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Telechelic polyesters of ethane diol and adipic or sebacic acid by means of bismuth carboxylates as non-toxic catalysts

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Abstract

Dimethyladipate or dimethylsebacate were polycondensed with an excess of 1,2-ethane diol in bulk using two different temperature/time programs. Bismuth(III)*n*-hexanoate ($BiHex_3$), tin(II)2-ethylhexanoate ($SnOct_2$) and titanium tetrabutoxide were used as catalysts. Only the bismuth catalyst yielded clean telechelic polyesters having two ethylene glycol endgroups. With $SnOct_2$ cyclic oligoesters were obtained as byproducts. $Ti(OBu)_4$ yielded OH-terminated linear chains containing large amounts of diethylene glycol units (detectable up to three ether groups per chain). Furthermore, small amounts of cycles were also formed. Acid-catalyzed polycondensations of ethylene glycol with sebacic acid gave low yields of low oligomers, part of which contained diethylene glycol units.

Keywords: Biodegradable polyesters; Telechelics; Bismuth hexanoate

1. Introduction

Aliphatic polyesters derived from dicarboxylic acids and α-ϖ-dihydroxyalkanes are known since the pioneering work of Carothers [1,2]. Due to their relatively low melting temperatures (T_ms typically in the range of 50–120 °C) and due to their sensitivity to hydrolysis, these polyesters have not found any technical application for many decades. However, more recently the interest in such polyesters has rapidly increased due to their biodegradability and the non-toxic character of their degradation products.

The classical synthesis of such aliphatic polyesters is based on an acid catalyzed polyesterification of the dicarboxylic acids and diols with azeotropic removal of the liberated water (Eq. (1)). The most widely used alternative approach consists of a transesterification of dimethyl esters with an excess of α-ϖ-dihydroxyalkanes (Eq. (2)). This approach was also used for many decades for the technical syntheses of poly(ethylene terephthalate) and poly(butylene terephthalate). The most efficient and most widely used catalyst for this type of polycondensation is titaniumtetrabutoxide (or other tetraalkoxides) alone or in combination with additives [3–7]. For temperatures below 200 °C, tin(II) salts and tin(II) alkoxides have proven to be excellent transesterification catalysts particularly useful for ring-opening polymerizations of lactones and lactides [8–10]. However, these tin compounds are unstable at temperatures around or above 250 °C and they possess a rather high cytotoxicity.

Quite recently we have found that bismuth(III) carboxylates are efficient and versatile catalysts/initiators for ring-opening polymerizations of lactones and cyclic carbonates [11–14]. These bismuth salts are particularly interesting because of their extraordinarily low toxicity [15–18]. Therefore, they are promising as catalysts and initiators when the resulting polyesters are designed for pharmaceutical and medical applications. In this context it was the purpose of this work to study the usefulness of bismuth(III)*n*-hexanoate ($BiHex_3$) as transesterification catalyst for the preparation of telechelic oligo- and polyesters derived from 1,2-ethane diol and adipic or sebacic acid (**Lb** chains in Scheme 1).

2. Experimental

2.1. Materials

Dimethyladipate (DMA), dimethylsebacate (DMS), bismuth(III) acetate, sebacic acid and *p*-toluene sulfonic acid (monohydrate) were purchased from Aldrich Co. (Milwaukee,

