Poly(β-alanoid-block-β-alanine)s: synthesis via cobalt-catalyzed
carbonylative polymerization and self-assembly†

Shaohui Lin, a Xinfei Yu, a Yingfeng Tu, a Hongyu Xu, b Stephen Z. D. Cheng a and Li Jia a

Revised: 11th March 2010, Accepted: 14th April 2010
First published as an Advance Article on the web 19th May 2010
DOI: 10.1039/c0cc00324g

The titled diblock copolymers are synthesized via cobalt-catalyzed
living carbonylative polymerization of N-alkylaziridines under
moderate pressures followed by a deprotection step. The
poly(β-alanine) block is solubilized by the poly(β-alanoid) block
in chloroform and remains fully hydrogen-bonded in the form of
a sheet-like assembly.

β-Peptide oligomers and polymers have been explored in the
past decade due to their structural analogy to peptides and,
as such, their potential peptidomimetic applications.1 Folding
of such synthetic molecules into various helices has been
well-studied both experimentally and theoretically. In
comparison, investigations on sheet-like structures formed
by β-peptides have not been prevalent.2 Interestingly, the
simplest member in the family, poly(β-alanine) or nylon 3,
has been characterized by X-ray diffraction to exist as flat
sheets in the solid state3 in contrast to the pleated
sheets in the polymer in solution. Usually, chain terminations
are living in either solvents,4 especially when the intended number
of aziridines is present.5 We hence chose to use a protective group strategy
to produce poly(β-alanine) (βAla) instead directly from the
unsubstituted aziridine. The protected monomer to be used
was para-(methoxybenzyl)aziridine (1). N-Butylaziridine (2)
was adopted as the other co-monomer to give the solubilizing
block, poly(n-butyl-β-alanoid) (BuβA), in the diblock
copolymer. Catalyst CH₂COCo(CO)₃(P(η-tolyl))₃ (3) was used
for the polymerization.6

Numbers of empirical trials were conducted to optimize
the conditions for synthesis of the diblock copolymers by
sequential addition of 1 and 2. The results of the synthesis
under the optimal conditions are summarized in Table 1.
The solvent and pressure of the polymerization are key and
deserve some elaboration. The choice of the polymerization
solvents was between tetrahydrofuran (THF) and 1,4-dioxane
(ε = 7.6 and 2.2,7 respectively). Although the mercaptal
polymerizations of 1 or 2 are living in either solvents,
chain termination was difficult to avoid in THF after the
consumption of the first aziridine monomer and when the
second aziridine was added.6 Monoblock contaminations were
observable by gel permeation chromatography (GPC) in
the diblock copolymers synthesized in THF. The chain
termination was also accompanied by ring-expanding
polymerization of the second aziridine co-monomer to give
the corresponding β-lactam as the byproduct.5 When
1,4-dioxane was used as the polymerization solvent, chain
termination could be avoided as long as the second monomer
was added promptly after the consumption of the first.
However, at 1000 psi of CO and 50 °C, which we had
customarily adopted for the polymerization, a bimodal
molecular weight distribution of the first block was observed
by GPC (see ESI),8 especially when the intended number
average degree of polymerization (Χn, which theoretically
equals the monomer-to-catalyst molar ratio) was low. The
bimodality was more pronounced for poly(para-methoxybenzyl-β-alanoid) (pMOBβA) than for poly(BuβA). Although
the mechanism that causes the bimodal distribution is still not
clear, lowering the CO pressure unexpectedly alleviated the
problem. At 150 psi and 50 °C, the bimodal distribution of the
first block was no longer observable (Fig. 1). Even under such
a low CO pressure, poly(pMOBβA-block-BuβA)s were
produced in quantitative yields with no olefinic structures
detectable by ¹H NMR, indicating the absence of chain
termination by β-hydrogen elimination. The diblock
copolymers displayed relatively low polydispersity without
significant contamination of the monoblock dead chains
regardless whether poly(pMOBβA) or poly(BuβA) was
chosen as the first block (Fig. 1).

