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Poly[(*R*)-3-hydroxyalkanoates] – The Fourth Family of Biopolymers: Contributions of an Organic Chemist

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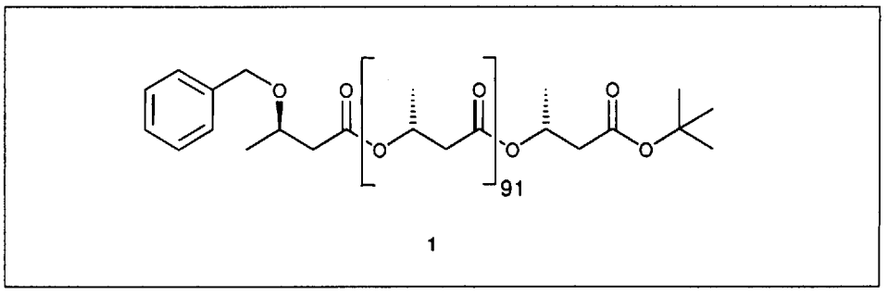
Originally, we considered PHB as a source of (*R*)-3-hydroxybutanoic acid (HB), a *chiral synthetic building block* [1], the enantiomer of the yeast reduction product of 3-oxo-butanoate [2]. We learned how to modify the structure of this simple molecule at each and every position of the C_4 skeleton [3–5] and to apply the principles developed with it to other 3-hydroxy- [6][7] and also to 3-amino-carboxylic acids [8][9].

Over the years, we became more and more interested in *biological, biochemical, medicinal*, and *material-science aspects* of PHB and the other poly(hydroxyalkanoates) (PHAs). PHB occurs in nature not only as the high-molecular-weight microbiological storage material (*s*-PHB, m.w. *ca.* 10^6 Dalton) but also as an oligomer of 100–150 units (*c*-PHB, m.w. around 10^4 Dalton) supposed to form complexes with various other materials. In her pioneering work, *Reusch* has shown that *c*-PHB is present in cell walls of prokaryotic and eukaryotic organisms [10][11], as well as in human blood serum [12]. The proposed function of *c*-PHB in biological systems called for fundamental synthetic and structural investigations!

We have developed a simple *exponential fragment coupling method for preparing linear oligomers* of very narrow molecular-weight distribution [13][14] which gave, for instance, a 93-mer **1** with $M_w/M_n \leq 1.001$ [15], and we found new methods



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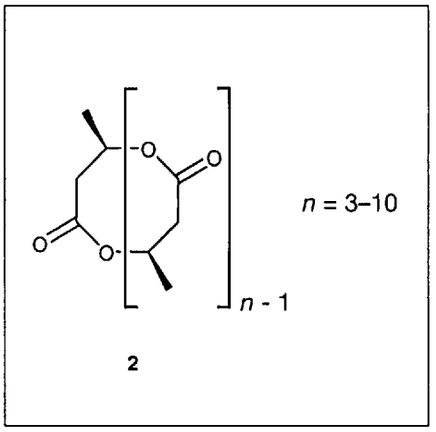

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of degrading PHB to oligomer fractions indicative of the dimension of folding in PHB crystallites [16][17]. Laser-desorption mass spectroscopy and gel-permeation chromatography were used for molecular-weight determinations, and the synthetic materials served as standards to calibrate these methods [15].

Cyclic oligomers (*oligolides*) **2** of 3-hydroxybutanoic acid were prepared from the monomer, using macrolactonization methods. Depending on the conditions, different ring sizes were preferred, and pure compounds containing three to ten HB units were isolated [13][14][18]. Especially the smaller oligolides can also be obtained directly from the polymer: under carefully controlled acid-catalyzed conditions, the triolid is prepared from PHB in *ca.* 50% yield [14][19]. A number of X-ray crystal structures [14][18] reveal the following facts: *i*) the larger oligolides (≥ 6 HB units) occur in several forms which differ in the folding of the rings (conformation) in the crystals; *ii*) the folded rings contain structural units from which known [20] and hitherto not detected helical structures of the linear polymer can be modelled [14][21]. A data bank of bond lenghts, bond angles, and dihedral angles for further modellings of polyester structures has become available. The crystal structures of the oligolides and their solid-state NMR spectra have been compared [22]. Finally, enzymatic degradation (*Pseudomonas delafieldii*) of the cyclic oligomers has been found to occur [23] contrary to expectation (so far enzymes have only been shown to degrade PHB from the *termini* of the chain).

Complexation and transport of ions through organic phases by various linear and cyclic HB oligomers have been studied [24]. Alkali and alkaline-earth ions are transported (nonspecific lipophilic order). A crystal structure reveals a first example of an ester-crown complex between Na^+ and the triolide, with an intriguing geometry [19].

The work presented at the Interlaken Meeting has been done by a group of enthusiastic coworkers: *Andreas Brunner, H. Michael Bürger, Urs Lengweiler, Roland Meier, Hans-Martin Müller, Dietmar A. Plattner, Ingrid Schwegler* (see also names in the list of references).

An extended abstract of a previous lecture on this topic has been published [25], and an extensive *review article* entitled 'Poly(hydroxyalkanoates), the Fifth Class of Physiologically Important Organic Biopolymers?' is appearing in the April 1993 issue of *Angew. Chem.* (260 references!). Reprints of the article or copies of the corresponding issue of the journal will be available at the conference.

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