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Polyanhydrides. 2. Thermotropic Poly(ester anhydride)s Derived from Terephthalic Acid, Substituted Hydroquinones, and 4-Hydroxybenzoic Acids

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ABSTRACT: Terephthaloyl chloride was condensed in bulk with mixtures of silylated hydroquinone, methylhydroquinone, or phenylhydroquinone and silylated 4-hydroxybenzoic acid, 3-methoxy-4-hydroxybenzoic acid, or 3,5-dimethoxy-4-hydroxybenzoic acid. In this way three classes of poly(ester anhydride)s were prepared in high yields. ^{13}C NMR spectra indicate complete transacylation. Most poly(ester anhydride)s are amorphous and form a nematic melt above the glass transition. Films of poly(ester anhydride)s are stable in neutral water for at least 6 months. In contact with alkaline water (pH 10.4) the rate of hydrolysis depends on the content of anhydride groups.

Introduction

Fully aromatic thermotropic polyesters were recently commercialized by various chemical companies because they possess a combination of numerous useful properties which render them attractive engineering plastics or high-strength fibers. Characteristic properties of this group of polyesters are high thermostability, low sensitivity to oxidation in combination with low inflammability, low melt viscosity due to a nematic mesophase, low thermal expansion coefficients, and high heat distortion temperatures.

In the past decade another group of polymeric materials, namely, biodegradable and resorbable polymers, has attracted much interest for the following reasons. Resorbable polymers yielding nontoxic degradation products such as lactic acid or β-hydroxybutyric acid are useful matrix polymers for drug delivery systems, as medical sutures, or for the internal fixation of bone fractures. Furthermore, various types of biodegradable materials may serve as films and foils for packaging or as engineering plastics. However, almost all groups of so-called biodegradable materials are entirely aliphatic or contain aliphatic units in their backbone.

In this connection the present work has the purpose of presenting an approach which allows one to impart a higher rate of biodegradation (e.g., by hydrolysis) into thermotropic, fully aromatic engineering plastics. This approach is based on the incorporation of anhydride groups into polyesters in such a way that its molar fraction and, thus, the rate of hydrolysis can be varied over a broad range. Such a variation is, of course, necessary for the optimization of the hydrolytic stability for potential applications under variable conditions. It was quite recently demonstrated[1] that aromatic poly(ester anhydride)s containing 50 mol % anhydride groups may be thermotropic.

Finally, it is to be mentioned that in the past decade numerous more or less aliphatic polyanhydrides were synthesized and, in some cases, studied as biodegradable materials for pharmaceutical or medical applications.[2-10]

Experimental Section

Materials. Terephthaloyl chloride was a gift of Bayer AG and was distilled in vacuo prior to polycondensation. Hydroquinone and 4-hydroxybenzoic acids were again gifts of Bayer AG, but used without purification. Methyl- or phenylhydroquinone and 3-methoxy- or 3,5-dimethoxy-4-hydroxybenzoic acid were purchased from Aldrich Chemical Co. (St. Louis, MO) and used without purification. All hydroquinone and hydroxybenzoic acids were silylated with hexamethyldisilazane in refluxing toluene (2-4 h) and isolated by distillation in vacuo.

Polycondensations. Terephthaloyl chloride (40 mmol), a mixture of a silylated diphenol and a silylated 4-hydroxybenzoic acid (together 40 mmol), and 10 mg of benzyltriethylammonium chloride were weighed under nitrogen into a cylindrical glass reactor equipped with gas-inlet and -outlet tubes. The reaction mixture was heated with stirring and under nitrogen from 120 to 290 °C over a period of ca. 4 h. Vacuum was then applied for an additional 0.5 h. The crude, cold reaction products were washed with dry tetrahydrofuran, dried in vacuo at 60-65 °C, and characterized without reprecipitation.

