Novel Heterocyclic Synthesis and Investigation on Radiation-Grafted Low-Density Polyethylene with 2-*N*-Vinylpyrrolidone

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ABSTRACT: Radiation-induced graft polymerization of low-density polyethylene with *N*-vinylpyrrolidone, LDPE-*g*-PNVP, was used as a starting material for the synthesis of polyfunctionally substituted heterocyclic products. Thus, LDPE-*g*-PNVP reacts with ylidenemalononitrile derivatives to give the Michael addition products. In multistep reaction, LDPE-*g*-PNVP reacts with *N,N*-dimethylformamide dimethyl acetal (DMFDMA), hydrazine hydrate and malononitrile, respectively, to give a hydropyrrolopyridazine derivative. The latter could also be prepared via the reaction of LDPE-*g*-PNVP with DMFDMA, followed by treating with cyanoacetohydrazide. Also, LDPE-*g*-PNVP reacts with malononitrile to give an adduct product, dimer malononitrile derivative 13. The latter reacts with sulfur element to afford the thiophene derivative. Furthermore, this adduct reacts with hydrazine hydrate to isolate the original starting material, LDPE-*g*-PNVP, and aminopyridine derivative. The resulted films were characterized by infrared (IR) spectroscopy, ^{1}H nuclear magnetic resonance (^{1}H-NMR) mass spectroscopy, elemental analysis, swelling behavior, and electron scanning microscope. © 1999 John Wiley & Sons, Inc. J Appl Polym Sci 74: 2963–2970, 1999

Key words: graft; low-density polyethylene; *N*-vinylpyrrolidone; malononitrile; thiophene

INTRODUCTION

Radiation-induced graft copolymers with polyfunctionally substituted heterocyclic ring derivatives comprise a very interesting class of polymer because of their significant biological and pharmaceutical activity.[1–7] Extensive work has been prompted on the radiation-induced graft polymerization of *N*-vinylpyrrolidone (NVP).[8–11] The use of NVP as hydrophilic grafting monomer is well known in the radiation grafting on various trunk polymers and was described for the preparation of biocompatible polymer surfaces.[12,13] In last few years, we have been involved in a program aimed to developing a new synthesis for polyfunctionally substituted heterocyclic ring system using a radiation-induced graft copolymer as a building block. In this article, the modification of the grafted polymer with biologically active reagents, for example, ylidenemalononitrile derivatives,[14–20] and, also, a synthesis of fused pyridazine and thiophene derivatives as required compounds for testing in the field of biological and medical uses.

EXPERIMENTAL

Materials

Low-density polyethylene (LDPE) films of 70 μm thickness (El-Nasr Co. for medical supplies, Egypt) were used as a polymer substrate. *N*-Vinyl-2-pyrrolidone (NVP; Merck, Germany) of pu-

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rity 99% were used without further purification. Other chemicals were of reagent grade and used without further purification.

Graft Polymerization

Strips of LDPE were washed with acetone, dried in a vacuum oven at 50°C, weighed, and immersed in the NVP–dimethyl formamide (DMF) solution in glass ampoules. Ferric chloride, 0.008 wt %, was added to the monomer–solvent to reduce the homopolymerization process during irradiation. The glass ampoules that contained polymer and monomer–solvent mixtures were deaerated by bubbling of nitrogen gas for 4–7 min, sealed, and then subjected to a ^{60}Co gamma source at a dose rate 1.60 Gy/s. The obtained grafted films were removed and washed thoroughly with hot, distilled water and soaked overnight in water to extract the residual monomer and homopolymer occluded in the film. The grafted films (1 in Scheme 1) were then dried in a vacuum oven at 50°C for 24 h and weighed. The degree of grafting was determined by an increase in weight percentage as follows:

$$\%G = \frac{W_g - W_o}{W_o} \times 100$$

where W_g and W_o represent the weights of grafted and initial films, respectively.

