was repeated several times. After the addition was complete, the reaction mixture was stirred for 1 h at room temperature, followed by the addition of hydrochloric acid (1 *N* aqueous). When the reaction mixture became acidic to pH paper, the solid (charcoal) was filtered. The filtrate was condensed under reduced pressure to yield a light yellow liquid. Sodium carbonate was added to this solution until the formation of CO_2 bubbles ceased (pH 8). The resulting solution was extracted with methylene chloride, and the combined organic phase was dried over K_2CO_3 , filtered, and evaporated to afford a pale yellow oil.

Procedure B. A solution of Polymer (7) (2.017 g, 0.00946 mol) in 100 mL DMF with a catalytic amount of Raney nickel was placed in a Parr bomb. The bomb was charged with hydrogen gas to 800 psi, and heated to 50°C for 2 h followed by 60°C for 6 h. The reaction mixture was then stirred overnight at

room temperature, and the catalyst was filtered. The resulting liquid was evaporated under reduced pressure at 50°C to afford a light brown oil (1.46 g 84.3%).

Analysis. Calculated for $C_{10}H_{21}N_3$: C, 65.52; H, 11.55; N, 22.93%.

Found: C, 64.21; H, 11.34; N, 22.20%.

1H NMR ($CDCl_3$, TMS): δ 1.00 (s), 1.5 (m), 2.2 (s), 2.95 (m, br), 5.55 (s, br).

^{13}C NMR ($CDCl_3$, 77.0): δ 25.66, 45.27, 55.12, 60.87, 67.59, 130.37.

Methylation of Polymer

Procedure A. The procedure reported by Pine and Sanchez [10] was modified as follows: In a 50-mL round-bottomed flask was placed Polymer (11) (2.81 g, 0.0179 mol), and the flask was cooled in an external ice bath. To this, formic acid (88 wt% aqueous, 3.6 g, 0.075 mol) was slowly added, followed by formalin solution (37 wt% aqueous, 5.1 g, 0.063 mol). The flask was equipped with a magnetic stirrer and a condenser and placed in an 80°C constant-temperature bath for 26 h. The mixture was cooled, and 10 mL of 6 *N* HCl was added. This was then extracted three times with 20 mL ethyl ether, and the combined ether extracts were washed with 10 mL H_2O and dried over K_2CO_3 overnight. Evaporation of ether gave a white solid (0.23 g). The aqueous layer was made basic with sodium hydroxide (50% w/v aqueous) and extracted three times with 20 mL methylene chloride. The combined organic layer was washed with 10 mL H_2O and dried over K_2CO_3 . Filtration and subsequent evaporation yielded a light brown, clear, viscous oil (1.52 g, 45.9% yield).

Procedure B. The method previously reported by Borch and coworkers [11, 12] was applied. To a stirred solution of Polymer (10) (2.81 g, 0.0179 mol) and formaldehyde (37 wt% aqueous, 11 mL, 0.136 mol) in 40 mL acetonitrile was added sodium cyanoborohydride ($NaBH_3CN$). Glacial acetic acid was added until the reaction mixture reached a pH of 6. Stirring was continued for 10 h, and the mixture was poured into 200 mL ether. The resulting mixture was washed four times with 75 mL of 2 *N* KOH solution and once with 60 mL saturated NaCl solution. The combined KOH wash was back-washed with 100 mL ether. The combined ether layer was dried over K_2CO_3 overnight and evaporated to yield a light brown, clear, viscous oil (1.72 g, 51.9%).

Analysis. Calculated for $C_{10}H_{23}N_3$: C, 64.81; H, 12.51; N, 22.68%.

Found: C, 63.55; H, 12.18; N, 22.07%.

¹H NMR (CDCl₃, TMS): δ 0.91 (s), 2.04 (s), 2.28 (s), 2.33 (s), 2.65 (m).

