Pd/charcoal-catalysed cleavage of benzyl ester protecting groups in poly(benzyl acrylate) and poly(benzyl methacrylate)

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The cleavage of benzyl protecting groups of poly(benzyl acrylate), poly(benzyl malolactonate) and poly(benzyl methacrylate) by Pd/charcoal-catalysed hydrogenolysis was investigated in order to show the consequences of chemical modification on the molecular structures of the resulting polymeric compounds. It is shown that such catalytic cleavage is a general reaction that depends very much on the structure of the porous charcoal and on the location of the Pd-metal catalyst, which can be either at the surface or well inside the pores, or both. The rate of cleavage depends on many factors, namely nature of the parent polyacid backbone, stirring rate, solvent, relative amounts of poly(benzyl ester) and of catalytic system, etc. However, molecular weights, molecular-weight distribution and the origin of the catalytic system seem to be the main factors. Data confirm that partial catalytic hydrogenolysis can lead to the formation of blocky acid/ester copolymers or to mixtures of homopolymers depending on the structure of the Pd/charcoal catalytic system.

(Keywords: chemical modification; surface studies; catalytic bond cleavage; poly(benzyl acrylate); poly(benzyl methacrylate))

INTRODUCTION

With the development of tailor-made polymers for therapeutic applications, protection of functional groups and cleavage of protecting groups are being developed in the field of synthetic polymers, as has been the case for years in the field of polypeptide chemistry. Benzyl alcohol is regarded as a worthwhile protecting compound for carboxyl-bearing polymers. Indeed, aromatic benzyl ester can be readily and selectively cleaved in the presence of aliphatic ester groups by catalytic hydrogenolysis using Pd/charcoal as the catalyst[1]. Benzyl alcohol has been used successfully for carboxyl protection in the synthesis of poly(β-malic acid) (PMLAH_{100})[2]. However, partial hydrogenolysis of poly(benzyl malolactonate) (PMLABe_{100}) has revealed that Pd/charcoal-catalysed cleavage of benzyl ester groups is a complex reaction, which leads either to copolymers or to mixtures of homopolymers depending on experimental conditions[3]. In the case of Pd/charcoal-catalysed hydrogenolysis of poly(benzyl glutamate), failure to achieve 100% cleavage has been reported[4]. A limit was also found for poly(benzyl malolactonates) of rather high molecular weights[3]. Furthermore, it has been shown that copolymers, when formed during partial hydrogenolysis of poly(benzyl malolactonate), were not random but presented physico-chemical characteristics of amphiphilic block copolymers[3,5]. In particular, it was shown that such copolymers with very low contents of hydrophobic benzyl ester units are soluble in water, where they form large aggregates, in contrast to random copolymers of the same gross composition[5].

In order to obtain better understanding and better control of the Pd/charcoal-catalysed cleavage of benzyl ester protecting groups in polymers, we have undertaken a detailed investigation of the behaviour of two poly(carboxylic acid benzyl esters) of the acrylic series, namely poly(benzyl acrylate) (PAABe_{100}) and poly(benzyl methacrylate) (PMABe_{100}), and compared the data obtained with those previously obtained for PMLABe_{100}. Several Pd/charcoal catalysts of different origins have been considered because it appeared that the origin of the catalytic system is of great importance for the evolution of the cleaving reaction.

EXPERIMENTAL

Chemicals

Benzyl acrylate (AABe) (b.p. = 50°C at 10^{-2} mmHg) and benzyl methacrylate (MABe) (b.p. = 43°C at 10^{-2} mmHg) were supplied by Orkem (France). Both were purified by vacuum distillation before polymerization.

Johnson 37 and Johnson 65 Pd/charcoal catalysts were purchased from Johnson-Matthey France, whereas the Janssen one was obtained from the corresponding company. All the catalytic systems were used without further treatments.

Polymerizations

First 50 g of monomer and 200 cm^3 of toluene were mixed in a polymerization tube together with 200 mg of azobisisobutyronitrile in the case of AABe and 70 mg in the case of MABe. The tube was evacuated and sealed and allowed to stand at 70°C for 72 h. The recovered polymers, PAABe_{100} and PMABe_{100} respectively, were dissolved in toluene and fractionated by selective precipitation with ethanol in order to eliminate the low-molecular-weight compounds.

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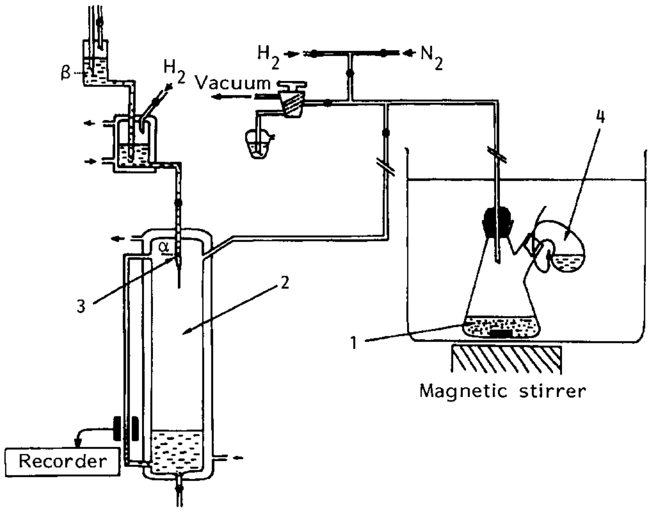

