Effective Molarities from Distributions of Cyclic Oligomers in the Synthesis of Polythiolactones

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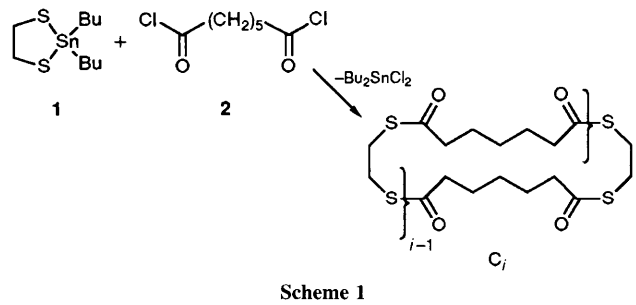
Effective molarities for closure of oligomeric polythiolactones with polymerisation degree up to 4 have been extracted from precise yield data in the reaction of 1,3,2-dithiastannolane with pimeloyl chloride.

Distribution among cyclic oligomers in macrocyclisation reactions depends not only on dilution[1] but also on the ring-closing tendencies (effective molarities, EM_i)[2] of the various cyclic '*i*-mers'. However, in spite of long-standing efforts,[3] there has been only a limited success in the evaluation of reliable EMs from ring distributions. A major reason for this is the paucity of systematic investigations of the effect of reactant concentrations on yields and distributions of cyclic oligomers. The present investigation is aimed at filling this gap.

Recently, we have reported[4] an improved procedure for the synthesis of macrocyclic polythiolactones *via* reaction of 2,2-dibutyl-1,3,2-dithiastannolane **1** with diacyl chlorides, *e.g.* pimeloyl chloride, **2**, Scheme 1, in refluxing $CHCl_3$. We now report that a careful scrutiny of the crude reaction mixtures by ^1H NMR spectroscopy and HPLC analysis revealed a virtually quantitative production of cyclic oligomers with the total exclusion of linear oligomers as well as of undesired side-products. Fig. 1 shows a typical HPLC chromatogram of the crude reaction product obtained from a batch-wise experiment with equal initial concentrations of reactants (0.050 mol dm^{-3}). It is apparent that the given reaction lends itself admirably to the purpose of an accurate determination of the cyclic oligomer distribution as a function of initial reactant concentration.

Absolute yields of cyclic oligomers, obtained by a comparison of the HPLC peak intensities with an internal standard, are given in Table 1 and graphically shown in Fig. 2. As expected, increasing dilution causes a composition shift towards the smallest oligomers. In the experiment run at the highest dilution the only detectable rings are C_1 and C_2, the sum of which accounts for virtually all of the starting materials.



Scheme 1

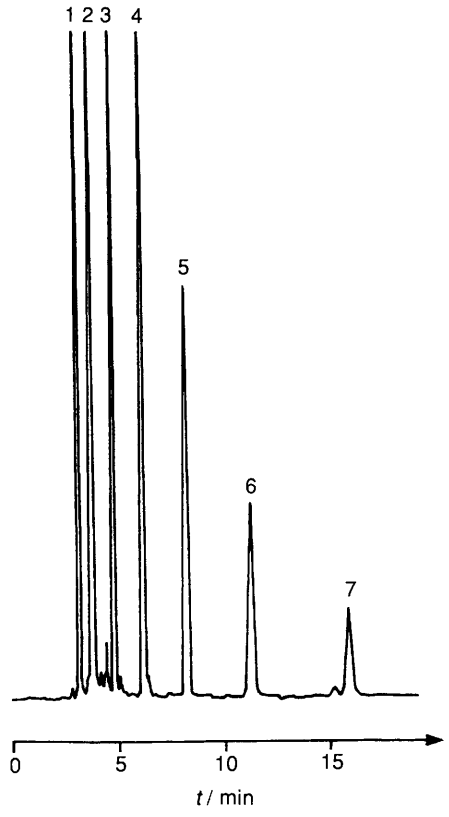


Fig. 1 Typical HPLC chromatogram of the reaction mixture obtained in a batch experiment where $[\mathbf{1}]_0 = [\mathbf{2}]_0 = 0.050$ mol dm^{-3}. The number on each peak indicates the degree of polymerisation of the corresponding cyclic oligomer C_i.

Table 1 Experimental and calculated distributions of cyclic oligomers C_i in the synthesis of polythiolactones.[a,b]

$[\mathbf{1}]_0 = [\mathbf{2}]_0$/ mol dm^{-3}	% C_1	% C_2	% C_3	% C_4
0.001	91 (88)	8 (11)	— (<1)	— (<1)
0.005	65 (62)	28 (29)	6 (7)	2 (2)
0.010[c]	42 (45)	34 (34)	13 (13)	6 (5)
0.050[d]	14 (14)	26 (25)	12 (12)	6 (8)

[a] Reactions carried out under batch-wise conditions in refluxing $CHCl_3$ as reported in ref. 4. [b] Values in brackets refer to calculated yields. EM_1 1.6×10^{-2}; EM_2 6.3×10^{-2}; EM_3 3.0×10^{-2} and EM_4 2.2×10^{-2} mol dm^{-3}. [c] C_5 (3%) and C_6 (1%) were also detected in the HPLC trace. [d] C_5 (5%), C_6 (3%) and C_7 (2%) were also detected in the HPLC trace.