Refluxing poly(pMOBβA-block-BuβA)s in trifluoroacetic
acid (TFA) selectively cleaved the N-methoxybenzyl group9
to give the corresponding poly(βAla-block-BuβA)s. The
completeness of deprotection is evidenced by the absence
of methoxy and phenyl resonances in the ¹H NMR of the
product (see ESI).9 The poly(βAla-block-BuβA)s with a
relatively long β-Ala block (entries 3 and 4 in Table 1) are
insoluble in common organic solvents. Those with a short
β-Ala block (entries 1 and 2 in Table 1) dissolve in chloroform

† Electronic supplementary information (ESI) available: NMR,
DSC, GPC traces, additional XRD data and unit cell sketch of
poly(βAla), and dynamic and static light scattering data. See DOI:
10.1039/c0cc00324g

Department of Polymer Science, University of Akron, 170 University
Avenue, Akron, Ohio 44325, USA. E-mail: lijia@uakron.edu,
scheng@uakron.edu

Department of Chemistry, Lehigh University, 6 East Packer Avenue,
Bethlehem, Pennsylvania, 18015, USA

Chem. Commun., 2010, 46, 4273–4275 | 4273

This journal is © The Royal Society of Chemistry 2010

COMMUNICATION
www.rsc.org/chemcomm | ChemComm
Table 1 Synthesis of diblock polymers

<table>
<thead>
<tr>
<th>Entry</th>
<th>Monomer</th>
<th>1st block</th>
<th>Diblock</th>
<th>PDI&lt;sub&gt;c&lt;/sub&gt;</th>
<th>PDI&lt;sub&gt;c&lt;/sub&gt;</th>
<th>PDI&lt;sub&gt;c&lt;/sub&gt; after deprotection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 (10)</td>
<td>2 (40)</td>
<td></td>
<td>1.50</td>
<td>1.44</td>
<td>9.87</td>
</tr>
<tr>
<td>2</td>
<td>1 (10)</td>
<td>2 (60)</td>
<td></td>
<td>1.50</td>
<td>1.44</td>
<td>11.8</td>
</tr>
<tr>
<td>3</td>
<td>1 (20)</td>
<td>2 (60)</td>
<td></td>
<td>2.55</td>
<td>1.26</td>
<td>13.2</td>
</tr>
<tr>
<td>4</td>
<td>2 (20)</td>
<td>1 (60)</td>
<td></td>
<td>2.25</td>
<td>1.26</td>
<td>13.0</td>
</tr>
</tbody>
</table>

<sup>a</sup> 150 psi of CO, 50 °C, 79 mg of 3 in 200 mL of 1,4-dioxane (0.80 mM), quantitative yield.  <sup>b</sup> Numbers in the parenthesis are the monomer-to-3 ratio.  <sup>c</sup> Relative to polystyrene standards by GPC with a refractometric detector using chloroform as the eluent.  <sup>d</sup> GPC with a refractometric detector using HFIP for GPC traces, ES-I for GPC traces.  

Fig. 1 GPC trace of polymers from entries 2 (left) and 4 (right) in Table 1. Red line: first block; blue line: diblock. The samples were collected directly after polymerization without any fractionation. The peaks labelled with asterisks are due to P(o-tolyl)₃ and OP(o-tolyl)₃ from the catalyst.