Figure 1 Schematic representation of the apparatus set-up for catalytic hydrogenolysis: (1) reaction compartment of the reactor: (2) hydrogen reservoir; (3) Mariotte system for permanent regulation of H_2 pressure according to atmospheric pressure; (4) side compartment for delayed polymer introduction into the reaction compartment

Hydrogenolysis

Typically, 40 mg of catalyst were introduced in the main compartment of a glass flask equipped with a side compartment and containing 20 cm^3 of the selected solvent medium and a magnetic bar (*Figure 1*). Then 300 mg of the polymer to be debenzylated were dissolved in the same solvent medium (5 cm^3) and introduced into the side compartment. The flask was then connected to the hydrogenation apparatus, which was designed to remain at normal pressure during the reaction time, and immersed in a water bath thermostated at 25°C and finally purged twice with nitrogen before being filled up with pure hydrogen. When hydrogen pressure was balanced, the main compartment was allowed to stir in order to disperse the catalyst and to saturate it with hydrogen. Pouring of the polymer solution from the side compartment into the main compartment marked the beginning of the hydrogenolysis reaction, which was maintained until the desired volume of hydrogen was consumed. Hydrogen was then replaced by nitrogen before opening the flask. The solid catalyst was separated from the polymer solution by filtration through a no. 5 sintered glass filter and rinsed with dioxane. After evaporation of the filtrate, the polymer was allowed to dry for 48 h in vacuum at 40°C.

Hydrolysis

$PAABe_{100}$ (2 g) was dissolved in a mixture of 50 cm^3 acetic acid, 12.5 cm^3 hydrochloric acid and 25 cm^3 water. The mixture was refluxed for 48 h, 15 cm^3 aliquots being withdrawn from the reaction mixture every day. The partially hydrolysed polymers were recovered after evaporation of the solvents and neutralization with 2 N NaOH. The solutions thus obtained were then dialysed against distilled water using Spectrapor (3500 g mol^{-1} cut-off) dialysis tubes and finally evaporated to yield the desired copolymers. The degree of hydrolysis of each was determined potentiometrically after percolation of aliquots through an H^+ ion-exchange column.

Measurements

The i.r. spectra were recorded with a Perkin–Elmer 1760 *FT*i.r. spectrometer.

The 60 MHz ^1H n.m.r. spectra were obtained by using a Varian T 60 A spectrometer.

Potentiometric titrations were performed with a Tacussel Ionoprocessor II pH-meter using titration cells thermostated at 25.0 ± 0.1°C. All the polymer concentrations are expressed in moles of repeating units per litre (mol l^{-1}).

Size exclusion chromatography was performed with a Waters apparatus equipped with PL Gel Mixed columns working in dioxane. For aqueous s.e.c., chromatograms were obtained with a Pharmacia f.p.l.c. apparatus using a Sephacryl S 200 gel (5000–10 000 g mol^{-1} range) or Pharmacia Sepharose CL6B (5000–300 000 g mol^{-1} range) as stationary phases and 0.15 M LiBr or 1 M NaCl/0.15 M phosphate buffer mixtures respectively as mobile phases, the detection being done by a Hewlett-Packard 1040A multi-wavelength u.v. detector.

RESULTS AND DISCUSSION

Pd-catalysed hydrogenolysis of benzyl protected poly(carboxylic acids) was carried out in a special apparatus (*Figure 1*), the key point of the selected setting being the use of a Mariotte system. Accordingly, any H_2 consumption in reactor 1 decreases the pressure in the reservoir 2, which is immediately counterbalanced by the water flowing from the Mariotte flask 3 so that the pressure in 1 is kept at equilibrium with the local atmosphere. The sensitivity of the system was in the range of 0.1 cm^3 gas consumption, detection being achieved by using a photoelectric device. Saturation of the catalyst with H_2 (40 cm^3/100 mg) had to be done before starting the reaction. This was made possible by using a two-compartment flask where the polymer and the catalytic system were initially separated as shown in *Figure 1*, the content of both compartments being mixed after the saturation of the catalytic system with H_2. As the stirring rate appeared to be a critical factor below 1300 r.p.m., magnetic stirring was always done at 2500 r.p.m. Under these conditions, the relative error was evaluated as less than 5%.

In a first series of experiments, hydrogenolysis of $PAABe_{100}$ was performed comparatively with three catalytic systems, namely Janssen, Johnson 37 and Johnson 65 in dimethylformamide (DMF) at 42°C. *Figure 2* shows that $PAABe_{100}$ was turned to PAA within 6 min by Johnson 37 and 12 min by Janssen, whereas no reaction was detected after 40 min in the case of Johnson 65. *Table 1* shows some characteristics of the catalytic systems, especially location of the metal and distributions of pore sizes. The comparison between *Figure 2* and *Table 1* shows that the rate of hydrogenolysis was maximum for the catalytic system with the lowest content of active metal and the greatest proportion of large pores (300–10 000 Å). In contrast, the Johnson 65 system, which had no metal at the surface and a large proportion of small pores, was not able to hydrogenolyse the protected poly(carboxylic acid). Therefore, the inactivity of Johnson 65 has been assigned to size exclusion effects.

