
Influence of potassium fluoride on the syntheses of methylpiperazine-modified poly(vinyl chloride)s for use as fixed-site proton carrier membranes

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Received 30 August 1996; accepted 15 May 1997

Abstract: Aminated poly(vinyl chloride) (PVC) membranes were prepared that had a Nernstian response over a wide range of pH. The reaction between PVC and methylpiperazine (MePIP) in dimethylformamide (DMF) was studied over a wide range of time and temperature, and in the presence of the catalyst, potassium fluoride (KF). Time, temperature, and KF increased the nitrogen (N) content of the resulting polymers, but sometimes at the expense of decreasing their specific viscosities (molecular weights). Activation energies of processes that occurred in different temperature ranges were estimated assuming an Arrhenius relationship. A Nernstian response occurred once the N content ap-

proached to about 0.3 w/w %, and was accelerated by the presence of KF at elevated temperatures. Increasing the N content above about 3% led to a loss of the Nernstian response either because of an increase in the double bond content and a subsequent decrease in polymer mobility, or because of a decrease in the molecular weight of the copolymer and concomitant difficulties in film preparation. © 1998 John Wiley & Sons, Inc. *J Biomed Mater Res*, **39**, 667–672, 1998.

Key words: amination; biosensors; catalyst; membranes; poly(vinyl chloride)

INTRODUCTION

In the past, potentiometric sensors were fabricated from highly plasticized poly(vinyl chloride) (PVC) membranes using mobile neutral carriers such as valinomycin and tridodecylamine to measure K^+ and H^+ analytes, respectively, after adding negative sites via the addition of a lipophilic salt, potassium tetrakis(*p*-chlorophenyl)borate. Unfortunately, the plasticizer along with the mobile carriers (both the neutral and negative sites) tend to leach out of the membranes and form an intervening layer that compromises biocompatibility, reduces analyte diffusivity, increases surface resistance, and consequently modifies response times and measured values. While the long-term goal is to integrate the sensor chemistry for electrophysiology into a single multifunctional molecule, the near-term goal is to attach functional groups or fixed sites onto the PVC backbone so that ionic charge can be selectively transported through the membrane. To

measure pH changes, the functional group of choice has been an amine.

In 1965, reactions of PVC with primary, secondary, and tertiary amines were studied by Teplyakov et al.¹ In 1987, Gurgiolo et al. filed a patent describing the attachment of amine groups onto the backbone of PVC.² A year later, Ma et al. fixed aminated sites onto PVC chains.³ Then, in 1990, Ma and Meyerhoff aminated PVC with both mono- and diamines by refluxing in methanol for 3–45 h.⁴ The pH response was linear, with slopes ranging from –24.0 to –55.1 mV/pH unit over a pH range from 5 to 12, although ranges >5 pH units were never found in any PVC membrane. In the same year, Kusy and Whitley began aminating PVC with 1,4-diaminobutane, followed by other members of that homologous series as well as with 1,2-diaminopropane, *trans*-1,4-diaminocyclohexane, 1,8-diamino-*p*-methane, and 1,4-bis(3-amino-propyl) piperazine.⁵ Two years later, Kusy et al. first aminated PVC powders based on the strong base of diethylenediamine (piperazine), and measured the electromotive force potentials of a series of electrodes prepared from the respective membranes.^{6,7} In these reactions, investigators noticed that not only did amination and a dehydrochlorination occur, but also crosslinking; con-

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sequently, they started to use *N*-methyl-diethyl-*endo*amine (methylpiperazine) (MePIP) for these reactions. All of the abovementioned reactions were run in either methanol (MeOH) or dimethylsulfoxide (DMSO).