Hydrolysis. Disks with a diameter of 30 mm and a thickness of approximately 0.15 mm were prepared with a pressure of 60 bar at 210 °C for 5 s. These disks were immersed at 20 °C either in neutral water (200 mL) containing a phosphate buffer (Merck Co., Darmstadt, Germany) or in alkaline water which was 0.1 M in Na_2CO_3 and 0.1 M in $NaHCO_3$. Before weighing, the wet disks were washed with distilled water, acetone, and diethyl ether and finally dried at 80 °C for 45 min.

Measurements. DSC measurements were conducted with a Perkin-Elmer DSC-4 under nitrogen in aluminum pans at a heating rate of 20 °C/min.

Inherent viscosities were measured with an automated Ubbelohde viscometer thermostated at 20 °C.

IR spectra were obtained on a Nicolet SXB 20 FT spectrometer. The poly(ester anhydride)s were dispersed in liquid paraffin (Uvasol, Merck AG, FRG).

The ^{1}H and ^{13}C NMR spectra (Figures 4 and 5) were measured from solutions of a poly(ester anhydride) (300 mg) in a mixture (3 mL) of $CDCl_3$ and trifluoroacetic acid (volume ratio 4:1) containing TMS. A Bruker AC-100 FT spectrometer was used for the ^{1}H NMR measurements and a Bruker MSL 300 FT spectrometer for the ^{13}C NMR measurements.

Results and Discussion

Syntheses. As reported recently[1] thermotropic poly(ester anhydride)s could be synthesized by polycondensation of terephthaloyl chloride with silylated hydroxy acids such as 4-hydroxybenzoic acid (eq 1, Scheme I) or 6-hydroxynaphthoic acid. These poly(ester anhydride)s demonstrated for the first time that a high content of anhydride groups is well compatible with a thermotropic character of the resulting polymers. Furthermore, the condensation of silylated hydroxy acids with terephthaloyl chloride has proved to be a useful synthetic method and, thus, was also used throughout this work.

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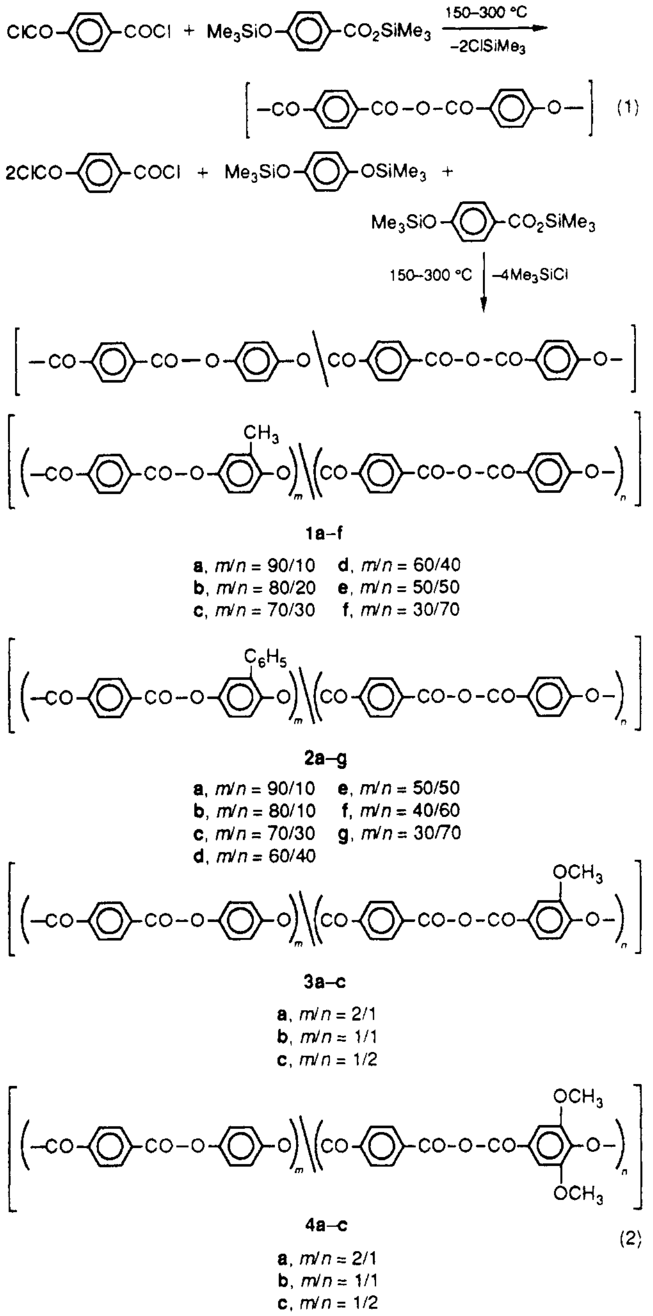
Scheme I