The decrease of the reaction rate with time that is observed in the case of the Janssen catalyst depended on the concentration of the polyester and on the quantity of the catalytic system present in the reaction medium. Considering the whole set of data and the various H_2

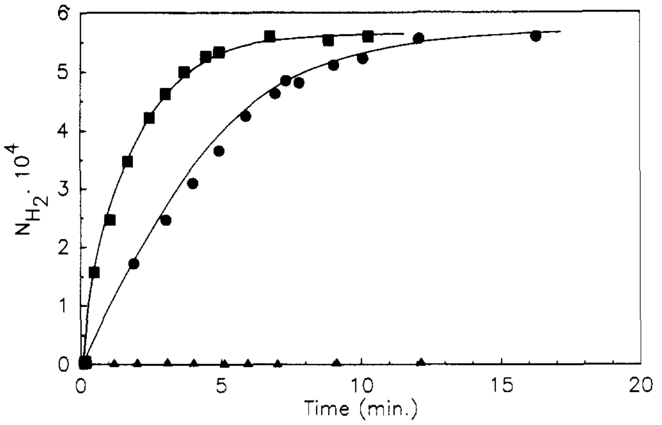

Figure 2 Variations of hydrogen consumption *versus* time for various Pd/charcoal catalytic systems ((●) Janssen, (■) Johnson 37, (▲) Johnson 65) under similar conditions: 40 mg catalytic system; 100 mg PAABe$_{100}$; $\bar{M}_w = 29\,000$, $\bar{M}_w/\bar{M}_n = 1.4$; solvent, DMF (25 cm^3); $T = 42°C$

Table 1 Characteristics of the commercial catalytic systems used

	Johnson 37	Johnson 65	Janssen
Pd amount (%)	5	5	10
Specific area (m^2 g^{-1})	960	740	760
Porous volume (cm^3 g^{-1})			
pore size <300 Å	0.63	0.61	Unknown
300 < pore size < 10 000 Å	0.81	0.23	0.23
Location of the metal	At surface	In pores	Unknown

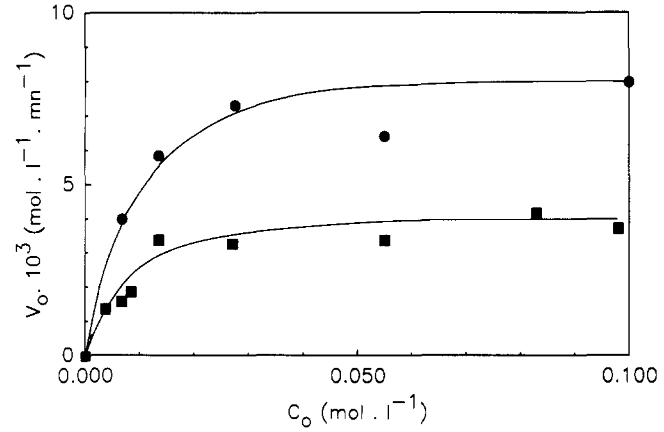

Figure 3 Variations of the initial rate of hydrogenolysis V_0 *versus* PAABe$_{100}$ ($\bar{M}_w = 74\,000$, $\bar{M}_w/\bar{M}_n = 1.6$) concentration for two amounts of the Janssen Pd/charcoal catalytic system ((■) 40 mg, (●) 100 mg) under similar conditions: DMF (25 cm^3); $T = 42°C$

consumption *versus* time plots obtained with the Janssen catalytic system, it was found that the rate $V_t = d[NH_2]/dt$ varies as [polyester]$^\alpha$ in large ranges of polymer concentration ($4 \times 10^{-3} < C_p < 10^{-1}$ mol l^{-1}) and amounts of catalytic system (20 to 400 mg/25 cm^3) provided α was given the value 0.7. None of the curves obtained for the Johnson 37 system varied as [polyester]$^{0.7}$, in agreement with the difference in profiles as compared with the Janssen system (*Figure 2*). Therefore, the α parameter appeared to be characteristic of the Janssen catalytic system and was regarded as a phenomenological internal order. Because data could not be characterized by simple kinetic laws, most of the following discussions have been based on V_0, the initial rate at time $t = 0$ given by the slope at $t = 0$ in H_2 consumption *versus* time plots. At low initial polymer concentration, V_0 increased linearly and then levelled off, thus showing that, for $C_0 > 0.03$ mol l^{-1}, the initial rate became independent of the polymer concentration (*Figure 3*). *Figure 4* shows data obtained for three fixed polymer concentrations and increasing amounts of the Janssen catalytic system. V_0 increased linearly in the presence of low amounts of catalytic system and levelled off for amounts above 250 mg/25 cm^3, i.e. in a large weight excess of the catalytic system with respect to the polymer present in the reaction medium. Further experiments were carried out in different solvent media, namely DMF, dioxane and 50/50 v/v ethyl acetate/ethanol mixture, with the Janssen catalytic system (*Table 2*). The initial hydrogenolysis rate V_0 decreased according to the order DMF > ethyl acetate/ethanol > dioxane. Interestingly, it was found that all the PAABe$_{100}$ molecules were hydrogenolysed in DMF and dioxane, as shown by i.r. and ^{1}H n.m.r., whereas only those low-molecular-weight molecules which were soluble in the ethyl acetate/ethanol mixture were converted in this medium.

