Synthesis of 1,3-Oxazole and Benzimidazole Pendant Groups From Polyacrylonitrile Hydrolysis Products

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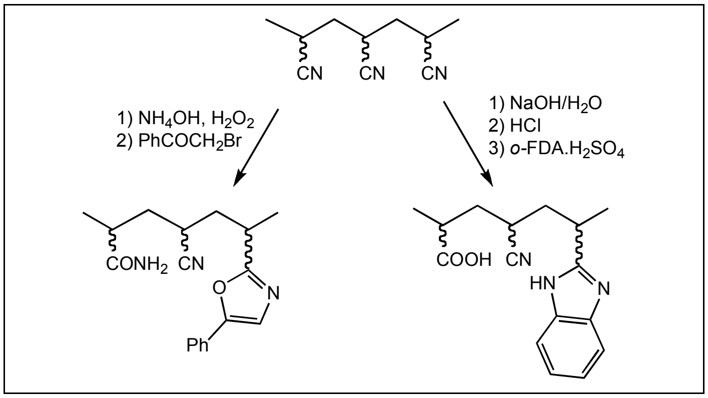
Received May 31 2007



New terpolymers containing heterocyclic pendant groups, such as 1,3 oxazole and benzimidazole are obtained by hydrolysis of polyacrylonitrile (PAN). These materials are spectroscopically characterized and their solubility, viscosity and thermal behavior are analyzed.

J. Heterocyclic Chem., **45**, 429 (2008).

INTRODUCTION

When commercial homopolymers are chemically modified, they possess interesting properties quite different from their precursors. For example, polyacrylonitrile (PAN) is modified attaching tetrazole units to the polymer backbone, producing in this way polyelectrolyte properties, close to polyacrylic acid [1]. These properties can be regulated through reaction time. This is an important advantage of this methodology since the traditional strategy of mixing monomers has its limitations because the relative reactivity of the different monomers restricts the number of units of each kind included in the copolymer chains. In previous works, synthesis of terpolymers containing 3,5-disubstituted 1,2,4-, 1,3,4-oxadiazole, and 1,3-oxazole as pendant groups on the heterocycles were described [2-4]. The rheological properties as well as their thermal stability were studied, showing remarkable differences from the starting materials. In these opportunities, we pointed out that the changes in behavior among the same terpolymer series had to do with the substituents variations or conversion time modifications. When conversion times were altered, the most affected property turned out to be the rheological one.

Oxazole were first synthesized by Zinin in 1840 [5]. These heterocycles show typical aromatic properties. In the present work, one of the objectives was the synthesis of terpolymers containing 1,3 oxazolic pendant groups attached to the polymer backbone. Among the different methods to obtain 1,3-oxazole, the reaction of amides with α−haloketones or α−haloaldehydes [6-9] was the method chosen. The synthetic pathway was based on basic hydrolysis of polyacrylonitrile (PAN) as the first step of reaction. The copolymer obtained contains amide groups in its structure. Afterwards, the terpolymer containing 1,3-oxazole rings was obtained. In this case, the heterocycles are linked to the polymer chain instead of being attached to a small molecule.

On the other hand, due to the broad spectrum of pharmacological activities that benzimidazoles possess, their synthesis was explored by several authors. In 1957, Leavitt *et al.* obtained 2-aryl and 2-alkyl-substituted benzimidazoles using polyphosphoric acid as condensing agent [10]. Then, the synthesis of benzimidazoles by condensation of *o*-phenylenediamine with organic acids was developed by Hooper and coworkers [11]. In the present work, different conversion time terpolymers, containing benzimidazole pendant groups coming from *o*-phenylenediamine condensation with the carboxilic groups formed during the partial basic hydrolysis of PAN followed by neutralization is also reported. Again, we took advantage of reactions previously described for small molecules to synthesize benzimidazole attached to macromolecules.

Apart from the synthesis of these new terpolymers and taking into account that the properties of these materials are often different from their precursors, the effect of pendant groups on viscosity behavior and thermal stability were also analyzed.

