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Syntheses of diblock copolymers: poly(2-methylpropene)-b-poly(α-amino acid)

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Summary : Diblock copolymer poly (2-methylpropene)-b-poly (α-amino acid) was obtained by polymerization of the corresponding N-caboxy anhydride initiated by a poly (2-methylpropene) bearing a terminal amine in dioxane/CH_2Cl_2 mixture. Copolymers were analyzed by FT IR, ^1H and ^{13}C NMR. $\overline{M}n$ of the α-amino acid segment determined by ^1H NMR fits well with those obtained by a theoretical calculation.

Introduction.

Block copolymers can be synthetized via two ways : a) by polycondensation of two functional oligomers A and B; b) by polymerization of a monomer B initiated by an oligomer A bearing terminal function known as efficient initiator for B. In the first case, the molecular weight $\overline{M}n$ of the diblock is controlled by the $\overline{M}n$ of each block and in the second case, this latter depends on the well-defined and well-controlled polymerization of B. Poly (α-amino acid)s have been investigated for a possible use in various biomedical applications. Thus, it is of interest to carry out the synthesis of biomaterials containing poly (α-amino acid)s as one component. Nakajima et at (1) have investigated the formation, the structure, and the functional properties of A-B-A triblock copolymers in which A is a poly (α-amino acid) and B is a polybutadiene. Teyssié et at (2,3) have synthetized poly (lactone)-b-poly (peptide)s and poly (lactide)-b-poly (peptide)s in view to study their biocompatibility, biodegradation and surfactant properties. In the course of our research, we have synthetized poly (2-methylpropene) azide (PMPAZ) (4) by an "apparent living polymerization" of 2-methylpropene (MP) initiated by azide / Lewis acid systems. PMP amine (PMPAM) can be obtained quantitavely by reduction of PMPAZ. In the mean time, the synthesis and polymerization of N-carboxyanhydride (NCA) of α-amino acids were also investigated in our laboratory. It is interesting to synthetize diblock poly (2-methylpropene)-b-poly (α-amino acid) by polymerization of NCA initiated by the function amine of PMP. This paper reports the results of this investigation.

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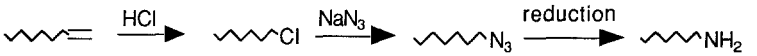
Experimental.

Reactants are purified and dried according to the technique used in our laboratory :

NCA of α-amino acids can be obtained by reaction of α-amino acids with phosgene (5).

PMP with unsaturation end (Exxon, Parabol 950, $\overline{M}n$ = 950, functionality = 1) was functionalized into PMPAM according to the reaction steps (4) :



A typical polymerization was carried out as follows : In a flask equipped with magnetic stirrer and flushed with nitrogen were introduced 1g of PMPAM (1,05 mmol.), 20ml of a mixture of solvents dioxane - dichloromethane (3 : 1) and 0.25 - 0.36g of NCA (10,5 mmol.) in this order (NCA concentration : 0.07 - 0.08 M). The solution was stirred at room temperature. The course of polymerization was followed by FT IR (the decreasing of the carbonyl peaks of NCA at 1865 cm^{-1} and 1849 cm^{-1}). The total disappearance of these latters occurs after 3 - 4 days. The reaction was stopped by pouring the reaction mixture in ether. The copolymers were obtained by filtration, rinsed and dried..

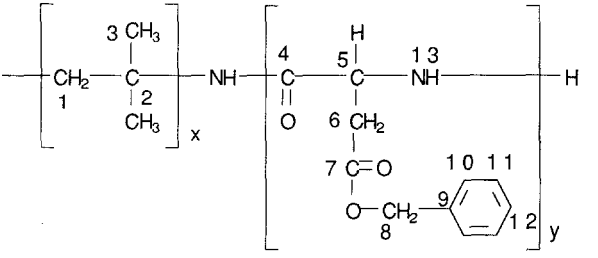
Copolymers were analyzed by FT IR (Bruker IFS 45, KBr window) and by ^1H NMR (Bruker WP 200, TFA/$CDCl_3$ mixture as the solvent).

Results and Discussion.

Two NCAs have been choosen for this study : β-benzyl aspartate (BZA) and L-leucine (LEU).

Poly (MP)-b-poly (BZA).

PMPAM homopolymer is soluble in hexane. A treatment of the crude product by this solvent leaves an insoluble and the evaporation of the filtrate does not show the presence of unreacted PMPAM meaning that all of this latter participates to the initiation of BZA polymerization. According to Teyssié et at (3), in ^1H NMR analysis the presence of a peak at 3,46 ppm corresponding to N-amide methylene protons attests for the blocky structure in absence of any homopolymers. The same event is observed in our case (Fig.3;arrows; methyl peaks at 3,55 and 3,75 ppm). The copolymer poly (MP)-b-poly (BZA)



is insoluble in most of the common solvents except in the mixture trifluoroacetic acid (TFA) / chloroform.

