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MACROCYCLIC POLYMERIZATION - A NEW APPROACH TO MOLECULAR ENGINEERING

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Abstract: 2,2-Dibutyl-2-stanna-1,3-dioxacycloalkanes were used as cyclic initiators for the ring-opening polymerization of various lactons. This method exclusively yielded series of macrocyclic polylactones without any competition with linear polymers. Under optimized reaction conditions these macrocyclic polymerizations obey the pattern of "living polymerizations". The living chain ends allow the syntheses of macrocyclic blockcopolymers. The macrocyclic polylactones react with carboxylic acid chlorides by ring-opening yielding telechelic oligo or polylactones. Furthermore, the tin containing macrocyclic polylactones can be used as difunctional "monomers" for polycondensations with dicarboxylic acid dichlorides.

INTRODUCTION

Biodegradable polymers of various structures have recently attracted increasing interest in fundamental research and also for pharmaceutical or medical applications. The most widely studied and most widely produced biodegradable materials are polylactones and particularly polylactides. The initiators preferentially used for the ring-opening polymerization of the lactones are metal carboxylates, such as Sn(II)2-ethylhexanoate[1-8)] and Zn(II)lactate[9, 10)] or metal alkoxides such as Al(isopropoxide)$_3$[11-13)], Ti(isopropoxide)$_4$[14)] or Bu$_3$Sn O Me[15, 16)]. At least in the case of these covalent metal alkoxides it is clear that the chain growth proceeds by a so-called coordination-insertion mechanism which involves the reaction of the covalent metal-O bond with the CO-O bond of the lactone[11, 14)]. Thereby, the alkoxide yields an alkylester endgroup (eq. 1).

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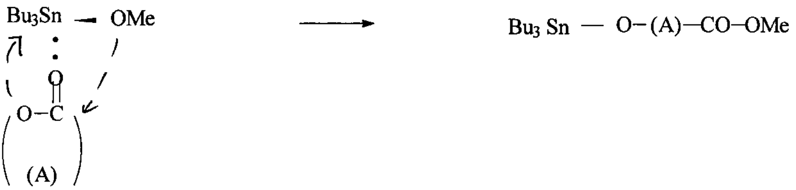
The present paper deals with a new class of coordination initiators which are characterized by a cyclic structure and certain at least one tin atom and one reactive Sn-O bond.



(1)

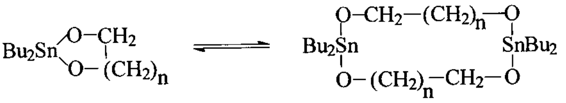
RESULTS AND DISCUSSION

Syntheses of macrocyclic polylactones

Cyclic tin alkoxides such as the 2-stanna-1,3-dioxacycloalkanes 1a - 3a were synthesized and characterized by several research groups[17 - 22]. It has been shown that the five and six-membered rings spontaneoulsy dimerize yielding the more stable crystalline macrocycles 1b and 2b respectively. This dimerization is a consequence of energetically unfavorable conformations in the smaller rings of 1a and 2a which relax upon ring expansion. Obviously the seven-membered ring of 3a is large enough to avoid unfavorable conformations, and thus, remains stable in the monomeric form. Dimerization was also observed, when one oxygen in the six-membered ring was replaced by sulfur (4a / 4b), whereas the 2-stanna-1,3-dithiacycloalkanes 5 and 6 are stable in the monomeric state.

The 2-stanna-1,3-dioxacycloalkanes react with neat lactones above 25°C by insertion of the lactones into all Sn-O bonds according to a coordination-insertion mechanism, and thus, macrocyclic polylactones (7) are formed (eq. 2). In the case of the initiator 4a, b the more stable Sn-S bond does not react and the resulting macrocycles have the structure (8). This spectroscopic result is in good agreement with the finding that the 2-stanna-1,3-dithiacycloalkanes 5 and 6 are not reactive as initiators at least at temperatures $\leq 120°C$. Higher temperatures are unfavorable because of transesterification and back-biting degradation. The structures of the supermacrocyclic (i.e. macrocycles containing more than 100 ring atoms) was confirmed by ^{1}H-, ^{13}C- and ^{119}S-NMR spectroscopy[23-25].