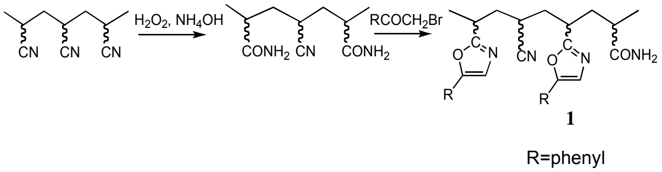
RESULTS AND DISCUSSION

In a previous paper, we described the polyacrylamide (PAM) modification to obtain copolymers of amide-5-phenyl-1,3-oxazole (APOC) [4]. Now, we describe the synthesis of nitrile-amide-4-phenyl-1,3-oxazole terpolymer (NAPOT), using in this case PAN as starting material. Scheme 1 presents the synthetic pathway carried out to arise the 1,3-oxazolic derivatives:

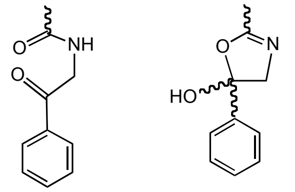
In the first step of NAPOT synthetic route, polyvinyl-amide-nitrile copolymer was obtained from partial basic hydrolysis of PAN with ammonia hydroxide in presence of hydrogen peroxide. The second step involves the condensation of the amide groups with an α-haloketone to give the 2,4-disubstituted-1,3-oxazole derivative.

The spectroscopical technique of ^{13}C nmr was crucial to confirm the presence of heterocyclic rings in the terpolymers. The structure of NAPOT was confirmed by this technique (see Experimental). All the spectra were performed using deuterated dimethyl sulfoxide-d$_6$ as solvent. The signals appearing at 139.3, 147.8 and 175.4 ppm correspond to C5, C4 and C2 of 1,3-oxazole ring. Interestingly, apart from the oxazolic pendant groups, whose structures are stabilized by resonance due to their aromaticity, the spectrum also showed some signals that were attributed to the presence of an intermediate cyclic structure. This intermediate structure is the consequence of the lack of elimination process in some of the heterocycles present in the backbone. Figure 1 shows the possible structure for the intermediate heterocycle. The signals appearing at 66.5 ppm may correspond to C5 of the intermediate cyclic structure attached to the copolymer, and the peak at 88.7 ppm to C4 of the same structure.

Scheme 1



The signals appearing between 192.6-200 ppm could be attributed to carbonyl carbons coming from the intermediates of reaction (intermediate I) at different conversion times. These possible intermediates are shown in Figure 1 and their presence was confirmed by ^{1}H nmr technique.



I II

Figure 1

^{1}H nmr spectra were performed in dimethyl sulfoxide-d$_6$, but drops of deuteriomethanol, hydrochloride acid and sodium hydroxide both prepared with deuterated water were added to each nmr experiment. The spectra obtained were compared. Although these spectra were too complex to elucidate the structure of this terpolymer, they helped to confirm the presence of carboxyl and hydroxyl groups.

In presence of deuteriomethanol, deuterated hydrochloric acid and sodium hydroxide, peaks at 6.99, 7.27 and 10.65 ppm disappeared. Thus, the lack of these two first signals may correspond to hydroxyl groups attached to the heterocycle (intermediate II). They suffered H interchange in these conditions. On the other hand, the absence of 10.65 ppm peak may indicate the presence of some carboxyl groups attached to the polymer structure that may come from partial hydrolysis of some amide groups as consequence of unexpected side reactions.

With regard to solubility, NAPOT precursor, as it was predictable, turned out to be soluble in water and aqueous solutions, because it comes from high degree of transformation of nitrile groups into amide ones. NAPOT of 2 hours conversion time is insoluble in water and solvents with rather low polarity, slightly soluble in aqueous solution of hydrochloride acid (1 *N*) and soluble in sodium hydroxide (1 *N*) solution. It is also partially soluble in aprotic solvents such as dimethyl sulfoxide or dimethylformamide.

The viscosity developed by two hours conversion time NAPOT in alkaline aqueous solution (NaOH 1 *N*), was 3 cp which turns out to be really low if it is compared with the viscosity developed by a copolymer of amide-4-phenyl-1,3-oxazole (APOC) of the same conversion time (235 cp) [4]. Probably, the quantity of carboxylic groups coming from the hydrolysis of nitrile present in NAPOT is such, that the terpolymer is solved in basic medium and the repulsive charges between chains makes them get away avoiding their interaction and gel formation.

Calorimetric (DSC) results showed that NAPOT precursor is stable up to 90°C approximately. Above this temperature solvent elimination took place, especially bonded water.

In general, polymers that contain a large number of amide groups in their structure when they are heated above 250°C could suffer cyclization reactions followed by ammonia liberation [12]. Above 350°C large scale thermal degradation occurs with liberation of hydrogen, carbon monoxide and ammonia [13]. Although the DSC thermogram for this material is quite complex, several endothermic peaks, appearing between 170 and 250°C, support these assumptions.