Since the formation of $2i - 1$ intermolecular bonds plus the final intramolecular bond is required for the monomer molecules to build up into a cyclic 'i-mer', the cyclic oligomer distributions presented in Table 1 are the result of a formidable competition between inter- and intra-molecular processes. Recently, we have developed kinetic models in which competition between inter- and intra-molecular processes occurring in simple[5] and double[6] ring-closure reactions are taken into account. In order to adapt to the present reaction the model that describes the double ring closure of two symmetrical bifunctional monomers A–A and B–B, where A and B are two functional groups that react irreversibly with each other only, the actual reaction mechanism has to be taken into account. It has been suggested[4] that reaction of **1** with –COCl groups affords species with a reactive

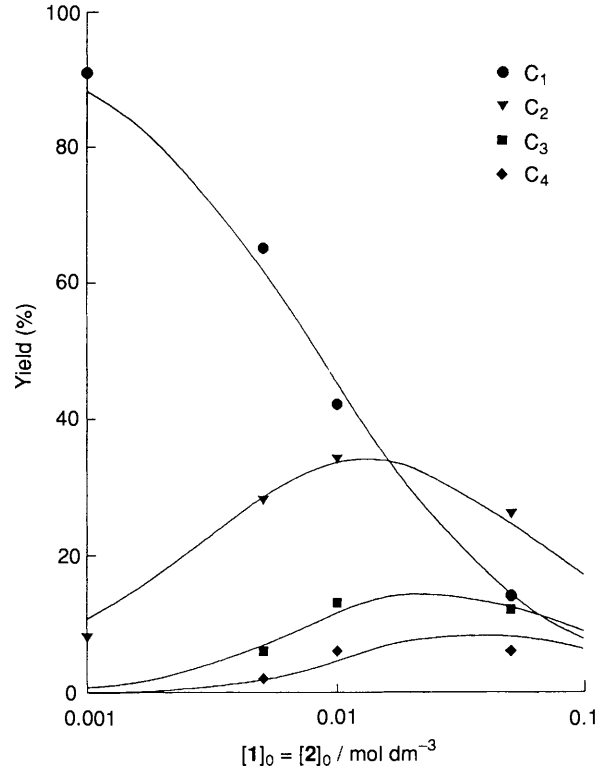
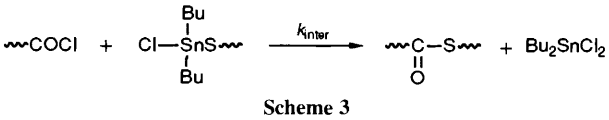
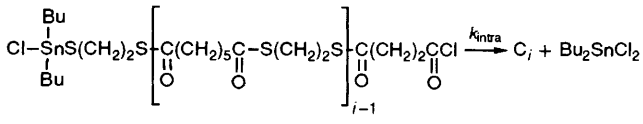


Fig. 2 Distributions of cyclic oligomers C_i as a function of initial reactant concentrations. The points are experimental (Table 1) and the curves are calculated.

Scheme 2



Scheme 3



Scheme 4

–$SSnBu_2Cl$ group (Scheme 2).† which is responsible for intermolecular (Scheme 3) and intramolecular (Scheme 4) processes. To sum up, the reactive species present in solution are **1** and linear oligomers having as terminal groups two –COCl functions, two –$SSnBu_2Cl$ functions, and one –COCl plus one –$SSnBu_2Cl$ function. Under the usual assumption of end group reactivity independent of chain length the reaction is characterized by the second-order rate constants k'_{inter} and k_{inter}, and by as many first-order rate constants $k_{(intra)i}$ as the number of cyclic oligomers being formed. It can be shown that the final product distribution is a function of the initial reactant concentration and of the k'_{inter}/k_{inter} and $k_{(intra)i}/k_{inter}$ ratios, the latter being the effective molarities EM_i of the cyclic 'i-mers'.

† The coefficient 2 in Scheme 2 is a statistical factor due to the existence of two equivalent sulfur atoms in **1**.

An optimization procedure based on numerical integration of the pertinent set of differential rate equations has been carried out. The input data are the initial reactant concentrations, the k'_{inter}/k_{inter} ratio,‡ and the experimental yields of cyclic oligomers. The EMs are treated as adjustable parameters to improve fit of calculated to experimental yields. In Table 1 are listed the yields calculated by the final EM_i values (in mol dm^{-3}).

The good agreement between calculated and experimental yields confirms the reliability of our kinetic model as well as of the computational procedure. The calculated EM_i values from EM_2 onward are practically coincident with available EM values of large, strainless rings, where the cyclisation tendency is solely determined by the conformational entropy loss upon ring closure.[2b] EM_1 is lower than the EMs of the next higher oligomers, but substantially higher than many of the values recorded for closure of 11-membered rings,[2b] showing that the presence of two bare sulfur atoms and two trigonal carbon atoms relieves most, if not all, of the eclipsing and transannular interactions which are major sources of strain in typical medium rings.[7]

So far, effective molarities for kinetically controlled ring-closure reactions have been obtained by direct measurements of rates of cyclisation and of the intermolecular model reaction.[2] The results reported in this communication show that a proper analysis of precise yield data of oligomers formed in a well-behaved macrocyclisation reaction is a valuable source of effective molarities.

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‡ Evaluated as 0.068 from independent measurements.

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