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Protonated Amino Acid-Induced One-Handed Helicity of Polynorbornene Having Monoaza-18-crown-6 Pendants

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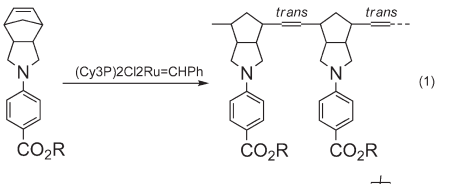
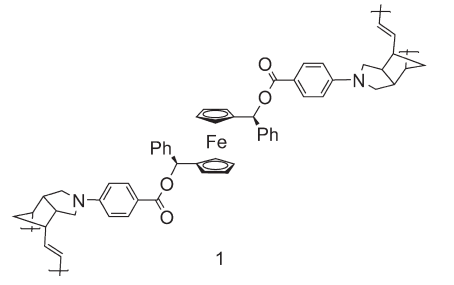
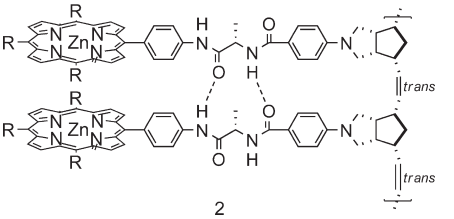
ABSTRACT: Upon complexation with protonated amino acids, one-handed helical polynorbornenes appended with monoaza-18-crown-6 (**7a**) are obtained. The cooperativity is observed as revealed by the sergeant−soldier effect and the majority rule. When sterically hindered amino acids such as phenylalanine, isovaline or proline, esters of amino acids, and aminoalcohols are used, the $\Delta\varepsilon$ values in CD spectra are significantly reduced. The protonated ammonium ion may form complex with a crown ether moiety whereas the carboxylic acid may form hydrogen bonding with the adjacent crown ether pendant resulting in unidirectional orientation of the pendants leading to a helical scaffold. The corresponding dimer **10** with the same isotactic stereochemistry as that of polynorbornene **7a** behaves similarly to exhibit bisignate CD curve upon treatment with protonated alanine. On the other hand, polynorbornene with monoaza-15-crown-5 (**7b**) does not exhibit any CD response under the same conditions.

Introduction

Polynorbornenes obtained by metal-catalyzed ring-opening metathesis polymerization (ROMP)[1] of the corresponding norbornene derivatives having different kinds of pending groups have been demonstrated to be useful for catalysis,[2] light harvesting and photoinduced electron transfer,[3] ion conductivity,[4] and optoelectronic applications.[5−9] We recently established that ROMPs of nobornenes having 5,6-endofused *N*-arylpyrrolidine catalyzed by the first generation Grubbs catalyst give isotactic single stranded polynorbornenes with all double bonds in trans configuration and all pendants aligned coherently toward the same direction (eq 1).[10,11] Presumably, $\pi-\pi$ interactions between these pending aryl groups might take place during the course of the polymerization and would be responsible for the stereoselectivity.[12] This protocol has been successfully used for the synthesis of relatively rigid polynorbornene-based double stranded polymeric ladderphanes[13] and for the replication of a single stranded polynorbornene into the corresponding complementary polynorbornene.[14] Amalgamation of chiral auxiliaries into the polymer through hydrogen bonding has offered a powerful platform for the one-handed helical polymers.[15−18] Incorporation of chiral linkers is known to afford one-handed helical double stranded ladderphane **1**.[13b] Alternatively, the use of bisamidic chiral alanine linkers between the pending porphyrins and the polynorbornene backbone has been shown to induce one-handed helical structures for these polymers **2** owing to hydrogen bonding between the adjacent linkers.[18] Both polymers **1** and **2** exhibit characteristic exciton coupling between adjacent aminobenzoate pendants as revealed by the circular dichroitic (CD) profiles.[13b,18] A stereoregular poly(phenylacetylene) bearing the azacrown ether pendants forms a one-handed helix upon complexation with protonated amino acids as revealed by the enhanced CD attributed by the significant cooperative interactions in the polymer backbone.[15,16] These studies has not only addressed the formation of one-handed helical polymers through complexation, but also provided useful information on the stereoregularity of the polymers.[15−17] We now wish to report the first one-handed single stranded helical polynorbornene having crown ethers as pendants.







Results and Discussion

Synthesis. Monoaza-18-crown-6 appended norbornene monomer **3a** was obtained in 40% yield from the reaction

