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Communications to the Editor

2-Oxepane-1,5-dione: A Precursor of a Novel Class of Versatile Semicrystalline Biodegradable (Co)polyesters

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The steadily increasing concern of the general public with the protection of our daily environment has largely contributed to the advent and growth of biodegradable polymers. Among them, poly(ϵ-caprolactone),[1] PCL, has a central position because of highly desired combination of biocompatibility and good mechanical properties. Nevertheless, the melting temperature (T_m) of PCL is too low for it to be usable as packaging material. With the purpose to modify PCL properties, a series of (α and γ)-substituted lactones have been synthesized.[2] This communication aims at reporting on the synthesis and polymerization of 2-oxepane-1,5-dione (OPD), which has the same structure as ϵ-caprolactone, except for the central methylene group which is replaced by a carbonyl. This new monomer paves the way to a novel class of (co)polyesters with potential applications as packaging material and constitutive component of biomedical devices.

Synthesis of 2-oxepanedione relies on the classical Baeyer−Villiger oxidation of 1,4-cyclohexanedione by *m*-chloroperbenzoic acid in dichloromethane (Scheme 1, route 1). Only traces of the diester formed by the Baeyer−Villiger oxidation of OPD have been detected. Substitution of a polarized ketone function (C═O) for the central methylene group of the cyclic ϵ-caprolactone strengthens the intermolecular interactions and thus increases the melting temperature from −1 °C up to 110−112 °C.

Polymerization of 2-oxepane-1,5-dione has been initiated by 1-phenyl-2-propanol added with 0.5 equiv of tin octoate in toluene at 90 °C. The collected polyester (89% yield) is semicrystalline with a high T_m (147 °C) and a T_g of 37 °C. Its physical properties are actually identical to those of the polyester we recovered by deacetalization of poly(1,4,8-trioxaspiro[4.6]-9-undecanone) a few years ago[3] (Scheme 1, route 2). A crystallographic study showed that the unit cell for this polyester is orthorhombic in the $P2_12_12_1$ space with two molecules extended along the *c*-axis just as PCL.[3]

Dibutyltin dimethoxide has proved efficiency to synthesize random copolymers of ϵ-caprolactone, ϵ-CL, with 2-oxepane-1,5-dione under different conditions (Table 1). The distribution of the comonomers is dictated by a combination of two effects, i.e., the higher reactivity of OPD with respect to ϵ-CL and transesterification reactions. These copolymers are semicrystalline over the whole composition range investigated in this study. T_m increases regularly and monotonically from 60 to ca. 150 °C as result of cocrystallization as supported by wide-angle X-ray scattering (WAXS) analysis. This is the first report, at least to our knowledge, of such a phenomenon

Table 1. Bulk Copolymerization of ϵ-CL and OPD Mixtures of Various Molar Compositions (f_{OPD})

entry	M/Sn	f_{OPD}	T (°C)	time	yield (%)	F_{OPD} [a]	T_m (°C)[b]	ΔH_m (J g^{-1})[b]
1	600	0.08	110	4 min	99	0.07	63	55
2	600	0.30	25	48 h	99	0.29	94	52
3	600	0.30	80	2 min	46	0.55	114	67
4	600	0.65	110	10 min	92	0.72	137	75

[a] F_{OPD}, the molar content of OPD in the copolymer, was determined by ^{1}H NMR. The polydispersity index measured by SEC is ca. 1.7. [b] T_m and ΔH_m (DSC data) were reported for the second heating run.

