Polynorbornene Replication

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From Polynorbornene to the Complementary Polynorbornene by Replication**

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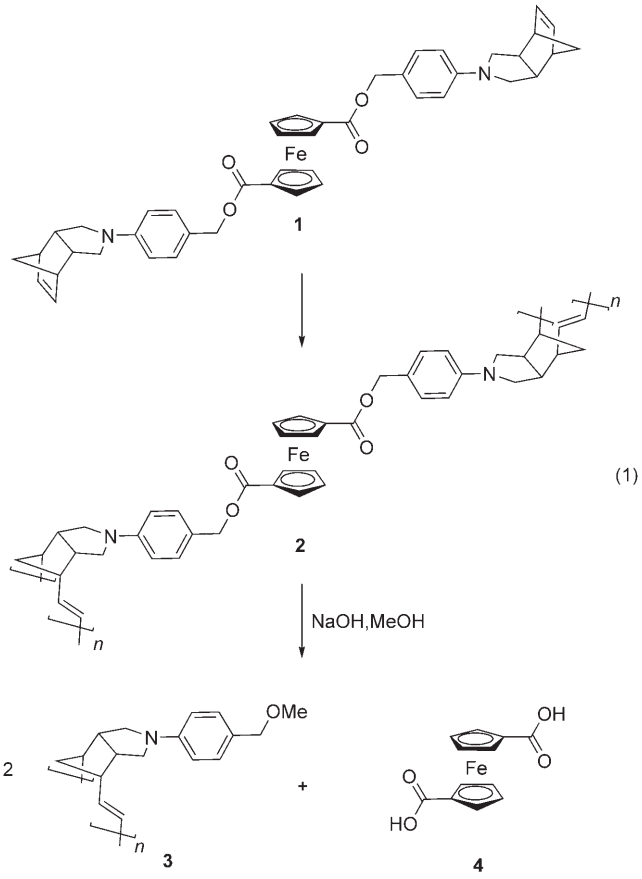
The double-helical structure, the act of replication linked to the cell cycle, and the ability of transcription leading to RNA synthesis are unique features of DNA.[1] Many approaches to simulate the biological processes by replicating a host molecule into its complementary molecule are known in the literature.[2–6] Particular attention has been focused on the use of oligonucleotide hosts to furnish the nonenzymatic synthesis of complementary oligonucleotides[3] or related analogues.[4] Peptides[5] and other synthetic systems[6] have also been used as templates for self-replication. We recently reported the first helical double-stranded polymer **2** by ring-opening metathesis polymerization (ROMP)[7] of a bisnorbornene derivative **1** [Eq. (1)].[8] The structure of **2** was unambiguously proved by chemical hydrolysis, spectroscopic means, and STM images. It is noteworthy that the linker between two norbornene moieties in **2** is derived from 4-aminobenzyl ester and ferrocene dicarboxylate. The aminobenzyl fragment in **2** is known to be particularly labile towards hydrolysis[9] to afford the corresponding single-stranded polymer **3** and ferrocene dicarboxylic acid **4** [Eq. (1)].[8]



(1)

Recently, we have also established that single-stranded polynorbornenes having *endo* pendant groups are rigid and that all pendant groups may align coherently in the same direction.[10] In particular, single-stranded polymers that have an electron-withdrawing substituent on the aryl pendant group (for example, **3**), directly obtained from the corresponding norbornene monomer by the Grubbs I catalyst, has been shown to exhibit isotactic stereochemistry.[10b] Accordingly, another norbornene monomer may be able to link to these pendant groups. Because the neighboring norbornene moieties may be in close proximity, ROMP may then take place, leading to a double-stranded polymer. After hydrolysis, a complementary polymer resulting from the replication of the original polymer may be obtained. This strategy is outlined in Figure 1. Herein, we report the first example of the use of a polynorbornene derivative as a template to exhibit replication ability for the formation of a complementary polymer.

