Solid Support for High-Throughput Screening of Conducting Polymers

Diego F. Acevedo, María C. Miras, and César A. Barbero*

Departamento de Química, Universidad Nacional de Río Cuarto, 5800-Río Cuarto, Argentina

The increased use of combinatorial synthetic methods in drug discovery[1−3] is based on performing the synthetic reactions in the solid phase on polymer beads or crowns (pins). The method allows easy handling of the reaction system, avoiding complex workout.[4] The procedure was devised after the use of cross-linked polystyrene beads in peptide synthesis by Merrifield and co-workers.[5] The most common form of solid support consists of polymer (e.g., cross-linked polystyrene) beads derivatized with reactive groups (e.g., chloromethyl groups). On the other hand, the use of polymer films has been studied to a much lower extent.[6]

Although combinatorial methods in materials research were used in the 1970s by Hanak,[7] the use of the combinatorial chemistry to determine new materials, such as polymers or catalysts, is less explored than its drug synthesis counterpart.[8] Recently, it has been shown that different polymers could be synthesized and screened in a combinatorial way.[9]

Intrinsic conductive polymers (ICPs) have attracted attention not only for the fundamental scientific interest, but also for practical applications, because of their novel properties.[10] Post-modification is a promising method for introducing novel properties to the polymer backbone, because the conductivity of the polymer is usually less disturbed.[11] Keeping this in mind, we propose to achieve chemical modification of ICP backbones using a combinatorial approach. The application of combinatorial synthesis to the post-modification of IPC is hindered by the lack of a suitable method to support the polymer in a rigid matrix such as Merrifield resins. This is relevant because there are few reports on the production of conjugated polymers by combinatorial methods,[12] probably because of the problems inherent to working from solution-based synthesis.

Here, we report a novel solid support of conducting polymer films, which allows high-throughput screening of the polymer modification using Fourier transform infrared (FT-IR) and/or ultraviolet−visible (UV−vis) spectroscopy. Low-density polyethylene (LDPE) thin films are used to support the conducting polymer during modification of the conductive polymer backbone. The high transparency of the support polymer in the mid-infrared (mid-IR) and UV−vis region of the spectrum allows us to test the occurrence of

modification reactions. We show that this method can be used with different conducting polymers (polyaniline, polypyrrole, etc.).

To produce a solid support for the polymers, thin (2 μm thick) films of LDPE (Polisur, Argentina) were immersed in a stirred polymerization solution to produce a supported film of ICPs. Polyaniline and polypyrrole were produced by the oxidative polymerization of monomer solutions, which was performed as described previously.[13,14]

To modify the polymers, we used two types of reactions: diazonium ion coupling reactions[15,16] and nucleophilic addition.[17,18] In the first case, diazonium ions, which are produced by diatozation of primary aromatic amines or azo dyes bearing primary amino groups,[19] were made to react with polyaniline (PANI). Nucleophilic addition was produced by reacting nucleophiles (amines, thiols, sulfinic acids, carbanions, cyanide ion, sulfite ions, etc.) with the oxidized form of polyaniline[18] or polypyrrole.[20] The chemical structures of the modified polymers synthesized using those reactions are shown in Scheme 1.

To examine the modification reactions, we measured the FT-IR spectra of the conducting polymer films supported on LDPE. As Figure 1 shows, LDPE has few bands in the mid-IR region. [The band at 2920 cm^{-1} could be assigned to the asymmetrical stretching mode C−H of the methyl group, the band at 2850 cm^{-1} to the symmetrical stretching mode C−H of the methyl group, the band at 1463 cm^{-1} to C−H bending vibrations of the methyl group, and the band at 710 cm^{-1} to the rocking vibration of the methylene group.] Therefore, the IR spectra of the supported film can be easily measured without a cumbersome workout. Figure 1 also shows the FT-IR spectrum of a PANI (emeraldine base) film deposited on LDPE, with the LDPE absorption subtracted. The spectrum of PANI shows all characteristic bands of the polymer: at 1588 cm^{-1} (assigned as the C=C stretching of the quinoid rings), 1496 cm^{-1} (the C=C stretching of benzenoid rings), 1306 cm^{-1} (the C−N stretching mode), and 1164 cm^{-1} (N=Q=N, where Q represents the quinoid ring).[21] The fact that all IR bands of PANI can be assigned is a good evidence that LDPE can be used as a support for studies regarding the modifications on the polymer skeleton. Only in the region between 2750 and 3050 cm^{-1}, the strong C−H stretching vibration of the LDPE could not be subtracted; therefore, new bands due to the modification reaction could not be detected in that region.

