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SYNTHESIS OF POLY(ADIPIC ANHYDRIDE) BY USE OF KETENE

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ABSTRACT

Polyadipic anhydrides were prepared (a) from the mixed anhydride of adipic acid and acetic acid, (b) from the mixed anhydride of adipic acid and ketene in tetrahydrofurane solution (0°C), (c) by melt polycondensation of adipic acid with ketene, and (d) from the seven-membered ring adipic anhydride. The polymers were characterized by means of NMR, IR, DSC, and GPC. The polymer with the highest melting temperature was obtained by melt polycondensation of adipic acid with ketene (T_{peak} 76°C). The heat of fusion was approximately 40 J/g in all four methods. The number-average and weight-average molecular weights of the polyanhydrides were 2000 and 3000, respectively.

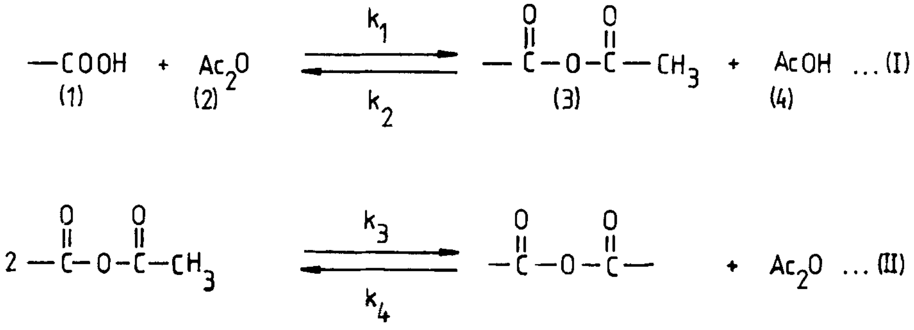
INTRODUCTION

Following our studies on degradable polymers [1], where we used polyesters, and the design of thermoplastic elastomers [2, 3], we now focused on polyanhydrides as possible species for hard, crystalline segments in thermoplastic copolymers. Neither the polyanhydrides nor their degradation products have been found to be mutagenic or cytotoxic, and they have low teratogenic activity [4-6]. The polymers of aliphatic dibasic acids with acetic acid are known to be unstable even in air due to uptake of moisture [7]. These properties could be utilized in the design of rapidly degrading systems for use in surgery and medicine.

Aliphatic polyanhydrides were synthesized in 1932 by Hill and Carothers [7]. They studied the behavior of diacids toward anhydride formation. Malonic acid forms only a polymeric linear anhydride, whereas succinic and glutaric acids form only the monomeric cyclic anhydrides. Adipic acid forms both a monomeric and a polymeric anhydride, but higher diacids yield only linear products. The work in this field was extensively revised by Yoda in 1969 [8]. The simplest method of preparation of linear polyanhydrides is the reaction of acetic anhydride with a dicarboxylic acid [7, 9]. In the first stage of the reaction, the acetic anhydride (2) reacts with the acid, forming a mixed anhydride (3) and acetic acid (4). In a later stage the mixed anhydride decomposes to acetic anhydride and the original acid anhydride (5) [9] (Scheme 1).

It is obvious that the acetic acid present is able to degrade the polyanhydride formed. One way of avoiding this equilibrium would be by the use of ketene gas, which has been known for many years as a way of preparing mixed acid anhydrides [10, 11]. This paper describes four methods of obtaining linear aliphatic polyanhydrides: (a) by continuous preparation of polymer by the reaction of adipic acid with excess acidic anhydride, (b) by reaction of adipic acid with ketene at low temperature, (c) by reaction of adipic acid with ketene at 160°C, and (d) by polymerization of cyclic adipic anhydride monomer.

