

## OMCOS for functional polymers—double-stranded DNA-like polymers\*

Tien-Yau Luh<sup>‡</sup>, Hui-Chun Yang, Nai-Ti Lin, Shu-Yi Lin, Shern-Long Lee, and Chun-hsien Chen

*Department of Chemistry, National Taiwan University, Taipei 106, Taiwan*

**Abstract:** The first helical double-stranded polymer by ring-opening metathesis polymerization (ROMP) of a bisnorbornene derivative and the replication of a single-stranded polynorbornene leading to its complementary polynorbornene derivative are described. Base-promoted hydrolysis of this polymer affords the corresponding single-stranded polymer and the linker, ferrocene-1,1'-dicarboxylic acid, in excellent yield. Three forms (helical, supercoil, and ladder) of the polymer have been observed by scanning tunneling microscopy (STM) and simulated by molecular mechanical and dynamical calculations. The polymer thus obtained has a structural resemblance to DNA by having similar width, number of monomeric units per pitch, five-membered rings in the polymeric frame, perpendicular linkers to the backbones, and similar spacing between neighboring monomeric units. In the replication study, the single-stranded polynorbornene acts as a template for norbornene monomer adhesion via ester linkage. This polymer is treated with Grubbs-I catalyst to proceed the ROMP to afford the corresponding unsymmetric double-stranded polymer. After hydrolysis, a complementary polynorbornenecarboxylic acid is produced. This approach may provide a versatile entry for the design, synthesis, and physicochemical investigations of new types of polymers for simulation of biological systems as well as materials applications.

**Keywords:** ring-opening metathesis polymerization; bisnorbornene; double-stranded polymers; replication; STM image.

### INTRODUCTION

The use of organometallic chemistry directed toward polymer synthesis has a long history. The discovery of the Ziegler and Natta catalysts have opened a new era for polyalkene synthesis [1]. Since the 1980s, ring-opening metathesis polymerization (ROMP) using well-defined organometallic catalysts has provided a powerful method for the molecular-level design of macromolecular materials with high selectivity and functional group tolerance [2]. Cross-coupling reactions have furnished a versatile entry for the synthesis of a wide range of polymeric semiconductive materials [3]. Synergies between organic chemistry and polymer synthesis have paved the way for constructing macromolecules of diverse structural varieties. Biopolymers exhibit unique structural features and fascinating functions that artificial polymers are still far from matching (Table 1). The synthesis of polymers compatible with biopolymers therefore remains a great challenge for synthetic chemists. In line with the context shown in Table 1, our initial endeavor has focused on the synthesis of alternating silylene-divinylarene copolymers hav-

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<sup>‡</sup>Corresponding author

ing donor and acceptor chromophores arranged in regioregular manners for light-harvesting and electron-transfer investigations [4]. In addition, by employing a convergent/divergent strategy, we have recently synthesized alternating monodispersed benzene-furan oligomers with molecular weights up to several thousands [5]. Different substituents can be regioselectively incorporated in these oligomers so that the molecules can have no repetitive units. In this account, we summarize our approach on the synthesis and chemistry of the first DNA-like double-stranded polymers including replications [6,7].

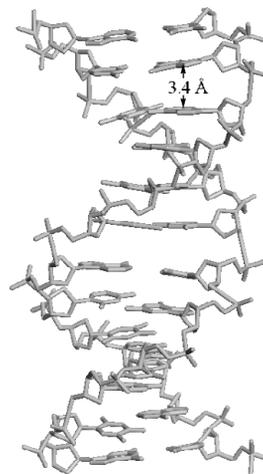
**Table 1** Biopolymers vs. synthetic polymers.

Characteristics	Biopolymers	Synthetic polymers
Dispersity	unity	>1
Repetitive units	no, but with well-defined defined sequence	yes, but occasionally with poorly defined sequence
Chirality	yes	yes (with chiral auxiliary)
Catalytic behavior	yes	rare
Double-stranded	yes	possible
Replications	yes	unknown

## STRATEGY

The unique structural features and certain characteristics of a DNA molecule are summarized in Fig. 1. Much effort has been focused on the helical double-stranded oligomers where the two single chains are linked by chelation to metal ions [8–10] complexation through hydrogen-bondings [11,12],  $\pi$ - $\pi$  stacking [13], or inclusion complexes [14]. Ladder-like organic polymers having two strands connected by covalent, dative, or ionic bonds have been briefly explored [15–18].