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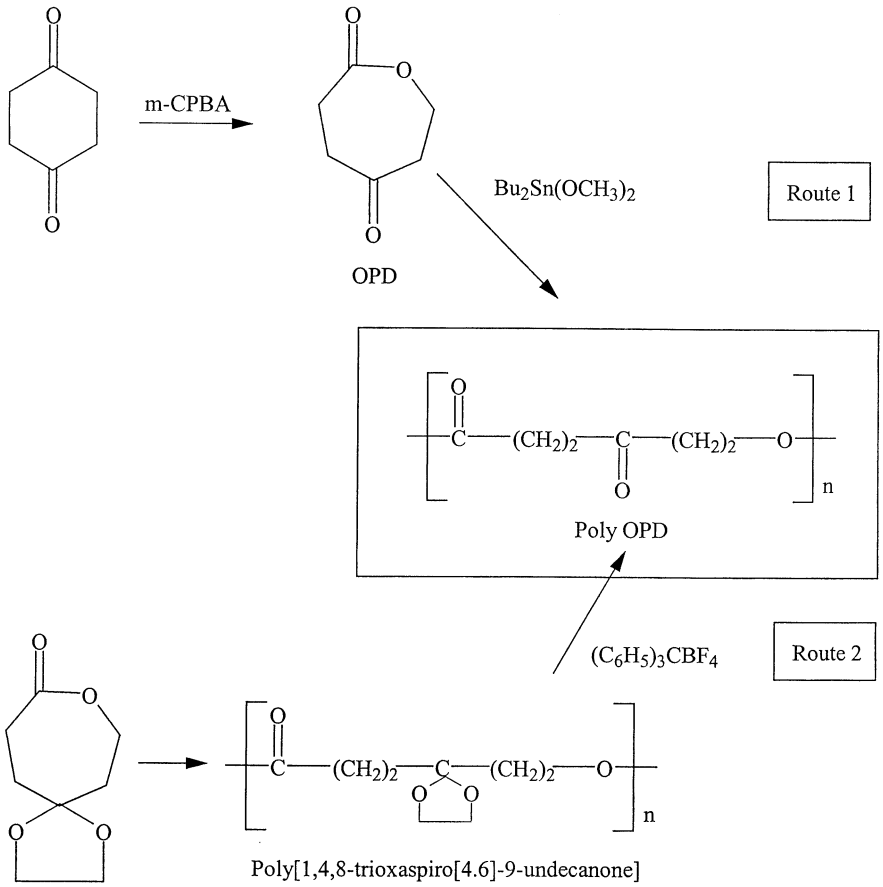
Scheme 1. Comparative Routes for the Synthesis of Poly(2-oxepane-1,5-dione)



occurring in polyesters. Also consistent with a regular increase of the intermolecular interactions with the OPD content, T_g obeys the Fox equation[4] (eq 1), which indicates that the composition of the amorphous phase may be approximated to the overall composition determined by ^{1}H NMR.

$$1/T_g = (w_1/T_{g1}) + (w_2/T_{g2}) \quad (1)$$

where w_i is the weight fraction of compound i and T_{gi} is the glass transition temperature (in kelvin) of the parent homopolymer.

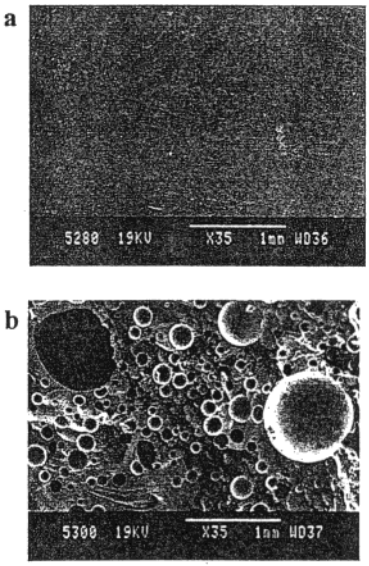


Figure 1. SEM images of a poly(OPD-*co*-CL) containing 30 mol % of OPD before and after immersion in a phosphate buffer (pH = 7.4) at 37 °C: (a) $t = 0$; (b) $t = 14$ weeks.

The mechanical properties of copolyesters with an OPD content until 30 mol % are quite reminiscent of PCL of comparable molecular weight. For instance, a poly(2-oxepane-1,5-dione-*co*-ϵ-caprolactone) of M_n 65 000 and 30 mol % OPD shows an elongation at break of 800% and an ultimate tensile strength of 26 MPa, compared to 1000% and 36 MPa, respectively, for PCL of same M_n.[5] The ketone increases the polyester hydrophilicity and thus its sensitivity to hydrolysis, as convincingly supported by Figure 1, which compares the scanning electron micrographs (SEM) for the copolyester before and after immersion in a phosphate buffer at 37 °C. After 14 weeks, the copolyester shows obvious signs of hydrolytic degradation.[6] Indeed, 13% of water absorption and 8% of weight loss[6] are observed, in sharp contrast to PCL which remains unchanged.