Effect of polymer molecular weight

Figure 5 shows the consumption of hydrogen *versus* time for PAABe$_{100}$ fractions of different molecular weights at the same concentration in DMF and for a fixed amount of the Janssen catalytic system corresponding to the zone of the plateau that is observed in *Figure 3*. The rate of hydrogenolysis was found to decrease with the advance of the reaction and with the increase of

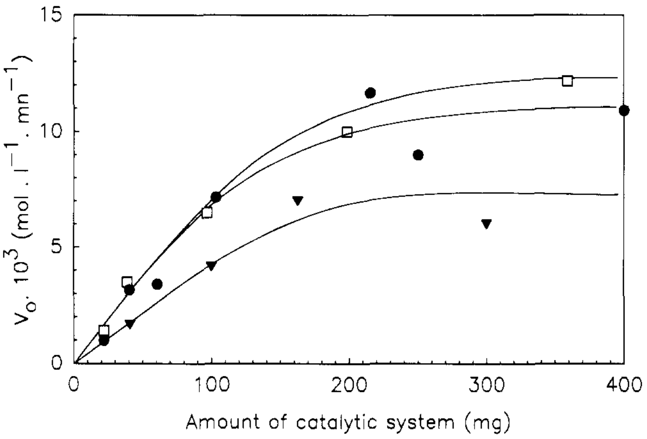

Figure 4 Variations of the initial rate of hydrogenolysis V_0 *versus* amount of Janssen catalytic system for three PAABe$_{100}$ ($\bar{M}_w = 74\,000$, $\bar{M}_w/\bar{M}_n = 1.6$) concentrations ((▼) 6.2×10^{-3}, (●) 24.7×10^{-3}, (□) 49.4×10^{-3} mol l^{-1}) under similar conditions: DMF (25 cm^3); $T = 42°C$

Table 2 Influence of solvent and temperature on the initial rate of hydrogenolysis: Janssen catalytic system, 60 mg; solvent, DMF (25 cm^3); PAABe$_{100}$ ($\bar{M}_w = 8400$, $I = 1.4$)

Solvent	Ethyl acetate/ ethanol (3/2 v/v)	Dioxane	DMF	DMF
Temperature (°C)	23	25	23	42
$V_0 \times 10^3$ (mol l^{-1} min^{-1})	1.2	0.9	4.8	20.0

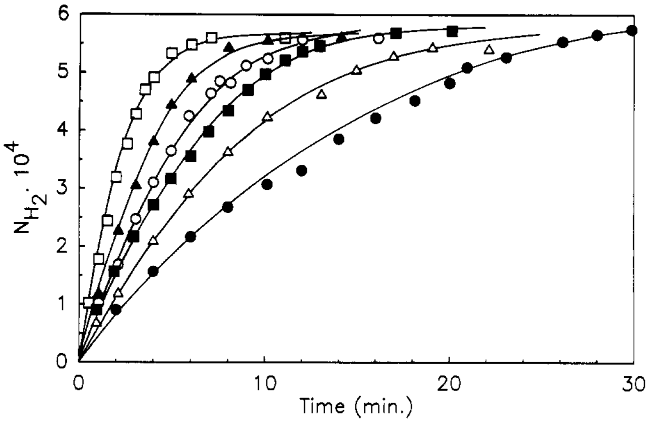

Figure 5 Hydrogen consumption *versus* time plots for PAABe$_{100}$ polymers with different molecular weights ((□) 7300, (▲) 19000, (○) 28000, (■) 88000, (△) 106000, (●) 134000) under similar conditions: PAABe$_{100}$ (40 mg); Janssen catalytic system (40 mg); DMF (25 cm^3); $T = 42°C$

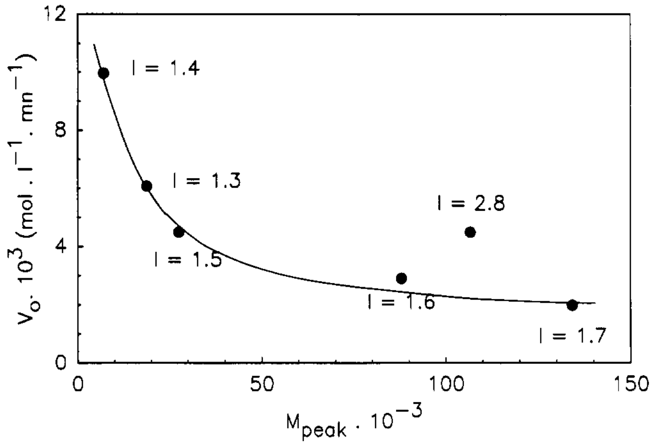

Figure 6 Values of the initial rate of hydrogenolysis for various molecular weights and molecular-weight distributions as defined by $I = \bar{M}_w/\bar{M}_n$ (for experimental conditions, see *Figure 5*)