We have previously shown that the ferrocene moiety provides a unique linker for double-stranded polymers because it may serve as a filling to prop up the two polymeric backbones. Moreover, the ferrocene unit may increase the solubility of the polymer because of the flexibility of the

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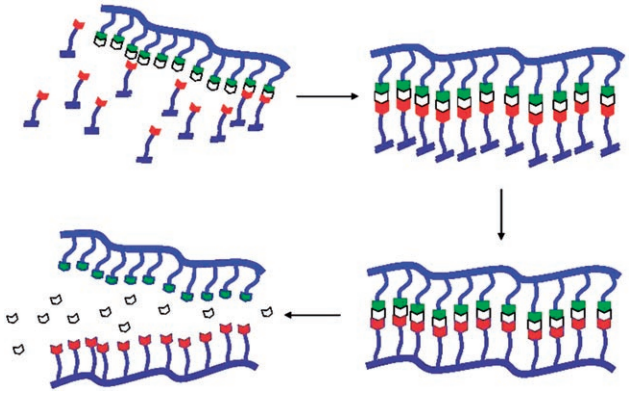
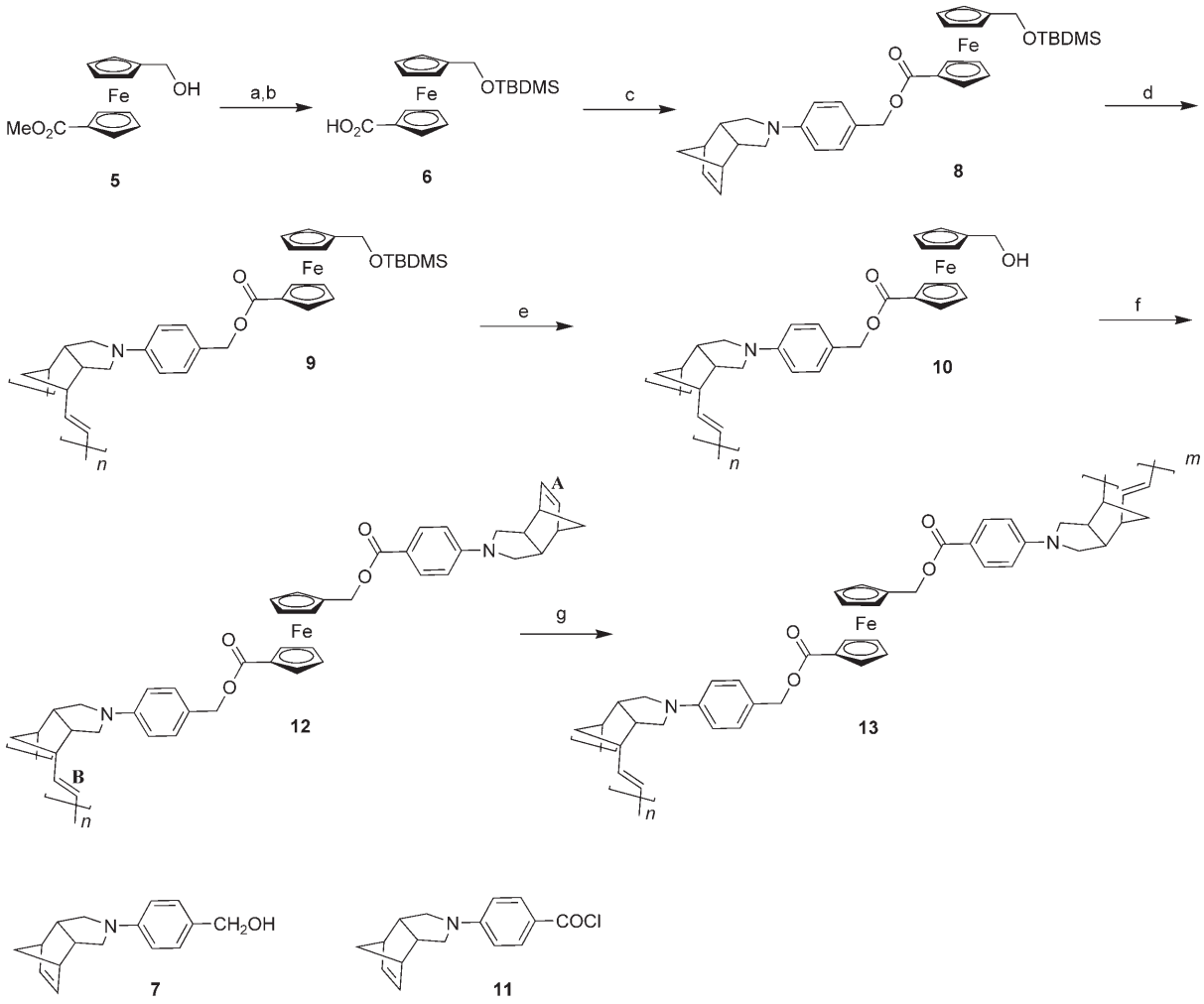