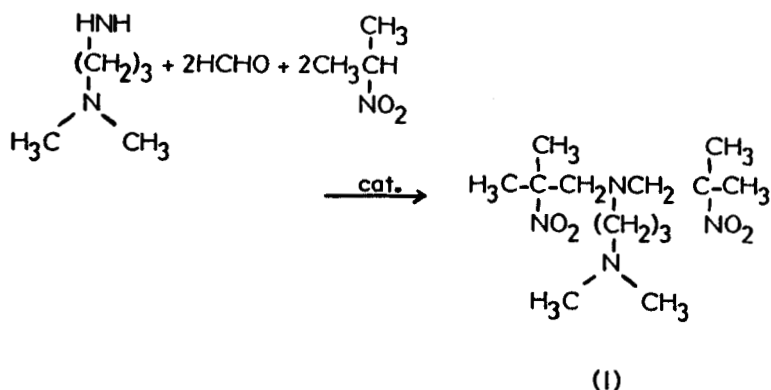
¹³C NMR (CDCl₃, 77.0): δ 16.67, 36.94, 46.98, 59.12, 64.04, 93.01.

IR (neat): 3320 (m, br), 2940 (s, sh), 2840 (s, sh), 2800 (s, sh), 1660 (m), 1450 (s), 1370 (m), 1350 (w), 1325 (w), 1280 (m), 1270 (m, sh), 1235 (w), 1195 (w), 1170 (w), 1145 (m), 1130 (m), 1090 (s, sh), 1060 (m), 1040 (m), 1010 (w), 975 (w), 960 (w), 940 (w), 905 (w), 890 (m), 810 (w, br), 750 (w) cm⁻¹.

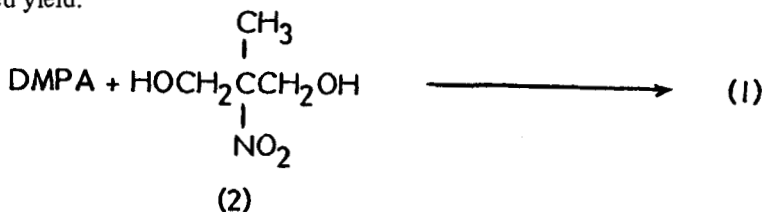
RESULTS AND DISCUSSION

Model Compounds

A series of reactions between 2-nitropropane, formaldehyde, and *N,N*-dimethyl-1,3-propanediamine (DMPA) was carried out to yield Model Compound (1).



In order to determine the conditions that would afford the highest conversion, several different reactions conditions were studied. Higher temperature was less favorable than a lower temperature, and the catalyst, being basic or acidic, did not drastically alter the degree of conversion of the reaction. The adduct of 2-nitropropane and formaldehyde, (2), which was obtained in almost quantitative yield, was reacted with DMPA to afford Compound (1) in much improved yield.