Characteristic Methods

IR spectra were recorded using a model 2000 Perkin–Elmer FT Spectrometer in KBr disks. ^{1}H nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a Bruker AC-80 Spectrometer in dimethyl sulfoxide (DMSO). Mass spectra were obtained on Finnigan GCQ system. The ionization mode was the ion methane CI, and the column used was the polar column. The scanning electron micrographs were examined in a model JSM-6300 JEOL scanning electron microscope (SEM) at 20 kV. Analytical data were obtained from the Analab, Chemistry Department, Kuwait University.

Synthetic Procedures

Ylidenemalononitrile derivatives were prepared as described earlier.[21] Inhibitor concentration, influence of monomer concentration, and IR spectroscopy of grafted and modified copolymers were also described by our group.[2]

Reaction of the Modified Grafted Films with Ylidenemalononitrile Derivatives (2a–c)

Colorless grafted films (2 × 3 cm) was immersed in a solution prepared from 2a–c (~ 3 g) and a few pellets of sodium hydroxide (~ 0.5 g) in ethanol (50 mL). The reaction mixture was refluxed for 20 h. The colored films (pale brown and deep violet) was removed and washed with distilled water and ethanol, followed by air drying.

Reaction of N,N-Dimethylformamide Dimethyl Acetal with Grafted Polymer (1)

Colorless grafted film (2 × 3 cm) was immersed in a solution prepared from DMFDMA (~ 6 mL) and a few pellets of sodium hydroxide (~ 0.5 g) in ethanol (50 mL). The reaction mixture was refluxed for 24 h. The colored film (pale yellow) was removed and washed with distilled water and ethanol, followed by air drying.

Reaction of Hydrazine Hydrate with Dimethylamine Derivative (6)

A product film, obtained from reaction of grafted polymer with DMFDMA, was immersed in a solution prepared from hydrazine hydrate (~ 5 mL) and ethanol (50 mL). The reaction mixture was refluxed for 24 h. The colored film (yellow) was removed after cooling and washed with distilled water and ethanol, followed by air drying.

Reaction of Cyanoacetohydrazide with Dimethylamine Derivative (6) or Malononitrile with Hydrazide Derivative (7)

A product film, obtained from reaction of grafted polymer with DMFDMA or that obtained from reaction of hydrazine hydrate with 6 was immersed in a solution prepared from cyanoacetohydrazide (~ 5 g) or malononitrile (~ 3.3 g), respectively, and a few pellets from sodium hydroxide (~ 0.5 g) in ethanol (50 mL). The reaction mixture was refluxed for 24 h. The colored film (brown) was removed after cooling and washed with distilled water and ethanol, followed by air drying.

Reaction of Grafted Polymer (1) with Malononitrile or Dimer Malononitrile

Colorless grafted film (2 × 3 cm) was immersed in a solution prepared from malononitrile (~ 6.6 g) and a few pellets of sodium hydroxide (~ 0.5 g) in ethanol (50 mL). The reaction mixture was re-