Double stranded  
 Helical structures  
 No repetitive units  
 Pending group perpendicular to backbone  
 Two antiparallel complimentary strands  
 Hydrophilic interactions (hydrogen bondings)  
 Hydrophobic interactions ( $\pi$ - $\pi$  interactions 3.4 Å)  
 Isotactic  
 Chiral  
 Conformational changes  
 Replication  
 Charged  
 Triple helix formation  
 Electron hopping between base pairs

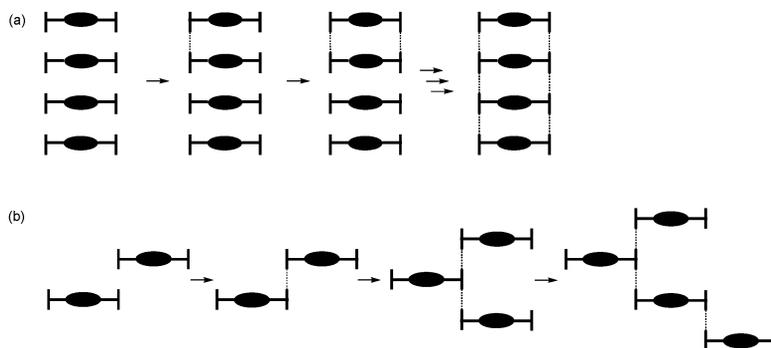


**Fig. 1** Certain characteristics of a DNA molecule.

Our strategy toward a synthesis of a DNA-like polymer involves polymerization of the monomer containing two polymerizable groups linked by an appropriate linker (Fig. 2a). In order to avoid polymerization leading to a scattered structure (Fig. 2b), several important factors are indispensable for the success of the synthesis of a double-stranded polymer. They are: (1) the nature of the polymerizable group; (2) the stereochemistry and conformation of the polymers; (3) the nature of the connecting group; and (4) elucidation of the structure of the polymers.

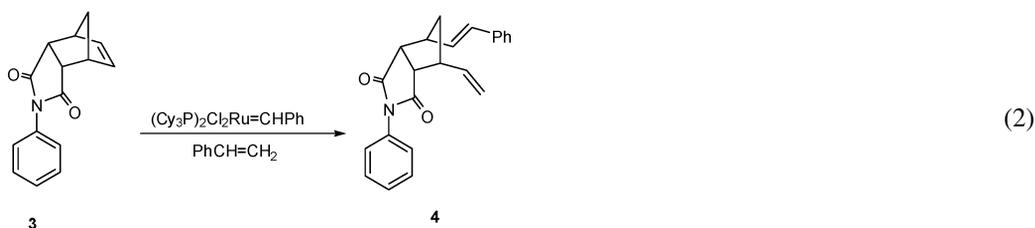
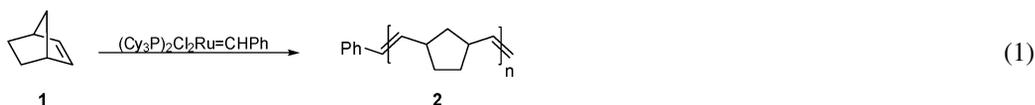
## NATURE OF THE POLYMERIZABLE GROUP

As shown in Fig. 1, one of the important structural features in a DNA molecule is the 3.4 Å-spacing between base pair layers due to  $\pi$ - $\pi$  interactions. It is believed that such hydrophobic interactions may play an important role, inter alia, for the DNA molecule holding the double-stranded structure. Based on this strategy, it seems unlikely that polymers derived from  $\alpha$ -olefin could be used as the backbones of double-stranded polymers because the space occupied by each monomeric unit may be around 2.5 Å, which is far shorter than the required 3.4 Å for  $\pi$ - $\pi$  interactions.