The amination of PVC (the alkylation of the amine by PVC) is a well-known substitution-type or SN₂-type reaction.⁸ At the same time, however, elimination of HCl occurs as an E₂-type reaction. In the present work, the reaction between PVC and MePIP in a good aprotic solvent for PVC and solvent for MePIP [*N,N*-dimethylformamide (DMF)] was investigated versus time, temperature, and the presence of a catalyst [potassium fluoride (KF)]. In total, about 50 batches of powders were made. After preparing membranes from these formulations, their pH responses were measured in appropriate potentiometric cells. Consistent with the role of a catalyst, we found that Nernstian pH response could be attained for membranes cast from formulations made in the presence of KF for shorter reaction times and lower reaction temperatures.

EXPERIMENTAL

General amination procedure

For each batch, 0.02 mol of PVC beads (*M_w* = 110,000; Polyscience) was dissolved in 50 mL of DMF (HPLC grade; Sigma-Aldrich) in a round-bottomed flask that contained a polytetrafluoroethylene-coated magnetic stirring bar. Thereafter, 0.04 mol of 1-methylpiperazine (MePIP; Aldrich) was poured into the flask. In those experiments in which a catalyst was used, 0.002 mol KF (Fluka-Chemika) was added, after being dried at 100°C in a vacuum oven for 24 h. In some cases, which will be discussed later, 0.0004 and 0.01 mol of KF were also used. A Claisen adapter was connected to each flask. In the straight arm of this adapter, a second adapter was attached that had a gas inlet for argon and a center opening for a thermowell. A Graham condenser, which had a gas trap attached to its top opening, was connected to the curved arm of the Claisen adapter. Argon purged the system during the whole experiment. Temperatures were maintained from 50° to 110°C via a small heat tape. The temperature was regulated via a controller that used a thermocouple, which was placed in the thermowell. Each reaction time was measured in hours once the solution reached the desired reaction temperature (usually after 10 min). At the end of the desired time, which ranged from 1 to 30 h, the controller was turned off and 60 mL MeOH (HPLC grade; Mallinckrodt Chrom AR) was added to each flask to quench the reaction. The solutions with precipitated polymer were left standing for 24 h at room temperature (RT = 23°C). Then the solvent was removed with a Buchner funnel having a 3–15 mesh pore size. The polymer was washed by portions of MeOH until the pH of the filtrate became neutral (usually 250 mL) as determined with pHDrion paper. Finally, the

aminated PVC product (AmPVC) was dried in a vacuum at RT overnight.

Viscosity measurement

The specific viscosity η_{sp} of an 1% solution of AmPVC in tetrahydrofuran (THF; Aldrich) was measured with an Ubelode viscometer at 24°C according to the equation $\eta_{sp} = (t_s - t_{THF})/t_{THF}$, where t_s and t_{THF} are the flow times for the solution of AmPVC in THF (t_s) and THF (t_{THF}), respectively. For comparison, the unreacted, as-received PVC was also measured. Based on the standard deviations of all viscosity data, the precision of these measurements is $\pm 2\%$.

Nitrogen analysis

The nitrogen content, which indicated the possible extent of amination, was assayed using CHNS/O analyzer (2400 Series II; Perkin Elmer). Classical organic elemental analysis techniques are used in this analyzer: combustion in a pure oxygen environment to convert the sample elements to simple gases of CO₂, H₂O, and N₂. The system uses a steady-state, wavefront chromatographic approach to separate the measured gases. This approach involves separating a continuous homogenized mixture of gases through a chromatographic column. These gases are detected via thermal conductivity. Based on a secondary organic standard (acetanilide; Perkin-Elmer No. 0240-1121), each N analysis had an accuracy of ± 0.02 w/w %.