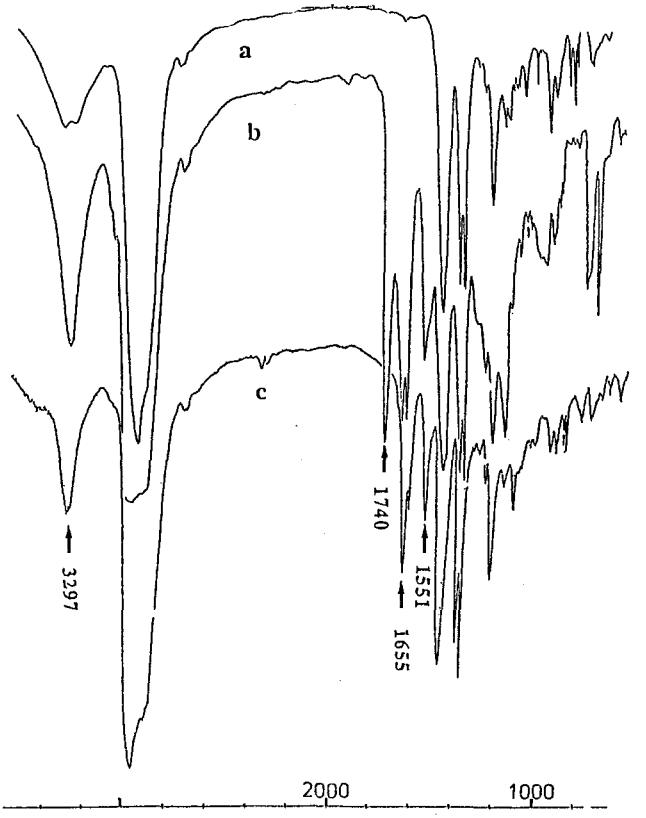


Fig.1 : FT IR spectra of : (a) PMPAM; (b) poly (MP)-b-poly (BZA) and (c) poly (MP)-b-poly (LEU).

Figure 1 presents FT IR spectra of PMPAM (**a**) with characteristic peaks at 3245-3304 cm^{-1} (NH_2) ; 3000-2800 cm^{-1}, 1472-1391-1368 cm^{-1} (CH_2, CH_3 of PMP) and of copolymer poly (PMP)-b-poly (BZA) (**b**) where, besides peaks of PMP, peaks at 3297 cm^{-1} (NH), 1740cm^{-1} (C=O ester), 1661 cm^{-1} (C=O amide I), 1553 cm^{-1} (C=O amide II) are detected. No peaks at 1865-1849 cm^{-1} corresponding to unreacted BZA (at the end of polymerization) indicating that the whole monomer was consummed during the polymerization.

The structure of the diblock copolymer was confirmed by ^{13}C NMR (Fig.2) and by ^{1}H NMR (Fig.3) where chemical shifts are listed in table 1 and 2.

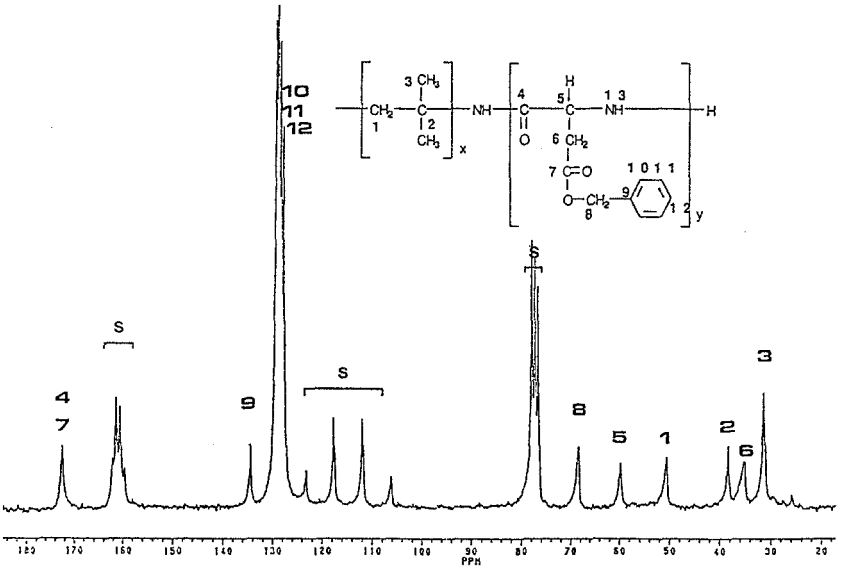


Fig.2 : ^{13}C NMR spectrum of poly (MP)-b-poly (BZA).