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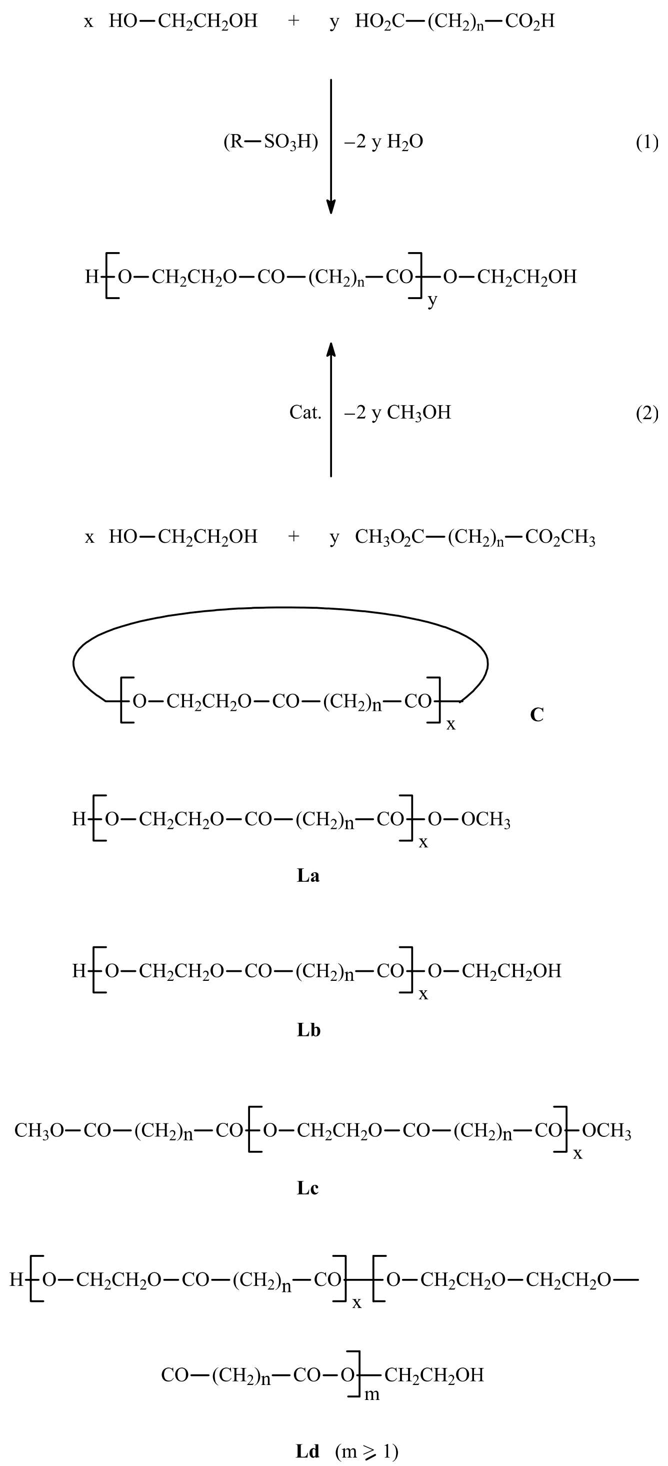

Scheme 1. Potential reaction products of polycondensations of ethane diol with dimethyl adipate ($n=4$) or sebacate ($n=8$).

WI, USA) and used as received. Bismuth(III) hexanoate, $BiHex_3$, was prepared from bismuth acetate and *n*-hexanoic acid as described previously [12]. Tin(II)2-ethylhexanoate ($SnOct_2$) was also purchased from Aldrich Co. and purified as described previously [9]. Ethane diol was kindly supplied by BASF AG (Ludwigshafen, Germany). It was azeotropically dried with toluene and distilled in vacuo.

2.2. Polycondensations (typical procedures)

(A) with dimethylsebacate and $BiHex_3$ up to 260 °C

Dimethylsebacate (30 mmol), ethane diol (120 mmol) and $BiHex_3$ (0.03 mmol) were weighed into a cylindrical glass reactor equipped with mechanical stirrer, gas-inlet and gas-outlet tubes. The reaction vessel was immersed into an oil bath preheated to 100 °C. After rapid heating to 180 °C, the following time/temperature program was applied: 1 h/180 °C, 0.5 h/220 °C, 0.5 h/240 °C, 2 h/200 °C + 0.5 h vacuum. The cold product was dissolved dichloromethane and precipitated into methanol.

(B) With sebacic acid and *p*-toluene sulfonic acid

Sebacic acid (100 mmol), ethane diol (400 mmol) and *p*-toluene sulfonic acid monohydrate (1.0 mmol) were weighed into a 250 mL three-necked flask equipped with mechanical stirrer, distillation head (+cooler) and dropping funnel. Toluene (100 mL) was added and the reaction vessel was placed into an oil bath preheated to 120 °C. The temperature was raised until the toluene slowly began to distill. The distilled toluene was continuously replaced using a dropping funnel. After 6 h, the reaction mixture was cooled to 20 °C. The white product which had crystallized was isolated by filtration, washed with toluene and dried at 25 °C in vacuo. The filtrate was concentrated in vacuo and the remaining product was characterized.