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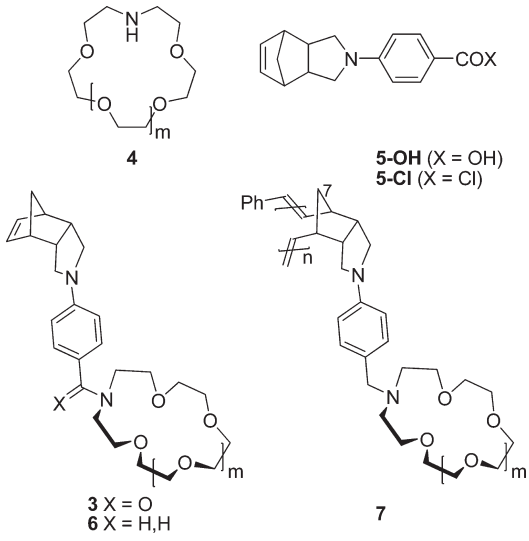
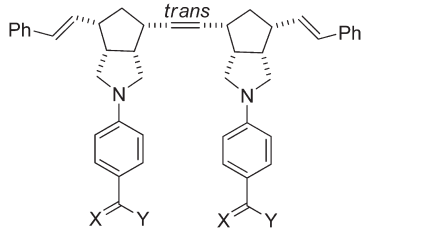
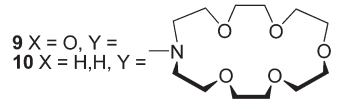
of **4a** with acid chloride **5-Cl**. Treatment of **3a** with excess $LiAlH_4$ gave the corresponding amine **6a** in 61% yield. ROMP of **6a** with 3 mol % of $(Cy_3P)_2Cl_2Ru=CHPh$ followed by quenching with $EtOCH=CH_2$ afforded the corresponding polymer **7a** in 90% yield (M_n = 14 700, PDI = 1.18). The ^{13}C NMR spectrum of **7a** showed two peaks of equal intensity at δ 36.1 and 36.3 ppm attributed to C_7,[19] which is characteristic for isotactic polynorbornene with endofused *N*-arylpyrrolidine pendants having all double bonds in trans configuration.[11b] In a similar manner, **7b** was obtained in overall 32% yield from **4b**, and the details are described in the Experimental Section.







In order to scrutinize the helicity of the complex of **7** with different protonated amino acids, dimer **10** was synthesized from **8**[18] in 48% overall yield and the details are described in the Experimental Section.

Reactions of 7a with Protonated Amino Acids. An equal volume (10 mL) of **7a** (4.1 mM based on the molecular weight of **6a**) in CH_2Cl_2 and an aqueous solution of $HClO_4$ (0.1 M) containing 82 mM of amino acid was stirred at room temperature for 18 h. The organic phase was separated and subjected to CD measurements. The absorption spectra of **6a** and **7a** are shown in Figure 1a. Like all polynorbornenes with *N*-arylpyrrolidine pendants,[11] the λ_{max} for **7a** appeared at slightly shorter wavelength than that of the corresponding monomer **6a**. The CD curves for the alanine−**7a** complexes are shown in Figure 1b and those of the complexes with other amino acids, amino esters and aminoalcohols and chiral amines are shown in the Supporting Information. The second Cotton wavelengths and the corresponding $\Delta\varepsilon$ values of these complexes are summarized in Table 1. A positive Cotton effect was observed with protonated L-amino acids and vice versa, and the wavelength region was consistent with the absorption maximum of the 4-aminobenzyl chromophore. In addition, the CD curves were reversibly temperature dependent (Figure 1c), the intensities decreasing with increasing temperature. It is noteworthy that a mixture monomer **6a** and protonated L-alanine prepared under the same conditions was CD inactive.

As shown in Figure 1 and Table 1, mirror image CD curves were obtained for a pair of enantiomeric protonated alanines. The $\Delta\varepsilon$ values were comparable but had opposite sign. It is interesting to note that neutral (entries 1−4), basic (entries 5 and 6), acidic (entries 7 and 8), and hydroxyl-substituted (entry 9) amino acids gave similar $\Delta\varepsilon$ values.

Crown ethers are known to form one to one complexes with protonated amines.[20] The stoichiometry of the complex formed from **7a** and D-alanine−$HClO_4$ in CF_3CH_2OH was examined.[21] A plot of $\Delta\varepsilon$ values against the molar ratio of D-alanine−$HClO_4$ versus total crown ether in **7a** is shown in Figure 2 and the details are shown in Figure S2 in the Supporting Information. The $\Delta\varepsilon$ values reached a plateau when the molar ratio of alanine and crown ether reached 1. A similar plot using D-valine−$HClO_4$ is also shown in Figure 2. These results indicate that each of the crown ether moieties in **7a** would form one to one complex with the ammonium ion. It is noteworthy that the $\Delta\varepsilon$ values for the complexes formed from protonated D-alanine and D-valine and **7a** under these conditions were comparable to those obtained by the extraction procedure shown in Table 1. In addition, when CD_2Cl_2 was employed as the solvent for the extraction of protonated D-alanine, the organic solution was analyzed by ^1H NMR (Figure S21). The ratio of the methyl protons of D-alanine to those of aminobenzyl moieties in **7a** suggests that a one to one complex between **7a** and protonated alanine was formed. Furthermore, certain protons of the crown ether moieties in this complex shifted to lower field, presumably due to complexation.

The presence of sterically bulky substituent(s) of the amino acids such as phenylalanine or isovaline (entries 10 and 11) somewhat reduced the $\Delta\varepsilon$ values. As mentioned above, the spacing occupied by each of the monomeric units would be around 0.5−0.6 nm.[11] Presumably, these amino acids may be more difficult to insert into the space between two adjacent crown ethers resulting in decrease in $\Delta\varepsilon$ values. Protonated proline also gave poor CD response (entry 12). Unlike other protonated amino acids, protonated proline has only two N−H bonds for hydrogen bonding to the crown ether moiety in **7a**. Complexation of protonated proline with **7a** would therefore be less selective, leading to small $\Delta\varepsilon$ value.