Table 1 : ^{13}C chemical shifts (ppm) of poly (MP)-b-poly (BZA)

Block	CH_3	CH_2	CH	C	C=O	Φ
PMP	31.25	59.68		38.23		
	(3)	**(1)**		**(2)**		
PBZA		35.19 et 68.30	50.51	134.28	172.24	128.06-127.32
		(6) **(8)**	**(5)**	**(9)**	**(4)** **(7)**	**(10)** **(11)** **(12)**

Table 2 : ^{1}H NMR chemical shifts (ppm) of poly (MP)-b-poly (BZA)

Block	CH_3	CH_2	CH	NH	Φ
PMP	1.15	1.49			
	(3)	**(1)**			
PBZA		2.98 5.05	4.95	8.01	7.19
		(6) **(8)**	**(9)**	**(13)**	**(10)** **(11)** **(12)**

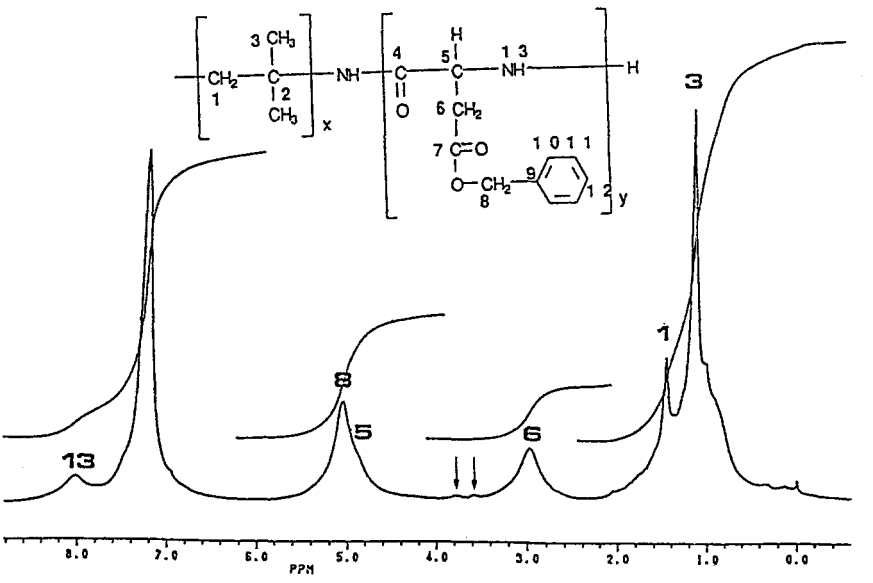


Fig.3 : ^{1}H NMR spectrum of poly (MP)-b-poly (BZA).

According to the structure of the copolymer, we can determine **x** and **y** segments by the integrations of CH_2+CH_3 of MP (h_1) and CH_2 (peak 6) of BZA (h_2):

$$\frac{8x}{2y} = \frac{h_1}{h_2}$$

$$\frac{x}{y} = 1{,}65$$

$$\frac{\overline{M}n_{PMP}}{\overline{M}n_{PBZA}} = \frac{x \,.\, 56}{y \,.\, 205}$$

$$\overline{M}n_{PBZA} = \frac{\overline{M}n_{PMP} \,.\, y \,.\, 205}{x \,.\, 56} = 2100$$

$$\overline{M}n_{copol.} = \overline{M}n_{PMP} + \overline{M}n_{PBZA} = 950 + 2100 = 3050$$

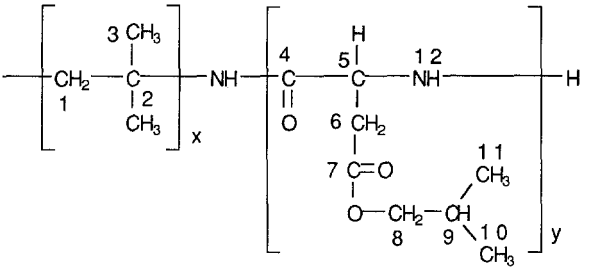
Theoretical calculation : 1,05 mmol. of PAPAM and 10,5 mmol.of BZA lead to a $\overline{DP}$ = 10 for PBZA which correspond to $\overline{M}n_{PBZA}$ = 2050.

$\overline{M}n_{copol.}$ = 950 + 2050 = 3000.

The $\overline{M}n$ determined by ^{1}H NMR fits well with those calculated.

Poly (MP)-b-poly (LEU).

The same results were obtained in the polymerization of LEU. The IR spectrum of the copolymer (Fig. 1c), for instance;



presents the characteristic peaks at 3298 cm^{-1} (NH), 1655 cm^{-1} (amide I) and 1549 cm^{-1} (amide II) corresponding to PLEU block. However, poly (MP)-b-poly (LEU) is not very soluble in the mixtute TFA/$CDCl_3$ so that ^{13}C and ^1H NMR spectra give peaks not well-defined by splitting but their estimated chemical shifts correspond approximatively to these of PMP and of PLEU (by comparison with those of poly (MP)-b-poly (BZA)).

From these results, we have shown the possibility of the synthesis of block copolymers poly (MP)-b-poly (amino acid)s by polymerization of NCA initiated by an oligomer bearing amine end. In the mean time, it confirms that the functionalization steps from unsaturation to amine applied to oligomer (see experimental) give a quantitative yield. The PMP segment is hydrophobic and not biocompatible; the poly (BZA) and poly (LEU) segments are hydrophilic and biocompatible. Obviously, the diblock copolymers are not biocompatible but may present surfactant properties which are actually studied..

Reference.

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