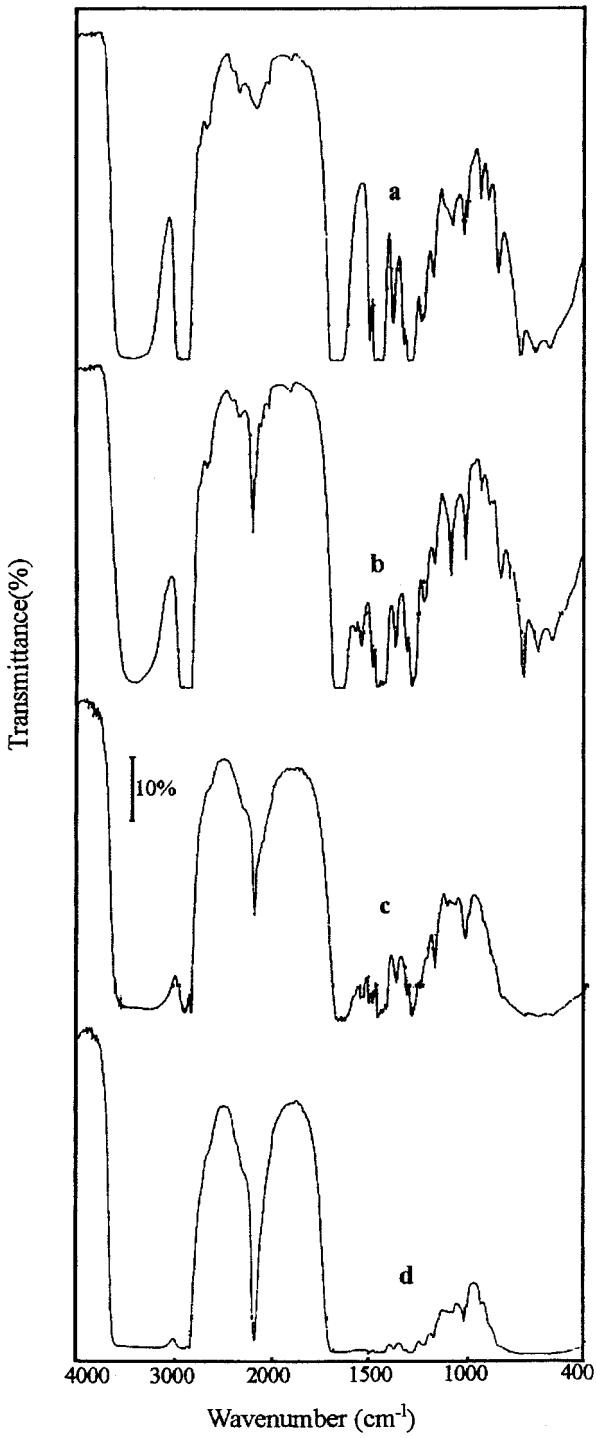


Figure 1 IR spectra of (a) LDPE-*g*-PNVP copolymer and (b) its modified grafted films with *p*-chlorobenzylidenemalononitrile, (c) *p*-methoxybenzylidenemalononitrile, and (d) furfurylidenemalononitrile, having the same degree of grafting (70%).

fluxed for 20 h. The colored film (brown) was removed and washed with distilled water and ethanol, followed by air drying.

Reaction of Sulfur Element with Compound (13)

A product film, obtained from reaction of grafted polymer with malononitrile, was immersed in a solution prepared from sulfur element (~ 3.2 g) and few pellets from sodium hydroxide (~ 0.5 g) in ethanol (50 mL). The reaction mixture was refluxed for 24 h. The colored film (pink) was removed after cooling and washed with distilled water and ethanol, followed by air drying.

Reaction of Compound (13) with Hydrazine Hydrate

A product film, obtained from reaction of grafted polymer with malononitrile, was immersed in a solution prepared from hydrazine hydrate (~ 5 mL), a few pellets of sodium hydroxide (~ 0.5 g), and ethanol (50 mL). The reaction mixture was refluxed for 24 h. The film was removed after cooling and washed with distilled water and ethanol, followed by air drying. To extract the organic compound 25, the mother liquor was treated by diethyl ether and then dried over sodium sulfate anhydrous. Then, the solid product was collected by evaporation of the ether and then crystallized from DMF (mp > 250°C).

Swelling Measurements

The clean, dried LDPE-*g*-PNVP and modified films with ylidenemalononitrile derivatives were immersed in distilled water for 24 h. The films were removed, blotted by absorbent paper, and immediately weighed. The swelling percentage was calculated as follows:

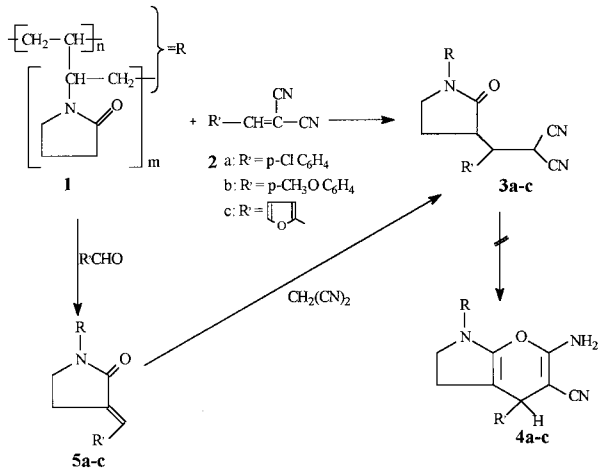
$$\text{Swelling } \% = \frac{W_s - W_g}{W_g} \times 100$$

where W_s and W_g represent the weights of initial grafted modified and swelled grafted modified films, respectively.