The DSC curve shows a broad initial endotherm corresponding to the release of moisture and bonded water (Figure 2). A broad endotherm with its maximum at 224°C should be the product of cyclization reactions mentioned above and over 360°C other complex degradative reactions took place.

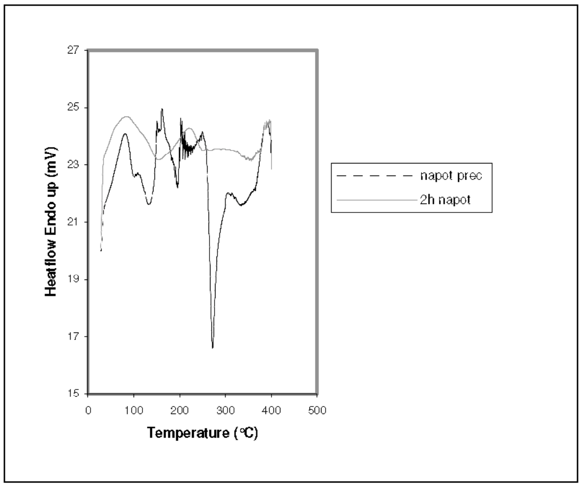
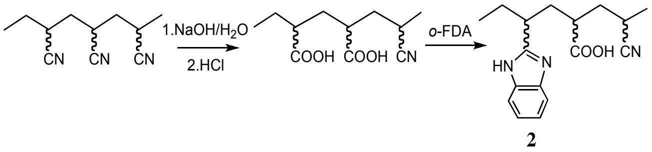


Figure 2

On the other hand, nitrile-carboxyl-benzimidazole terpolymer (NCBT) was synthesized within two steps. The first one involves the basic hydrolysis of some nitrile groups to obtain carboxylic groups in the polymer backbone, previous neutralization with hydrochloric acid. After having prepared *o*-phenylenediamine sulfate [11], the copolymer was treated with this reactant to obtain the NCBT. Scheme 2 shows the synthetic pathway:

Scheme 2



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Again, the structures of NCBT at different conversion times were confirmed by ^{13}C nmr technique and the conversion degrees were calculated by elemental analysis.

The solubility of the NCBT series is quite similar to NAPOT. They are insoluble in organic solvents of medium to low polarity, but soluble in aprotic polar solvents such as dimethyl sulfoxide or dimethylformamide. They are also soluble in alkali aqueous solution and partially soluble in acid medium and slightly soluble in hot water.

The results of elemental analysis for NCBT series and its precursors are listed in Table 1.

According to these results, the NCBT precursor that showed the highest conversion yield was the one corresponding to two hours conversion time. The precursor of six hours exhibited a comparable conversion yield, and no conversion occurred during the first hour of reaction. Thus, the percentage of carbon and nitrogen of one hour conversion time NCBT precursor was almost the same as PAN (starting material).

With respect to NCBT, two hours conversion time terpolymer showed a conversion yield of 24%. However, six hours conversion time NCBT showed a remarkably lower value. This difference might come from the formation of cyclic anhydrides between two neighboring carboxylic groups attached to the polymer chains. When the temperature is high and the reaction time is incremented, this kind of side reaction takes place. This cyclization avoids the later attack of *o*-phenylenediamine sulfate to carboxylic groups lowering in this way the final conversion yield. This assumption was confirmed by IR spectra of six hours conversion time NCBT precursor where peaks at 1822 and 1748 cm^{-1} were observed. These signals correspond to stretching vibrations of anhydrides C=O.

Table 1

Elemental analysis

	Composition (wt%)			Yield (wt%)
Compounds	**C**	**N**	**H**	
PAN	64.7	18.4	5.3	100
NCBT prec 1h	65.2	18.8	5.7	0
NCBT prec 2h	42.3	5.3	5.4	71.3
NCBT prec 6h	43.5	5.9	5.1	68.0
NCBT 1h	65.3	18.6	5.8	0
NCBT 2h	52.3	9.9	5.5	24.0
NCBT 6h	47.1	7.1	6.0	9.0

Regarding viscosity measurements, the values obtained for NCBT series are listed in Table 2. It can be observed that the viscosity of one hour conversion time NCBT and its precursor is almost the same, indicating that these two compounds are the same polymer. This is evidence that no reaction occurred during the first hour of reaction. With respect to precursors, their viscosity values were quite low. This trend could be explained by saying that great amount of carboxylic groups were formed during the first step of reaction, causing the copolymer solubilization when it is put into the basic solution. When bezimidazole groups are present in the terpolymer the viscosity had a slight increment but, according to the elemental analysis results, the conversion of carboxylic groups into the heterocycles was rather low not affecting in a remarkable way the viscosity values of the NCBT in any of the conversion times studied.