1a–f

a, m/n = 90/10 d, m/n = 60/40
b, m/n = 80/20 e, m/n = 50/50
c, m/n = 70/30 f, m/n = 30/70

2a–g

a, m/n = 90/10 e, m/n = 50/50
b, m/n = 80/10 f, m/n = 40/60
c, m/n = 70/30 g, m/n = 30/70
d, m/n = 60/40

3a–c

a, m/n = 2/1
b, m/n = 1/1
c, m/n = 1/2

4a–c

a, m/n = 2/1
b, m/n = 1/1
c, m/n = 1/2

In order to vary the content of anhydride groups and other properties of the poly(ester anhydride)s under investigation, copolymers were prepared by cocondensation of silylated hydroquinones and silylated 4-hydroxybenzoic acids with terephthaloyl chloride (eq 2 and formulas 1–4, Scheme I). When unsubstituted hydroquinone and unsubstituted 4-hydroxybenzoic acid were combined (eq 2), the reaction mixture solidified in the course of the polycondensation. The resulting poly(ester anhydride)s were more or less insoluble in all common inert solvents (strong acids cause rapid degradation), and they only melted above 400 °C, where rapid thermal degradation affects the melting process.

Therefore all further syntheses were either conducted with substituted hydroquinones (**1a–f** and **2a–q**) or with substituted 4-hydroxybenzoic acids (**3a–c** and **4a–c**). Hydroquinone, methylhydroquinone, 4-hydroxy-3-methoxybenzoic acid (vanillic acid), and 4-hydroxy-3,4-dimethoxybenzoic acid (syringic acid) were used as monomers, because they occur in plants in the form of glycosides. Hence these monomers may be considered to be biocompatible degradation products.

The resulting poly(ester anhydride)s were not reprecipitated for two reasons. Most samples were only soluble in acidic solvents and undergo gradual degradation in these solutions. Furthermore, precipitation into alcohols results in partial alcoholysis, whereas precipitation into ligroin does not improve the purity. Therefore, the crude reaction products were characterized as such. As demonstrated previously[6,9,10] for syntheses of various polyanhydrides, the "silyl method" is well suited for the preparation of polymers that are not suited for purification by precipitation or extraction due to their sensitivity to hydrolysis. The bulk condensation of silylated monomers does not require solvents, and the volatile chlorotrimethylsilane is the only byproduct. At the end of the polycondensation all reaction mixtures were stirred in a high vacuum for 0.5 h at 300 °C, so that all low molecular weight byproduct or starting materials could distill off or sublime. Hence it is not surprising that the crude reaction products gave in most cases satisfactory elemental analyses (Tables I–III).

Characterization. Chemical Structure. The low solubility of aromatic poly(ester anhydride)s in inert organic solvents and their sensitivity to hydrolysis in particular under acidic or alkaline conditions strongly limit the number of methods useful for their characterization. It has been reported that the rate of degradation of poly(ester anhydride)s prepared according to eq 1 rapidly increases with increasing acidity of the solvent. Nonetheless, solvent mixtures containing trifluoroacetic acid were required in the present work, because almost all polymers were insoluble when formic acid or acetic acid was used as acidic component. The viscosity data of series **1a–f** and **2a–e** listed in Tables I and II show a downward trend with increasing molar fraction of anhydride groups. This trend is at least partially the result of a more rapid degradation. The inherent viscosities of undegraded samples should be higher. The viscosity data also demonstrate the solubilities are particularly low in series **3a–c** and **4a–c**.