Hydrogen bonding to the adjacent crown ether module appeared to be essential to control the helicity of the polymer. Amino alcohols behaved similarly, albeit the $\Delta\varepsilon$ intensities were about 50% of those for the corresponding amino acids (entries 13 and 14). The $\Delta\varepsilon$ values were significantly reduced when the methyl esters of the amino acids were used (entries 15−18).

Chiral alkyl amines **11** and **12** gave very low CD responses (entries 19 and 20). These results suggest that the presence of the other protic substituents would be essential to direct the orientation of the adjacent crown ether pendants leading to one handed helicity.

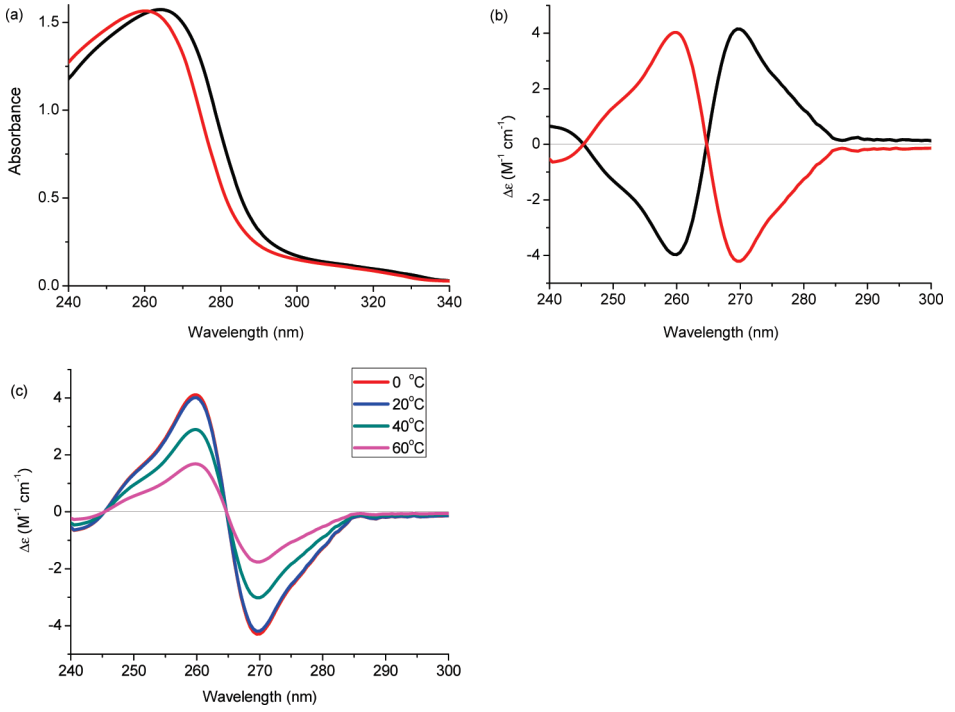
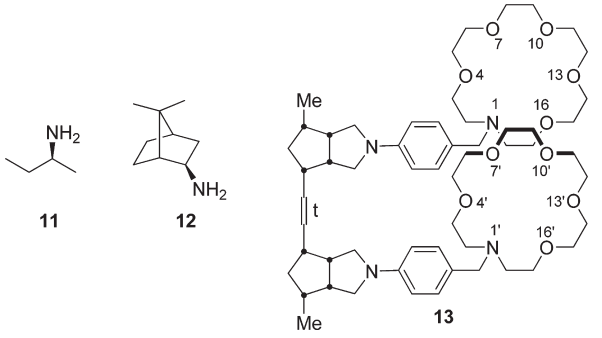


Figure 1. (a) Absorption spectra of monomer **6a** (black) and polymer **7a** (red) in CH_2Cl_2. (b) CD curves of complexes of L-alanine−$HClO_4$ (black) and D-alanine−$HClO_4$ (red) with **7a** in CH_2Cl_2. (c) Reversible temperature dependent CD profiles of D-alanine−$HClO_4$ with **7a** in CH_2Cl_2. All spectra were measured at the [**7a**] = 2 mg/mL equivalent to 4.1 μmol of monomer units per milliliter.



The similar shape of the CD profiles indicates that the nature of binding of the protonated amino acids and the **7a** may be similar. The helicity of the complexes between **7a** and protonated amino acids can be understood within the framework of exciton chirality method.[22] In other words, exciton coupling between pending aminobenzyl moieties would reflect the helicity of the complexes. The exciton couplet amplitudes among these complexes would be related to the interchromophore distance as well as the dihedral angle of the interacting moments.[22] As meniontedearlier, all pending groups in **7a** would align coherently toward the similar direction, and the spacing occupied by each of the monomeric units in polynorbornenes would be about 0.5−0.6 nm.[10,11] The dihedral angle of the interacting chromophores would likely offer a platform to dictate the intensity of the couplet. The uniformity of the orientation of these interacting chromohores in these complexes would determine the amplitude of the CD curves.

Majority Rule and Sergeant−Soldier Effect. In order to establish the cooperative effect toward helicity, the $\Delta\varepsilon_{second}$ values using different enantionmeric mixtures of L-valine and of D-alanine were measured and the results are shown in Figure 3 and details are shown in Figure S3. The nonlinear relationship suggests that the helicity of these complexes follows the majority rule[23,24] and there is cooperative effect in the complex formation of **7a** with protonated amino acids.