Membrane preparation

AmPVC, potassium tetrakis (*p*-chlorophenyl)borate (KTpC1PB; Fluka), and *o*-nitrophenyloctyl ether (*o*-NPOE; Fluka) were dissolved in THF in the proportions 100:2:200. The addition of the lipophilic salt KTpC1PB reduced the membrane resistance, anion interference, and response time. The highly polar *o*-NPOE was a monodisperse, low-molecular-weight plasticizer that provided good electrochemical characteristics in PVC membranes. For every 300 mg of polymer, negatively charged sites, and plasticizer, 4 mL of THF was added as a solvent for membrane casting. This solution was cast into a glass ring with an inside diameter of 30.0 mm, fixed on a glass plate for solvent evaporation. Membrane disks that were about 200 μ m in thickness were recovered following solvent evaporation of THF for about 48 h. Reproducible thicknesses were obtained by casting the same amount of solution with the same concentration into the same surface area.

Electromotive force measurements (EMF)

Ion-selective pH electrodes were fabricated from membrane disks 0.7 cm in diameter. These were all precondi-

tioned for a minimum of 24 h in a pH 7 Tris buffer, which contained sodium as an ionic background. Using an Ag/AgCl external reference electrode (Orion Model 90-09), the EMF was measured across the membrane disks at RT with a pH/m V-meter (Orion Model 720) after being placed in Tris buffer with a 140.0 mM Na⁺ ion background [10.0 mM NaOH + 130.0 mM NaCl + 10 mM tris(hydroxy-methyl) amino methane], which was adjusted over a pH range from 4 to 12. Readings were taken only after the potential change was <0.2 mV/min. The slope of each EMF-pH response was calculated along with the pH range over which linearity existed. These pH values were validated by means of a hydrogen-selective glass electrode (Orion Model 81-56).

RESULTS

Fifty MePIP-modified batches of PVC were synthesized and characterized in this work. These AmPVCs are powders with different colors that can range from white through yellows and orange to brown, depending on the particular reaction conditions. Nonetheless, all of them are soluble in THF.

The kinetics of N content in PVC at 50°, 60°, and 90°C in the presence of the KF catalyst and without it showed a linear dependence (Fig. 1). At all temperatures, the amounts of N accumulated at a given time were greater in the presence of KF than without it, but the differences diminished as temperature decreased. No substantial difference existed between the data obtained at 50° and 60°C.

Figure 2 shows the N content versus temperature for 3 h syntheses in the presence of KF and without it. Although these curves appear to be continuous, they may be viewed as representing three different parts:

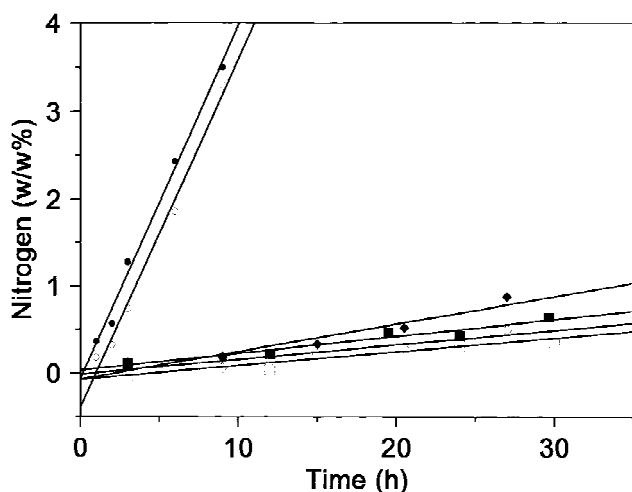


Figure 1. Kinetics of N content in AmPVC at 50° (■, □), 60° (◆, ◇), and 90°C (●, ○) in the presence of the KF catalyst (■, ◆, ●) and without it (□, ◇, ○). In all figures, DMF was the solvent and the molecular ratio of MePIP:PVC was 2:1.