It has been shown that deposition of PANI onto solid materials is quite reproducible;[22] therefore, modified and unmodified polymer films could be safely compared. The films are washed with excess water in an ultrasonic bath for 15 min to ensure that no reactant is retained in the film.

Figure 2a shows the FT-IR spectrum of a PANI film deposited on LDPE and modified by reaction with the diazonium salt of 4-aminobenzenesulfonic acid (**I**). Beside the typical bands due to polyaniline (see previous discussion), new bands can be observed at 1033 and 1008 cm^{-1}, which

* To whom correspondence should be addressed. Tel.: +54 358 4676157. Fax: +54 358 4676233. E-mail address: cbarbero@ exa.unrc.edu.ar.

Scheme 1. Chemical Structure of the Polymers Whose Spectra Are Shown in This Report.[a]

I   II

III   IV
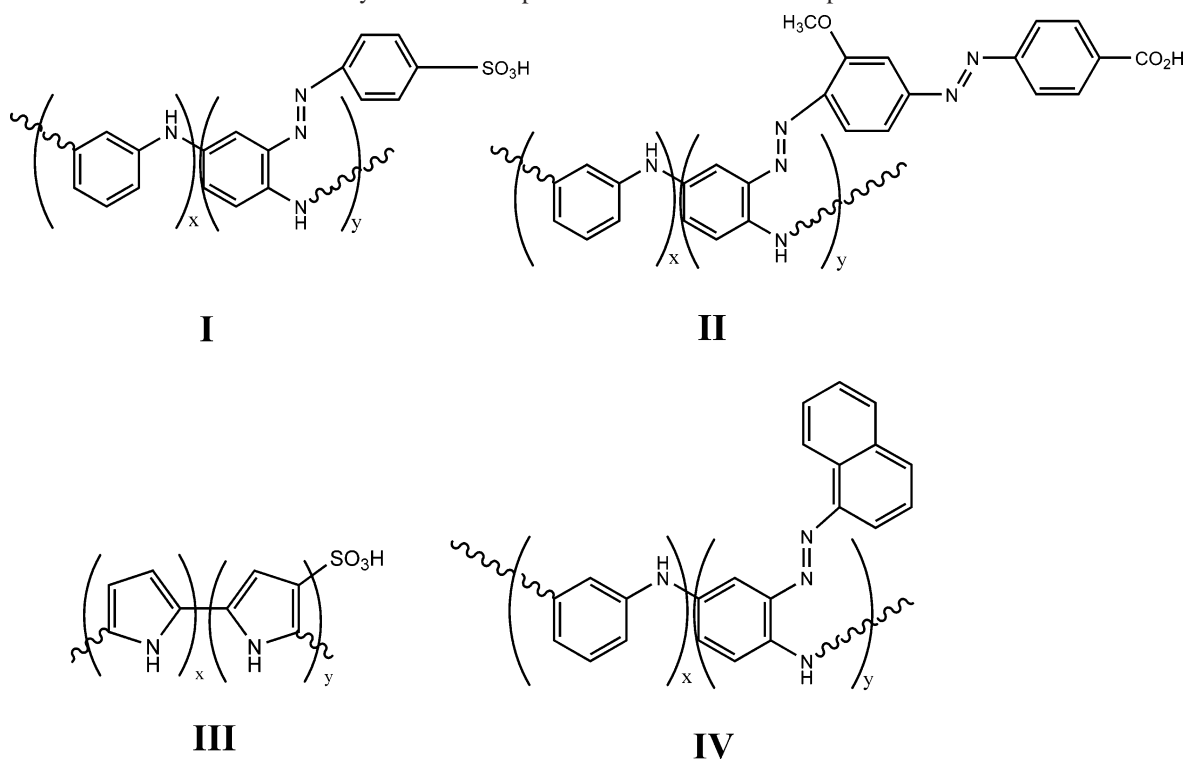
[a] The subscripts x and y denote the relative proportion of unmodified and modified polymer units, respectively.
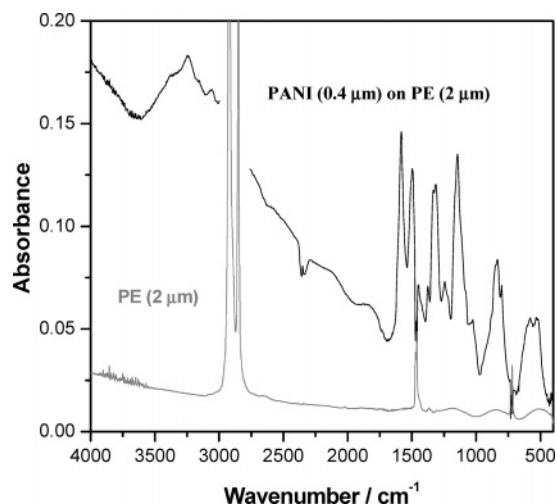