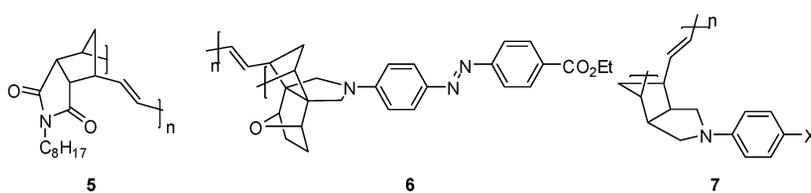
**Fig. 2** Synthetic strategy toward a double-stranded polymer.

ROMPs of norbornenes **1** are well documented [19]. Polynorbornenes **2** has mainly trans double bonds when Grubbs-I catalyst is employed (eq. 1) [20]. Like a DNA molecule, polynorbornenes have five-membered rings in the backbone. The span of each of the monomeric vinylcyclopentane moieties in polynorbornenes appears around 5–6.5 Å based on the X-ray structure of **4** obtained by cross metathesis of **3** with styrene (eq. 2) [21]. This distance provides a useful clue for the design of linkers for double-stranded polymers.

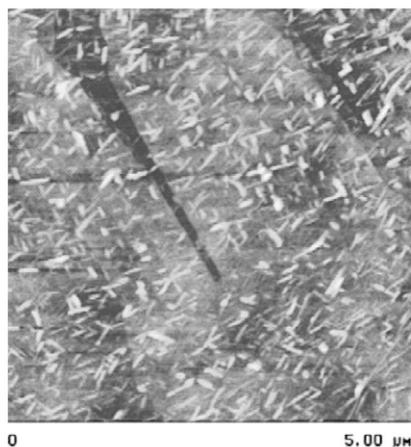


## STEREOCHEMISTRY AND CONFORMATION OF THE POLYNORBORNENES

The stereochemistries of polynorbornenes have been extensively examined, and it appears that the nature of the catalyst and the structure of the monomeric norbornenes may influence the tacticity and the double bond configurations of polymers [19,22–25]. ROMPs of norbornadiene diester and *exo,exo*-2,3-dicarbomethoxy-5-norbornene with a ruthenium catalyst reportedly give isotactic polymers with mainly trans double bonds [25], whereas **5** is atactic [23,24].

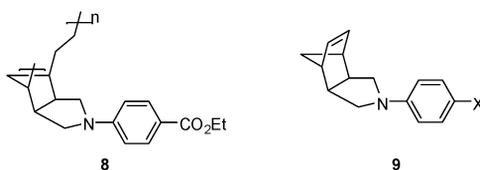


It is known that polynorbornenes obtained by ROMP using Grubbs-I catalyst have double bonds in *trans* configurations [20]. Atomic force microscopy (AFM) revealed that these polymers **6** may adopt rigid rod structures (Fig. 3) [21].



**Fig. 3** AFM image of **6**.

We have systematically examined the stereochemistry and conformation of polynorbornenes with 5,6-*endo* dipolar pending groups having substituted aryl chromophores **7** [21,26]. The extinction coefficients of **7** decrease with increasing degree of polymerization. Apparently, the pending chromophores may be in close proximity to form H-aggregation, resulting in decrease in extinction coefficients. In addition, the  $\beta$  values obtained from hyper-Rayleigh scattering method [27] or  $\mu\beta$  values measured by EFISH method for **7** or related polymers [26] are enhanced as the molecular weight of **7** increases. These results indicate that the dipolar pending groups may be coherently aligned in *syn* direction [26]. The presence of the double bonds in **6** appears to be inevitable for the rigidity of the polymer. Thus, the  $\mu\beta$  values of **7** ( $X = \text{CO}_2\text{Et}$ ) are compared with those of **8**, obtained by the diimide reduction of **7**, in Table 2. It is interesting to note that the  $\mu\beta$  values of **8** rapidly reach a plateau, whereas those of **7** ( $X = \text{CO}_2\text{Et}$ ) are molecular weight dependent.



**Table 2** Relative  $\mu\beta$  values of monomer **9** ( $X = \text{CO}_2\text{Et}$ ) and polymers **7** ( $X = \text{CO}_2\text{Et}$ ) and **8** of different molecular weights in  $\text{CHCl}_3$  using 1907 nm fundamental wavelength.