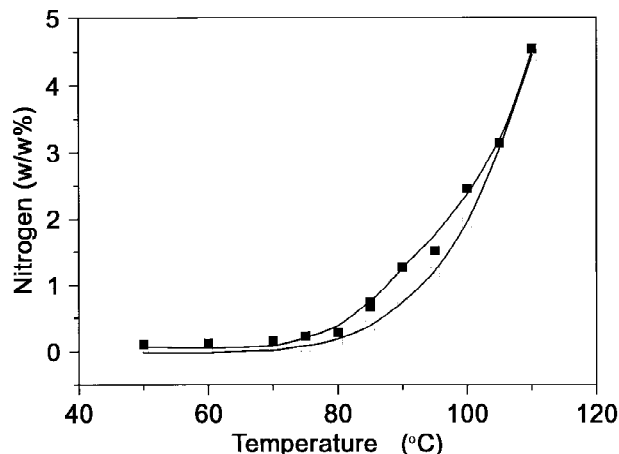


Figure 2. N content in AmPVC for 3-h syntheses in the presence of KF (■) and without it (□), after processing at different temperatures.

The first part corresponds to temperatures below 80°C, which is the glass transition temperature of PVC. Here, the N content is low and independent of temperature, regardless of the presence or absence of the catalyst. The second part occurs between 80° and 100°C, where the reaction goes faster as temperature increases. Here, the influence of the catalyst is substantial. The third part extends into the region of thermal degradation of PVC at the highest N content and is invariant, independent of KF.

The next three tables represent N content and viscosity data for prepared formulations. At high temperatures, Table I shows that the specific viscosity of AmPVC decreased as the reaction time increased. This effect was more pronounced in the presence of KF. Table II shows that when the reaction time was maintained constant, the viscosity of AmPVC decreased as the reaction temperature increased. The viscosity generally decreased with KF, regardless of its amount (Table III). Table III shows that the N content did not increase further once the level of KF exceeded 10 mol % of PVC.

Plots of the pH responses of AmPVC membranes

TABLE I
N Contents and Single-Point Viscosity Data for Some Formulations in the Presence and Absence of KF Versus Reaction Times at Different Temperatures

Temperature (°C)	Time (h)	With KF		Without KF	
		N (w/w %)	η_{sp}^*	N (w/w %)	η_{sp}^*
50	3	0.11	1.58	0.00	1.60
50	30	0.64	1.59	0.34	1.65
60	3	0.12	1.59	0.11	1.52
60	27	0.88	1.46	0.50	1.58
90	1	0.36	1.61	0.18	1.56
90	3	1.28	1.44	0.74	1.53
90	9	3.55	0.92	3.31	1.27

*For comparison, $\eta_{spPVC} = 1.69$.

TABLE II
N Content and Single-Point Viscosity Data for Some Formulations in the Presence and Absence of KF Versus Reaction Temperatures for 3-h Syntheses

Temperature (°C)	Time (h)	With KF		Without KF	
		N (w/w %)	η_{sp}^*	N (w/w %)	η_{sp}^*
50	3	0.11	1.58	0.00	1.60
60	3	0.12	1.59	0.11	1.52
80	3	0.29	1.41	0.18	1.53
90	3	1.28	1.44	0.74	1.53
105	3	3.14	0.83	3.08	1.14
110	3	4.55	0.65	4.43	0.78

*For comparison, $\eta_{spPVC} = 1.69$.

versus the duration of amination (Fig. 3) show that the pH responses increased sharply and approached Nernstian response at specific times which depended on both temperature and the presence of catalyst. When KF was present, this sharp increase generally took place at shorter reaction times than without it. As reaction times further increased, the pH responses decreased.

Plots of the pH responses of AmPVC membranes that were synthesized for 3 h versus reaction temperature (Fig. 4) show that a Nernstian response was attained at a lower temperature when KF was present. The very low pH responses of the two membranes, which were prepared from AmPVC made at 110°C, can be attributed to the poor structural quality of AmPVC membranes that were made from these low-viscosity (i.e., low-molecular-weight) polymers.

Finally, Figure 5 shows that a Nernstian response could be attained at a rather low level of N (about 0.3 w/w %), independent of the presence of catalyst. Further increases in the N contents, from about 0.3 to 3 w/w %, did not change the pH responses. As the N content increased further, the pH response decreased once again as a result of the poor structural quality of these low-molecular-weight polymers.