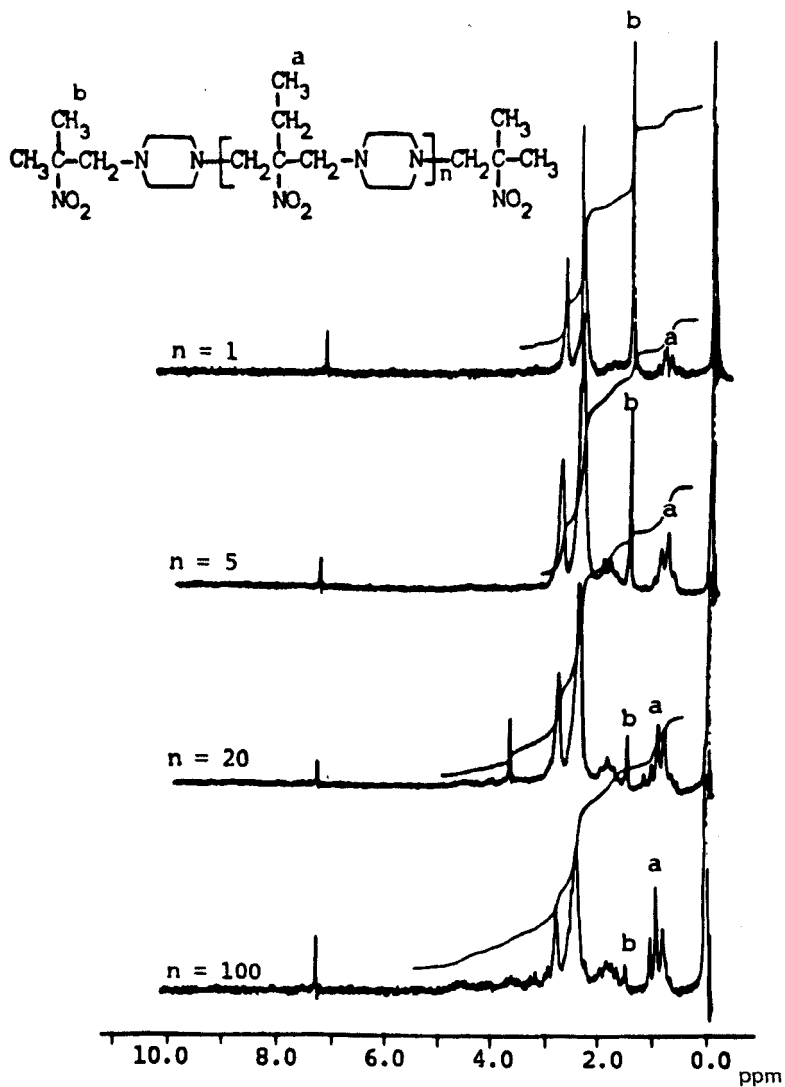
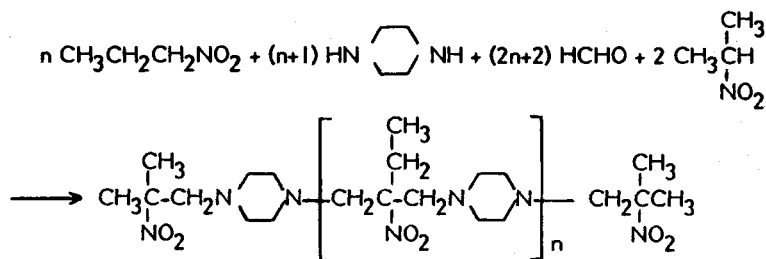


FIG. 1. $^1\text{H-NMR}$ spectra (in CDCl_3) of the model compounds utilizing 2-nitropropane as the chain-stopping reagent.

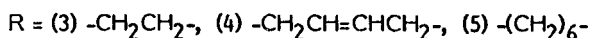
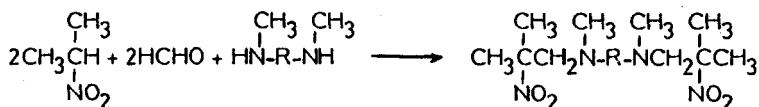
TABLE 1. Reactant Feed Ratio and Actual Chain Length from NMR Spectra

n	a	b	Ratio	Chain length
0	—	—	—	—
1	34	9	4:1	1
5	15	18	5:6	5
20	5	19	1:4	16
100	3	28	1:9	36

A series of model compounds was synthesized on the assumption that the reactivity of the proton of 2-nitropropane is equal to that of protons of 1-nitropropane. By varying the ratio of the two nitro compounds, one can theoretically control the length of the chain. As shown in Fig. 1, the ^1H spectra of these compounds were utilized to determine the actual number of repeating units by integration of the different methyl peaks. The actual degrees of polymerization of these compounds were shown to be 1, 5, 16, and 36 for the theoretical degrees of polymerization of 1, 5, 20, and 100, respectively (Table 1). This result shows that 1) the reactivity of the protons of 1-nitropropane is less than that of 2-nitropropane, thus the propagation stops before all the 1-nitropropane present is consumed; and 2) the conversion is not 100%, therefore the growth of the chain stops before all the reactants are consumed.

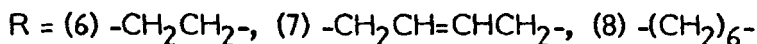
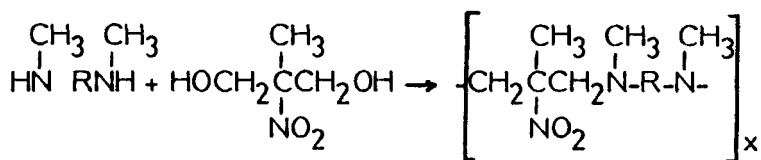


Other bis-secondary amines, i.e., N,N' -dimethylethylenediamine (DMEA), N,N' -dimethyl-2-butene-1,4-diamine (DMBA), and N,N' -dimethylhexamethylenediamine (DMHA), were utilized to produce the corresponding model compounds in good yields.