RESULTS AND DISCUSSION

Synthesis and Chemistry

In conjunction with our studies aimed at exploring the synthesis potential of the grafted polymer, low-density polyethylene grafted with 2-*N*-vinylpyrrolidone (LDPE-*g*-PNVP), 1, we report here several novel synthesis of heterocyclic ring system utilizing 1 as a starting material.[2] *N*-vinylpyrrolidone monomer can be viewed as a spe-



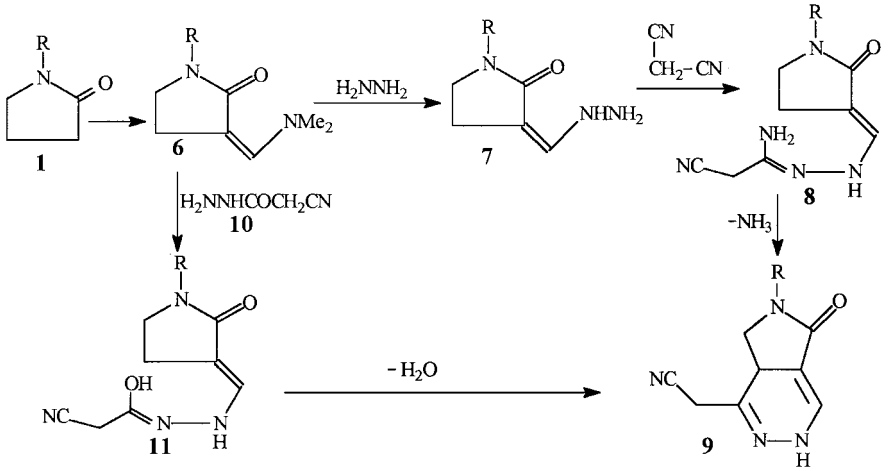
Scheme 1

cies containing the following three active sites: a vinyl group, a carbonyl group, and an active methylene function. These sites were reduced to two sites only after grafting process. The other two groups, a carbonyl group and a methylene function, show variety in the reactivity. The amide carbonyl group shows no reactivity toward the nucleophilic reagent, for example, hydrazine hydrate, and this may be due to the lowest reactivity in the amide carbonyl group or may be due to the chain steric effect. This result prompted us to investigate the reactivity of the α-methylene function.

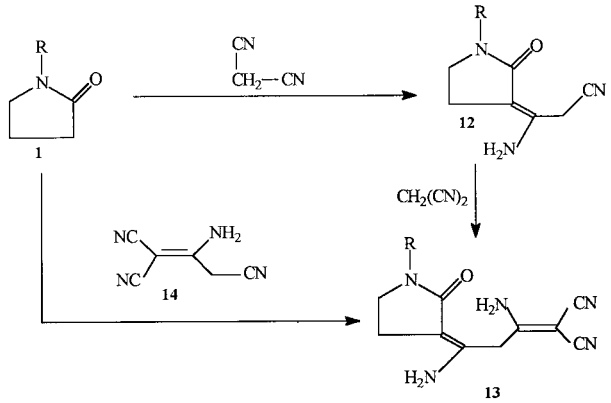
Thus, a graft copolymer 1 reacts readily with ylidenemalononitrile 2a–c to give 3a–c or 4a–c. Modified grafted polymers 4a–c were ruled out based on the infrared (IR) spectra, which reveal the presence of carbonyl group. Modified grafted polymer 3a was established based on the IR, which indicates the presence of cyano groups, which were absent in the LDPE-*g*-NVP. In addition to this, a carbonyl group appeared at 1659 cm^{-1} (cf. Fig. 1). Modified grafted polymer 3a was believed to be produced via Michael addition of the active methylene in 1 to an ethylenic double bond in a ylidenemalononitrile derivative 2a. Similarly, structures 3b–c were established. Modified grafted polymers 3a–c could also be prepared via reaction of an aldehyde with the grafted polymer 1 in a basic medium to give the nonisolated intermediate 5a–c, and then treated with malononitrile *in situ* to give the final isolated product 3a–c (cf. Scheme 1).