Table 2

Viscosity data for NCBT series

Compound	Viscosity (cp)
1h NCBT precursor	77
2h NCBT precursor	6
6h NCBT precursor	5
1h NCBT	74
2h NCBT	10
6h NCBT	8

Figure 3 corresponds to DSC thermograms of NCBT series. Thermal analysis showed that one hour conversion time precursor and its terpolymer has the same profile. Again, this is another proof that no reaction occurred during the first hour of heating. In all cases, endothermic peaks below 100 °C that come from the evaporation of bonded water and moisture are observed. Regarding to precursors, broad endothermic peaks between 150 and 250 °C were seen. They come from the dehydration process of carboxyl groups forming glutaric anhydride [14]. Then, above 250°C, water and carbon dioxide is generated. Chains scission occurs above 350°C [15]. NCBT of two and six hours conversion time also showed endothermic peaks over 200°C corresponding to terpolymer degradation.

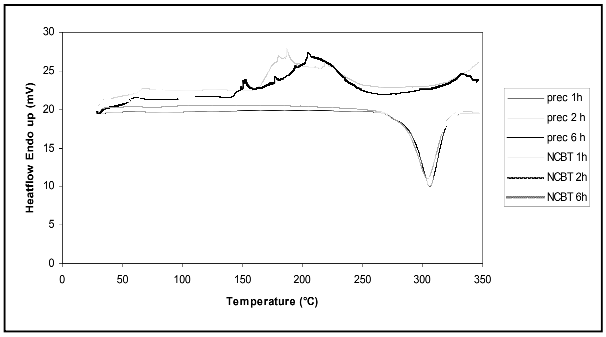

Figure 3

In conclusion, we can extend the traditional methodology to synthesize 1,3-oxazole and benzimidazole from small molecules to macromolecules. The properties of these new materials are different from the starting material. Besides, some different terpolymers could be obtained by treating PAN in basic media only by changing the reactants used, reaction times and temperature. It is interesting to point out the presence of different reaction intermediates and the lack of elimination process in some of the NAPOT´s heterocycles. The groups that surround the intermediate structure must be stabilizing this form. Besides, the reaction media is water which is not favorable for the elimination process.

With regard to thermal analysis, NCBT as well as NAPOT released moisture and bonded water during heating. Both terpolymers presented decomposition above 200 °C and no remarkable difference in stability existed between terpolymers of NCBT series.

The viscosity values turned out to be low in NCBT series, not showing any tendency with conversion time. NAPOT also presented a very low viscosity value.

EXPERIMENTAL

General Methods. DSC measurements were performed on a Perkin-Elmer 6 Pyris thermal analyzer. One dimensional ^{13}C nmr (50 MHz) and ^{1}H nmr (200 MHz) spectra were measured with a Bruker spectrometer in hexadeuterated dimethyl sulfoxide. The elemental analysis was performed on a Carlo Erba EA 1108. The infrared spectra were obtained from a Nicolet FT-IR Instrument Model: 510P. For this purpose, KBr and solid polymer pellets were prepared.

Regarding to viscosimetric assays, they were performed on a FANN 35S viscosimeter at 25 ºC and 31.42 sec^{-1} of shear rate, and solutions of 50 ml of NaOH 1 *N* and 1 g of the terpolymer were prepared.

Synthesis of terpolymers containing heterocycles pendant groups.

Nitrile-amide-4-phenyl-1,3-oxazole terpolymer (1). PAN powder (5 g) was added together with 200 ml of NH_4OH into a 500 ml glass flask equipped with an addition funnel with pressure-equalization arm under stirring and water bath. The whole system was heated to 50 °C. Aliquots of 10 ml of H_2O_2 were added to the flask helped by the addition funnel, until the reactants were soluble (*ca.* 170 ml of H_2O_2). Then, the solvent was evaporated under reduced pressure and a yellowish solid was obtained (Scheme 1, first step).