Table 1. Signs and Differences of the Second Cotton ($\Delta\varepsilon_{2nd}$) for the Complexes of 7a with Protonated Amino Acids, Amino Esters, Amino Alcohols, and Chiral Amines in CH_2Cl_2

entry	protonated amine	$\Delta\varepsilon_{second}$ (M^{-1} cm^{-1})/λ(nm)
1	L-Ala	−3.97/260
2	D-Ala	+4.02/260
3	L-Val	−4.87/260
4	D-Val	+4.73/260
5	L-Lys	−3.57/260
6	D-Lys	+3.51/260
7	L-Asp	−4.35/260
8	D-Asp	+4.37/260
9	L-Ser	−4.09/260
10	L-Phe	−2.80/260
11	L-isoval	−0.90/260
12	L-Pro	−0.30/260
13	L-valinol	−2.13/260
14	L-alaninol	−2.03/260
15	L-Ala-OMe	−1.38/261
16	D-Ala-OMe	+1.42/261
17	L-Val-OMe	−1.49/261
18	D-Val-OMe	+1.48/261
19	**11**	−0.35/260
20	**12**	+0.50/259

In a similar manner, a plot of the $\Delta\varepsilon_{second}$ values of the complexed **7a** against the molar ratio of protonated D-alanine in a mixture of D-alanine and glycine is shown in Figure 4. Again, the nonlinear relationship because of the sergeant−soldier effect[23,24] further supports the cooperative effect in the complex formation between **7a** and protonated amino acids.

Reaction of 10 with Protonated Alanines. Treatment of **10** in CH_2Cl_2 with L- and D-alanine in perchloric acid under the same conditions as described above gave the corresponding organic solution which was subjected to CD analysis and the results are shown in Figure 5. It is worthy noting that the

profiles exhibited same Cotton effect as those of the complexes of **7a** with alanines (cf. Figure 1) but with lower intensities.[25] The exciton coupling due to the adjacent aminobenzyl pendants would be responsible for the CD properties for both **7a** and **10**. These results offer convincing evidence to show that the helicity would be arisen from the complexation of protonated amino acid with the crown ether pendants in **7a** and **10**.

DFT Calculations of 14. In general, the $-NH_3^+$ moiety may form symmetrically hydrogen bonding with three alternating oxygen atoms of the 18-crown-6.[26] The relative hydrogen-bond acceptor abilities of amino nitrogen and ethereal oxygen depend not only on the basicity of the heteroatoms, but also on the relative orientation of the nonbonding orbital.[27] The crystal structures indicate that the substituent on nitrogen in monoaza-18-crown-6 ethers in general locates at the axial position.[28] The lone pair electrons on nitrogen of the crown ether moiety would likely orient along the equatorial position toward the center of the crown ether ring. In this regard, it seems likely that the $-NH_3^+$ moiety may preferentially form hydrogen bonding with O_4, O_{10} and O_{16} in a N-substituted monoaza 18-crown-6. On the basis of this assumption, density function theory (DFT) calculations were carried out to examine the possible conformations of **14** obtained from **13** and two equivalents of protonated L-alanine.[29]

As shown in Figure 6, the $-NH_3^+$ moiety would form hydrogen bonding with O_4, O_{10}, and O_{16} of one crown ether pendant and the carboxylic acid group would hydrogen-bond to either O_7' (**14a**) or O_{13}' (**14b**) of the adjacent crown ether pendant. It is noteworthy that these two oxygen atoms (O_7' and O_{13}') would be diastereotopic. The total energy difference between these two distereomers was 16.7 kcal/mol in favor of **14a**. The center to center distance between two crown ethers in **14a** was around 7.3 Å. The projected torsional angle of the two pendants defined by two lines from the center of the cyclopentane ring and the center of the crown ethers in **14a** was about 27° with a right handed rotation which is consistent with the experimental observation described above based on exciton chirality method.[22] Apparently, the configuration at the chiral center of the amino acid would direct the orientation of the carboxylic

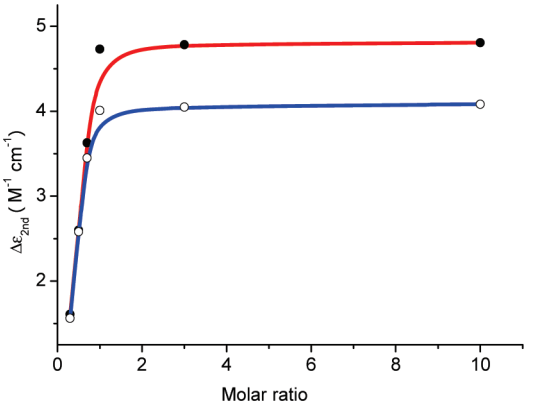


Figure 2. Plot of $\Delta\varepsilon_{second}$ values against the molar ratio of D-alanine–$HClO_4$ (open circle and solid line) and D-valine (solid circle and dotted line) versus momomeric crown ether unit in in **7a**. [**7a**] = 2 mg/mL in CF_3CH_2OH.