Furthermore, grafted polymer 1 reacts with *N,N*-dimethylformamide dimethyl acetal, $(CH_3)_2NCH(OCH_3)_2$, in basic medium to give 6. The latter reacts with hydrazine hydrate to give 7, which was reacted with malononitrile to afford 8. The intermediate 8 cyclized via elimination of ammonia to give the final isolated product 9. The latter 9 could also be prepared via another route, where compound 6 reacts with cyanoacetohydrazide 10 to give the nonisolated intermediate 11, which cyclized to give a product with the identical IR with 9. The reaction product may be formed via elimination of dimethylamine to give 11, which cyclized to 9 via elimination of water molecule (cf. Scheme 2).

Modified grafted polymer 1 reacts with malononitrile to give dimer malononitrile derivative 13. The latter was believed to be formed via addition of active methylene in pyrrolidone ring to the cyano group in malononitrile to afford 12, which further added to another molecule of malononitrile to give the final isolated product 13. In other



Scheme 2



Scheme 3

words, malononitrile may be dimerized first under the reaction condition to give 14, which was reacted with the grafted polymer 1 to give 13. The latter was established based on IR spectra, which reveals the presence of two cyano groups at 2178 and 2170 cm^{-1}; two amino groups at 3468, 3435, 3379, and 3370 cm^{-1}; and a carbonyl group at 1681 cm^{-1} (cf. Scheme 3 and Fig. 2).

The modified grafted copolymer 13 undergoes Gewald synthesis,[22–26] in which it reacts with sulfur element in ethanolic–sodium hydroxide to give 15, which was cyclized to 16 and then tautomerized to 17. Under the reaction condition, 17 converted to 18. Modified grafted polymer 18 was established, based on IR spectra, which reveals the presence of only one cyano group at 2188 cm^{-1} and two carbonyl groups at 1658 and 1690 cm^{-1}. Also, elemental analysis reveals the presence of sulfur in about 2% (cf. Table I and Scheme 4).

Modified grafted polymer 13 reacts with hydrazine hydrate to give the LDPE-*g*-PNVP 1 and aminopyridine 25. Such reaction products could be explained via the Japp–Klingemann reaction, in which the imine 19 converted under the reaction condition to the keto compound 20.[27] The latter was attacked by the base to give the intermediate 21, which undergoes bond cleavage, affording the anion of LDPE-*g*-PNVP, which was stabilized by resonance and finally separated as

