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Lipozyme-catalyzed transesterification of oligo(methylacrylate)s

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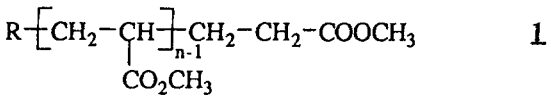
SUMMARY

Oligo(methylacrylate)s with ester end-group are transesterified by allyl alcohol in the presence of lipozyme as catalyst. The transesterification is regioselective : only end-group is modified. The structure of the modified oligomers is studied by ^{13}C NMR spectroscopy.

INTRODUCTION

Monofonctional and telechelic oligo(methylacrylate)s :



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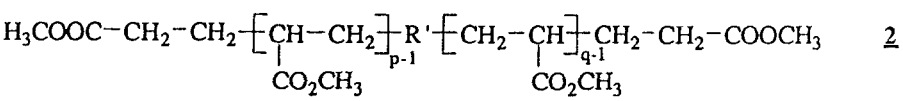
or :



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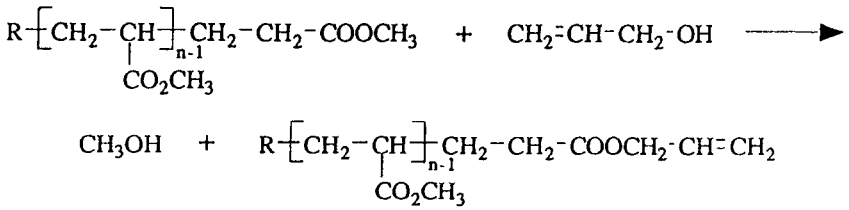
can be obtained by radical polymerization of methylacrylate (MA) in the presence of compounds, such as thiols, which behave as coinitiator and transfer agents (1, 2).

In this article, we study the regioselective transesterification of the end-groups of oligomers 1 by allyl alcohol :



The reactivity of the various ester-groups is roughly the same and that of the end-group is not sufficiently different from the others to allow a regioselective modification by classical transesterification processes.

To overcome this difficulty, we used lipozyme as transesterification catalyst (3-5). Due to the steric hindrance of its active site, this enzyme cannot catalyze the transesterification of the ester groups of 1 with the exception of the end-one whose steric neigbourhood is different from the others.

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EXPERIMENTAL

Allyl alcohol (Aldrich), hexane and toluene (Prolabo RP) were used without further purification. Lipozyme from NOVO is an immobilized lipase (EC 3.1.1.3) from *Mucor Miehei* (6). All experiments were conducted with a lipozyme concentration of 100 $g.l^{-1}$ and an optimal water content of 10 % (w/w) of supported enzyme.

1- Preparation of sample 3

Synthesis : A solution of AIBN (0.02 mol, 3.28 g), MA (1 mol, 86 g) and thiophenol (0.33 mol, 36.6 g) in CH_3CN (50ml) is heated to reflux (80°C) during five hours. After reaction, the solvent is evaporated and the residual fraction A is dried under vacuum for an hour at 60°C.

Fractionation : A mixture of fraction A (100 g) and hexane (1.5 l) is maintained at room temperature during 16 hours. The hexane-soluble fraction is separated and hexane is distilled off (rotating evaporator). The monoadduct is partly distilled off under vacuum. The undistilled fraction (sample 3) contains mainly diadduct 6 ; its $\overline{DP}_n$ is 2.3.

2- Synthesis of adducts of higher methylacrylates

Sample 4 ($\overline{M}_n$ = 403 $g.mol^{-1}$) : A solution of AIBN (0.004 mol, 0.656 g), MA (0.2 mol, 17.2 g) and thiophenol (0.0667 mol, 7.33 g) in CH_3CN (50 ml) is heated to reflux (80°C) during 5 hours. After reaction the solvent is distilled off (rotating evaporator) and the residual fraction is dried under vacuum at 60°C.

Sample 5 ($\overline{M}_n$ = 870 $g.mol^{-1}$) : The synthesis is carried out as that of sample 4 ; the thiophenol content is 3.30 g (0.03 mol).

3- Lipozyme-catalyzed transesterification of sample 3

Solution A : 3 (1 g) and allyl alcohol (1 ml) are introduced into a 50 ml graduate flask and liquid volume is completed to 50 ml with hexane.