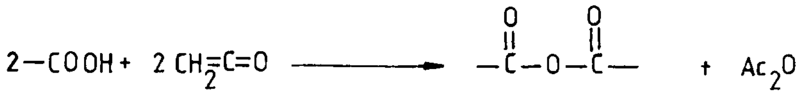
The polymers were characterized with regard to molecular weight as well as thermal and spectroscopic properties. Thus, this paper compares the classical route and ring-opening polymerization of the seven-membered ring adipic anhydride with two ketene routes. The ketene routes avoid the equilibrium between the acid, the mixed anhydride, and the polymer (Scheme 2).



$$\underset{(1)}{-COOH} + \underset{(2)}{Ac_2O} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \underset{(3)}{-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}-CH_3} + \underset{(4)}{AcOH} \quad \ldots(I)$$

$$2\,-\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}-CH_3 \underset{k_4}{\overset{k_3}{\rightleftharpoons}} -\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}- + Ac_2O \quad \ldots(II)$$

SCHEME 1. Reaction equilibria for polyanhydride formation.



$$2\text{—}COOH + 2\,CH_2{=}C{=}O \longrightarrow \text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}O\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—} + Ac_2O$$

SCHEME 2. Reaction of ketene with acid groups to give polyanhydride.

EXPERIMENTAL

Materials

Adipic acid (p.a.) was purified by vacuum sublimation. Acetone, THF, and chloroform were purified by distillation. Acetic anhydride (p.a.), petroleum ether (p.a.), and $ZnCl_2$ were used as received. All chemicals were purchased from Aldrich. Ketene was synthesized by pyrolysis of acetone, as described in Vogel [10].

Preparation of Polymers

(a) Synthesis of Poly(Adipic Anhydride) by the "Classical" Route

Adipic acid, 50 g (0.34 mol), and acetic anhydride, 40 mL, were held at reflux temperature for 1 h under nitrogen. Another 110 mL acetic anhydride was then added continuously through a dropping funnel while acetic acid and acetic anhydride distilled over. Optimum results were obtained if the starting point was a mixture of 1 mol adipic acid and approximately 0.5 mol acetic anhydride. When the distillation started, 2.5 mol acetic anhydride was added at a rate equal to the rate of distillation of the volatile constituents [8]. When no further distillation took place, a vacuum was applied and the temperature was raised to 160°C. The total reaction time was 6 h. The residual polymer was dissolved in chloroform, precipitated in dry ether, and stored over P_2O_5 in a desiccator.

(b) Synthesis of Poly(Adipic Anhydride) in THF with Ketene

Adipic acid, 10 g (0.0684 mol), was dissolved in 50 mL THF, and nitrogen was bubbled through the mixture for 15 min. The reaction vessel was then cooled with ice to 0°C, and ketene was bubbled through the reactants for 3 h. This reaction time was sufficient to react all acid groups to mixed anhydrides.

The reaction was followed by IR analysis. The mixed anhydride was isolated by rotary evaporation to remove THF. The mixed anhydride, 4 g of which was placed in a glass polymerization tube equipped with a side arm for distillation. A capillary reaching to the bottom of the tube was inserted. The polymerization tube was heated to 150°C in an oil bath, brought to that temperature after the tube was in position. Dry nitrogen was passed through the mixture, and acetic anhydride distilled over. After 30 min a vacuum of 0.9 mbar was applied. A slow stream of nitrogen was continuously passed through the melt, which became more and more viscous. After 2 h the polycondensation was terminated, and the polymer was allowed to crystallize. It was then dissolved in chloroform, precipitated in diethyl ether and stored over P_2O_5 atmosphere in a desiccator.

(c) Melt Polycondensation of Adipic Acid with Ketene

Adipic acid, 15 g (0.1026 mol), was melted at 160°C in a 50-mL flask equipped with a water-cooled condensing bulb under a continuous nitrogen sweep. Ketene was then introduced through the nitrogen stream into the stirred mixture. Acetic anhydride distilled off continuously during the 8-h reaction, and the mixture became more and more viscous. When no further distillation took place, the ketene supply was stopped. The reaction was terminated by cooling, and the polymer was allowed to crystallize. It was then dissolved in chloroform, precipitated in ether, and stored over P_2O_5 in a desiccator.