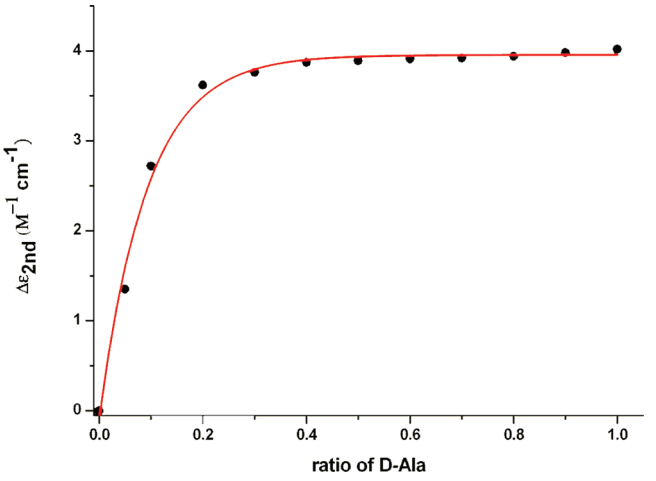


Figure 4. Changes in ICD intensity ($\Delta\varepsilon_{second}$) of **7a** against the molar ratio of D-alanine in a mixture of D-alanine and glycine.

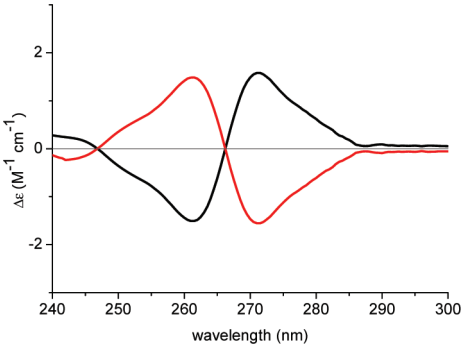


Figure 5. CD curves of complexes of L-alanine-$HClO_4$ (black) and D-alanine-$HClO_4$ (red) with **10** in CH_2Cl_2. [**10**] = 2.36 (4.1 μmol monomer units) mg/mL.

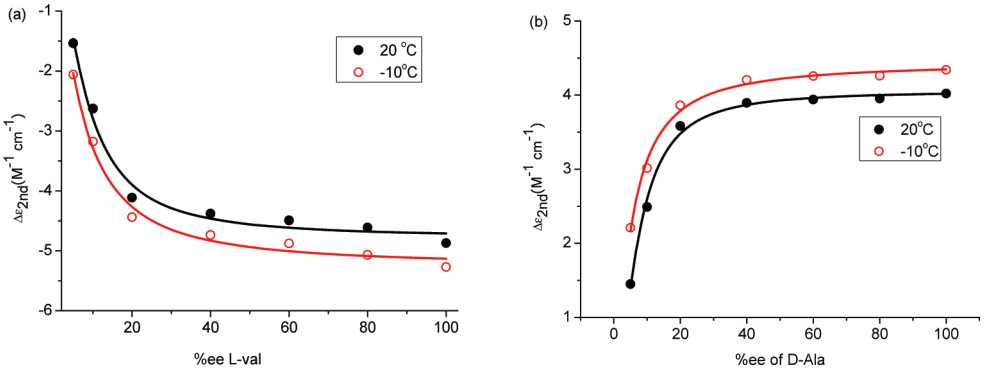


Figure 3. Changes in ICD intensity ($\Delta\varepsilon_{second}$) of **7a** against enantiomeric excess (%) of L-Val (a) and D-Ala (b) during the complexation with **7a** at 20 (black) and −10 °C (red) respectively. [**7a**] = 2 mg/mL in CH_2Cl_2.