All membranes had wide linear pH response range, from pH 4–6 to pH 10–12. Among the 19 batches that approximated a Nernstian response, 17 exhibited it over the pH range from 4 to 11, from 5 to 12, or from 6 to 12.

DISCUSSION

Substitution, elimination, and degradation

Although the amination of a polymeric alkyl halide (alkylation of amine by polymeric halide) obeys the laws inherent to similar chemical reactions of low-molecular-weight substances, this reaction also differs from them. For high-molecular-weight compounds,

the present processes may be termed polymer-analogous reactions.^{9,10} Usually, these processes are accompanied by the formation of double bonds and the degradation of main chains. The specific unique feature of these reactions is that a process which takes place in one unit of the chain can affect the processes in other units.

In contrast to the reaction between low-molecular-weight alkyl halides and piperazine, the likelihood that PVC will approach 100% amination, even under optimum conditions, is virtually impossible. Reacting Cl groups of PVC are relatively small and close to each other, whereas piperazine rings are bulky. Thus, the appearance of the MePIP group instead of the Cl atom in one unit of the PVC chain sterically prohibits another such group in a neighboring unit. At best, they probably can be substituted in every third or fourth Cl group of PVC. Attempts to make a polymer with a high N content may lead to cleavage of the main chain, which apparently took place in some of our syntheses. In addition, the process of elimination of HCl decreases the level of amination as the resulting double bonds decrease the mobility of each macromolecule and promote another elimination reaction on the next unit of the same macromolecular chain. These reactions will autoaccelerate and ultimately lead to the formation of chains of double bonds (conjugated double bonds). The formation of conjugated double bonds is accompanied by changes in coloring of the polymer. In this work, the time, temperature, and catalyst intensified both substitution and elimination, as the formulations contained more N and became more brown.

Degradation of AmPVCs takes place both as an independent process caused by heating and stirring of the reaction mixture, and as a process accelerated by the substitution reaction. The presence of KF accelerates degradation as well. When AmPVCs are made in presence of KF, they have a higher N content, are more colored, and also are more degraded.

Effects of solvent and temperature

In this work, a higher N content was achieved in PVC than in previous work.⁷ This improvement was accomplished by using a very specific solvent, DMF. DMF is a good solvent for PVC, so a homogeneous reaction occurs in solution. Furthermore, by being an aprotic solvent, DMF promotes the SN2 reaction (amination), although temperature influences the yield of the reaction. The change that occurred at the glass transition temperature (80°C) can be explained by the different state of the PVC molecules in solution. Below 80°C, not every group is available to react with the nucleophilic reagent, because PVC can be dispersed in

TABLE III
N Content and Single-Point Viscosity Data for Some Formulations Made at 60° and 90°C Versus the KF Amount for 3-h Syntheses

Temperature (°C)	Without KF		2 mol % KF from PVC		10 mol % KF from PVC		50 mol % KF from PVC	
	N (w/w %)	η_{sp}^*	N (w/w %)	η_{sp}^*	N (w/w %)	η_{sp}^*	N (w/w %)	η_{sp}^*
60	0.11	1.59	0.06	1.49	0.12	1.52	0.13	1.47
90	0.74	1.53	0.76	1.47	1.28	1.44	1.29	1.42

*For comparison, $\eta_{spPVC} = 1.69$.

a colloidal state. Above 80°C, PVC can be dispersed in a molecular state, so that almost all Cl groups are available for amination—at least in principle.