When the dimeric heterocycles 1b, 2b or 4b are used as initiators, they have certain disadvantages. The high melting temperatures (> 200°C) and poor solubilities in organic solvents including lactones. In consequence, the total initiation process is slow (even when the reaction of an individual dissolved molecule is rapid) and the chain growth is faster than the initiation. Therefore, the resulting molecular weights are higher than the monomer/initiator (M / I) ratio and difficult to control. However, polymerizations following nearly the "living pattern" can be achieved by means of the initiator 3a which is a monomeric liquid and miscible with most lactones. When 3a initiated polymerizations of ε-caprolactone were conducted in bulk at 80°C polydispersities around 1,5 ± 0,5



(2)

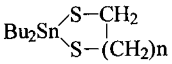
1a, n = 1 **1b**, n = 1

2a, n = 2 **2b**, n = 2

3a, n = 3

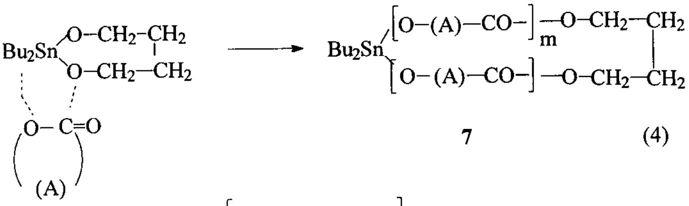
(3)

4a **4b**

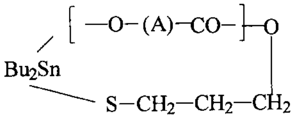


5, n = 1

6, n = 2



7 (4)



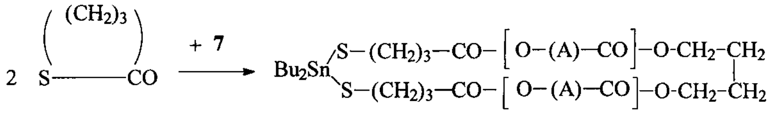
were obtained which are higher than those of a classical living polymerization, but the number average molecular weights (M_n's) follow exactly the M / I ratios. Therefore, 3a allows an easy control of the molecular weights at least up to M_n's of 10^5.

The living character of the covalent Sn-O bonds allows a broad variety of reactions after complete polymerization of a lactone. A stoichiometric reaction and useful modification of macrocyclic polylactones is the insertion of γ-thiobutyrolactone (eq. 3). This (commercial) lactone does not homopolymerize for thermodynamic reasons, but one insertion step is possible because a Sn-S bond is formed at the expense of the less stable Sn-O bond. The resulting macrocycles (9) are less sensitive to hydrolysis and alcoholysis, and thus, more suited for a variety of characterization methods such as SEC, fast atom bombardment (FAB) or MALDI-TOF mass spectroscopy. In fact FAB and MALD-TOF mass spectroscopy of the macrocyclic polylactones were only successful when the Sn-O bonds were replaced by Sn-S bonds (Figure 1).

Another interesting modification of the supermacrocycles 7 concerns the insertion of the 1,3-dithianone-2 (10). When conducted at temperatures ≥ 100°C, the first (slow) insertion step is followed by an elimination of Bu_2Sn S (a trimeric heterocycle) and tin-free supermacrocycles are formed (eqs. 4 - 5). Finally, it should be mentioned that the addition of another lactone to the supermacrocycles 7 results in a continuation of the polymerization process with the formation of macrocyclic blockcopolymers (1). Their structure can be checked by NMR-, DSC- and X-ray measurements[23-25)]. The perfection of the block-structure depends, of course, on the influence of transesterification reactions, which depend in turn on the reaction time and temperature.

Condensation reactions of macrocyclic polylactones

Nearly four decades ago members of the Bayer AG have reported[26,27)] on the isolation and polymerization of macrocyclic (i.e. tetrameric) bisphenol carbonates. Quite recently syntheses of macrocyclic esters or ethers and their use as monomers for the RIM technology has attracted increasing interest. In this work a new approach is presented for the first time, namely the application of tin-containing macrocycles and supermacrocycles as bifunctional monomers for (poly) condensation reactions.



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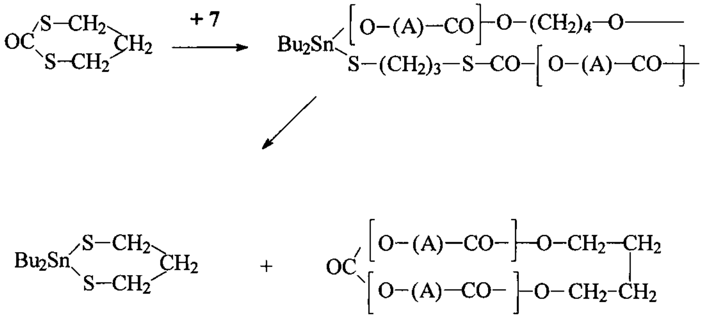
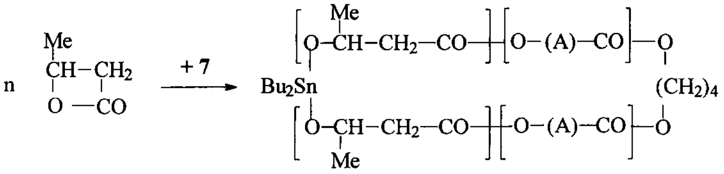