(C) With dimethyladipate and $Ti(OBu)_4$ up to 240 °C

Dimethyladipate (30 mmol) and ethane diol (120 mmol) were weighed into a cylindrical glass reactor equipped with mechanical stirrer, gas-inlet and gas-outlet tubes. $Ti(OBu)_4$ (0.03 or 0.06 mmol) was injected in the form of a 0.5 M solution in chlorobenzene. The reactor was placed into an oil bath preheated to 100 °C. The temperature was rapidly raised to 180 °C, after 1 h at 180 °C it was raised to 200 °C, for 1.5 h, to 220 °C, for 0.5 h and to 240 °C for 2 h. Finally, vacuum was applied for 0.5 h. The cold product was dissolved in dichloromethane (40– 50 mL) and precipitated into cold methanol (500 mL).

2.3. Measurements

The inherent viscosities were measured in dichloromethane with an automated Ubbelohde viscometer thermostated at 20 °C.

The 400 MHz ^1H NMR spectra were recorded on a Bruker ‘Avance 400’ NMR spectrometer in 5 mm o.d. sample tubes. $CDCl_3$ containing TMS served as solvent and shift reference. The MALDI-TOF mass spectra were measured with a Bruker Biflex III mass spectrometer equipped with a nitrogen laser ($\lambda=337$ nm). All spectra were recorded in the reflection mode with an acceleration voltage of 20 kV. The irradiation targets were prepared from chloroform solutions with dithranol as matrix and K-trifluoroacetate as dopant. The SEC measurements were performed with a home-made chromatograph

Table 1
Polycondensations of dimethyl sebacate (DMS) with ethylene glycol in bulk catalyzed by $BiHex_3$, $SnOct_2$ or $Ti(OBu)_4$

Exp. no.	Catalyst	DMS/catalyst	Final temp. (°C)	Yield (%)	η_{inh}[a] (dL/g)	DP (^1H NMR)	Reaction products (MALDI-TOF)[b]
1a	$BiHex_3$	1000/1	240	80[c]	0.11[c]	15[c]	**Lb**
1b[d]	$BiHex_3$	1000/1	240	82	0.12	16	**Lb**
2	$Ti(OBu)_4$	1000/1	240	92	0.16	–	**Lb**, **Ld** ($m=1,2$), **C**
3	$SnOct_2$	1000/1	240	88	0.14	–	**Lb**, **C**
4	$BiHex_3$	500/1	240	84	0.15	20	**Lb**
5	$Ti(OBu)_4$	500/1	240	82	0.16	–	**Lb**, **Ld** ($m=1,2$), **C**
6	$BiHex_3$	1000/1	260	83	0.22	29	**Lb**
7	$Ti(OBu)_4$	1000/1	260	80	0.11	–	**Lb**, **Ld** ($m=1$–3), **C**
8	$SnOct_2$	1000/1	260	84	0.12	–	**Lb**, **C**, (**Ld**)
9	$BiHex_3$	500/1	260	85	0.18	24	**Lb**, (**C**)
10	$Ti(OBu)_4$	500/1	260	84	0.20	–	**Lb**, **Ld** ($m=1$–3), **C**

[a] Measured at 20 °C with $c=2$ g/L in CH_2Cl_2.
[b] Symbols in brackets mean only traces were detectable.
[c] $M_n=3100$ Da, $M_w=6000$ Da.
[d] Repetition of 1a with upscaling of monomer and catalyst quantities by a factor of 4: $M_n=3300$ Da, $M_w=6300$ Da.

equipped with UV and RI detectors. Tetrahydrofuran served as eluent at 25 °C. The measurements were calibrated with commercial polystyrene standard and finally evaluated with the M.H. Eq. (3) [19].

$$[\eta] = 1.395 \times 10^{-4} \times M_W^{0.786} \quad (3)$$

3. Results and discussion

3.1. Polycondensations of dimethyl sebacate

The present work is based on polycondensations of two dimethylesters, namely those of adipic acid and sebacic acid. Most polycondensations were conducted with dimethyl sebacate, because its higher boiling point is favorable for experiments above 200 °C. In preliminary polycondensation experiments (not described here in detail) it was found that reaction temperatures ≤220 °C are too low for high conversions within a time frame of 1 day. Therefore, two temperature/time programs were elaborated in Section 2 which were characterized by a final temperature of 240 °C or 260 °C. Since telechelic oligo-/polyesters having two OH-endgroups were desired as endproducts, an excess of ethane diol was necessary, and in all polycondensations of this work (so far dimethyl esters served as reaction partners) an excess of 300 mol% was used.