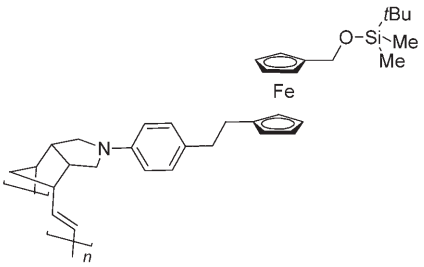
Figure 1. Strategy for polynorbornene replication.

skeleton that results from twisting of the two cyclopentadienyl ligands.[8] Accordingly, we have incorporated the ferrocene moiety into the single-stranded polymer (Scheme 1). Treatment of **5**[11] with TBDMSCl in the presence of imidazole and subsequent hydrolysis of the ester with "anhydrous hydroxide" (5 equiv KO*t*Bu, 2 equiv H_2O, THF)[12] gave **6** in 70% yield. Mitsunobu reaction[13] of **7** with **6** (DIAD, Ph_3P) gave **8** in 40% yield. ROMP of **8** with 7 mol% Grubbs I catalyst[7] afforded polymer **9** as a pale yellow solid in 92% yield. Gel permeation chromatography (GPC) analysis suggested that **9** had an M_n value of 12000 (PDI = 1.3),[11] corresponding to an average of 20 repeat units, which were consistent with the data from the end-group analysis based on ^{1}H NMR spectrum (an average of 19 repeat units). Attempts to use MALDI-TOF MS for the absolute molecular-weight determination were unsuccessful, presumably owing to the instability of the aminobenzyl ester moieties in **9**.

To test the stability of ferrocene-containing polynorbornene under MALDI-TOF MS conditions, polymer **14**, with an ethylene bridge between the ferrocene unit and the 4-aminophenyl group, was synthesized.[11] Because of the absence of the aminobenzyl ester group in **14**, the MALDI-TOF mass spectrum was obtained satisfactorily. It is noteworthy that the average molecular weights for **14** obtained by gel permeation chromatography (M_n = 12000, PDI = 1.1),



Scheme 1. Reaction conditions: a) TBDMSCl, imidazole, RT, 4 h, quantitative; b) KO*t*Bu, H_2O, RT, 20 h, 70%; c) DIAD, PPh_3, **7**, THF, RT, 40%; d) 7 mol% $[(Cy_3P)_2Cl_2Ru{=}CHPh]$, CH_2Cl_2, RT, 2 h, 92%; e) TBAF, THF, 0°C, 5 h, quantitative; f) DMAP, Et_3N, **11**, RT, 10 h, 80%; g) 5 mol% $[(Cy_3P)_2Cl_2Ru{=}CHPh]$, CH_2Cl_2, RT, 50 min, quantitative.



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MALDI-TOF ($M_n = 12000$, PDI = 1.3), and end-group analysis with ^{1}H NMR spectroscopy (number of repeat units: 21) were comparable. These results suggested that GPC or end-group analysis may provide reliable results for the analysis of ferrocene-containing polynorbornenes.

The silyl protective groups in **9** were removed (TBAF, 0 °C, 5 h, quantitative) to give the alcohol **10**, which was esterified with acid chloride **11** (DMAP/Et_3N, RT), leading to the formation of polymer **12**. This latter esterification procedure was repeated and the ^{1}H NMR spectrum showed that at least 94 % of **12** was incorporated into this polymer. GPC analysis suggested that **12** had an M_n value of 12000 (PDI = 1.2), corresponding to an average of 17 repeat units. However, the end-group analysis based on the ^{1}H NMR spectrum showed that **12** may have an average of 19 repeat units. Again, it was not possible to determine the molecular weight of **12** by MALDI-TOF MS owing to instability of the polymer under laser-bombardment conditions.