molecular weight. *Figure 6* represents the variation of the initial rate V_0 as a function of M_{peak}, the relative molecular weight at the s.e.c. peak, and of $I = \bar{M}_w/\bar{M}_n$, the polydispersity index. Interestingly enough, the V_0 value found for the fraction with $I = 2.8$ fell far from the curve common to all the other fractions with comparable polydispersity indices ($1.3 < I < 1.7$). Furthermore, it was found that Pd/charcoal-catalysed partial hydrogenolysis can fractionate a polydisperse PAABe$_{100}$ mixture made by a (50/50 w/w) blending of two fractions with very different molecular weights (*Figure 7A*). At 40% gross conversion, the partially hydrogenolysed polymeric compound recovered after filtration and evaporation of the solvent appeared to be a mixture of a fraction insoluble in water and composed of large and slightly hydrogenolysed macromolecules (*Figure 7B*) and a fraction composed of small water-soluble molecules with high degree of hydrogenolysis (*Figure 7C*). Therefore, molecular weight appeared as a critical factor for the rate of hydrolysis. An attempt to normalize the data of *Figure 6* was made by combining size exclusion chromatography and kinetics data assuming that hydrogenolysis rate V_t at time t actually reflects the hydrogenolysis of molecules with a given size. For this, molecules with the same s.e.c. molecular weight M_i in a polydisperse population have been considered as reacting at the same rate V_i after a degree of hydrogenolysis Y % at which all the molecules with molecular weight $M_j < M_i$ were modified. Under these conditions, the fraction of modified macromolecules can be approximated from the ratio ($M_0 < M < M_i$) area/total area of the s.e.c. chromatograms. With this approximation, it has been possible to correlate the s.e.c. chromatograms and the kinetics plots of the different fractions through Y values taken as the experimental yields at times t in kinetics plots. *Figure 6* was thus turned to a master curve shown in *Figure 8*, where data corresponding to the different fractions now fit the same curve, regardless of polydispersity. At least two phenomena can be invoked to account for the fact that low-molecular-weight compounds react faster than high-molecular-weight ones: preferential adsorption of

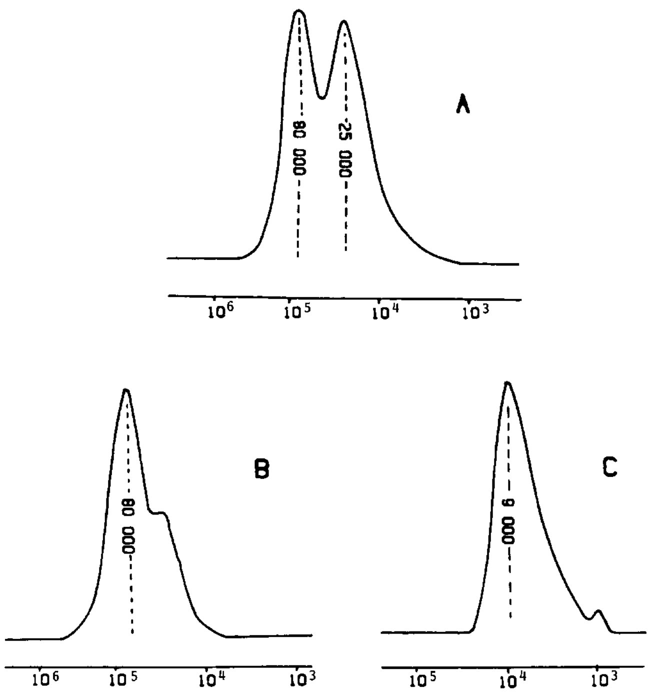

Figure 7 S.e.c. chromatograms for a mixture of two PAABe$_{100}$ fractions of different molecular weights before hydrogenolysis (A) and at 40% gross conversion: water-insoluble soluble fraction (B) and water-soluble fraction (C)

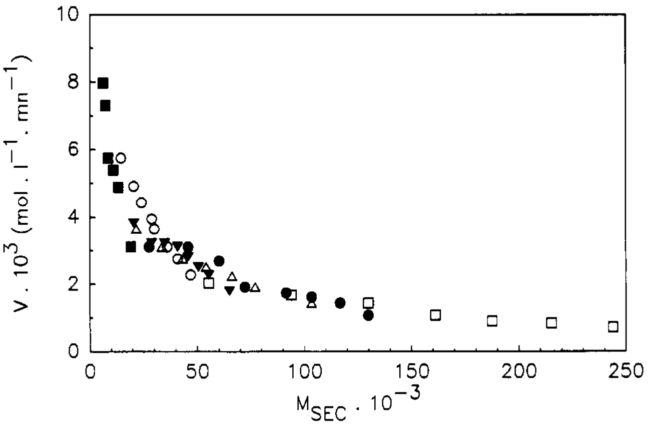

Figure 8 Molecular-weight dependence of the rate of hydrogenolysis as deduced from kinetics and s.e.c. molecular-weight distributions assuming that small macromolecules always react before larger ones