The catalytic activity of $BiHex_3$ was compared to that of $SnOct_2$ and $Ti(OBu)_4$ under identical conditions. In a first small series of polycondensations, the DMS/catalyst ratio was fixed at 1000/1 (Nos 1–3 and 6–8, Table 1).

The MALDI-TOF mass spectra (m.s.) of the reaction products gave the following results. Clean OH-terminated telechelics (**Lb**, Scheme 1) were obtained from $BiHex_3$ as illustrated in Fig. 1. With $Ti(OBu)_4$ the **Lb** chains were again the main product, but analogous chains containing one or two diethylene glycol units (**Ld**, $m=1$, 2) were present in sizable amounts. Furthermore, cyclic oligoesters were detectable. With $SnOct_2$ as catalyst, cycles and **Ld** chains were formed as byproducts (Fig. 2). When the final reaction temperature was

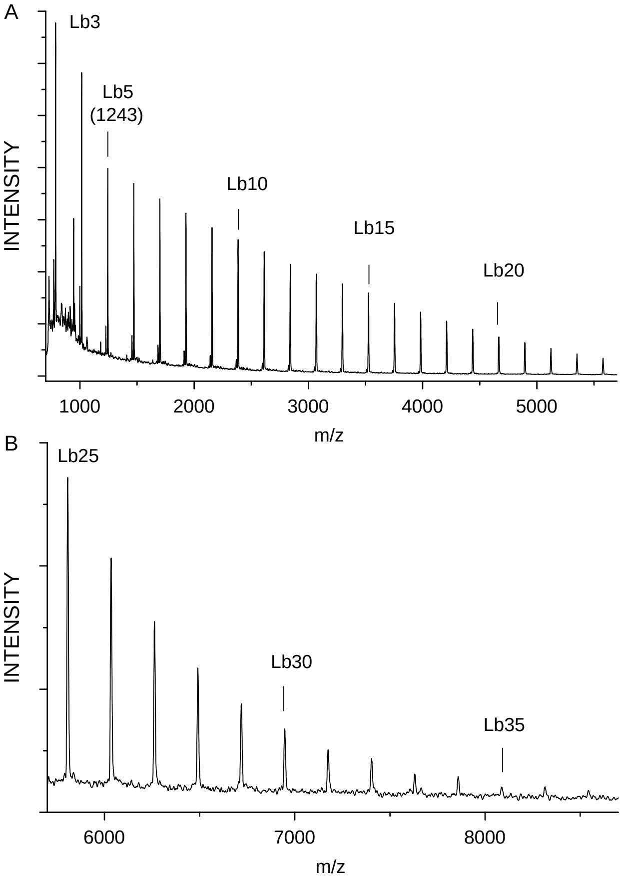

Fig. 1. MALDI-TOF mass spectrum of the telechelic polyester No. 1, Table 1, prepared from dimethyl sebacate with $BiHex_3$ as catalyst at 240 °C.