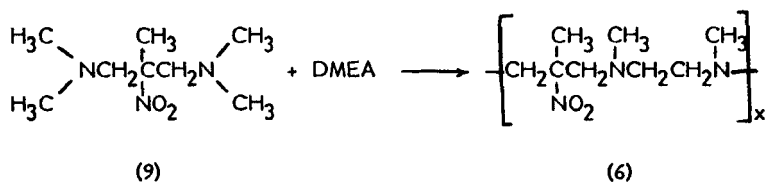
Polymers

An investigation of the polymerization of DMEA with an adduct of nitroethane and formaldehyde, (2), was then carried out. The reaction produced an excellent yield of Polymer (6).



This polymer, however, showed a molecular weight of only 2200 by vapor pressure osmometry. The low molecular weight could be the result of the relatively low conversion.

DMBA and Adduct (2) were then polymerized under identical conditions to afford the corresponding polymer, which showed a low molecular weight (2500) by VPO. The ^{13}C -NMR spectrum of this polymer is shown in Fig. 2. Similarly, DMHA and Adduct (2) were polymerized under identical conditions to yield the corresponding polymer. Since these polymers did not have very high molecular weight, the method reported by Angeloni and coworkers was employed [8, 9, 13, 14]. Thus, 2-methyl-2-nitro-1,3-bis(dimethylamino)propane (9) was prepared and treated with DMEA to afford Polymer (6), identical to the polymer previously obtained by the reaction of (2) and DMEA. Similarly, (9) was treated with DMBA and DMHA to yield the corresponding Polymers (7) and (8), also identical with the polymers obtained previously by the reaction of (2). The molecular weights of these polymers also ranged from 2000 to 2500.



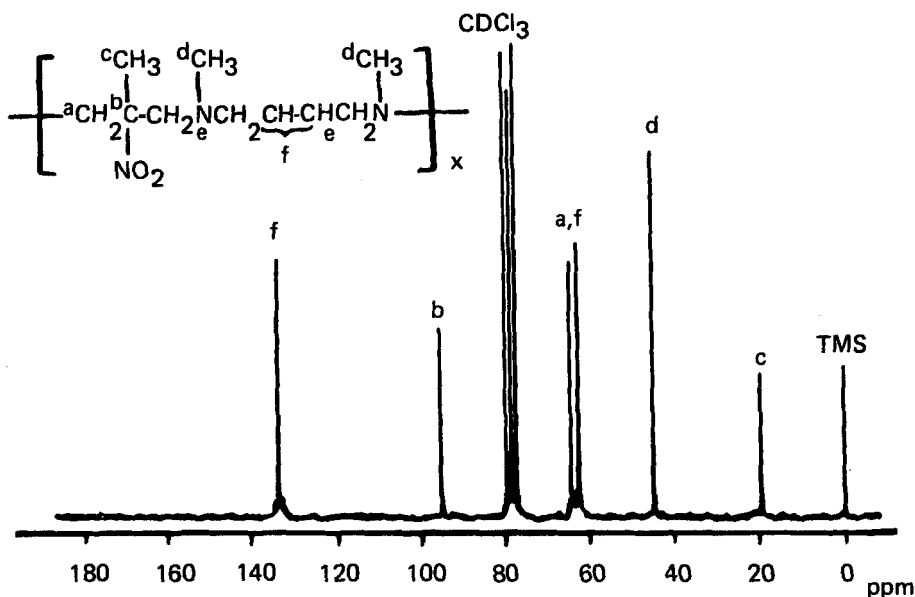


FIG. 2. Proton decoupled ^{13}C -NMR spectrum of Polymer (7) in CDCl_3 .

Compound (9) was also polymerized with piperazine under similar conditions. However, the white solid which precipitated from this reaction mixture was not soluble in most of the common organic solvents.