Attempts were made to estimate the activation energies, assuming an Arrhenius relationship of all processes that occurred between 80° and 100°C and above 100°C (Fig. 6). Between 80°C and 100°C, the activation energies of amination in the presence and absence of KF are 26.6 and 34.5 kcal/mol, respectively. Above 100°C, the activation energies are 17.4 and 23.3 kcal/mol, respectively. The lower values of activation energies at high temperatures occur because degradation dominates. Thus, the polymer has a lower molecular weight and more sites available, since these reaction sites are sterically less restricted near the ends of the polymeric chains.

pH response and properties of polymers

The present work shows that the pH response of membranes depends on the structure of the modified PVC from which they are made. At the very least, three factors influence the pH response: the N content,

the double bond content and its distribution, and the polymeric molecular weight.

Given the present composition of our membranes, which intentionally lacked mobile neutral carriers, we had to make membranes with fixed sites from an N-containing polymer if we wanted the slope of the EMF-pH response to differ from zero. The growth of N in AmPVC occurred gradually, but the pH response changed suddenly at an N content of about 0.3 w/w %. That observation suggests a cooperative phenomenon within the modified PVC. Probably, the growth of the N content was accompanied by other changes in the AmPVCs—for example, an opening up of the structure or an increase in mobility of the chain—and as a consequence, a change in the glass transition temperature. Unfortunately, this factor is not yet adequately understood. Thus, the influence of the double bond content and its distribution is not yet clear. At present, we can only say that the best properties have AmPVCs with a moderate brown color, which results from excessive elimination. Finally, the molecular weights of these AmPVCs are of great significance, since films must be fabricated from structurally sound materials. The molecular weight has to be adequate to make strong films from these polymers, but not so great as to impede its fixed-site mobility—as in crosslinked chains. This factor requires further investigation as well.

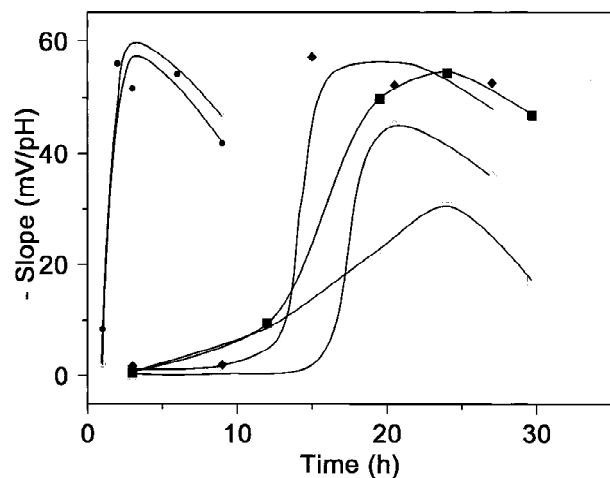


Figure 3. Slopes of the potentiometric responses of the membranes cast from AmPVCs versus the duration of amination at three different temperatures: 50° (■, □), 60° (◆, ◇), and 90°C (●, ○), in the presence of KF (■, ◆, ●) and without it (□, ◇, ○).

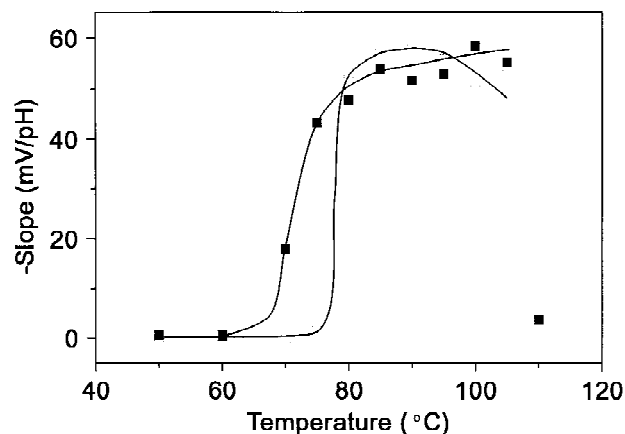


Figure 4. Slopes of the potentiometric responses of the membranes cast from AmPVCs that were synthesized for 3 h versus the temperature of amination in the presence of KF (■) and without it (□).