In order to obtain some crude information on the chemical structure of these poly(ester anhydride)s, IR spectra and ^{13}C NMR spectra were measured in the case of series **1a–f** and **2a–e**. The IR spectra obtained from a suspension of poly(ester anhydride)s in paraffin (Figure 1) demonstrate that the molar fraction of anhydride groups (CO band at 1790 cm^{-1}) increases with the feed ratio of hydroxybenzoic acid/hydroquinone.

The ^{13}C NMR were obtained from freshly prepared solutions of poly(ester anhydride)s in a mixture of $CDCl_3$ and trifluoroacetic acid (4:1 by volume). They are particularly easy to interpret when the molar ratio of hydroquinone and hydroxybenzoic acid is close to 1:1. The best resolution of carbonyl signals which are most sensitive to sequence effects was obtained for samples **2e** and **2f** (containing phenylhydroquinone). As shown in Figure 2, six relatively strong CO signals are observable. Taking into consideration that poly(phenylhydroquinone terephthalate) (measured separately) exhibits only one CO signal (a in Figure 2), four CO signals are expected according to the above formula of **2e**. However, it was demonstrated in a previous paper that the synthesis of polyanhydrides by the "silyl method" involves rapid transacylation.[9] Therefore two of the six CO signals may originate from the corresponding homoanhydrides formed according to eq 3. Furthermore, three weak CO signals (x, y, and z in Figure 2) were detectable, which result either from trans-

Table I
Properties of Poly(ester anhydride)s Prepared from Silylated Methylhydroquinone and 4-Hydroxybenzoic Acid

						elem anal.		
polymer	Hqu/Hba[a]	η_{inh},[b] dL/g	T_g,[c] °C	T_i,[d] °C	elem form (form wt)		% C	% H
1a	90/10	0.78		420–430	$C_{150}H_{98}O_{41}$	calcd	70.48	3.86
					(2556.4)	found	69.08	4.08
1b	80/20	0.73	104	450–470	$C_{75}H_{48}O_{21}$	calcd	70.09	3.76
					(1285.2)	found	69.15	3.79
1c	70/30	0.58	108	450–480	$C_{150}H_{94}O_{43}$	calcd	69.71	3.67
					(2584.4)	found	69.38	3.91
1d	60/40	0.46	95	470–490	$C_{75}H_{46}O_{22}$	calcd	69.34	3.57
					(1299.2)	found	68.57	3.56
1e	50/50	insol	108	430–450	$C_{30}H_{18}O_9$	calcd	68.97	3.47
					(522.47)	found	68.74	3.43
1f	30/70	insol	113	450–470	$C_{150}H_{86}H_{47}$	calcd	68.24	3.28
					(2640.3)	found	68.32	3.14

[a] Feed ratio of methylhydroquinone to 4-hydroxybenzoic acid. [b] Measured with c = 2 g/L in $CHCl_3$/TFA (4:1 by volume) at 20 °C. [c] From DSC measurements with a heating rate of 20 °C/min. [d] Microscopic observation at a heating rate of 20 °C/min.