Compd.	$M_n$ (PDI)	$\mu\beta_o^p/\mu\beta_o^m$	Compd.	$M_n$ (PDI)	$\mu\beta_o^p/\mu\beta_o^m$
<b>9</b> ( $X = \text{CO}_2\text{Et}$ )	283	1			
<b>7a</b>	4200 (1.2)	8.7	<b>8a</b>	4200 (1.2)	2.0
<b>7b</b>	6500 (1.1)	16.5	<b>8b</b>	6500 (1.1)	3.0
<b>7c</b>	9100 (1.2)	22.4	<b>8c</b>	9100 (1.2)	3.0
<b>7d</b>	17 000 (1.4)	35.3	<b>8d</b>	17 200 (1.4)	3.3

$^{13}\text{C}$  NMR has been extensively used for the tacticity of polynorbornenes [19]. Figure 4 shows the possible structures of the syn conformations of isotactic and syndiotactic polymers **7**. The syndiotactic structure has  $C_2$  symmetric axis bisecting the carbon–carbon double bond. As such, the environment for each of the neighboring monomeric units is the same, and only one set of the  $^{13}\text{C}$  NMR signals would be expected. On the other hand, there is a plane of symmetry perpendicular to the polymeric backbone and bisecting each monomeric unit in isotactic structure with the syn conformation. The two planes of symmetry ( $\sigma$  and  $\sigma'$ ) in two neighboring units, however, are different and therefore two sets of the  $^{13}\text{C}$  NMR signals might be anticipated.

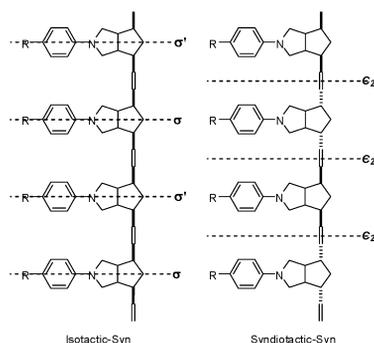
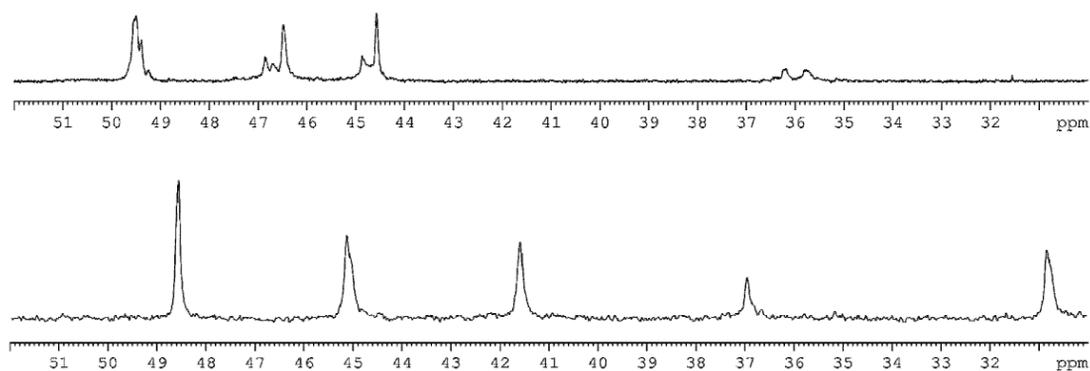
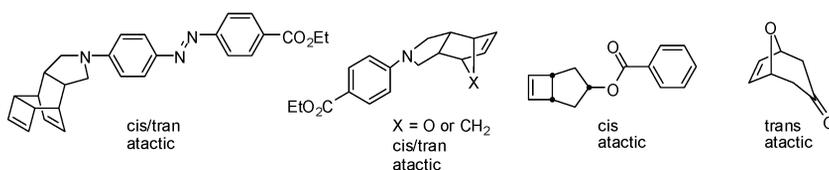
**Fig. 4** Symmetry of **7** with syn conformations.

Figure 5 shows the  $^{13}\text{C}$  NMR spectra of **7** ( $X = \text{CO}_2\text{Et}$ ) and the corresponding hydrogenated polymer **8**. The high field signals assigned to  $C_7$  [27] for **7** ( $X = \text{CO}_2\text{Et}$ ) exhibit as two peaks of equal intensity at  $\delta$  35.75, 36.21. It seems likely that **7** may adopt an isotactic structure with syn conformation. Upon reduction, these signals are merged into a single peak. The simplicity of the spectrum for **8** suggested that this polymer may adopt a single tacticity [19]. It is believed that interactions between pending chromophores may play an important role in dictating the stereochemistry of these polynorbornenes **7**.