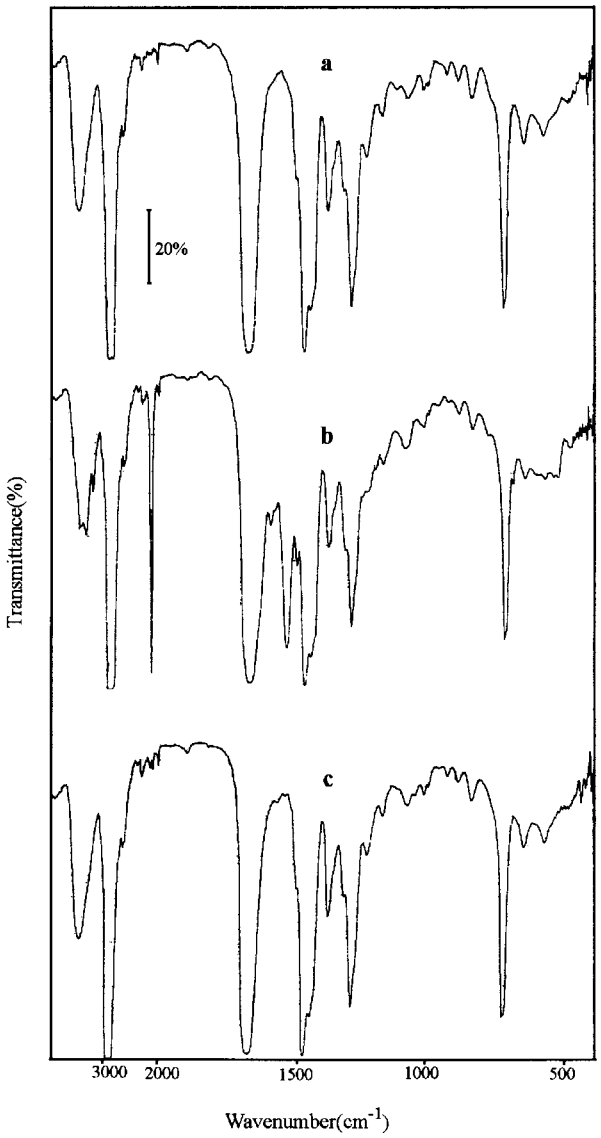
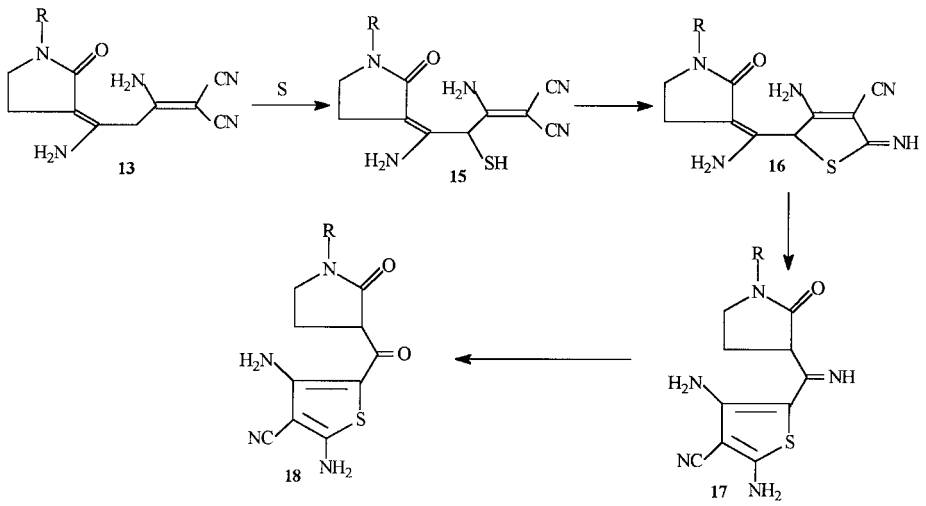


Figure 2 IR spectra of (a) LDPE-*g*-PNVP copolymer and (b) its modified grafted films with malononitrile or dimer malononitrile, and (c) the same latter film after treating with hydrazine hydrate, having the same degree of grafting (15%).

LDPE-*g*-PNVP on abstraction of a proton from the reaction medium. This was established based on IR spectra, which shows the identical IR spec-

Table I IR Spectra of the Synthesized Compounds and Modified Grafted Copolymer Films (cm^{-1})

Compound No.	OH	NH_2	CN	CO	C═C	←C—N	C—S
7	—	3400, 3338, 3320	—	1658	1559	1162	—
9	—	3433	2144	1665	1629	1217, 1174	—
18	—	3200–3468	2188	1690	1658	1230, 1288	650
25	3560	3411, 3336–3237	—	—	1600	1184	—