Table II
Properties of Poly(ester anhydride)s Prepared from Silylated Phenylhydroquinone and 4-Hydroxybenzoic Acid

						elem anal.		
polymer	Hqu/Hba[a]	η_{inh},[b] dL/g	T_g,[c] °C	T^{i},[d] °C	elem form (form wt)		% C	% H
2a	90/10	0.80	133	470–490	$C_{195}H_{116}O_{41}$	calcd	75.19	3.75
					(3115.1)	found	75.30	4.03
2b	80/20	0.72	141	460–480	$C_{95}H_{56}O_{21}$	calcd	74.41	3.68
			(150)		(1533.5)	found	73.64	3.69
2c	70/30	0.50	134	400–420	$C_{185}H_{108}O_{38}$	calcd	73.60	3.61
					(2938.8)	found	73.51	3.71
2d	60/40	0.50	130	440–460	$C_{90}H_{52}O_{22}$	calcd	72.77	3.53
			(140)		(1485.38)	found	71.62	3.60
2e	50/50	0.48	125	400–420	$C_{35}H_{20}O_9$	calcd	71.92	3.45
					(584.54)	found	71.37	3.58
2f	40/60	0.34	132	370–390	$C_{85}H_{48}O_{23}$	calcd	71.03	3.37
					(1437.3)	found	70.48	3.38
2g	30/70	insol	133	380–400	$C_{165}H_{92}O_{47}$	calcd	70.11	3.28
					(2826.5)	found	68.84	3.31

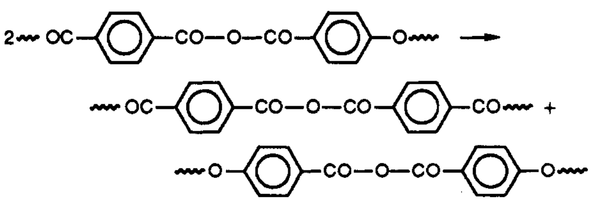
[a] Feed ratio of phenylhydroquinone to 4-hydroxybenzoic acid. [b] Measured with c = 2 g/L in $CHCl_3$/TFA (4:1 by volume) at 20 °C. [c] From DSC measurements with a heating rate of 20 °C/min; values in parentheses originate from the second heating. [d] Microscopic observation at a heating rate of 20 °C/min.

Table III
Properties of Poly(ester anhydride)s Prepared from Silylated Hydroquinone and 3-Methoxy- or 3,5-Dimethoxy-4-hydroxybenzoic Acid

						elem anal.		
polymer	Hqu/Hba[a]	η_{inh},[b] dL/g	T_g,[c] °C	T_i,[d] °C	elem form (form wt)		% C	% H
3a	2/1	insol	117	not detected	$C_{44}H_{26}O_{14}$	calcd	67.87	3.36
			(130)		(778.7)	found	66.53	3.33
3b	1/1	insol	128	440–460	$C_{30}H_{18}O_{10}$	calcd	66.92	3.37
			(130)		(538.5)	found	65.93	3.19
3c	1/2	0.31	124	410–450	$C_{46}H_{28}O_{16}$	calcd	66.03	3.37
			(132)		(836.7)	found	65.18	3.48
4a	2/1	insol	124	not detected	$C_{45}H_{28}O_{15}$	calcd	66.83	3.49
			(131)		(808.7)	found	66.11	3.55
4b	1/1	insol	162	430–460	$C_{31}H_{20}O_{11}$	calcd	65.50	3.55
			(168)		(568.5)	found	64.63	3.46
4c	1/2	0.27	170	isotropic	$C_{48}H_{32}O_{18}$	calcd	64.29	3.60
			(200)		(896.8)	found	62.98	3.76

[a] Feed ratio of hydroquinone to hydroxybenzoic acid. [b] Measured with c = 2 g/L in $CHCl_3$/TFA (4:1 by volume) at 20 °C. [c] From DSC measurements at a heating rate of 20 °C/min; values in parentheses originate from the second heating. [d] Microscopic observation at a heating rate of 20 °C/min.

esterification or from end groups. Low molecular weight model compounds of the end groups, such as 4-acetoxybenzoic acid of monomethyl terephthalate, did not prove to be useful for reliable assignments. Therefore, the synthesis of **2e** was repeated at lower maximum reaction temperature (T_{max} = 250 °C), and a polymer of lower molecular weight (η_{inh} = 0.23 dL/g) was obtained (**2e′**). Under these conditions signals of end groups should be more intense, and signals resulting from transesterification should be weaker or absent. In fact, the intensities of signals x, y, and z were higher by a factor of 2. This finding indicates the absence of transesterification, in agreement with previous results.[9]