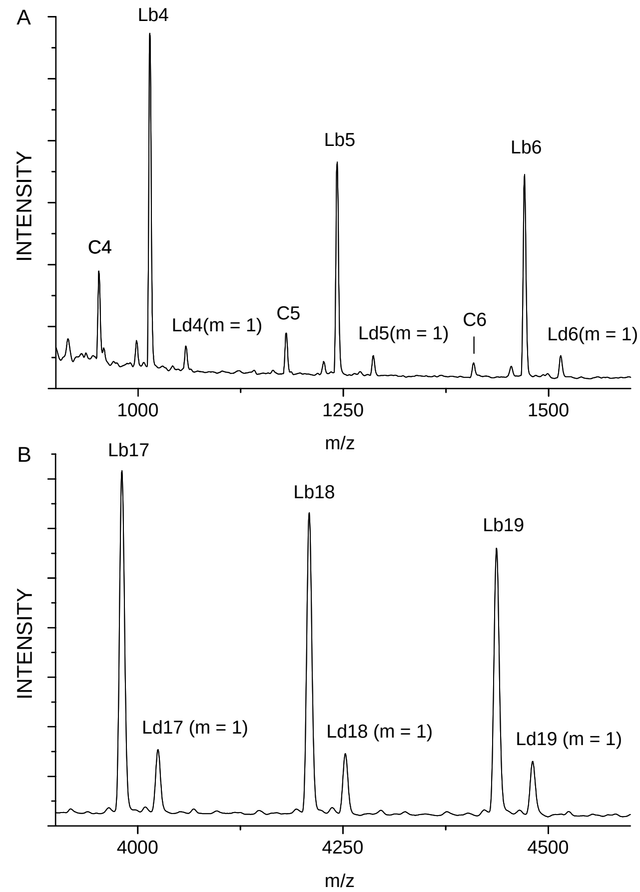

Fig. 2. MALDI-TOF mass spectrum of the polyester No. 3, Table 1, prepared from dimethyl sebacate with SnOct$_2$ at 240 °C.

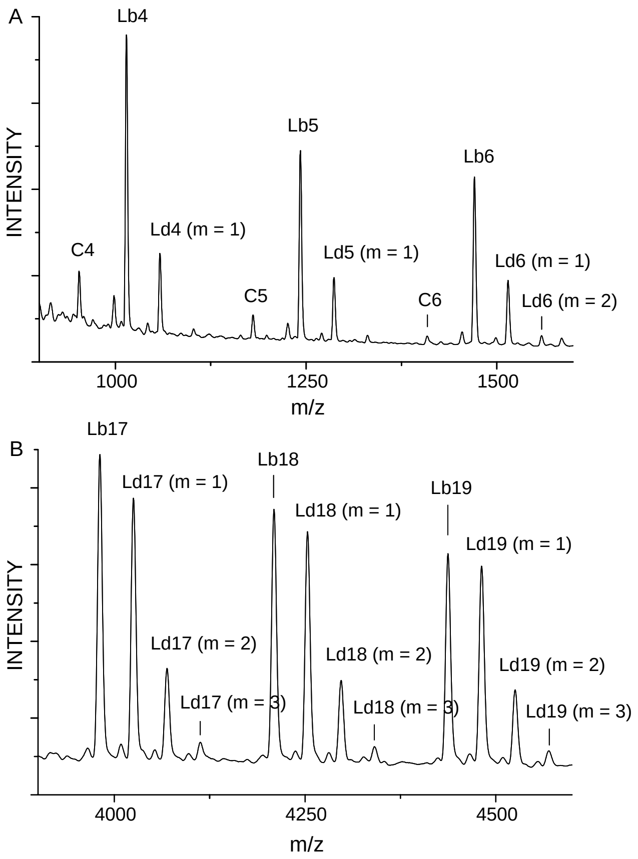

Fig. 3. MALDI-TOF mass spectrum of the polyester No. 6, Table 1, prepared from dimethyl sebacate with Ti(OBu)$_4$ at 260 °C.

raised to 260 °C, a quite similar pattern of products was found. BiHex$_3$ exclusively yielded **Lb** telechelics. However, Ti(OBu)$_4$ and SnOct$_2$ produced even more side reactions. The Ti(OBu)$_4$-catalyzed polyester contained **Ld** chains with up to three diethylene glycol units as demonstrated in Fig. 3. The existence of ether groups is also documented in the ^{1}H NMR spectrum by a triplet signal at 3.7 ppm (Fig. 4). With SnOct$_2$ a larger fraction of cycles was formed and also a larger fraction of **Ld** telechelics containing one diethylene glycol unit ($m=1$).

The polycondensations performed with monomer/catalyst ratios of 500/1 (Nos 4+5 and 9+10, Table 1) gave the expected result that side reactions were more intensive, regardless of catalyst and temperature. Even BiHex$_3$ produced traces of cycles when the temperature was raised to 260 °C (No. 9), but **Ld** telechelics were not detectable. In summary, a much cleaner polycondensation process was catalyzed by BiHex$_3$ than by both other catalysts.