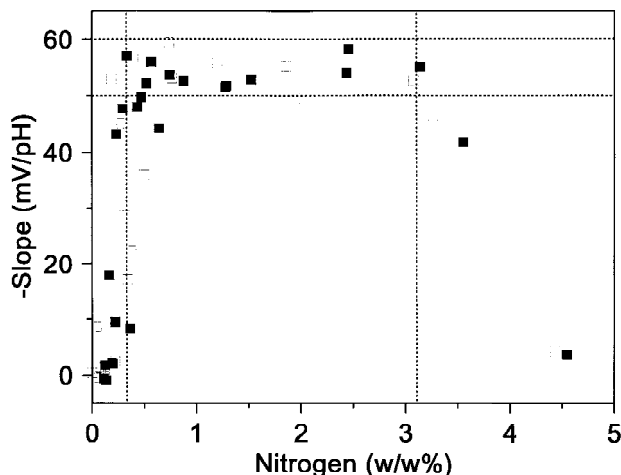


Figure 5. Slopes of the potentiometric responses versus N content for all formulations in the presence of KF (■) and without it (□). The two horizontal and vertical dotted lines encompass the region of acceptable responses.

Significance and future work

The pH responses and properties show that certain catalyzed MePIP-modified PVCs may be very promising for proton carrier membranes for pH electrodes or other enzyme-protein reactions for which the ultimate analyte is a proton. As such, these polymers can provide the foundation upon which further configurational modifications can be achieved. These include determining which plasticizer moiety would be most appropriate to accommodate either into the backbone of the polymer; or, more likely, what interpenetrating vinyl polymer would be best integrated into the sensor chemistry to facilitate proton transfer without the detrimental effects of leaching. This amination work represents the achievement of the first polymer requirement.

CONCLUSIONS

Aminated PVCs can be prepared using MePIP in a good aprotic solvent, DMF, and presence of the catalyst KF. The conditions of amination of PVC by MePIP in DMF in the presence or absence of the catalyst KF have been documented. The N content was observed over a wide range from 0 to 4.5 w/w %.

The amination (via N content) and degradation (via single-point viscometry) have been studied versus time, temperature, and the presence of KF. All three factors increase N content and degradation.

A Nernstian pH response can be attained for membranes cast from AmpVCs with N contents between about 0.3 and 3 w/w % and a moderate brown color.

A Nernstian pH response can be attained for membranes cast from formulations made in presence of KF

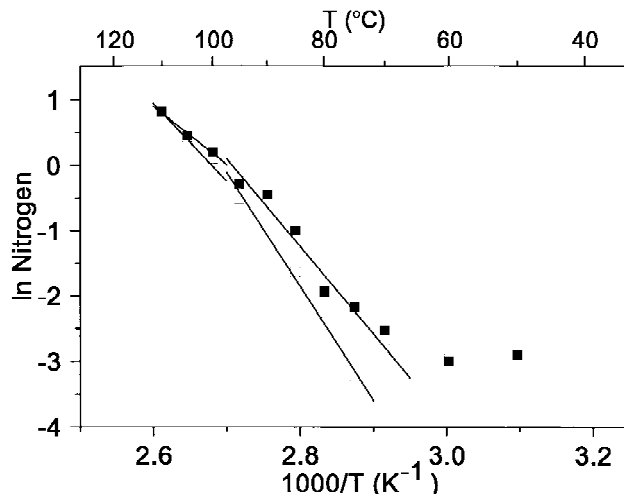


Figure 6. Arrhenius plot of one-half the fraction of nitrogen versus $1/T$ for amination between 80° and 100°C (lower lines) and above 100°C (upper lines) in the presence of KF (■) and without it (□).

for shorter reaction times and lower reaction temperatures.

The activation energies of amination were estimated for various temperature ranges: 26.6 and 34.5 kcal/mol between 80° and 100°C, and 17.4 and 23.3 kcal/mol above 100°C in the presence and absence of KF, respectively.

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