(6)

(7)

5



(8)

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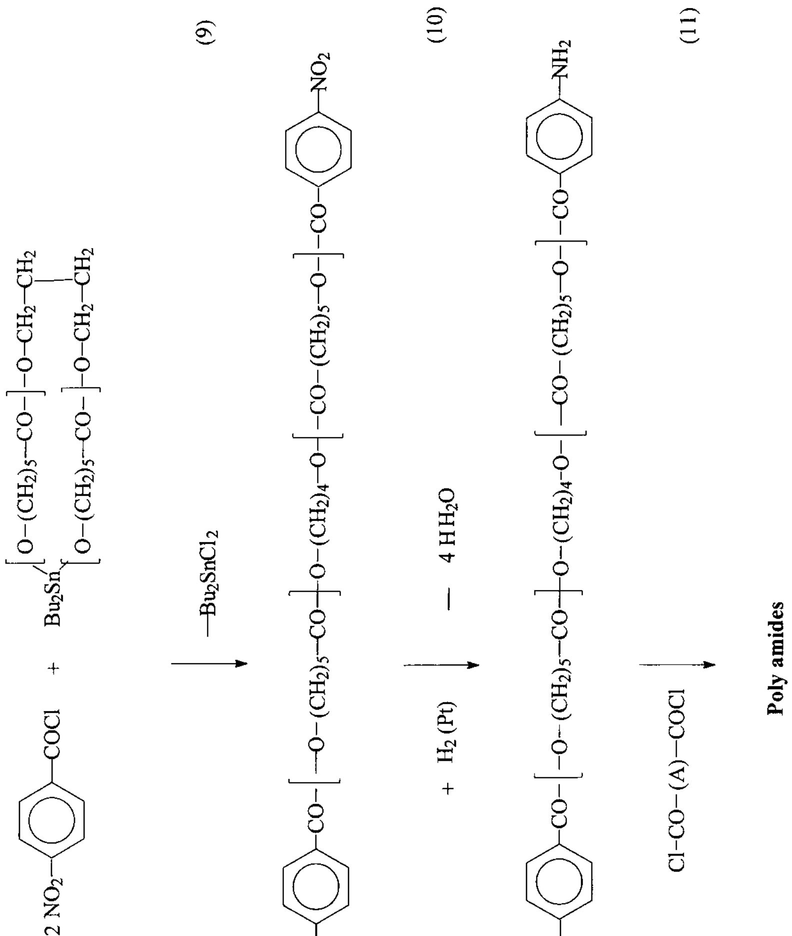
This new approach comprises two strategies:

I) Syntheses of telechelic oligolactones or polylactones followed by a chain extension.

II) Direct polycondensations of the tin-containing (super) macrocycles with dicarboxylic acid dichloride.

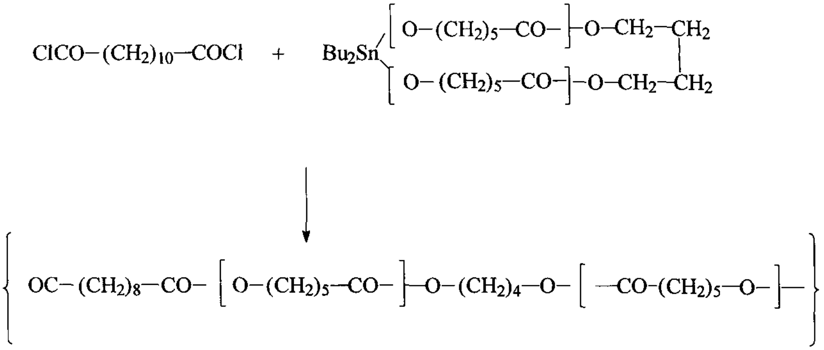
A characteristic example illustrating strategy I is outlined in eqs. (9) - (11). Further examples are described in a forthcoming publication28). Eq. (12) illustrates strategy II29). When this strategy is applied to macrocyclic block copolymers, it allows the syntheses of multiblock copolymers in an "one-pot procedure". Further studies in this direction are in progress.



(9)

(10)

(11)



$$ClCO{-}(CH_2)_{10}{-}COCl \;+\; Bu_2Sn\begin{cases}\left[O{-}(CH_2)_5{-}CO{-}\right]{-}O{-}CH_2{-}CH_2\\ \left[O{-}(CH_2)_5{-}CO{-}\right]{-}O{-}CH_2{-}CH_2\end{cases}$$

$$\downarrow$$

$$\left\{OC{-}(CH_2)_8{-}CO{-}\left[O{-}(CH_2)_5{-}CO{-}\right]{-}O{-}(CH_2)_4{-}O{-}\left[{-}CO{-}(CH_2)_5{-}O{-}\right]{-}\right\}$$

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