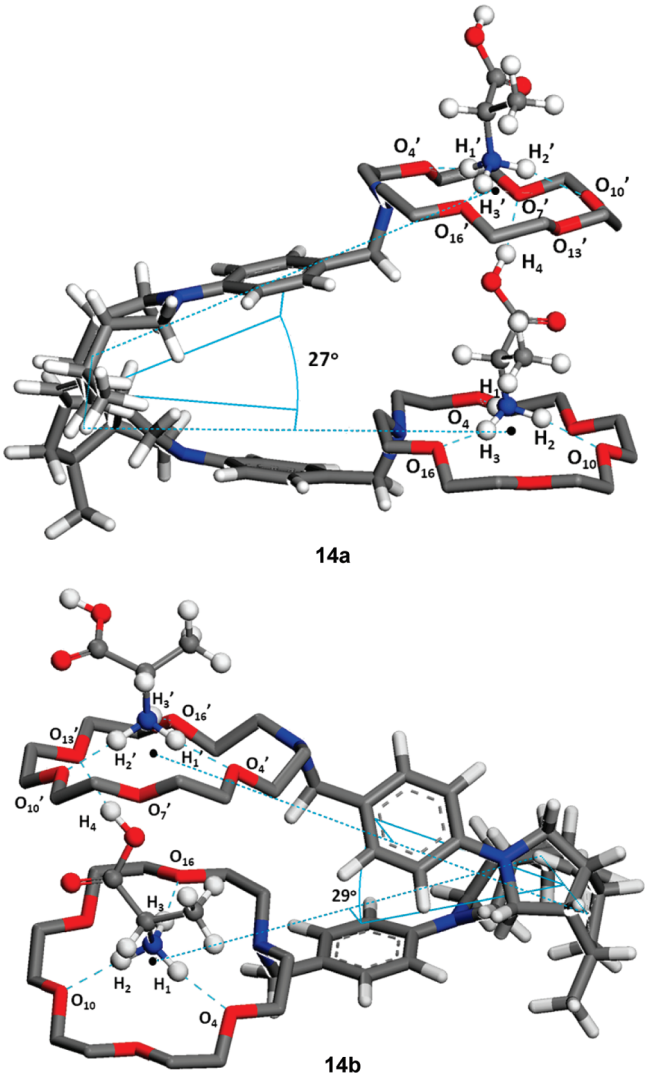


Figure 6. DFT calculations of **14a** (right handed) and **14b** (left handed). Seleced distances for **14a**: H_1O_4, 1.86 Å; H_2O_{10}, 2.00 Å; H_3O_{16}, 2.01 Å; H_4O_7', 1.79 Å; $H_1'O_4'$, 1.89 Å; $H_2'O_{10}'$, 2.02 Å; $H_3'O_{16}'$, 2.00 Å; **14b**: H_1O_4, 2.02 Å; H_2O_{10}, 1.94 Å; H_3O_{16}, 1.99 Å; H_4O_{13}', 1.82 Å; $H_1'O_4'$, 1.99 Å; $H_2'O_{10}'$, 1.82 Å; $H_3'O_{16}'$, 1.83 Å.

acid groups so that the pending groups in **7a** may oriented uniformly leading to a helical scaffold.

Reaction of 7b with with Protonated L-Alanine. In order to establish the importance of the diastereoselective formation of hydrogen bonding predicted by DFT calculations, polymer **7b** having monoaza-15-crown-5 ether pendants was synthesized. Interestingly, no CD response was observed when **7b** was treated with protonated L-alanine under the same conditions as described above. These results are different from those of poly(phenyleneacetylene)derivative bearing same monoaza-15-crown-5 ether pendants.[16d] The ^{1}H NMR experiment using CD_2Cl_2 as the extracting solvent indicates that only less than 25% of protonated D-alanine was extracted from the aqueous layer into the organic phase (Figure S21). This organic solution again showed no CD response (Figure S22).

Unlike 18-crown-6 ethers, the crown ether pendant in **7b** has only five heteroatoms (four O's and 1 N) available for hydrogen bonding. It is worthy noting that the complex between a chiral *N*-benzylmonoaza-15-crown-5 and the $-NH_3^+$ moiety is held together by hydrogen bonds between the two protons of the ammonium ion and nitrogen and three oxygen atoms of the crown ether as revealed by the crystal structure.[30] The complex formation might therefore be unselective because no diastereotopic oxygen atoms would be present for hydrogen bonding with the carboxylic acid end of the complexed amino acid.

Conclusion

In summary, we have addressed for the first time one-handed helicity of single stranded polynorbornenes appended with monoaza-18-crown-6 **7a** and the corresponding isotactic dimer **10** induced by protonated amino acids. The protonated ammonium ion may form complex with a monoaza-18-crown-6 whereas the carboxylic acid may form hydrogen bonding with the adjacent crown ether resulting in unidirectional orientation of the pendants leading to a helical scaffold. A homogeneous stereochemistry (double bonds and tacticity) of **7a** would be crucial for the helical formation. It is striking to note that polynorbornene with monoaza-15-crown-5 **7b** does not exhibit any CD response under the same conditions. The uniqueness of monoaza-18-crown-6 pendants in **7a** and **10** appeared to be consistent with the model based on DFT calculations.

Expermental Section

General Data. Gel permeation chromatography (GPC) was performed on a Waters GPC machine using an isocratic HPLC pump (1515) and a refractive index detector (2414). THF was used as the eluent (flow rate = 1.0 mL/min). Melting points were measured on a SPSIC WRS-2A melting point apparatus and were uncorrected. CD spectra were taken at 20 °C unless otherwise specified on a JASCO J-810 spectropolarimeter in a 3 mL cell. Absorption spectra were measured with a Hitachi U-331 spectrophotometer.

Monomer 3a. To a mixture of **4a**[31] (0.80 g, 3.0 mmol) and Na_2CO_3 (2.12 g, 20.0 mmol) in CH_2Cl_2 (30 mL) was added the freshly prepared **5-Cl** (1.22 g, 4.5 mmol) in CH_2Cl_2 (30 mL) at 0 °C. The mixture was gradually warmed to room temperature and stirred for 17 h. After filtration, the solvent was removed in vacuo and the residue was chromatographed on silica gel (CH_2Cl_2/MeOH = 19:1) to give **3a** (0.60 g, 40%) as a solid: mp 165−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (d, J = 8.4 Hz, 1 H; H_7 on norbornene), 1.61 (d, J = 8.4 Hz, 1 H; $H_{7'}$ on norbornene), 2.89−2.97 (m, 4 H), 3.07−3.11 (m, 2 H), 3.21−3.27 (m, 2 H), 3.62−3.77 (m, 24 H; H on crown ether), 6.16 (s, 2 H; olefinic-H), 6.38 (d, J = 8.4 Hz, 2 H; Ar H), 7.29 (d, J = 8.4 Hz, 2 H; Ar H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.3, 46.4, 50.3, 51.9, 53.3, 69.7, 70.3, 70.5, 70.6, 110.9, 122.6, 128.5, 135.6, 148.1, 172.7; MS (ESI, m/z) 501 (M^+ + H). Anal. Calcd: C, 67.18; H, 8.05; N, 5.60. Found: C, 67.09; H, 8.05; N, 5.58.