Reduction

Since the study of reduction of the model compound indicated that Raney nickel-catalyzed hydrogenation yielded the best results, the polymers were reduced under similar conditions. The IR spectra of these reduced polymers showed little nitro absorptions. For comparison, Polymer (6) was reduced by NaBH_4 in the presence of palladium/activated charcoal to yield an almost identical product. However, the relative intensities of the nitro absorptions are stronger than those of the previously obtained polymer.



$\text{R} = \text{(10) } -\text{CH}_2\text{CH}_2-$, $\text{(11) } -\text{CH}_2\text{CH}=\text{CHCH}_2-$, $\text{(12) } \text{-(CH}_2\text{)}_6-$

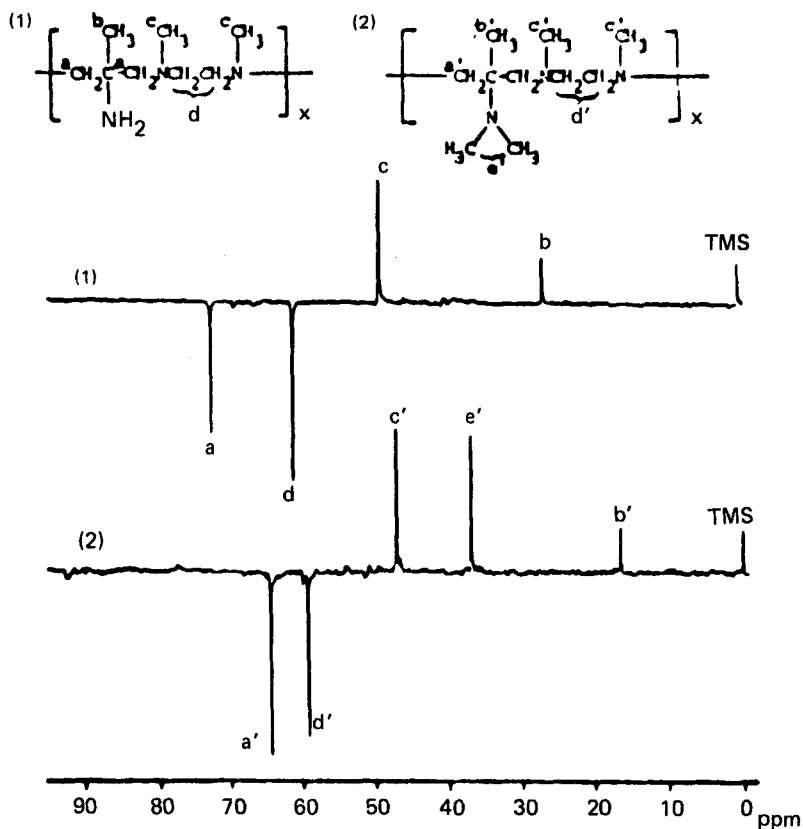
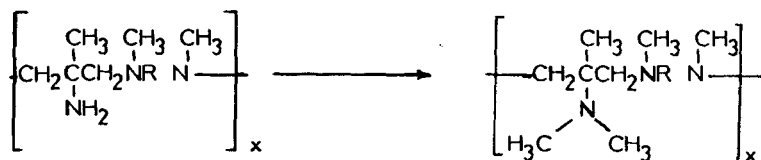


FIG. 3. INEPT ^{13}C -NMR spectra of Polymers (10) and (13).

Methylation

Methylation of Polymer (10) was carried out with sodium cyanoborohydride and formaldehyde [11, 12]. The NMR spectrum showed a shift of methyl and methylene peaks as well as a new methyl peak (Fig. 3). Polymer (10) was then methylated with formic acid and formaldehyde [10]. The resulting polymer was identical with the previously obtained polymer. Similarly, Polymer (11) was methylated by formic acid and formaldehyde to yield the desired polymer, whose structure was confirmed by NMR spectra.



R = (13) $-\text{CH}_2\text{CH}_2-$, (14) $-\text{CH}_2\text{CH}=\text{CHCH}_2-$

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