Figure 1. Fourier transform infrared (FT-IR) spectra of a low-density polyethylene (LDPE) (gray line) and a polyaniline (PANI) film deposited onto LDPE (black line). In the latter spectra, the spectrum of LDPE was subtracted.

could be assigned to the symmetric stretching of the S(=O)$_2$ group.[23] Another band, at 634 cm^{-1}, is assigned to the C$-$S stretching of the sulfonate group.

Figure 2b shows the FT-IR spectrum of PANI film (deposited on LDPE) modified by reaction with the diazonium salt of 4-(4-amino-2-methoxy-phenylazo)-benzoic acid (**II**). In this case, a new band (compared with PANI) appears at ca. 1692 cm^{-1}, which could be assigned to the stretching of the >C=O moiety of the carboxylic group present in the group added by coupling with the diazonium ion. Although the bands due to the polyaniline backbone remain in the same energy values, some intensity changes

occur because of the effect of the added group on the electron delocalization and/or protonation of the polymer.

The procedure could also be used to obtain structural information in polypyrrole (PPy). The spectra of an unmodified PPy film, deposited onto LDPE, and the product of its modification by nucleophilic reaction of sulfite ions (**III**) are shown in Figure 3.

As can be seen, the FT-IR spectrum of the modified PPy film (**III**) shows bands at 1045 and 1007 cm^{-1}, which could be assigned to the symmetric stretching of the sulfonate group,[23] and the band at 680 cm^{-1} could be assigned to C$-$S stretching of the same group.[23] Such a group is added to the polymer backbone during the modification reaction.

The reproducibility of the modification procedure could be assessed by comparing the FT-IR spectra of polymer films modified under the same conditions. It was found that, when the different procedures (LDPE treatment, PANI deposition, and PANI modification) were performed on separate samples (>5), the spectra of the films obtained are almost identical.

The reaction time should be enough to allow for the reaction to modify the film significantly. In the case of diazonium ion coupling with PANI, Liu and Freund[24] demonstrated that the reaction is very fast and is controlled by the reactant diffusion inside the film. In the case of the nucleophilic addition, the reaction is slower. In both cases, it was found that, after 30 min, there are no noticeable changes in the FT-IR spectra of the treated films. Such behavior was observed for 86 diazonium ions and 18 nucleophiles (reacted either with PANI or PPy). Therefore, the time period used here (60 min) seems to be sufficient for the reaction to occur, even taking into account the different reactivity of the reactants. It was also found that, after 15 min of washing of the film, no noticeable change in
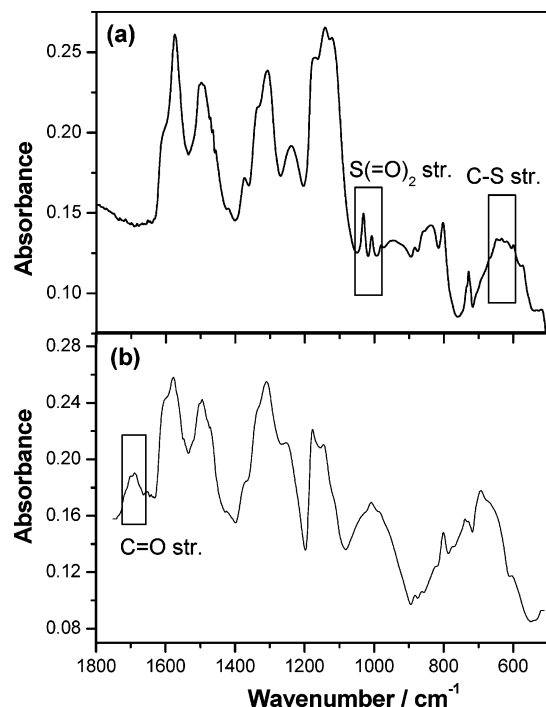
Figure 2. FT-IR spectra of polyaniline films on LDPE, modified with azo groups containing (a) a sulfonic group and (b) a carboxylic acid group.
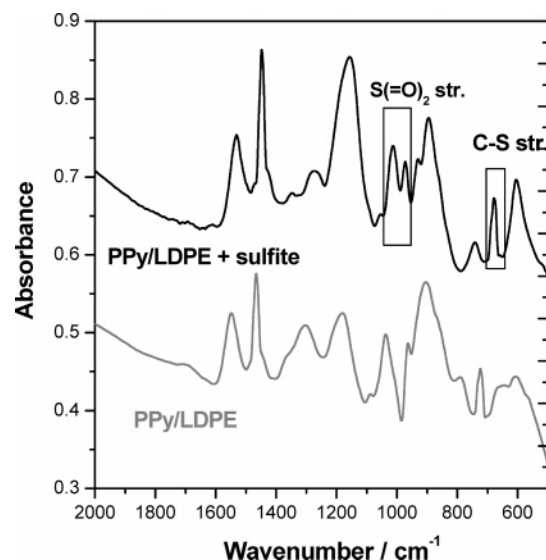