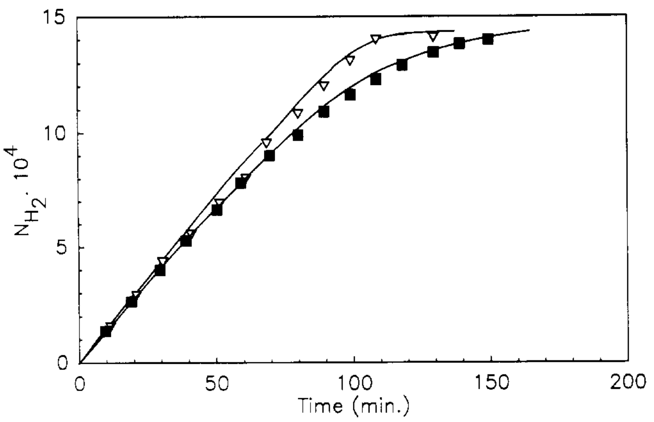

Figure 9 Variations of hydrogen consumption *versus* time for $PAABe_{100}$ (5.8×10^{-3} mol l^{-1}) (■) and for a $PAABe_{100}$ (5.8×10^{-3} mol l^{-1}) + $PAAH_{100}$ (5.8×10^{-3} mol l^{-1}) mixture (▿) under similar conditions: Johnson 37 (40 mg); dioxane (25 cm^3)

the smaller molecules on the surface of the active metal; and size exclusion effects based on the porosity of the catalytic system, assuming that the rate of hydrogenolysis of an isolated benzylated repeat unit is independent of molecule length. Theoretical considerations have been reported in the literature that involve interactions between macromolecules and surfaces in static situations[6–11]. For instance, it has been suggested that adsorption of macromolecules on smooth surfaces is molecular-weight-dependent with loop-forming mechanisms[12]. It was also proposed that the number of adsorbed repeat units is relatively greater for small macromolecules whereas the amount of adsorbed matter is relatively greater for large macromolecules[10]. In other words, small macromolecules spread more on a given surface than large ones, which tend to form more or longer loops. In the case of hydrogenolysis on the surface of a charcoal-supported Pd metal, only the initial stage is static. As soon as the reaction starts, the whole system becomes dynamic in the sense that adsorbed macromolecules react and thus are chemically transformed. Therefore, surface affinity of the adsorbed molecules changes dramatically as the reaction proceeds. In order to evaluate the relative affinities of the different macromolecules present in the medium for the catalyst surface, competition experiments were carried out by allowing $PAABe_{100}$ to react with hydrogen in the presence of poly(acrylic acid) ($PAAH_{100}$), the normal end-product of the hydrogenolysis reaction. *Figure 9* shows that 50% w/w $PAAH_{100}$ did not significantly perturb the reaction on $PAABe_{100}$ up to rather high values of the degree of conversion (>55–60%). Therefore, it has been concluded that $PAABe_{100}$ macromolecules interacted preferentially with the catalytic surface compared with $PAAH_{100}$ ones.

Competition experiments were also performed by mixing $PAABe_{100}$ with another poly(carboxylic acid) having a polyester backbone, namely poly(β-malic acid). In this case, V_0 was found to be almost half of the value normally given by $PAABe_{100}$ alone at a similar content of benzyl units. This finding shows that the polyester backbone of poly(β-malic acid) competed with $PAABe_{100}$ for the catalyst surface and validates the absence of effects of $PAAH_{100}$.

Whether preferential adsorption related to molecule size can act in favour of low- or high-*MW* macromolecules and thus can account for the higher reactivity of low-molecular-weight molecules is still unknown. Only radiolabelling techniques could provide conclusive information on this particular point. As far as the influence of porosity is concerned, size exclusion effects should work in favour of low-molecular-weight molecules. Basically, small molecules should have easier access to the metal located within small pores and thus should use a larger fraction of the active catalyst with respect to large molecules. Size exclusion effects and the fact that the Pd catalyst is located exclusively well inside the pores fit with the inactivity of the Johnson 65 catalyst as mentioned before. Size exclusion phenomena could also well explain the *MW* dependence of V_0 that is observed for the Janssen catalytic system in DMF, on the basis of a selective permeation according to molecular weights.

In order to collect more information on the relationships between catalytic action and molecular size, the molecular-weight dependence of V_0 was investigated in DMF at 42°C, for two different catalytic systems, namely Janssen and Johnson 37 (*Figure 10*). The curves were obtained by considering the same set of $PAABe_{100}$ fractions, which differed by molecular weight only, polydispersity indices being quite similar ($1.3 < I < 1.7$). In contrast to the monotonic decrease of V_0 found with the Janssen system when molecular weight increased, the Johnson 37 system gave rise to a sigmoidal curve with almost constant V_0 values for low-molecular-weight fractions, a dramatic decrease in the range of 30 000–40 000 g mol^{-1} and then no further change for higher molecular weights up to 150 000 g mol^{-1}. Unfortunately, we did not get any precise information about the location of the metal from the supplier for this particular catalytic system. Anyhow, the differences of behaviour exhibited by the Janssen and the Johnson 37 catalytic systems account well for the fact that only the first one gave hydrogenolysis rates varying as $[\text{polymer}]^{0.7}$.