**Fig. 5** Partial  $^{13}\text{C}$  NMR spectra of **7** ( $X = \text{CO}_2\text{Et}$ , upper panel) and **8**.

Polymers with other skeletons obtained from the ROMP of the corresponding strained cyclic olefins have been examined, and representative results are summarized in Fig. 6. It seems that polynorbornenes fused with endo *N*-aryl pyrrolidine moiety (like **7**) appear to be unique in the stereoselectivity in Grubbs-I catalyst mediated ROMP reactions [28].



**Fig. 6** ROMP of strained cyclic olefins with Grubbs-I catalyst.

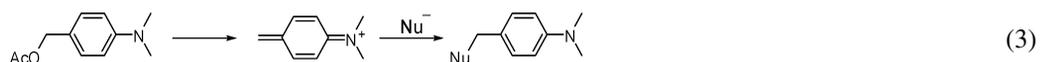
### NATURE OF THE LINKER

As mentioned earlier, the spacing occupied by each monomeric unit in **7** would be around 5–6 Å. It is therefore important to tailor the dimension of the linker within this range so that appropriate interactions between linkers might take place to assist the orientation of the polymerization process leading to a double-stranded structure.

In addition, the linker should be relatively rigid but somewhat flexible. Last but not least, the linker should be easily cleaved so that two single-stranded polymers may be isolated. This strategy would be very useful for structural elucidation of the double-stranded polymer thus obtained.

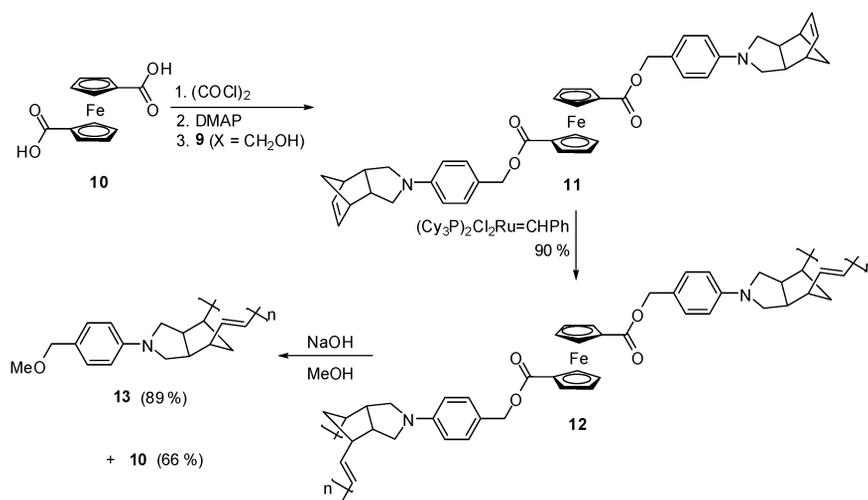
A ferrocene moiety would be a right choice because the Fe–Fe distances in single crystals of ferrocene derivatives are 5.5–5.9 Å [29]. The size is just right, and the ferrocene moiety is rigid but also flexible. In addition, it is redox active.

As described in the previous section, the single-stranded polymers **7** consist of *N*-arylpyrrolidine moieties. It is known that 4-aminobenzyl ester is extremely labile upon treatment with nucleophiles (eq. 3) [30]. Accordingly, this moiety may serve as an appropriate linker which may be readily cleaved upon hydrolysis.