(d) Ring-Opening Polymerization of Adipic Anhydride

A solution of 15 g (0.1026 mol) adipic acid in 150 mL acetic anhydride in a dry reaction vessel equipped with a magnetic stirrer and reflux condenser was held at reflux temperature for 4 h while nitrogen was continuously bubbled through the solution. The acetic acid formed in the reaction and the excess acetic anhydride were removed by distillation in a vacuum. The residue was transferred to a Claisen flask and heated under vacuum. After removal of the residual acetic anhydride at 0.9 mbar, no further distillation took place up to a bath temperature of 250°C. The distillate consisted of a liquid containing a small amount of crystalline material. $ZnCl_2$ (1 wt%) was added at room temperature to a solution of 6 g (0.05 mol) adipic anhydride in 50 mL methylene chloride. The run time was 6 h. The reaction was terminated by pouring the reaction mixture into dry ether to precipitate the polymer. The resulting white powder was filtered and washed with dry ether and stored over P_2O_5 in a desiccator.

Measurements

The resulting polymers were characterized by GPC, DSC, IR, and NMR. A Waters 6000 A pump with two Shodex columns (GPC AC-80M/S) connected to a differential refractometer was used for GPC with chloroform as the solvent and a flow rate of 1 mL/min. The apparatus was run at 28°C with a solvent pressure of 45.5 MPa. Polystyrene standards were used for calibration. The apparatus used for DSC was a Perkin-Elmer DSC-2 with a heating rate of 10°C/min, cooling rate 20°/min, giving the samples the same thermal history. The FTIR used was a Perkin-Elmer 1710. Spectra were taken on polymer films cast from chloroform solution on NaCl cells. The NMR instruments used were a JEOL JNM-PMX 60 SI and a Bruker WP 200. Samples were dissolved in deuterochloroform.

RESULTS AND DISCUSSION

Results of the Synthesis Methods

Results of the four polymerization routes are summarized in Tables 1 and 2. In the continuous preparation of polymer (a), the mixed anhydride is not isolated before polycondensation, i.e., acetic acid is present in the system, whereas in Method b the mixed anhydride is isolated between the treatments with acid and with ketene. This is possible due to the low reaction temperature, 0°C, which inhibits the development of oligomers because of the slow rate of anhydride exchange, so that there is no acetic acid present. After purification, the monomer is subjected to melt polycondensation in a polymerization tube at elevated temperature and high vacuum. In the second ketene

TABLE 1. Results of the Four Synthesis Routes

Synthesis method[a]	Yield, wt%	$\bar{M}_n$	$\bar{M}_w$
a	62	1929	3060
b	72	1933	2987
c	68	1980	2850
d	75	1693	2851

[a] See Experimental section.

TABLE 2. Results of DSC Analysis

Synthesis method[a]	ΔH_f,[b] J/g	T_{peak}, °C
a	43.4	72
b	40.2	70
c	37.1	76
d	44.3	71

[a] See Experimental section.
[b] Heat of fusion.