Quite interestingly, OPD imparts sensitivity to photo-cross-linking to this novel class of materials. Indeed, solubility in common organic solvents is lost, and the melt viscosity is sustained up to high temperatures upon UV irradiation of OPD containing copolyesters. This characteristic feature might find application in photolithography. The photo-cross-linking mechanism, which is under current investigation, is thought to rely on the formation of radicals by abstraction of an hydrogen in the α-position of the ketone.

So a series of major properties of PCL (T_m, T_g, mechanical performances, hydrophilicity, biodegradability, cross-linking) may be easily tuned by copolymerization of ϵ-caprolactone with various contents of 2-oxepane-1,5-dione, as will be shown in forthcoming papers. This novel class of (co)polyesters has potential

in different application areas, such as packaging materials, biomedical devices, agricultural films, etc.

Experimental Section. A. Synthesis of 2-Oxepane-1,5-dione (OPD). 1,4-Cyclohexanedione (12 g, 0.107 mol) and purified *m*-CPBA[7] (22 g, 0.127 mol) were weighed in a 500 mL reactor. 130 mL of dichloromethane was then added to the reactor, and the solution was refluxed for 3 h at 40 °C. After solvent evaporation under reduced pressure, the crude reaction product was washed (3 times) with 200 mL of diethyl ether, filtered, and dried under vacuum. It was redissolved in toluene (0.5% w/w) under N_2, and the solution was added with CaH_2 (5 g) and stirred for 16 h at room temperature. After filtration, the solvent was partially evaporated under reduced pressure (OPD concentration of ca. 2% w/w), and the solution was cooled to 4 °C for one night. The crystallized OPD was recovered and dried at ambient temperature under reduced pressure for 24 h. Yield: 45%. Melting point: 110−112 °C. ^{1}H NMR ($CDCl_3$, δ ppm): 4.4 (t, 2H, CH_2O), 2.8 (t, 2H, CH_2COO), 2.6 (m, 4H, CH_2CO). ^{13}C NMR ($CDCl_3$, δ ppm): 204.9 (*C*O), 173.3 (*C*OO), 63.3 (*C*H_2O), 44.6 (*C*H_2CO), 38.4 (*C*H_2CO), and 27.8 (*C*H_2COO). GC-MS: $M^+ = 128$, $M/Z = 55$ (base peak). No impurity was detected by GC, and the purity of OPD proved to be high enough for the polymerization to be successful.

B. OPD Polymerization. OPD (5 mmol) was weighed in a glovebox and dissolved in dry toluene (2 mL) at 90 °C, before being added to the reactor, followed by 1-phenyl-2-propanol (0.01 mmol) and $Sn(Oct)_2$ (0.005 mmol) (dissolved in 0.5 mL of dry toluene). The reaction mixture was maintained under stirring in an oil bath at 90 °C. PolyOPD precipitated as a white powder in the polymerization medium. It was recovered by filtration and washed abundantly with cold methanol before being dried under vacuum up to a constant weight.

C. ϵ-CL/OPD Copolymerization. In a typical experiment, OPD (2.27 mmol) was weighed in a glovebox and added to a flame-dried flask, followed by ϵ-CL (4.56 mmol). $Bu_2Sn(OMe)_2$ (0.011 mmol) was added to the comonomer mixture, which was maintained under stirring in an oil bath at 110 °C for 5 min. HCl excess was added, followed by chloroform (15 mL). The final solution was poured into heptane (150 mL), and the copolymer was precipitated, filtered, washed with cold methanol, and dried.

Mechanical properties were recorded with an Instrom universal tensile tester (model DY 24) at a tensile rate of 20 mm min^{-1}. SEM pictures of transversal cross sections of cylindrical samples were collected with a JEOL JSM-840 A microscope after coating with platinum for 120 s under an argon atmosphere. DSC was carried out with a Dupont 910 DSC thermal analyzer calibrated with indium, at a scanning rate of 10 °C/min under N_2.

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