Monomer 6a. Under argon atmosphere, a solution of **3a** (0.5 g, 1.0 mmol) in CH_2Cl_2 (8 mL) was added dropwise to $LiAlH_4$ (152 mg, 4.0 mmol) in ether (4 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred for an additional 18 h, quenched with H_2O (1 mL) and filtered. The organic layer was dried ($MgSO_4$) and evaporated in vacuo to give the residue which was chromatographed on silica gel (CH_2Cl_2/MeOH = 15:1) to give **6a** (296 mg, 61%) as a white solid: mp 152−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, J = 10.8 Hz, 1 H), 1.57 (d, J = 10.8 Hz, 1 H), 2.75 (br, 4 H), 2.83−2.86 (m, 2 H), 2.92 (br, 2 H), 3.01 (br, 2 H), 3.15−3.17 (m, 2 H), 3.54−3.65 (m, 22 H), 6.12 (s, 2 H), 6.36 (d, J = 8.4 Hz, 2 H), 7.10 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.2, 46.2, 50.3, 50.4, 51.9, 59.3, 69.7, 70.1, 70.51, 70.59, 111.3, 125.4, 129.6, 135.5, 146.5; LRMS (ESI, m/z) 487 ([M + H]$^+$). Anal. Calcd: C, 69.11; H, 8.70; N, 5.76. Found: C, 69.12; H, 8.68; N, 5.76.

Polymer 7a. Under argon atmosphere, a solution of $(Cy_3P)_2Cl_2Ru{=}CHPh$ (190 mg, 0.24 mmol) in CH_2Cl_2 (30 mL) was added to **6a** (3.5 g, 0.72 mmol) in CH_2Cl_2 (15 mL). The mixture was stirred at room temperature for 80 min, quenched with ethyl vinyl ether (5 mL) and poured into Et_2O (25 mL). The solid was collected and washed with EtOAc and Et_2O to afford **7a** as a tan solid (2.7 g, 90%): M_n = 14700; M_w = 17300; PDI = 1.18; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (br, 1 H), 1.47 (br, 1 H), 2.75−2.89 (br, 8 H), 3.14 (br, 4 H), 3.62−3.67 (m, 22 H), 5.48 (br, 2 H), 6.57 (br, 2 H), 7.17 (br, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.0, 36.3, 45.0, 45.2, 46.3, 46.5, 50.3, 53.3, 59.3, 69.7, 70.1, 70.5, 70.6, 112.7, 126.4, 128.2, 129.6, 131.3, 131.5, 147.3, 147.4; IR (KBr) ν = 3060, 2928, 2853, 1612, 1518, 1480, 1450, 1366, 1357, 1331, 1115, 967, 951, 818, 735, 720, 527 cm^{-1}.

Monomer 3b. To a mixture of **4b**[32] (1.0 g, 4.5 mmol), NEt_3 (1 mL, d = 0.728, 1.4 mmol) and a catalytic amount of DMAP in CH_2Cl_2 (15 mL) was added **5-Cl** [freshly prepared from **5-OH** (1.28 g, 5.0 mmol) and oxalyl chloride (1 mL, d = 1.478, 11.7 mmol) in CH_2Cl_2 (10 mL)] at 0 °C. The mixture was gradually warmed to room temperature and stirred for 24 h, poured into water and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$), filtered, and the filtrate was evaporated in vacuo to give the residue which was chromatographed on silical gel (CH_2Cl_2/EtOAc = 1/2) to give **3b** as a yellow liquid (1.5 g, 71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (d, J = 8.4 Hz, 1 H), 1.61 (d, J = 8.4 Hz, 1 H), 2.88−2.90 (m, 2 H), 2.91−2.92 (m, 2 H), 3.00−3.08 (m, 2 H), 3.20−3.26 (m, 2 H), 3.61−3.68 (m, 18), 3.76 (t, J = 6.0 Hz, 4 H), 6.15 (s, 2 H), 6.36 (d, J = 8.2 Hz, 2 H) 7.29 (d, J = 8.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.5, 46.6, 50.5, 52.1, 69.9, 70.27, 70.29, 71.1, 110.9, 122.6, 128.5, 135.6, 148.1, 172.6; IR (KBr) ν 3053, 2914, 2850, 1608, 1523, 1460, 1411, 1316, 1293, 1252, 1194, 1125, 982, 933, 823, 764, 729 cm^{-1}. HRMS (FAB) m/z: calcd for $C_{26}H_{36}N_2O_5$, 456.2624; found, 456.2626.

Polymer 7b. Under nitrogen, a solution of **3b** (200 mg, 0.44 mmol) and $(Cy_3P)_2Cl_2Ru{=}CHPh$ (16 mg, 0.05 equiv) in dried CH_2Cl_2 (5 mL) was stirred at room temperature for 1 h. The mixture was quenched with ethyl vinyl ether (1 mL) and then poured into pentane (20 mL). The solid was collected and redissolved in CH_2Cl_2 and precipitated again with pentane. This procedure was repeated twice to afford the polymer as a grayish solid. (150 mg, 75%) M_n = 6800, M_w = 8100, PDI = 1.18; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38−1.54 (br, 1 H), 1.78−1.90 (br, 1 H), 2.60−2.80 (br, 2 H), 2.80−3.00 (br, 2 H), 3.00−3.40 (br, 4 H) 3.50−4.00 (br, 20 H), 5.30−5.40 (br, 2 H), 6.30−6.60 (br, 2 H), 7.10−7.30 (br, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.4, 36.7, 44.9, 45.1, 46.5, 46.9, 49.8, 67.9, 69.7, 70.2, 71.0, 111.8, 123.6, 125.9, 128.5, 131.6, 131.9, 148.8, 172.5.