The resulting telechelics with **Lb** structure had melting temperatures in the range of 71–73 °C. The average degrees of polymerization were calculated from the CH$_2$OH-endgroups by ^{1}H NMR spectroscopy (Table 1). This method is expected to give reliable results in the absence of cycles. Therefore, it was of interest to compare the number average molecular weights (M_ns) to those obtained from SEC measurements. For this purpose the polycondensation No. 1a of Table 1 was repeated with a four-times larger quantity of monomers and catalyst to check the reproducibility which was found to be satisfactory (No. 1b). Afterwards, both samples were subjected to SEC measurements in THF. From SEC measurements of poly(ε-caprolactone) it was known that the usual calibration with commercial polystyrene standards overestimates the real

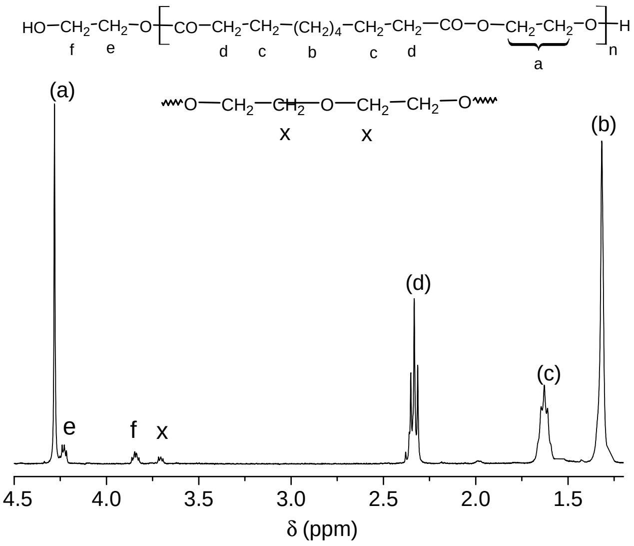

Fig. 4. Four hundred megaHertz ^{1}H NMR spectrum of the polyester No. 7, Table 1, prepared from dimethyl sebacate with Ti(OBu)$_4$ at 260 °C.

Table 2
Polycondensations of sebacic acid with ethane diol in boiling toluene catalyzed by *p*-toluene sulfonic acid

Polyc. no.	Sebacate acid/catalyst	Molar excess of ethane diol (%)	Yield (%)	η_{inh}[a] (dL/g)	Reaction products
1	1000/1	10	58[a]	0.05[b]	30–35% sebacic acid
2	100/1	10	62[b]	0.04[b]	20–25% sebacic acid
3	100/1	120	62	0.05	**Lb**, **Ld**, **Lc**

[a] Measured at 20 °C with $c = 2$ g/L in CH_2Cl_2.

[b] After separation from unreacted sebacic acid.

molecular weights by 50–100% [19–23] (depending on the range of molecular weights). More realistic M_ns were obtained [22] when the SEC curves were calibrated with the M.H. Eq. (3) [19], a procedure which corresponds to the universal calibration. The M_ns then obtained overestimated the M_ns of poly(εCL) determined by ^{1}H NMR endgroup analyses by approximately 10%. Acceptable results were also found in this work, when the SEC curves of the polyester samples Nos 1a and 1b (Table 1) were calibrated with Eq. (3). The M_n data listed in the footnotes of Table 1 were about 10% lower than those calculated from the average degrees of polymerization determined by ^{1}H NMR endgroup analyses. Polydispersities close to 2.0 are in good agreement with Flory's theory of step-growth polymerizations [24] in the absence of cyclization.