(3)

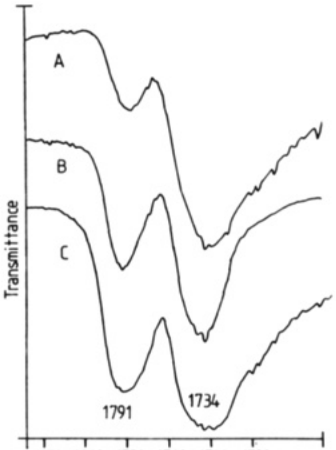


Figure 1. IR spectra of poly(ester anhydride)s (A) **1b**, (B) **1d**, and (C) **1f**.

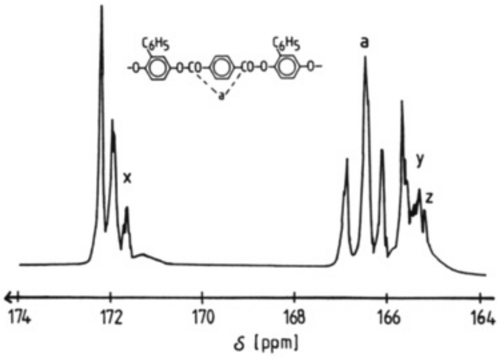


Figure 2. 75.4-MHz ^{13}C NMR spectrum of the carbonyl signals of poly(ester anhydride) **2f** measured in $CDCl_3$/trifluoroacetic acid (4:1 by volume).

Thermal Properties. The complex and obviously random sequences of several ester and anhydride groups are in good agreement with the observed amorphous character of all samples. The WAXS patterns display an amorphous halo, and a low degree of crystallinity is detectable only in the case of **3a** and **4a**, obviously due to short blocks of hydroquinone and terephthalic acid.

The DSC heating traces only display a glass-transition step. The glass-transition temperatures (T_g's) are lowest in the case of **1a–f** (Table I) and 20–30 °C higher in series **2a–g**. It is obvious that the phenyl substituent reduces the segmental mobility. Surprisingly, no significant trend is detectable with regard to the molar composition of series **1a–f** and **2a–g**. However, such a trend is obvious in series **4a–c**. Increasing the molar fraction of 4-hydroxy-3,5-dimethoxybenzoic acid considerably raises the T_g (Table III).

Microscopic observation with crossed polarizers revealed the formation of nematic mesophases for all members of series **1a–f** and **2a–g**. An example of the typical "schlieren textures" is shown in Figure 3. The isotropization temperatures are so high that they are affected by thermal degradation. Since the nematic melt is formed above T_g, the temperature range of the mesophase is very broad and allows processing from the melt at convenient temperatures. In the case of **3a** and **4a** the melt viscosity is so high and the thermal degradation above 450 °C is so rapid that development of a schlieren texture could not be observed. The mobile nematic melt of **3b** and **4b** was clearly detectable; yet surprisingly the melt of **4c** was isotropic. These results suggest that it is more promising from the viewpoint of a processable thermotropic engineering plastic to combine substituted hydroquinones with unsubstituted 4-hydroxybenzoic acid than vice versa.

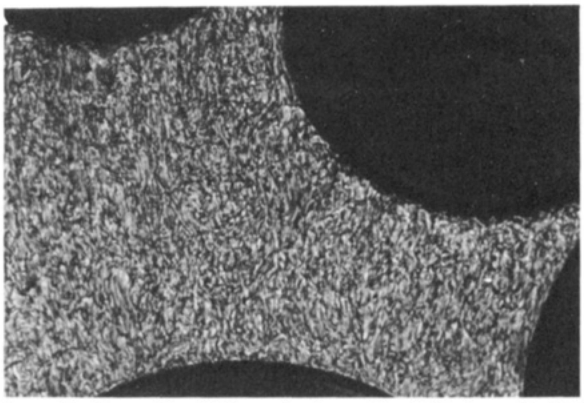


Figure 3. Nematic schlieren texture of poly(ester anhydride) **2c** at 350 °C (original magnification ca. 300×; the photo has been reduced to 65% of its original size for publication purposes).