The solid coming from the first step (2.4 g) was added together with 100 ml of water into a 500 ml flask under stirring and reflux. Then, 6.7 g of 2-bromoacetophenone were added to the solution. A sample was taken at 2 hours conversion time. The sample was poured in acetone and the insoluble resultant solids were filtered under vacuum and washed with ethanol. The copolymer obtained was dried with a vaccum pump to constant weight. Terpolymer **1** was isolated as an amorphous solid, ^{13}C nmr (dimethyl sulfoxide-d$_6$): δ 27.3 (CH_2), 34.7 (CH), 120.2 (C≡N), 125.3-135.0 (aromatic carbons), 139.3, 147.8, 175.4 (1,3-oxazolic carbons), 176.2 (amide carbons) and 192.6-200 ppm (carbonyl carbons); ir: 1600-1690 (C-N of amide), 2240 (C≡N), 3292 (HN of amide) cm^{-1}. *Anal.* Found: C, 58.1; H, 5.9; N, 17.0. Conversion degree: 17.3.

Nitrile-carboxyl-benzimidazole terpolymer (2). PAN powder (6 g) was added together with 300 ml of NaOH 1 *N* into a 1000 ml flask. The whole system was heated at 80 °C with a water bath under mechanical stirring. Aliquots of 100 ml were taken at different reaction times (one, two and six hours). These portions were neutralized with HCl 1 *N* to obtain the nitrile-carboxylic acid copolymers.

In order to condensate the copolymers formed in the previous step with the diamine, *o*-phenylenediamine sulfate was prepared.

A mixture of *o*-phenylenediamine sulfate (1 g) and copolymer (2 g) was heated under reflux with 30 ml of ethylene glycol for

3 h. Then, the reaction mixture was cooled to room temperature and poured into 50 ml of water. The pH of the solution was adjusted to 9 with NaOH. The product was filtered and washed with ethanol. The copolymer obtained was dried with a vacuum pump to constant weight. Terpolymer **2** was isolated as an amorphous solid, ^{13}C nmr (dimethyl sulfoxide-d_6): δ 26.1-28.5 (CH_2), 31.5-37.0 (CH), 115.0, 120.4, 122.5, 136.8, 156.0, (heterocyclic carbons), 174.0-176.0 ppm (COOH); ir: 3448 (HO of carboxyl groups), 2915, 2847, 2243 (C≡N), 1710, 1595, 1429, 1014, 780 cm $^{-1}$.

Acknowledgements. Financial support from CONICET, Agencia Nacional de Promoción Científica y Tecnológica (ANPCyT, project 06-13922) and UBA are gratefully acknowledged. The authors thank CONICET-San Antonio-Pride S.A. for the fellowship to I.N.V. Dr. N. B. D´Accorso is a research member of CONICET.

REFERENCES

[1] Annenkov, V. V.; Kruglova, V. A.; Alsarsur, I. A.; Shvetsova, Zh. V.; Aprelkova, N. F.; Saraev, V. V. *Vysokomol. Soed,* **2002**, *44*, 2053.

[2] Vega, I. N.; Morris, W.; D´Accorso, N. B. *React. Funct. Polym.* **2006**, *66*, 1609.

[3] Vega, I. N.; Sánchez, L.; D´Accorso, N. B. *J. Heterocyclic Chem.* **2007**, *44*, 389.

[4] Vega, I. N.; Sánchez, L.; D´Accorso, N. B. *React. Funct. Polym.* **2007**, doi:10.1016/j.reactfunctpolym.2007.09.003 (in press).

[5] Zinin, N. *Ann.* **1840**, *34*, 186.

[6] Blümlein, F. *Ber.* **1907**, *40*, 2578.

[7] Hantzsch, A. *Ber.* **1888**, *21*, 942.

[8] Lewy, M. *Ber.* **1887**, *20*, 2576.

[9] Lewy, M. *Ber.* **1888**, *21*, 924.

[10] Hein, D. W.; Alheim, R. J.; Leavitt, J. J. *J. Amer. Chem. Soc.* **1957**, *79*, 427.

[11] Dubey, P. K.; Kumar, R.; Kumar, C. R.; Grossert, J. S.; Hooper, D. L., *Synth. Comm.* **2001**, *31*, 3439.

[12] Silva, M.; Dutra, E.; Mano, V.; Machado, J. *Polym. Deg. Stab.* **2000**, *67*, 491.

[13] Minsk, L.; Kotlarchik, C.; Meyer, G.; Kenyon, W. O. *J Polym. Sci. Polym.* **1974**, *12*, 133.

[14] Li, L.; Hsieh, Y-L.; *Polym.* **2005**, *46*, 5133.

[15] de la Fuente, J. L.; Wilhelm, M.; Spiess, H. W.; Madruga, E. L.; Fernández García, M.; Cerrada, M. L. *Polym.* **2005**, *46*, 4544.