Fig. 2 IR spectra of 4 (bottom) in CDCl₃ solution (1 mg mL⁻¹) and poly(βAla) (top) in the solid state pressed into a pellet.
The antiparallel sheet-like structure. Corroborates the propensity of the forces between the (002) planes. The WAXD study therefore expands in the normal direction to the (002) planes than that of the WAXD pattern of pure poly(bA40 block of poly(bBuA) at 190 °C), which is also included in Fig. 3, the three halos are attributed to the (010), (200) and (002) diffractions \(d_{010} = 0.476 \text{ nm}, \ d_{200} = 0.400 \text{ nm}, \text{and} \ d_{002} = 0.377 \text{ nm}\) of the antiparallel sheets stacked in a monoclinic unit cell formed by the βAla block of 4. The crystals in this sample possess very small crystallite sizes within several nanometres based on the Scherrer equation. The βBuA30 block of 4 crystallizes during heating to exhibit Bragg diffractions as shown in the WAXD pattern taken at 150 °C in Fig. 3. By comparison with the WAXD pattern of the crystals of pure poly(βBuA), the diffractions of 4 with d-spacings of 0.82 nm, 0.49 nm, 0.43 nm and 0.41 nm are attributed to the crystals of the βBuA block (the crystal structure of pure poly(βBuA) is not available at this moment). Above the melting temperature of the crystals of βBuA block at 190 °C, two Bragg diffractions, which originate from the crystals of βAla block, remain as shown in Fig. 3. One is assigned to the (010) diffraction, and the other is a merger of the (200) and (002) diffractions. This merge is previously known for poly(βAla) and confirmed in our laboratory (see ESI) and is due to the larger thermal expansion in the normal direction to the (002) planes than that in the normal direction to the (200) planes. The phenomenon can be easily understood since the interaction is van der Waals forces between the (002) planes, while hydrogen bonding between the (200) planes. The WAXD study therefore corroborates the propensity of the βAla blocks in 4 to form the antiparallel sheet-like structure.

In summary, diblock poly(β-alanoid-block-β-alanine) have been synthesized via the catalytic carbynylative polymerization of aziridines followed by selective cleavage of the N-protective group. The diblock copolymers with a short βAla block form soluble supramolecular aggregates in chloroform. IR spectroscopic evidences suggest that the βAla block assembles into antiparallel sheets in the solution state via intermolecular hydrogen bonding. The WAXD studies support the notion that the antiparallel sheet conformation is highly favored by the βAla block.

We thank the NSF for supporting this research (CHE-0965060 and DMR-0906898) and funding University of Akron Magnetic Resonance Center to purchase the NMR instrument (CHE-9977144) used in this work. We are grateful to Tosoh Bioscience for running GPC analysis in HFIPA.

Notes and references

† Monomer 1 was dried over CaH2 and kept over n-Bu2Mg, and 2 was dried and kept over Na/K alloy. They were freshly distilled before polymerization. The polymerization was carried out in a 300-mL stainless-steel reactor equipped with a mechanical stirrer and a thermal couple (Autoclave Engineer). A stainless-steel tube was fitted to the top of the reactor via a ball-vein joint for monomer addition. The reactor was located in a ventilated hood, around which CO detectors were placed.

In a typical polymerization, a solution of 3 under CO (1 atm) and anhydrous 1,4-dioxane making the total volume 200 mL was charged into the reactor under a gentle CO flow. The reactor was then pressurized to 100 psi and heated to 50 °C. After the temperature stabilized, the first monomer was added through the addition tube pressurized to 150 psi. The polymerization was mechanically stirred at 500 rpm and monitored by ATR-IR via a SICOM probe (ReactIR IC, Mettler-Toledo) attached to the bottom of the reactor. When the polymerization of the first monomer reached completion (conversion frequency ~10 and ~20 h−1 for 1 and 2, respectively), the second monomer was added into the reactor via the slightly over-pressurized addition tube. The reaction was allowed to continue for an additional 5 h and stopped by releasing the pressure. Poly(MOBβA-block-βBuA) was collected after removal of 1,4-dioxane under vacuum, washing with ether, and drying under vacuum at room temperature. The yields were essentially quantitative.

Deprotection of poly(MOBβA-block-βBuA) was carried out in refluxing TFA for 4 h. After removal of TFA under vacuum, chloroform was added to the glassy residue to give either a solution or a slurry depending on the length of the βAla block. Diethyl ether was added to precipitate the poly(βAla-block-βBuA) product into a powder. The powder was collected after filtration and drying in vacuum. The yields were >90%.