Lipozyme : Lipozyme (0.5 g) is mixed with water (0.05 ml) and the mixture is introduced into a 10 ml flask ; 8 flasks numbered from 1 to 8 are prepared in the same way.

Reactional mixtures : 5 ml of solution A are introduced in each flask ; then the flasks are placed in a thermostated bath (40°C). After 6 hours flask 1 is sampled ; the same operation is carried out with flasks 2, 3, 4 etc..., after 9 hours and 1, 2, 3, 5, 7 and 9 days respectively. Each sample is filtrated in order to recover the supported catalyst, then the solvent and the allyl alcohol in excess are distilled off and the precipitate is analyzed by ^1H NMR.

4- Lipozyme-catalysed transesterification of samples 4 and 5

Solutions of oligo(methylacrylate)s : Sample 4 (0.247 g) or 5 (0.533 g) and allyl alcohol (0.1 ml) are placed in a 10 ml graduate flask ; the liquid volume is completed to 10 ml by toluene. Two flasks containing the sample and the lipozyme were prepared exactly as in the case of adduct 3. They were sampled after 8 days and the samples were treated as before.

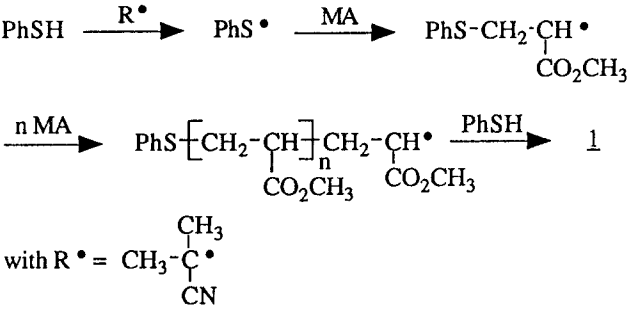
5- Alkaline hydrolysis of 4

Two drops of 6 are introduced into a 5 mm NMR tube with a mixture of C_2D_6CO and D_2O (5/1, v/v) and the first spectrum is recorded (fig. 5a). Then, two drops of a 30 % sodium deuteroxide solution in D_2O are added ; spectra 5b and 5c are recorded at times t_1 and t_2.

RESULTS AND DISCUSSION

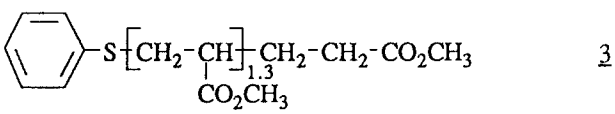
1- Synthesis and characterization of oligo(methylacrylate)s 1

They were prepared by AIBN initiation of MA polymerization in the presence of thiophenol (PhSH) which behaves as a transfer agent (2) :



The characteristics of the samples obtained in various experimental conditions are reported in table 1.

A sample (3) containing mainly diadduct (n = 2)



was obtained by elimination of the heavier fraction ($n \geq 2$) by selective precipitation and of monoadduct (n = 1) by distillation under vacuum. Its $\overline{DP}_n$ (2.3) was determinated by GPC (UV-detection ; fig. 1 and table 1) and by comparison of the peak areas of its ^1H NMR spectrum (fig. 2 ; table 2).

2- Lipozyme-catalyzed transesterification of 3 by allyl alcohol

The reaction was carried out in the conditions reported in the experimental part. The spectrum of the modified product (fig. 3) shows clearly the presence of allylic protons : CH_2OOC-, $-CH_2$-, -CH= at 4.6, 5.2 and 6 ppm respectively ; peak relative to $-COOCH_3$ protons is at 3.65 ppm.

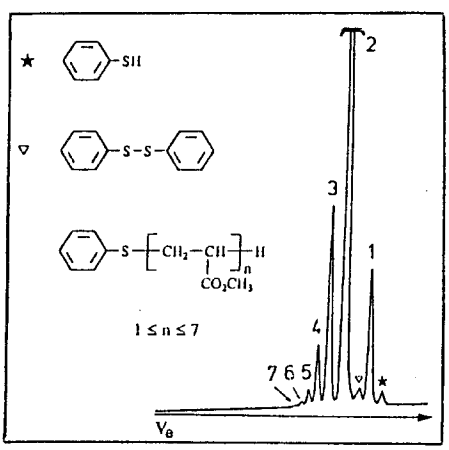


Figure 1 : GPC chromatogram of sample 3
Solvent THF - Detector UV
Columns : 100 Å + 50 Å
n is indicated above each peak