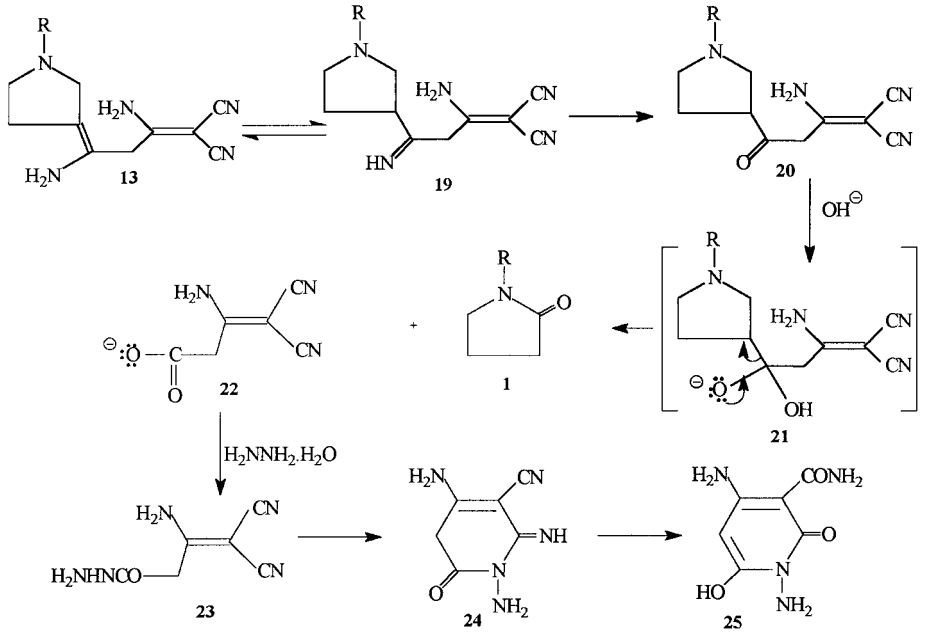


Scheme 4

tra of the blank one (cf. Fig. 2). Furthermore, the carboxylate 22 reacts with hydrazine hydrate to give the hydrazide derivative 23. Hydrazide 23 cyclized to 24 and then hydrolyzed to give the final isolated product 25. Aminopyridine derivative 25 was established based on mass spectroscopy, which shows a m/z = 184 (M^+). ^{1}H-NMR shows a protons at δ 10.41 (s, 1H, OH); 8.00 (s, 1H, Pyridine—CH); and 7.90, 6.96, and 5.40 (6H, $3NH_2$ groups) (cf. Scheme 5, Fig. 2, and Table II).

Swelling Behavior

It is known that the presence of hydrophilic groups introduced by the grafting of NVP should increase the water uptake of the trunk polymer.[12,13] Table III shows the water uptake percentage of the grafted polymer and that of the modified grafted polymer with ylidenemalononitrile. It can be seen that the water uptake of the modified films is higher than that of the grafted one. Modified grafted polymer with *p*-methoxybenzylidene malononitrile 2b shows a higher swelling percentage than that of the modified films with 2a and 2c. In general, the modified films can be arranged in the order of increased swelling behavior, as follows: modified film with 2b > modified film with 2c > modified film with 2a. This may be due to the pres-



Scheme 5

Table II Elemental Analysis of the Grafted Film and Different Modified Films at 140% Grafted Yield

Compound No.	C%	H%	N%	S%	M^+
1	82.660	13.420	0.0926	0.000	—
6	69.077	11.392	4.932	0.000	—
18	68.119	11.630	5.157	1.966	—
25	Calcd 39.124	4.387	30.456	0.000	184
	Found 39.403	4.701	30.230	0.000	

Table III Swelling Percentage of the Modified Films

	% Grafting (70%)		
Compound	W_g	W_s	% Swelling
LDPE-*g*-PNVP	0.1188	0.1387	16.75
Grafted film with 2a[a]	0.0670	0.0888	32.50
Grafted film with 2b[b]	0.0675	0.1700	151.85
Grafted film with 2c[c]	0.0493	0.1055	113.90

[a] 2a is *p*-chlorobenzylidenemalononitrile.
[b] 2b is *p*-methoxybenzylidenemalononitrile.
[c] 2c is furfurylidenemalononitrile.

ence of oxygen atom in both of 2b and 2c, which may be able to form hydrogen bonding with water molecules.