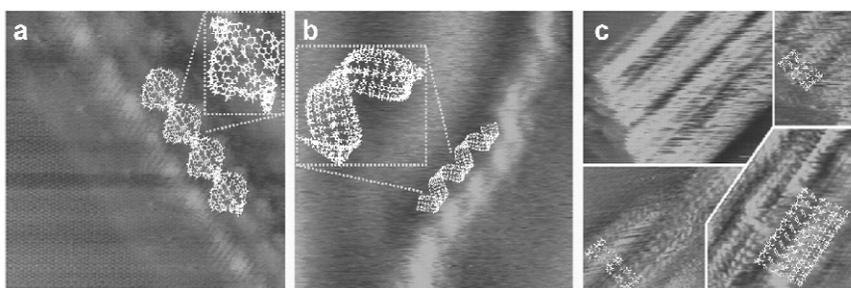
## SYNTHESIS AND CHARACTERIZATION OF BISNORBORNENE DOUBLE-STRANDED POLYMERS

Based on the preliminary investigations on the strategy for the design and synthesis of bisnorbornene double-stranded polymer, the synthesis according to Scheme 1 has been executed [6]. Grubbs-I catalyst catalyzed ROMP of **11** affords the corresponding double-stranded polymer **12** in excellent yield. The structure of **12** is unambiguously proved by spectroscopic means, scanning tunneling microscopy (STM) images, and chemical degradation. Thus, base-promoted methanolysis of double-stranded polymer **12** yields the corresponding single-stranded polymer **13** and the ferrocene linker **10** in excellent yield. The ability for hydrolytic dissociation into two single-stranded polymers adds interesting resemblance to DNA molecules. Like a DNA molecule, the double-stranded polymer **12** is highly fluxional in  $\text{CHCl}_3$  solution as revealed by the  $^1\text{H}$  NMR.



**Scheme 1**

Three forms (helical, supercoil, and ladder) of the double-stranded polymer **12** have been observed by STM and simulated by molecular mechanical and dynamical calculations (Fig. 7) [6]. In helical form (Fig. 7a), the average spacing between stripes and the pitch length are  $0.45 \pm 0.04$  and  $5.2 \pm 0.2$  nm, respectively, and each pitch consists of 12–13 monomeric units. For the supercoil structure (Fig. 7b), the average spacing per turn, the apparent height, and the nominal width are ca. 7.1, 3.2, and 3.0 nm, respectively, consistent with the structure of a hollow coil. The ladder structures shown in Fig. 7c display an apparent uniform width throughout the feature and exhibit parallel lines or bright spots, for example, going from the upper right to the lower left corner in Fig. 7c. Vertical to these parallel lines are fine rows making the topographic feature ladder-like. The width of ladders is ca. 2.2–2.4 nm, and the spacing between the rows falls in between 0.45 and 0.55 nm.



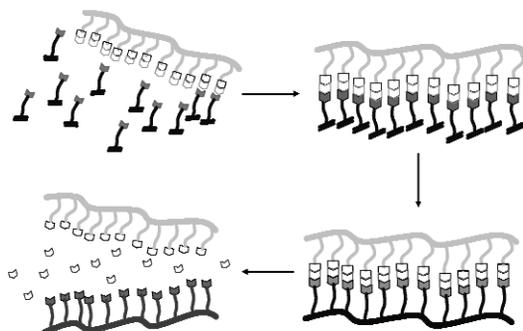
**Fig. 7** STM images of **12** on HOPG at flat terrace [6]. The values in parentheses are the corresponding imaging sizes and conditions: (a) helical structure ( $16.8 \times 16.8$  nm;  $E_{\text{bias}}$  0.19 V;  $i_{\text{tunneling}}$  200 pA); (b) supercoil ( $58 \times 58$  nm;  $E_{\text{bias}}$  0.19 V;  $i_{\text{tunneling}}$  20 pA); and (c) ladder (clockwise from the upper left one:  $35 \times 28$  nm,  $5.0 \times 6.5$  nm,  $7.0 \times 7.4$  nm,  $7.2 \times 5.3$  nm;  $E_{\text{bias}}$  0.24 V;  $i_{\text{tunneling}}$  20 pA).

The polymer thus obtained has a structural resemblance to DNA by having similar width, number of monomeric units per pitch, five-membered rings in the polymeric frame, perpendicular linkers to the backbones, and similar hydrophobic interactions between neighboring monomeric units.

Ferrocene is known to be redox active. Thus, electron transfer numbers of the ferrocenyl moieties in **12** and related polymers are examined by the chronoamperometric method [31] at a microelectrode or by the bulk-electrolysis experiments. On the average, about 70 % of the total ferrocenyl units in **12** and related polymers are electrochemically oxidized during a potential-step process [32].