Table 1 : Composition of sample 3 from GPC analysis - $\overline{DP}_n$ determination, n_i and T_i are relative to fraction i. T is defined in text.

n_i	T_i
1	0.1333
2	0.5790
3	0.1990
4	0.0616
5	0.0185
6	0.0055
7	0.0023

$$\overline{DP}_n = \Sigma\, n_i T_i = 2{,}28$$

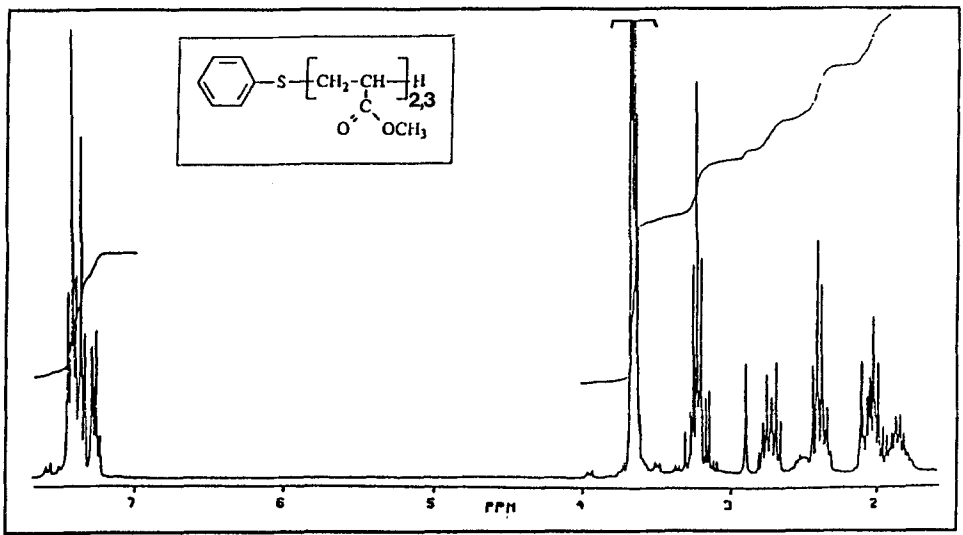


Figure. 2 : ^1H NMR spectrum (250 MHz) of sample 3 - C_2D_6CO solution - Reference TMS

Table 2 : Determination of the $\overline{DP_n}$ of sample 3 from its ^1H NMR spectrum (250 MHz)

Proton (*)	∂ ppm	Area
-COOCH$_3$ (proportional to the number of monomer units)	3.65	$A_1 = 55$
-S-CH$_2$- (proportional to the number of macromolecules)	3.2	$A_2 = 16$

(*) The characterization of the aliphatic protons is difficult as the sample is a mixture of several adducts.

$$\overline{DP_n} = \frac{1/3\ A_1}{1/2\ A_2} = 2.29$$

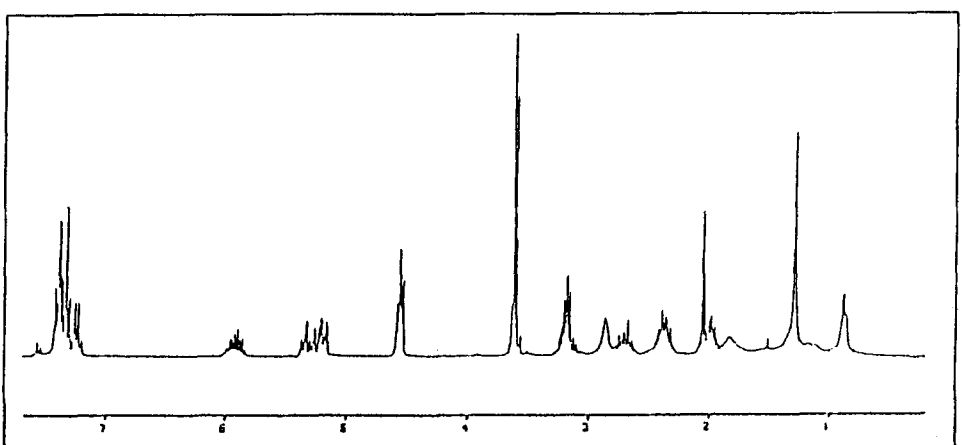


Figure 3 : ^1H NMR spectrum (250 MHz) of 3 after lipozyme-catalyzed modification by alcohol - C_2D_6CO solution - Reference TMS