Under high-dilution conditions, metathesis of **12** with Grubbs I catalyst (5 mol %)[7,14] gave efficiently the corresponding double-stranded polymer **13**. Owing to solubility problems, we were unable to determine the M_n value by GPC. The end-group analysis was also difficult because of significant overlap of characteristic peaks. The characteristic peak for the olefinic carbon atoms of the norbornene moiety in **12** ($\delta = 135.6$ ppm) was no longer observable for **13**. The signals at $\delta = 171.0$ and 166.5 ppm are attributed to the two carbonyl carbon atoms, whereas the signals at $\delta = 150.9$ and 148.5 ppm are characteristic for the *ipso* carbon atoms of the amino-substituted aryl rings. The simplicity of the spectrum indicated that **13** might adopt a regular rigid structure.

Scanning tunneling microscopy (STM) was employed to gain detailed structural information for **13**. Figure 2a shows four 52 × 52-nm frames acquired from different trials of experiments. It is noteworthy that no dendritic branching was observed for **13**. From more than 500 polymers **13**, the nominal width and length of **13** were 2.8 ± 0.2 and 10.5 ± 2.7 nm, respectively, where the standard deviation was derived from the Gaussian fitting shown in Figure 2c. Figure 2b exhibits the resolved STM image of one double strand of **13**. Although the contrast of the image is obscured from being exported from the NanoScopeIIIa program, there are clearly resolved fine rows nearly perpendicular to the polymer long axis with a spacing of about 0.56 nm. These results suggested that **13** may have an average of 19 repeat units and are consistent with the average number of repeat units of the precursors **9** and **12** described above.

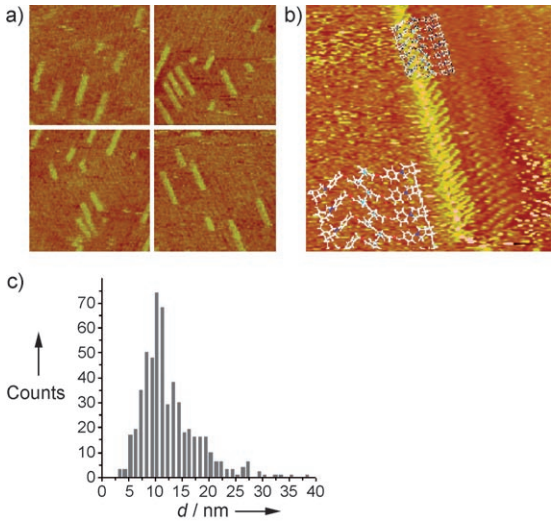
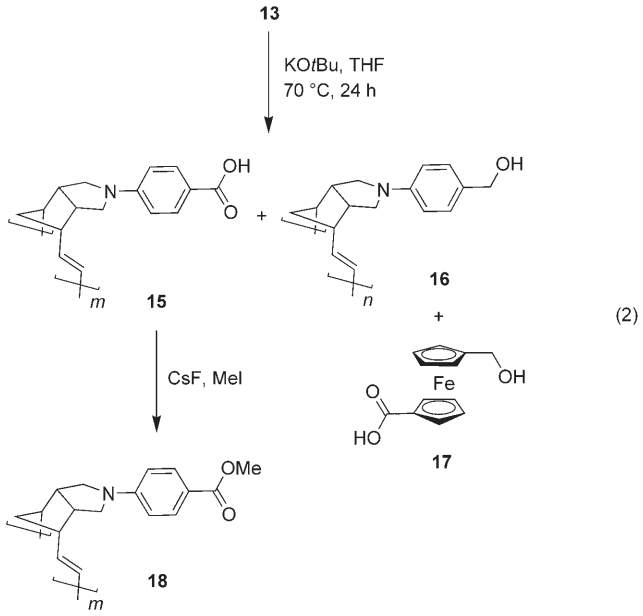