Structure and Morphology

For a medical polymer, it is very important that the material not only has certain strength and stability but also good biocompatibility.[28] The scanning electron micrographs of LDPE-*g*-PNVP membrane were indicated from Figure 3(a). The modification of the grafted film with sulfur element (polymer 18, scheme 4, Fig. 3b) shows that the structure of sulfur was embedded in the polymer matrix, which is similar to the "mountain"

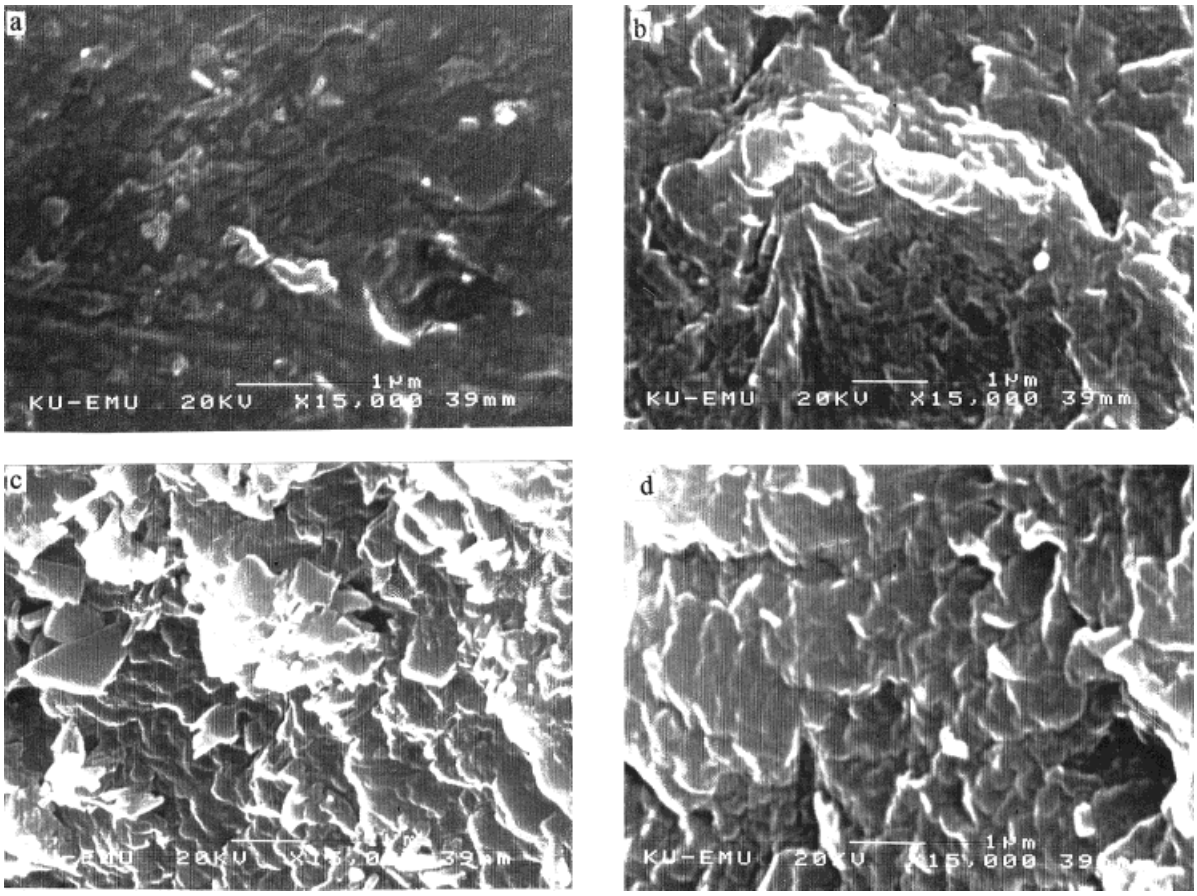


Figure 3 Scanning electron micrographs of LDPE-*g*-PNVP and some modified films: (a) micrographs of LDPE-*g*-PNVP, (b) micrographs of thiophene derivative 18, and (c) and (d) micrographs of pyridazine derivative 9, having the same grafting yield (140%).

type. However, modified grafted polymer 9, which is represented in Figure 3(c) and (d) appears to be a regular gathering structure similar to the sea horse type. This indicates that the grafted chain of PVNP, which modified with different organic materials, will increase the change in morphology of polymeric substance.

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