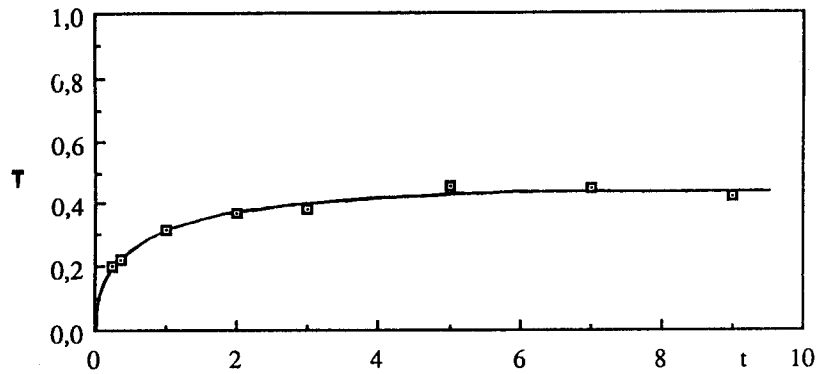


Figure 4 : Lipozyme-catalyzed transesterification of sample 3 by allyl alcohol
Variations of T against time t (days)

Let's T be the ratio of the number of allylacrylate groups to the number of methylacrylate groups in the oligomer :

$$T = \frac{1/2 \text{ Area } (-CH_2OOC-)}{1/3 \text{ Area } (-COOCH_3) + 1/2 \text{ Area } (-CH_2OOC-)}$$

The variations of T with respect to time are plotted in fig. 4.

Examination of fig. 4 shows that T tends toward a limit (0.44). Several assumptions can explain this phenomenum ; they are analyzed below.

- The system reached its thermodynamic equilibrium ; this explanation is hardly acceptable as the limit, in the case of chemical transesterification, is closed to 0.5 and since all the reactions were carried out in the presence of an excess of allyl alcohol.
- The enzyme is deactivated. This assumption must be eliminated as the enzyme recovered from the reaction mixture is active when used to catalyze another reaction.
- Only end ester-groups can react because the function in the chains are sterically hindered and are not reactive. To support this assumption, we compared the reaction limit to the contents in end-group (T_e) and in chain-groups (T_c) :

$$T_e = 1/DP_n = 0.44 \; ; \; T_c = 1 - T_e = 0.56$$

These values are in agreement with the assumption that the enzyme-catalyzed transesterification took place on the end-groups only. This selective modification of end-groups is confirmed by the NMR study (see part 4).

3- Lipozyme-catalyzed transesterification of sample 4 and 5

In order to confirm the results obtained with 3 we carried out the same reaction on samples 4 and 5 ; the results are reported in table 3. T_{ce} is the value of T corresponding to a complete conversion of ester end-groups ; T_{exp} is the experimental value.

Table 3 : Lipozyme-catalyzed transesterification of samples 4 and 5. T_{ce} and T_{exp} are defined in text. $[-CH_2COOCH_3]_0 = 0.06$ mol.l^{-1} - $[\text{Allyl alcohol}]_0 = 0.147$ mol.l^{-1}.
Solvent : toluene ; T(°C) = 40 - Reaction time = 8 days

Sample	$\overline{M}_n$ (g.mol^{-1})	$\overline{DP}_n$	T_{ce}	T_{exp}
4	403	3.4	0.293	0.267
5	870	8.8	0.113	0.110

Examination of table 3 shows that the conversion is almost complete in the case of 5 (97%) but below the expected value in the case of 4. However the agreement between T_{exp} and T_{ce} values is strongly in favour of a selective modification of the end-groups. This is confirmed by the structural analysis of the modified samples (part 4).

4- Characterization by ^{13}C NMR of the end-groups of 3

To confirm the assumption that only the end-group was modified we studied the structure of the transesterified polymer by ^{13}C NMR spectroscopy. Fig. 5 shows the spectra of non-modified (5a) and of modified (5b) sample 3 and the extension of the area around 51 ppm for these two spectra (5c and 5d).