Figure 3. FT-IR spectra of polypyrrole (PPy) (gray line) and PPy modified (**III**) by the nucleophilic addition of sulfite ion (black line). Both spectra are taken of conducting polymer films deposited on LDPE films, where the LDPE spectrum has been subtracted.

the FT-IR spectra is detected, suggesting that all soluble reactants are removed.

Obviously, the reaction conditions should be tested previously if one would like to use other reactions to modify the conducting polymers.

Because LDPE does not exhibit absorption in the UV−vis region, it is also possible to verify the modification using UV−vis spectroscopy. Figure 4 shows the UV−vis spectra of PANI (denoted by the gray line) and a modified PANI (**IV**) (denoted by the black line). The UV−vis spectrum of PANI presents three characteristic bands, at 349, 413, and
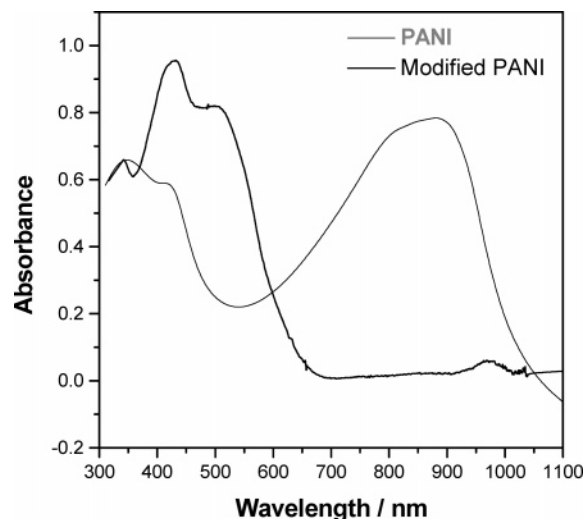

Figure 4. UV−visible spectra of PANI (gray line) and modified PANI (black line).

848 nm. The band at 349 nm is attributed to the $\pi \rightarrow \pi^*$ transition of the aniline ring, the band at 413 nm is assigned to the $n \rightarrow \pi^*$ transition of the localized radical cation, and the band at ca. 850 nm is assigned to the excitation from the highest occupied molecular orbital (HOMO) of the benzenoid rings (π_b) to the lowest unoccupied molecular orbital (LUMO) of the quinoid rings (π_q) in the quinoneimine units.[25] The spectrum of the modified PANI (**IV**), synthesized by reaction of the diazonium salt of 1-naphthylamine with polyaniline, presents an additional shoulder at 508 nm, which is assigned to the $n \rightarrow \pi^*$ transition of the azo chromophore. The band at ca. 850 nm, which is assigned to the exciton transition in the PANI backbone,[26] is strongly depressed in the modified polyaniline (**IV**), because of the inductive and steric effect of the naphthalenazo group. The effect is also present in the UV−vis spectra of modified polymer solutions in *N*-methylpyrrolidone. Therefore, the underlying LDPE substrate does not seem to have an effect. As expected, the decrease in the electron delocalization correlates with a clear diminution of polymer conductivity.[27] Although the UV−vis spectrum gives little structural information, it allows a quick and simple test of polymer changes.

Scheme 2 shows a comparison of the steps required for modifying and testing the reaction, using the proposed method and the traditional powder method. The use of supported polymers not only leads to less tasks but also allows us to significantly economize the reactants, because a polymer volume of only 5×10^{-5} cm³ is reacting. Although the total time reduction is significant, the reduction in screening time is nearly 6-fold. Therefore, it is reasonable to design a parallel scheme of conducting polymers modification, because the screening procedure will not become a bottleneck of the combinatorial search for modified conducting polymers.