Figure 2. High-impedance STM images of **13**. a) Typical images acquired from different runs (image size for each frame: 52 × 52 nm, $E_{bias} = 1.0$ V, $i_{tunneling} = 12$ pA, height mode). b) High-resolution STM image (15.7 × 15.7 nm, $E_{bias} = 0.7$ V, $i_{tunneling} = 20$ pA, current mode). The simulated structure is magnified and placed at the lower left part of (b). In these images, **13** adopts a ladderlike conformation which resides at the flat terrace rather than at a step edge or domain boundaries so that artefacts arising from the highly oriented pyrolytic graphite substrate would be unlikely.[15] c) Histogram of length (*d*) distribution plotted from 548 polymeric molecules (bin size: 1 nm).

A simulated structure is superimposed on the image of the double strand, and a magnified view of the structure is given at the lower left corner of the image (Figure 2b). One phenylene ring (on the left side of ferrocene in Figure 2b) might be tilted from the surface normal and positioned closer to the substrate surface than the other phenylene ring, which might hang above the substrate in between the norbornene and ferrocene units. Because of better tunneling conditions, the phenylene ring on the left side of the ferrocene moieties would exhibit a more distinct contrast than the right one.

Polymer **13** represents the first unsymmetrical double-stranded polymer in which the two constituent strands are complementary to each other and linked by the ferrocene units. Unlike **2**,[8] only ladderlike structures were observed by STM for **13**, and neither helical nor supercoiled structures were observed in the STM images. The relationship between the structure of the double-stranded polymer and the solid-state morphology remains unclear at this stage.

Polymer **13** was hydrolyzed under "anhydrous hydroxide" conditions (excess KO*t*Bu, 4 equiv H_2O in THF, 70 °C)[12] to afford **15** and ferrocene derivative **17** [Eq. (2)]. Attempts to isolate polymer **16** were unsuccessful.[16] Polymer **15**, obtained from the neutralization of the aqueous solution, was treated in situ with CsF and MeI[17] to give the corresponding methyl ester **18** (GPC: $M_n = 5000$, PDI = 1.3; MALDI-TOF: $M_n = 4500$, PDI = 1.2) in 50 % overall yield of isolated product from **15**. Polymer **18** showed spectroscopic properties identical to those of the polymer synthesized directly from the ROMP of the corresponding monomer[10] and had 18 repeat units, which were comparable to those of **12** and **13**. Since the number of the repeat units of **18** is comparable with those of the



precursors **9**, **10**, and **12**, it seems likely that the second polymerization (from **12** to **13**) might start from the terminal norbornene moiety in **12**.

In summary, we have demonstrated an unprecedented example on the replication of a single-stranded polynorbornene, leading to its complementary polynorbornene derivative. The process has been shown to involve an unsymmetrical double-stranded polymer **13**, which has been thoroughly characterized by spectroscopic means as well as by STM images. As described in our previous paper,[8] a bisnorbornene compound connected by an appropriate linker has provided a unique entry for the synthesis of a double-stranded DNA-like polymer. Since the double-stranded polymer can easily be transformed into two single-stranded polymers,[8] the present replication study adds another novel DNA-like feature to bispolynorbornenes. Further extension of this system is in progress in our laboratory.

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[11] a) The details are described in the Supporting Information; b) Abbreviations: TBDMS = *tert*-butyldimethylsilyl, DIAD = diisopropylazodicarboxylate, TBAF = tetrabutylammonium fluoride, DMAP = 4-dimethylaminopyridine.

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[14] Upon treatment of **12** (GPC: $M_n = 13\,000$, PDI = 1.1, 23 repeat units) with 10 mol % of the Grubbs I catalyst, **18** obtained after the same reaction sequence according to Scheme 1 and Eq. (2) has 15 repeat units (GPC: $M_n = 4000$, PDI = 1.3; MALDI-TOF: $M_n = 3673$, PDI = 1.1). Presumably, the reaction may take place from both ends of **12**, resulting in a decrease in the number of repeat units in **18**.

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