Peaks 1 and 2 (5c and 5d) are relative to the OCH_3 group ; after lipozyme-catalyzed transesterification (7 days) the intensity of peak 2 (fig. 5d) is strongly decreased. In the following we show that peak 2 is relative to the methoxy group of the terminal ester function.

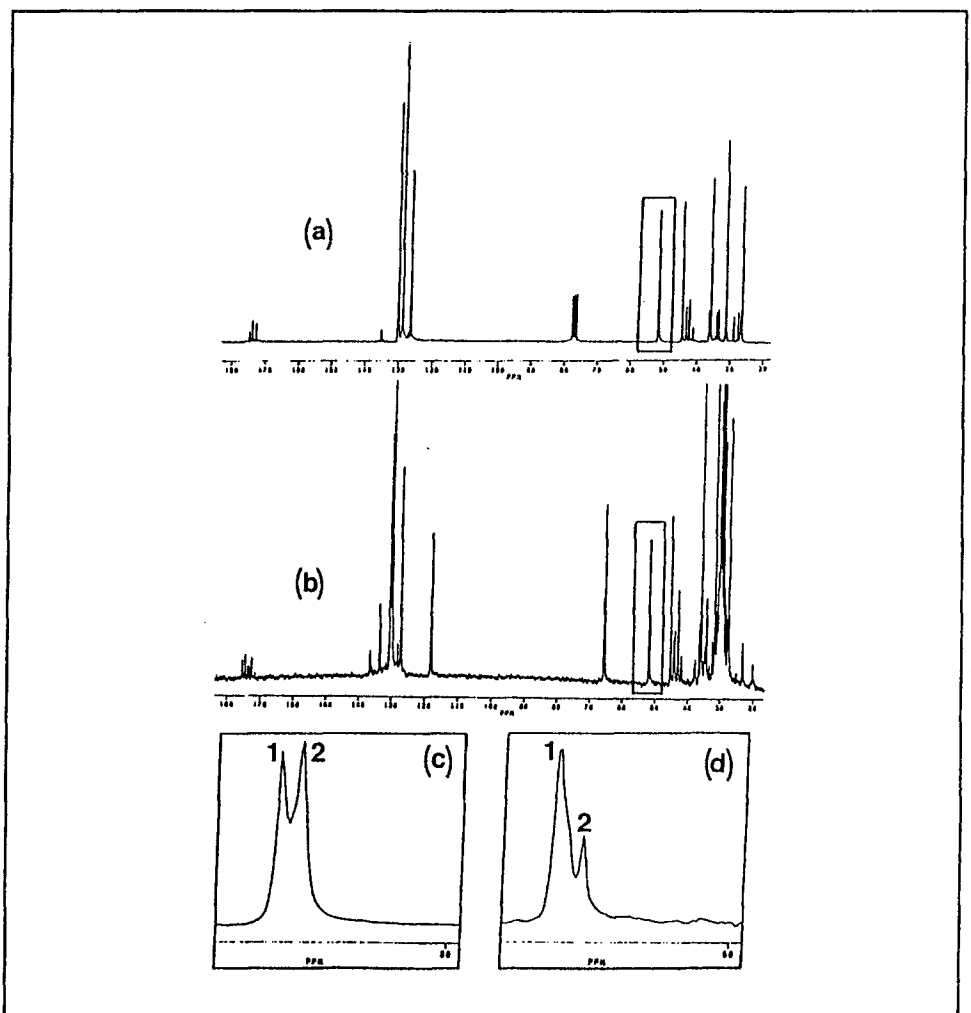
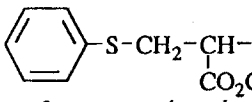


Figure 5 : ^{13}C NMR spectra (200 MHz) of 3 in $CDCl_3$ (a) and in C_2D_6CO (b)
(a) unmodified - (b) modified by lipozyme-catalyzed transesterification (7 days of reaction)

Studies on model (7) have unambigously shown that the rate of alkaline hydrolysis of the end-groups of our adducts is about 10 times that of the side-ester groups. We carried out the alkaline hydrolysis of sample 6 and recorded the ^{13}C NMR spectrum of the reactional mixture at different times (fig. 6).