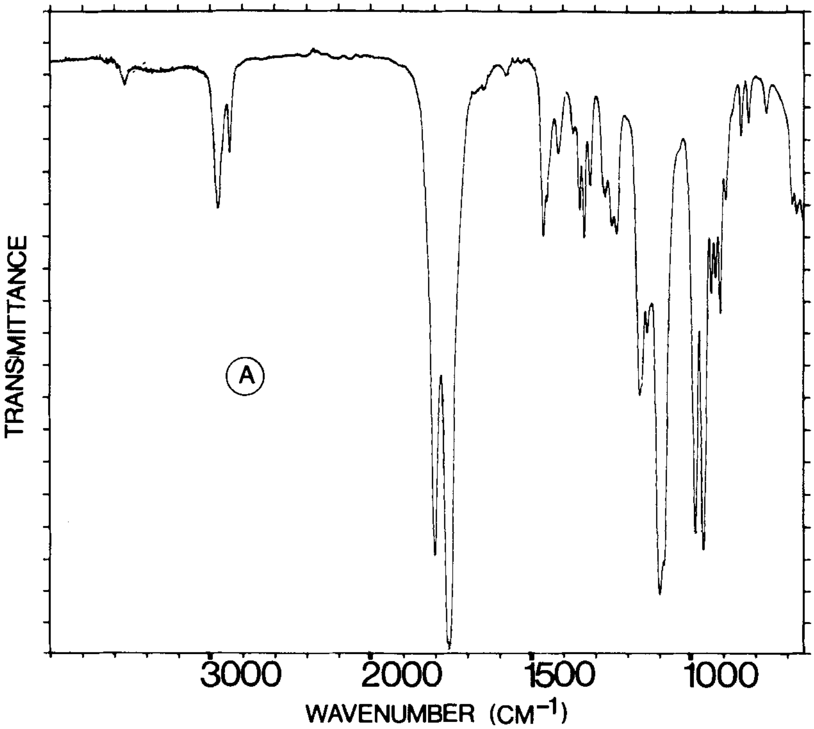


FIG. 1. Infrared spectra of (A) adipic anhydride and (B) poly(adipic anhydride).

route (c), melted diacid is reacted with ketene gas at ambient pressure without solvent and with no acetic acid present. The ring-opening polymerization of the seven-membered ring adipic anhydride (d) is carried out at room temperature in methylene chloride solution with $ZnCl_2$ as catalyst. All methods gave the same polymer, as indicated by the molecular weights in Table 1.

Results of NMR and IR Analysis

The IR spectra of adipic anhydride and poly(adipic anhydride) samples are shown in Fig. 1. All four methods gave materials with the same spectral characteristics. Characteristic absorption bands due to the anhydride group were observed at 1745 and 1800 cm^{-1}. Other absorption bands observed in the

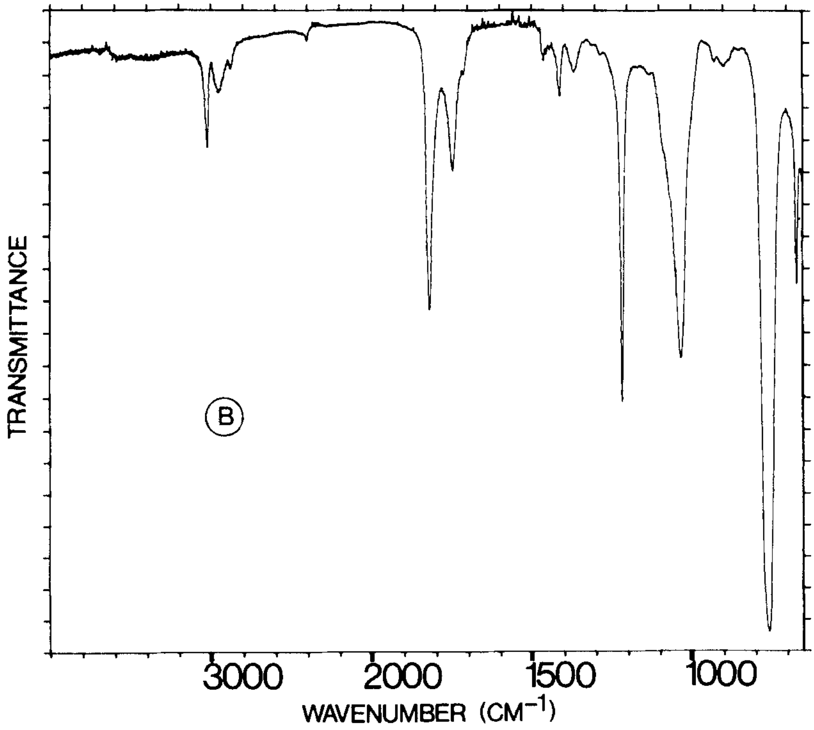


FIG. 1 (continued)