Absorption isotherms

One of the striking features of Pd/charcoal-catalysed hydrogenolysis of benzyl ester protecting groups borne by poly(carboxylic acid) macromolecules is the limited rate found when amounts of polymer or of catalytic system present in the reaction medium are increased. As

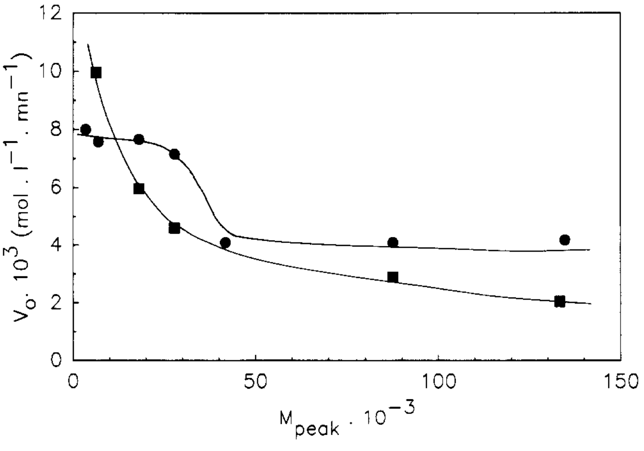

Figure 10 Variations of the initial rate of hydrogenolysis *versus* molecular weight as defined by the s.e.c. peak for the Janssen (■) and the Johnson 37 (●) catalytic systems under similar conditions: 100 mg of the polymer fractions (*Figure 6*); 40 mg of catalytic system; DMF at 42°C

it is well known that macromolecule absorption on a surface is also limited, attempts have been made to correlate both phenomena. PAABe$_{100}$ was allowed to stay in contact with the Pd/charcoal catalytic system under the conditions used for the previous kinetics studies. The concentrations of polymer before and after introducing the catalytic system were measured by u.v. spectrometry. *Figure 11* shows that the amount of polymer taken up by the catalytic system increased rapidly as the initial concentration increased and then levelled off to a limit close to 6% w/w. However, one has to remember that the catalytic system is composed of a porous support, which can absorb macromolecules, and of the active metal, which is deposited on the support and can adsorb macromolecules. At the moment, it is not possible to distinguish between the two phenomena. In an attempt to show the relative contribution of absorption of macromolecules by the porous charcoal support, hydrogenolysis reactions were conducted in the presence of catalytic and non-catalytic charcoal with similar levels of absorption of PAABe$_{100}$, namely 5% w/w. Data are given in *Table 3*. The presence of porous charcoal decreased the initial rate V_0 and the effect was dramatic when this charcoal was in large excess. However, it is of value to note that experimental rates V_0 observed under these conditions are lower than any possible rates calculated according to the variation of the polymer concentration in the solution phase (on the basis of 5% w/w uptake) or experimentally found so far, except if one takes into account exclusively the highest molecular weights investigated (*Figure 8*), a meaningless possibility. Accordingly, it is concluded that preferential absorption of molecules by the charcoal support and corresponding decrease of polymer concentration are not large enough to account for the observed decrease of V_0. At the moment, there is a lack of information to explain this feature.

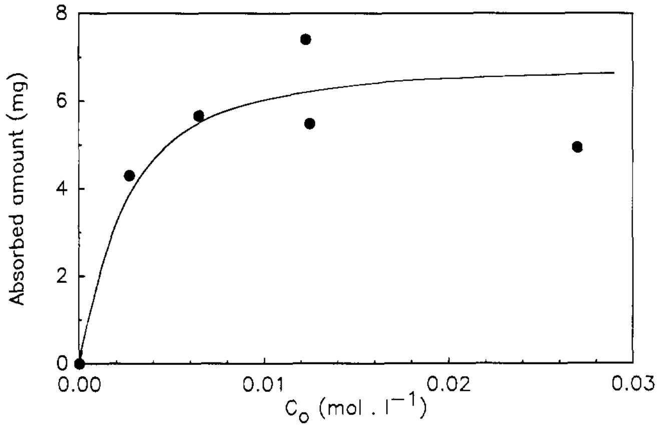

Figure 11 Variation of the amount of absorbed PAABe$_{100}$ ($\bar{M}_w$ = 74000, $\bar{M}_w/\bar{M}_n$ = 1.6) within 100 mg of Janssen catalytic system according to the initial polymer concentration C_0

Table 3 Initial rate of hydrogenolysis in the presence of catalytic and non-catalytic charcoal

Catalytic system (mg)	Non-catalytic charcoal (mg)	$V_0 \times 10^3$ (mol l^{-1} min^{-1})	Yield (%)
40	0	3.2	96
40	40	2.7	95
100	0	7.3	97
100	300	1.1	90

Partial hydrogenolysis of PAABe$_{100}$

Partial hydrogenolyses were carried out in different solvents and for two catalytic systems, namely Janssen and Johnson 37 (*Table 4*). In order to detect whether these reactions (i) affected all the macromolecules to yield copolymers of similar average gross composition or (ii) proceeded selectively to yield copolymer systems with a large range of compositions depending on molecular weights or (iii) yielded mixtures of copolymers and homopolymers, the recovered materials that gave milky mixtures in water were separated into water-soluble and water-insoluble fractions. Regardless of the degree of hydrogenolysis, the Janssen system yielded water-soluble fractions that were systematically 100% hydrogenolysed low-molecular-weight homopolymers. In contrast, the Johnson 37 system yielded insoluble ester-rich copolymer fractions and acid-rich copolymer fractions with rather narrow gross composition. Copolymers PAABe$_{10}$H$_{90}$