A combinatorial approach should provide fast and reliable generation of target libraries, selective and reproducible synthetic procedures, structural confirmation, and rapid testing for the required properties. In this work, we show an easy method to perform the last two requirements of the combinatorial approach by supporting intrinsic conductive

Scheme 2. Time for Tasks Comparison between Combinatorial and Conventional Modification and Screening.
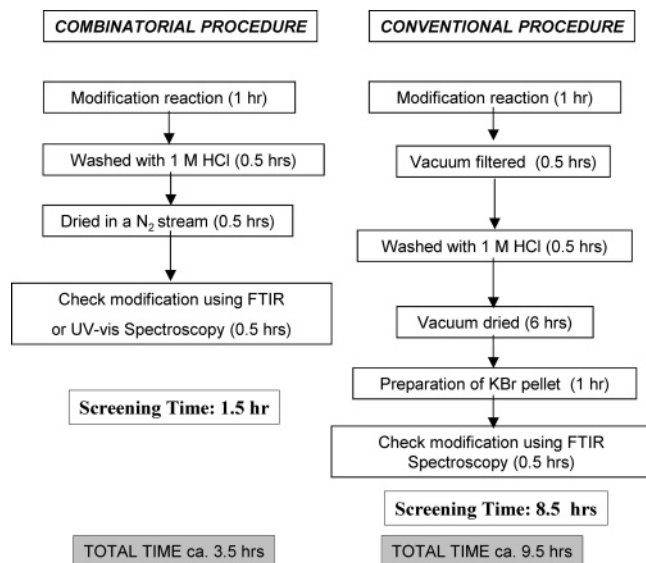
polymers on low-density polyethylene (LDPE). The support allows the use of Fourier transform infrared (FT-IR) spectroscopy to perform high-throughput screening of modification reactions on the polymer. The method of characterization is fast, and it seems quite general. It is also possible to study the UV–visible absorption of the polymer supported on LDPE. Therefore, the technique could be used to find lead compounds in conducting polymer libraries.

This method makes it possible to study different types of modification reactions on conductive polymers, such as nucleophilic addition of sulfite or coupling with diazonium salt. An extra advantage of the procedure is that it allows the researcher to not only optimize the reaction time but also economize the reactants significantly, without compromising its analytical capabilities.