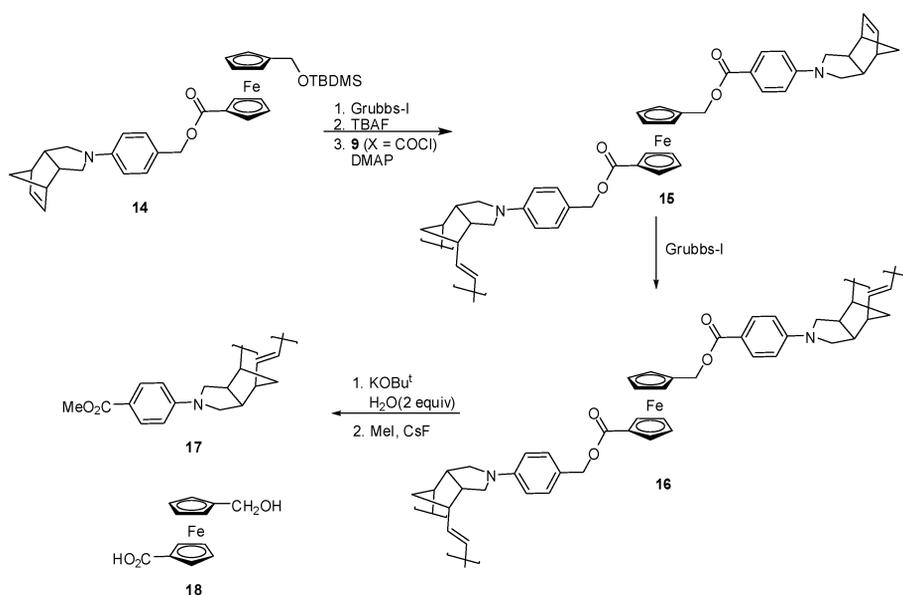
## REPLICATIONS

One of the most important features of a DNA molecule is the ability to replicate. Many approaches to simulate the biological processes by replicating a host molecule into its complementary are known in the literature [33–38]. Most of these approaches use oligonucleotides, peptides, or small molecules as the templates for replications. Our strategy is based on the successful synthesis of double-stranded polymer **12** from the corresponding bisnorbornene monomer **11** (Fig. 8). The details of the synthetic pathway are outlined in Scheme 2 [7].



**Fig. 8** Strategy for replication [7].

ROMP of **14** with Grubbs-I catalyst followed by the removal of the silyl protective group and repetitive esterification with **9** ( $R = \text{COCl}$ ) affords **15**. Under high dilution conditions, metathesis of **12** with Grubbs-I catalyst gave efficiently the corresponding unsymmetrical double-stranded polymer **16**. Interestingly, STM shows that **16** has only ladder-like structures and the average length is  $10.5 \pm 2.7$  nm.



Scheme 2

The relationship between the structure of the double-stranded polymer and the solid-state morphology, however, remains unclear at this stage. Polymer **16** was hydrolyzed under “anhydrous hydroxide” conditions [39] followed by esterification [40] yields **17**. Polymer **17** has the same number of repetitive units as those of **15** and **16**. These results have demonstrated an unprecedented example on the replication of a single-stranded polynorbornene, leading to its complementary polynorbornene derivative. Apparently, a bisnorbornene connected by an appropriate linker has provided a unique entry for the synthesis of a double-stranded DNA-like polymer. The present replication study adds another novel DNA-like feature of polybisnorbornenes.

## CONCLUSIONS

This account summarizes our recent results on the synthesis of the first helical double-stranded polymer by ROMP of a bisnorbornene derivative and the replication of a single-stranded polynorbornene leading to its complementary polynorbornene derivative. Grubbs-I catalyst appears to be unique in these polymerizations with high stereoselectivity. The polymers thus obtained have a structural resemblance to that of a DNA molecule by having similar width, number of monomeric units per pitch, five-membered rings in the polymeric frame, perpendicular linkers to the backbones, and similar spacing between neighboring monomeric units. This approach may provide a versatile entry for the design, synthesis, and physicochemical investigations of new types of polymers for simulation of biological systems as well as materials applications.

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