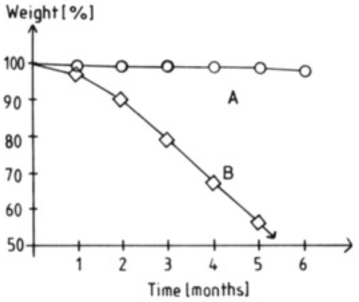


Figure 4. Loss of weight due to hydrolytic degradation in an aqueous solution of 1 M $NaHCO_3$ and 1 M Na_2CO_3: (A) polymer **2a**; (B) polymer **2e**.

Hydrolytic Stability. In order to obtain a crude idea on how sensitive the bulk poly(ester anhydride)s are to hydrolytic degradation, disks of **2a** and **2e** were immersed in neutral water of 20 °C over a period of 6 months. The washed and dried disks were weighed every 2 weeks. Interestingly no loss of weight was found. Because the disks were washed with acetone and diethyl ether before weighing, the constancy of the weight cannot be explained by insolubility of the degradation products in water. In a second series of hydrolysis, test disks of **2a** and **2e** were exposed to alkaline water containing $NaHCO_3$ (0.1 M) and Na_2CO_3 (0.1 M). The results plotted in Figure 4 demonstrate first that hydrolysis in alkaline water is, as expected, more pronounced and second that **2e** degrades more rapidly than **2a**. Nonetheless these preliminary studies indicate that the hydrolytic stability of poly(ester anhydride)s in bulk is fairly high. At this point it should be emphasized that the loss of mass studied here is, of course, not identical with the decrease of molecular weight or mechanical properties. A more detailed study of the degradation process is in progress and will be published separately. Nonetheless the loss of mass discussed is a crude measure of the hydrolytic stability, inasmuch as the disks were washed with acetone and diethyl ether before weighing to remove oligomers insoluble in water.

Thus, these preliminary results suggest that poly(ester anhydride)s with a low content of anhydride groups (<10 mol %) may be useful as engineering plastics even in moist air over a period of months. However, their properties in solution are quite different. When solutions in $CHCl_3$/TFA (volume ratio 4:1) are precipitated into methanol, the inherent viscosities of the precipitated materials are 20 ± 5% lower than those of the crude materials. This

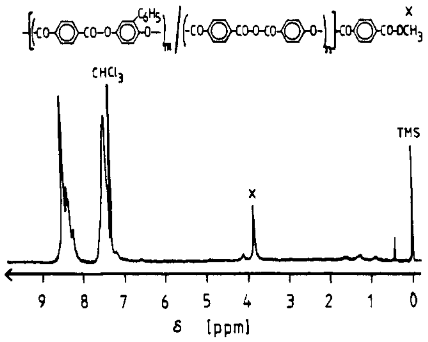


Figure 5. 100-MHz ^{1}H NMR spectrum of poly(ester anhydride) **2e** after precipitation with methanol.

observation suggests that in solution even a short contact with methanol results in partial alcoholytic cleavage of anhydride groups. This suggestion is supported by the finding of a methyl ester signal (3.8 ppm) in the ^{1}H NMR spectra of precipitated samples (Figure 5). The intensity of the methyl ester signal parallels the percentage of anhydride groups in the polymer. Thus, these results demonstrate that the chemical stabilities in bulk and in solution are quite different. This difference offers the chance to hydrolyze waste of poly(ester anhydride)s in an acceptable period of time after grinding and addition of detergents.

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