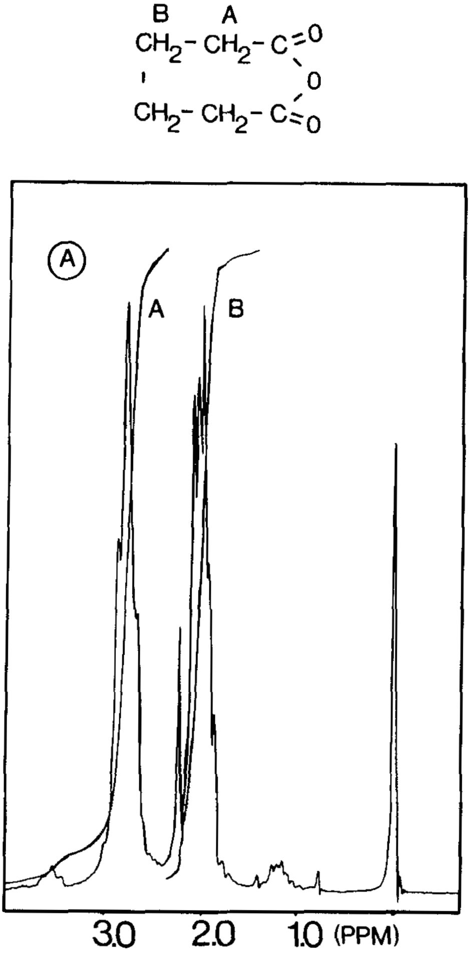


FIG. 2. 60 MHz ^{1}H-NMR spectra of (A) adipic anhydride, and 200 MHz ^{1}H-NMR spectra of (B) poly(adipic anhydride) in *d*-chloroform.

3020-2950 cm^{-1} region are characteristic of C—H stretching vibrations. The bands in the 1216 cm^{-1} region are attributed to —COO— bonds. The bands in the 1033 cm^{-1} region are characteristic of C—O stretching vibrations. The NMR spectra of adipic anhydride and poly(adipic anhydride) samples are shown in Fig. 2. Two distinct signals are evident: a singlet at 1.75 ppm due to methylene protons, and a sharp singlet at 2.50 ppm due to CO—CH_2 pro-

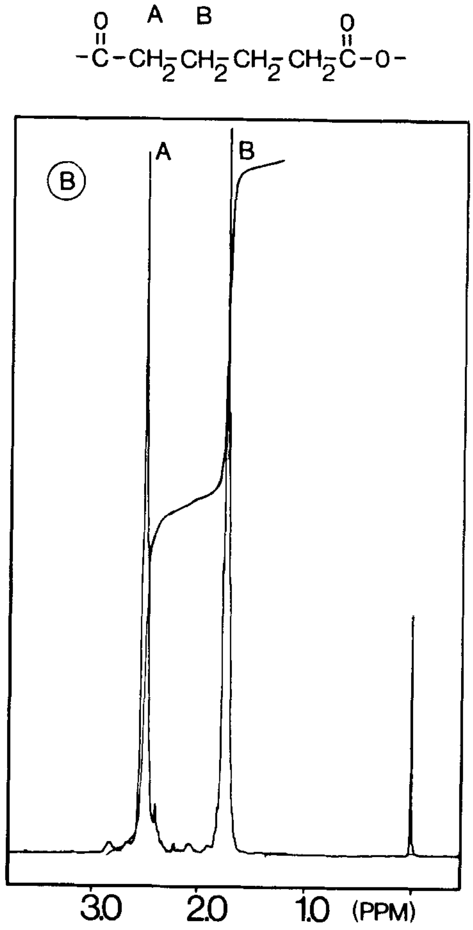


FIG. 2 (continued)

tons. Thus the spectral characteristics of the poly(adipic anhydride)s prepared by all four methods are explicable in terms of the proposed structure.