3.2. Polycondensations of sebacic acid

In order to find out how the classical polycondensation method (Eq. (1)) performs with a time limit of 8 h, three polycondensations of ethylene glycol with sebacic acid were conducted (Table 2). As usual 4-toluene sulfonic acid was used as catalyst and toluene as reaction medium for the azeotropic removal of the liberated water. When a monomer/catalyst ratio of 1000/1 was used (No. 1, Table 2) in analogy to the transesterification experiments of Table 1, 30–35% of unreacted sebacic acid crystallized from the reaction mixture upon cooling. A higher concentration of catalyst enhanced the conversion (No. 2, Table 2), but unreacted sebacic acid was still recovered. A larger excess of ethylene glycol had finally the consequence of a complete conversion of sebacic acid (No. 3). Nonetheless, only low oligomers of **Lb** structure were obtained and the m.s. indicated the formation of diethylene glycol units (**Ld** chains with $m = 1$) as expected when primary alcohols are reacted with an acidic catalyst. Therefore, this classical method proved to be inferior to the $BiHex_3$-catalyzed transesterification process (Eq. (2)).

3.3. Polycondensations of dimethyl adipate (DMA)

Six polycondensations were performed with ethylene glycol and dimethyl adipate using again a feed ratio of 4:1. $BiHex_3$ and $Ti(OBu)_4$ were compared at DMA/catalyst ratios of 1000/1 and 500/1. Furthermore, the final reaction temperature was varied from 240 to 260 °C with a DMA/catalyst ratio of 1000/1. The results (compiled in Table 3) showed the same trends as those observed of dimethyl sebacate. The conversion of methyl ester groups was complete, so that no **La** and **Lc** were detectable. With the lower catalyst concentration, $BiHex_3$ yielded clean telechelics of **Lb** structure (Nos 1 and 5, Table 3). When the catalyst concentration was doubled (Nos 3 and 6), traces of **Ld** chains were formed and at the higher temperature also traces of cycles became detectable. $Ti(OBu)_4$ produced small amounts of cycles under all conditions. However, the most conspicuous result is the large fraction of linear chains containing one or more diethylene glycol units (**Ld** with $m = 1$–3). Their content was distinctly higher than in the worst case of DMS-based polycondensations (Fig. 3). In summary, the results obtained from polycondensations of DMS were fully confirmed by the polycondensations of DMA. After these results were obtained polycondensations Nos 1 and 5 were repeated and the crude reaction products were examined by MALDI-TOF mass spectrometry. Their m.s. were almost identical with those of the precipitated polyesters. However, small amounts of byproducts having molecular weights below

Table 3
Polycondensations of dimethyl adipate (DMA) with ethylene glycol in bulk catalyzed by $BiHex_3$ or $Ti(OBu)_4$

Exp. no.	Catalyst	DMS/catalyst	Final temp. (°C)	Yield (%)	η_{inh}[a] (dL/g)	DP (^{1}H NMR)	Reaction products (MALDI-TOF)
1	$BiHex_3$	1000/1	240	79	0.25	25	**Lb**
2	$Ti(OBu)_4$	1000/1	240	78	0.11	–	**Lb**, **Ld**, **C**
3	$BiHex_3$	500/1	240	83	0.13[b]	21[b]	**Lb**, (**Ld**)
4	$Ti(OBu)_4$	500/1	240	79	0.12	–	**Lb**, **Ld**, **C**
5	$BiHex_3$	1000/1	260	75	0.11	18	**Lb**
6	$BiHex_3$	500/1	260	75	0.12	–	**Lb** (**C**+**Ld**)

[a] Measured at 20 °C with $c = 2$ g/L in CH_2Cl_2.

[b] $T_g = 47$ °C, $T_m = 51$ °C from DSC measurements with a heating rate of 10 °C/min.

1000 Da are not detectable due to the matrix signals. Therefore, it cannot be excluded that small amounts of cyclic dimmers, trimers or tetramers were formed.

4. Conclusions

The polycondensations studied in this work revealed that $BiHex_3$ is, in fact, an efficient and particularly useful transesterification catalyst because it enables the preparation of clean telechelic oligo- and polyesters having two OH-endgroups (**Lb** chains). This synthetic approach seems to be applicable to most, if not all, aliphatic dicarboxylic acids. The absence of cycles and other byproducts allows for the determination of $\overline{DP}$s from endgroup analyses. This fact is in turn a useful basis for a variety of chain extension reactions. Therefore, these telechelics are certainly useful building blocks for a variety of biodegradable block copolymers in as much as $BiHex_3$ is a catalyst of particularly low toxicity.

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