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Comparison of spectra a, b and c with the results obtained by Sakurada (7) shows unambigously that peak 2 is relative to terminal OCH_3 and confirms the fact that when lipozyme-catalyzed transesterification of the adducts is carried out, only the end-group is modified. This results fits those obtained by Miller (8) when studying lipozyme-catalyzed esterification.

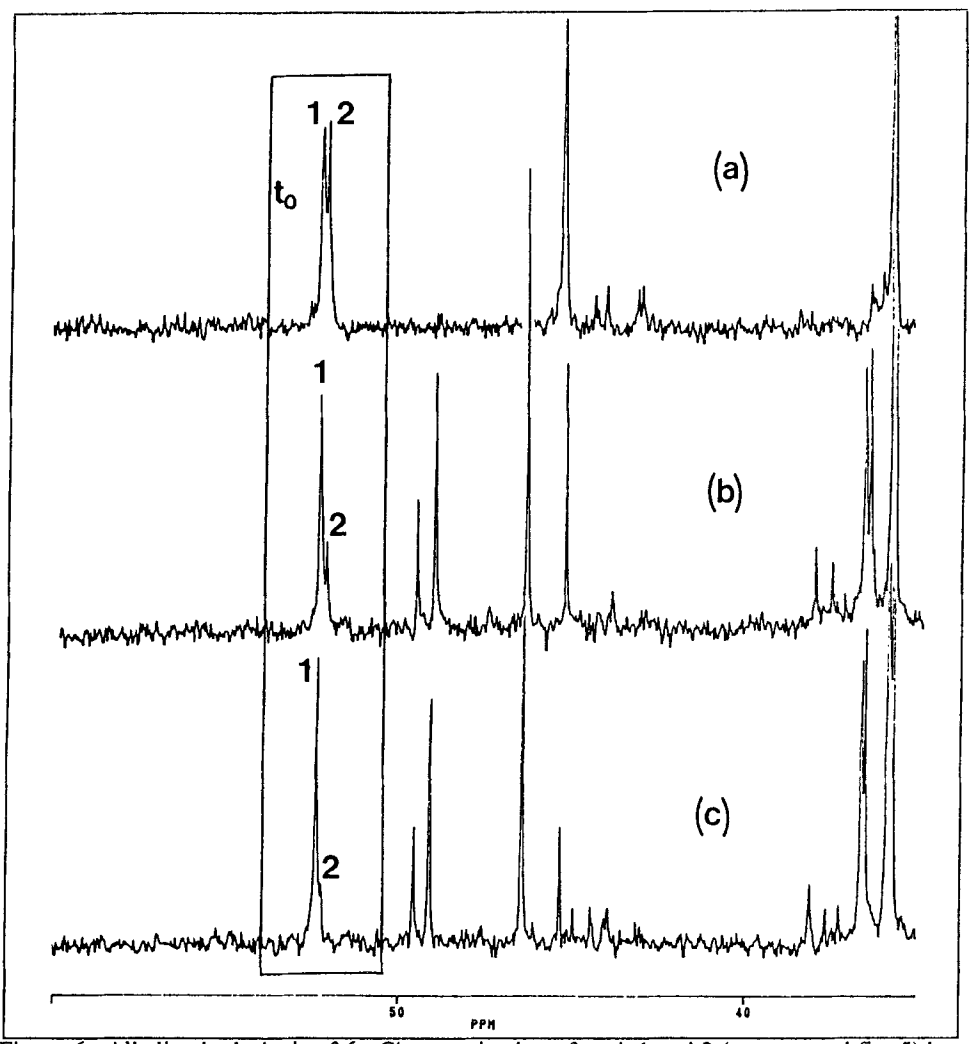

Figure 6 : Alkaline hydrolysis of 6 - Characterization of peak 1 and 2 (see text and fig. 5) by ^{13}C NMR (200 MHz) - Solvents : C_2D_6CO, D_2O (5/1 v/v)

CONCLUSION

We showed that the lipozyme-catalyzed transesterification of oligo(methacrylate)s leads to regioselective modification of the end-group. We already applied this method to telechelic oligo(methylacrylate)s and obtained oligomers with two allylic end-groups (9). Other alcohols and the use of these oligomers to prepare block copolymers are on study.

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