Supporting Information Available. Experimental section (complete with references) describing the materials, LDPE film treatment, chemical polymerization of the conducting polymers, chemical modification of the polymers, and polymer characterization (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Gallop, M. A.; Barrett, R. W.; Dower, W. J.; Fodor, S. P. A.; Gordon, E. M. *J. Med. Chem.* **1994**, *37*, 1233–1251.
(2) Plunkett, M. J.; Ellman, J. A. *Sci. Am.* **1997**, *256*, 55–61.
(3) (a) Chen, C.; Randall, A. A.; Miller, R. B.; Jones, A. D.; Kurth, M. J. *Tetrahedron* **1997**, *53*, 6595–609. (b) Gibbon, J. A.; Taylor, E. W.; Braeckman, R. A. In *Combinatorial Chemistry and Molecular Diversity in Drug Discovery*; Gordon, E. M., Kerwin, J. F., Eds.; Wiley: New York, 1998; pp 453–474. (c) Martin, E. J.; Critchlow, R. E. *J. Comb. Chem.* **1999**, *1*, 32–45.
(4) (a) Osborn, H. M. I.; Khan, *T. H. Tetrahedron* **1999**, *55*, 1807–1850. (b) Ito, Y.; Manabe, S. *Curr. Opin. Chem. Biol.* **1998**, *2*, 701–708.
(5) (a) Marglin, B.; Merrifield, R. B. *J. Am. Chem. Soc.* **1966**, *88*, 5051–5052. (b) Tam, J. P.; Tjoeng, F. S.; Merrifield, R. B. *J. Am. Chem. Soc.* **1980**, *102*, 6117–6127. (c) Sarin, V. K.; Kent, S. B. H.; Merrifield, R. B. *J. Am. Chem. Soc.* **1980**, *102*, 5463–5470.
(6) Berg, R. H.; Almdal, K.; Pedersen, W. B.; Holm, A.; Tam, J. P.; Merrifield, R. B. *J. Am. Chem. Soc.* **1989**, *111*, 8024–8026.
(7) Hanak, J. J. *J. Mater. Sci.* **1970**, *5*, 964–971.
(8) Jandeleit, B.; Schaefer, D.; Powers, T.; Turner, H.; Weinberg, W. *Angew. Chem., Int. Ed.* **1999**, *38*, 2494–2532.
(9) (a) Schmatloch, S.; Meier, M. A. R.; Schubert, U. S. *Macromol. Rapid Commun.* **2003**, *24*, 33–46. (b) Meier, M. A. R.; Hoogenboom, R.; Schubert, U. S. *Macromol. Rapid Commun.* **2004**, *25*, 21–33.
(10) (a) Shirakawa, H.; Louis, E. J.; MacDiarmid, A. G.; Chiang, C. K.; Heeger, A. J. *J. Chem. Soc. Chem. Commun.* **1977**, *16*, 578–580. (b) Heeger, A. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 2591–2611. (c) MacDiarmid, A. G. *Angew. Chem., Int. Ed.* **2001**, *40*, 2581–2590.
(11) (a) Yue, J.; Wang, Z. H.; Cromack, K. R.; Epstein, A. J.; MacDiarmid, A. G. *J. Am. Chem. Soc.* **1991**, *113*, 2665–2671. (b) Wei, X. L.; Wang, Y. Z.; Long, S. M.; Bobeczko, C.; Epstein, A. J. *J. Am. Chem. Soc.* **1996**, *118*, 2545–2555. (c) Salavagione, H. J.; Miras, M. C.; Barbero, C. *J. Am. Chem. Soc.* **2003**, *125*, 5290–5291 and references therein.
(12) Lavastre, O.; Illitchev, I.; Jegou, G.; Dixneuf, P. H. *J. Am. Chem. Soc.* **2002**, *124*, 5278–5279.
(13) MacDiarmid, A. G.; Chiang, J. C.; Richter, A. F.; Somarsiri, N. L. D.; Epstein, A. J. In *Conducting Polymers*; Alcacer, L., Ed.; Reidel Publishing Co.: Dordrecht, The Netherlands, 1987; p 105.
(14) (a) Brédas, J. L.; Street, G. B. *Acc. Chem. Res.* **1985**, *18*, 309–315. (b) Oh, K. W.; Park, H. J.; Kim, S. H. *J. Appl. Polym. Sci.* **2003**, *88*, 1225–1229.
(15) Barbero, C.; Salavagione, H. J.; Acevedo, D. F.; Grumelli, D. E.; Garay, F.; Planes, G. A.; Morales, G. M.; Miras, M. C. *Electrochim. Acta* **2004**, *49*, 3671–3686.
(16) Barbero, C.; Morales, G. M.; Grumelli, D. E.; Planes, G. A.; Salavagione, H. J.; Marengo, C. R.; Miras, M. C. *Synth. Met.* **1999**, *101*, 694–695.
(17) Salavagione, H. J.; Morales, G. M.; Miras, M. C.; Barbero, C. *Acta Polym.* **1999**, *50*, 40–44.
(18) Han, C.-C.; Lu, C.-H.; Hong, S.-P.; Yang, K.-F. *Macromolecules* **2003**, *36*, 7908 and references therein.
(19) Acevedo, D. F.; Salavagione, H. J.; Miras, M. C.; Barbero, C. A. *J. Braz. Chem. Soc.* **2005**, *16*, 259–269.
(20) Acevedo, D. F.; Ponzio, E. J.; Miras, M. C.; Barbero, C. Presented at the XIII Simposio Nacional de Química Orgánica, November 11–14, 2001, Huerta Grande, Argentina.
(21) Huang, K.; Oiu, H.; Wan, M. *Macromolecules* **2002**, *35*, 8653–8655.
(22) Sapurina, I.; Riede, A.; Stejskal, J. *Synth. Met.* **2001**, *123*, 503.
(23) Conley, R. *Infrared Spectroscopy*; Allyn and Bacon: Boston, 1966; pp 144–146.
(24) Liu, G.; Freund, M. S. *Chem. Mater.* **1996**, *8*, 1164–1166.
(25) Huang, W. S.; MacDiarmid, A. G. *Polymer* **1993**, *34*, 1833–1845.
(26) Masters, J. G.; Sun, Y.; MacDiarmid, A. G.; Epstein, A. J. *Synth. Met.* **1991**, *41*, 715–718.
(27) Acevedo, D. F.; DellaMea, J. M.; Miras, M. C.; Barbero, C. In *Green Chemistry Series No. 8*; INCA: Venice, 2002; pp 103–107.