Results of DSC Analysis

Typical thermograms are shown in Fig. 3. The melting temperature (T_{peak}) is about 70°C for the products of all four methods. Method c gave a polymer having the highest T_{peak} (76°C). Two-peak melting occurs, pre-

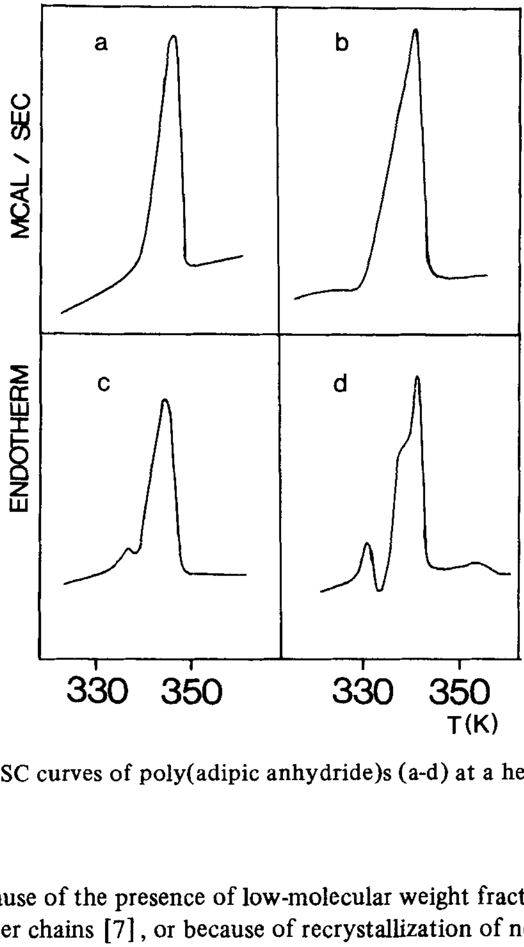


FIG. 3. DSC curves of poly(adipic anhydride)s (a-d) at a heating rate of 10°C/min.

sumably because of the presence of low-molecular weight fractions, such as rings or shorter chains [7], or because of recrystallization of nonequilibrium crystals. The area under the peak at ~70°C is used to calculate the heat of fusion (ΔH_f) (see Table 2).

DISCUSSION

Theoretically, it should be possible to synthesize polyanhydrides by reaction between acids with the elimination of water, but this leads to equilibrium rather than completion. The forward reaction is, however, favored if a mixed anhydride is used as the starting material. The mixed anhydride can be synthesized by reacting the acid with acetic anhydride. It is crucial to remove the acetic acid developed together with unreacted acetic anhydride by distillation, since the acetic acid, if present, is able to degrade the polyanhydride. The residue of mixed anhydride is subjected to polycondensation conditions. Due to the nonquantitative nature of the reaction, excess acetic acid anhydride must be used to generate the mixed anhydride, and the necessary excess can be considerable. There are thus several drawbacks in the synthesis of polyanhydrides from diacids.

The synthesis of polyanhydrides proceeds more smoothly if ketene is used. Ketene is allowed to react with the diacid at elevated temperature, and the mixed anhydride formed is melted and oligomerizes with the elimination of acetic acid anhydride. This bulk reaction takes place in a melt phase without solvent. It is also important that the intramolecular distance between the carbonyls shall be such that cyclic anhydrides cannot be formed. This requirement is fulfilled by adipic acid and sebacic acid. Another advantage of the preparation of mixed anhydride at 0°C with ketene is that it permits formation of mixed anhydrides of aliphatic and aromatic acid without anhydride exchange between the monomers. The result is a pure mixed anhydride with no isolation or purification problems.

CONCLUSIONS

We have shown here that linear poly(adipic anhydride)s resulting from the reaction of nonvolatile dicarboxylic acids with acetic anhydride can also be obtained by the use of ketene gas. This synthesis route has the advantage of avoiding the previously described equilibrium [9] because no acetic acid is formed which could force the reaction backward. The seven-membered ring adipic anhydride is easily polymerized at room temperature to molecular weights comparable with those obtained by the other methods.

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