Table 4 Partial hydrogenolysis of PAABe$_{100}$ under different conditions

$\bar{M}_w$	I	Catalytic system	Solvent	Partial yield (%)	Appearance in water	Carboxylic groups in water-soluble fraction (%)
8000	2.0	Janssen	Dioxane	20	Milky	100[b]
20000	1.3	Janssen	Dioxane	80	Milky	100[b]
20000	1.3	Janssen	DMF	80	Milky	100[b]
8000	2.0	Johnson 37	EA/EtOH[a]	80	Milky	77[b]
43000	1.4	Johnson 37	Dioxane	70	Milky	88[c]
23000	1.2	Johnson 37	Dioxane	25	Milky	90[c]
23000	1.2	Johnson 37	Dioxane	40	Milky	87[c]
23000	1.2	Johnson 37	Dioxane	50	Milky	82[c]
23000	1.2	Johnson 37	Dioxane	80	Milky	88[c]

[a] Ethyl acetate/ethanol (3/2 v/v)
[b] Controlled by ^{1}H n.m.r.
[c] Potentiometric determination

and $PAABe_{18}H_{82}$, which were apparently water-soluble, actually showed the typical characteristics of aggregated amphiphilic copolymers, as already mentioned in the series of poly(β-malic acid) derivatives[3]. In particular, a large peak was found at the exclusion volume in s.e.c. and solubilization of the water-insoluble Yellow OB dye was observed, thus reflecting the presence of lipophilic microdomains[13,14]. These features argue strongly in favour of a blocky structure for these copolymers. In order to support the existence of particular co-unit distributions, acid-rich copolymers obtained by hydrogenolysis ($PAABe_{10}H_{90}$ and $PAABe_{18}H_{82}$) were compared with copolymers of similar gross composition obtained by acidic hydrolysis of PAABe ($CoPAABe_{32}H_{68}$, $CoPAABe_{14}H_{86}$ and $CoPAABe_{4}H_{96}$). In contrast to the two copolymers obtained via hydrogenolysis, none of the equivalent copolymers obtained by simple hydrolysis showed the characteristics of aggregation recalled above. $CoPAABe_{32}H_{68}$ was able to increase the solubility of Yellow OB in water but it was because of a compact-coil conformation[13] and not because of aggregation as shown by the absence of any species at the exclusion volume in s.e.c.

Hydrogenolysis of $PMABe_{100}$

Poly(benzyl malolactonate) ($PMLABe_{100}$)[2] and $PAABe_{100}$ (this work) have been shown to be convertible to $PMLAH_{100}$ and $PAAH_{100}$ respectively by Pd/charcoal-catalysed hydrogenolysis under various conditions, and $PAABe_{100}$ was found to be less reactive than $PMLABe_{100}$.

With the Janssen catalytic system in DMF at 42°C, $PMABe_{100}$ was non-reactive whereas $PMLABe_{100}$ and $PAABe_{100}$ did react. In contrast, the same $PMABe_{100}$ polymer was turned to poly(methacrylic acid) ($PMAH_{100}$) at 120°C. With Johnson 37 in dioxane, total hydrogenolysis was feasible in 12 h at room temperature. The order of reactivities $PMLABe_{100} > PAABe_{100} > PMABe_{100}$ deduced from hydrogenolysis rates is the same as that corresponding to acid strengths of carboxylic groups in corresponding polyelectrolytes. At the moment, it is not possible to say whether this finding is fortuitous or results from a relation between ester cleavage and acid strength.

Insofar as partial hydrogenolysis is concerned, $PMABe_{100}$ behaved as the two other benzyl protected poly(carboxylic acids) and led to aggregated water-soluble copolymers under proper conditions, thus showing that the formation of blocky copolymers by hydrogenolysis of benzyl ester pendant groups on the surface of a solid catalyst is a general phenomenon.

CONCLUSIONS

In conclusion, it has been shown that it is possible to recover the parent poly(carboxylic acids) from benzyl ester protected derivatives by using a Pd/charcoal catalytic system provided proper conditions are used. Indeed, the completion of the reaction depends on many factors. We have shown that molecular weight, molecular-weight distribution, solvent and temperature are very important factors. However, it is remarkable that the catalytic system seems to be the key factor. Unfortunately, only very little is known on the structure and morphology of the catalytic systems commercially available. On the other hand, the characterization of such catalytic systems appears very difficult, as it must include not only porosity and pore-size distribution but also the active metal itself, which can be on the surface or well inside pores and thus can or cannot be accessible to macromolecules. This finding could well explain why total catalytic hydrogenolysis of poly(glutamic acid benzyl ester) has never been shown as a 100% efficient means to cleave benzyl ester protecting group and liberate poly(glutamic acid).

Beside the complexity of the reaction mixture, we have shown that partial hydrogenolysis is also dependent on many factors and can lead to different compounds depending on the catalytic system and the experimental conditions. For degrees of hydrogenolysis lower than 80%, the recovered macromolecular products are heterogeneous in chemical composition. Chemical molecular-weight fractionations are observed. Furthermore, blocky distributions of co-repeat units are sometimes obtained, which lead to water-soluble copolymers aggregated in aqueous media to form hydrophobic microdomains comparable to those observed for block copolymers synthesized as such by anionic polymerization. Last but not least, the water-soluble, or better, the water-dispersable, copolymers obtained by hydrogenolysis on the surface of the Pd metal supported by porous charcoal showed ester contents that were almost independent of the average degree of hydrogenolysis. Indeed, compositions of the water-soluble polymers were found to be almost constant for given polymer, temperature and catalytic system. This feature might reflect surface affinity phenomena.

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