To a slurry of $LiAlH_4$ (33 mg, 0.88 mmol) in Et_2O (10 mL) was added slowly the above polymer (100 mg, 0.22 mmol) in CH_2Cl_2 (5 mL), and the mixture was stirred at room temperature for 2 h. The reaction was quenched by water (1 mL) and the resulting suspension was filtered, and the organic layer was evaporated in vacuo to give the residue which was dissolved in CH_2Cl_2. The organic solution was dried ($MgSO_4$) and filtered, and the residue poured into pentane (20 mL). The solid was collected to afford **7b** as grayish solid. (36 mg, 36%) M_n = 6100, M_w = 6700, PDI = 1.10; IR (KBr) ν 2954, 2917, 2850, 1597, 1522, 1459, 1377, 1252, 1169, 1122, 1024, 948, 850, 805 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40−1.60 (br, 1 H), 1.70−1.90 (br, 1 H) 2.60- 3.00 (br, 8 H), 3.05−3.30 (br, 4 H) 3.50−3.80 (br, 18 H), 5.40−5.60 (br, 2 H), 6.50−6.70 (br, 2 H), 7.05−7.20 (br, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 46.3, 46.6, 47.2, 50.3, 53.6, 60.0, 69.5, 70.1, 70.3, 70.8, 112.8, 125.8, 128.3, 129.9, 131.3, 147.6.

Dimer 9. To a solution of **6**[17] (230 mg, 0.32 mmol) in THF (20 mL) and MeOH (5 mL) at 0 °C was added NaOH (55 mg, 1.37 mmol). The mixture was heated at reflux for 10 h and cooled to room temperature. After most of the solvent was removed, Et_2O (20 mL) and H_2O (30 mL) was added, and the aqueous layer was separated, and then acidified with 10% HCl (until pH = 6). The solid was filtered to give the diacid as a white solid, which was used for the next reaction without further purification.

To a solution of the diacid (100 mg, 0.15 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added oxalyl chloride (0.2 mL, 2.3 mmol) and DMF (one drop). The mixture was gradually warmed to room temperature and stirred for 1 h. The solvent was removed in vacuo to give crude acid chloride, which was taken up in CH_2Cl_2 (6 mL) and added to a cooled (0 °C) solution of **4a** (76 mg, 0.29 mmol), NEt_3 (0.5 mL) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 17 h. Saturated $NaHCO_3$ was added and the organic layer was washed with water, brine and then dried ($MgSO_4$). The solvent was removed in vacuo, and the residue was chromatographed on silica gel (CH_2Cl_2/MeOH/NEt_3 = 19:1:0.05) to give **9** as an oil (102 mg, 59%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59−1.65 (m, 2 H), 1.90−1.95 (m, 2 H), 2.81−2.83 (m, 2 H), 2.89−3.05 (m, 6 H), 3.17−3.29 (m, 8 H), 3.61−3.70 (m, 48 H), 5.47−5.50 (m, 2 H), 6.18 (dd, J = 7.2, 15.8 Hz, 1 H), 6.21 (dd, J = 7.2, 15.8 Hz, 1 H), 6.41 (d, J = 15.8 Hz, 1 H), 6.42 (d, J = 15.8 Hz, 1 H), 6.53 (d, J = 8.4 Hz, 2 H), 6.55 (d, J = 8.4 Hz, 2 H), 7.18−7.33 (m, 14 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.16, 36.24, 44.9, 45.1, 45.3, 45.4, 46.4, 46.67, 46.73, 49.84, 49.87, 50.0, 53.4, 69.7, 70.4, 70.6, 70.7, 111.94, 111.97, 125.8, 126.9, 128.31, 128.33, 128.5 130.4, 130.7, 131.6, 131.7, 137.1, 148.74, 148.77, 172.37, 172.39; IR (KBr) ν 3024, 2914, 2859, 1736, 1607, 1522, 1455, 1413, 1367, 1290, 1193, 1117, 965, 825 cm^{-1}. HRMS (FAB) m/z: calcd for $C_{70}H_{92}N_4O_{12}$ (M^+ + H), 1180.6716; found, 1180.6726.

Dimer 10. To a slurry of $LiAlH_4$ (30 mg, 0.79 mmol) in Et_2O (5 mL) was added slowly **9** (100 mg, 0.088 mmol) in CH_2Cl_2 (5 mL), and the mixture was stirred at room temperature for 1 h. EtOAc was carefully added, water (0.5 mL) was then introduced. The resulting suspension was filtered, and the organic layer was evaporated in vacuo to give a residue, which was triturated with CH_2Cl_2 repeatedly. The CH_2Cl_2 solution was dried ($MgSO_4$) and filtered. The solvent was removed in vacuo to give **10** as a oil (81 mg, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61−1.65 (m, 2 H), 1.85−1.90 (m, 2 H), 2.74−2.77 (m, 10 H), 2.86−3.02 (m, 6 H), 3.56−3.68 (m, 40 H), 5.54 (m, 2 H), 6.24 (dd, J = 7.6, 15.6 Hz, 1 H), 6.26 (dd, J = 7.6, 15.6 Hz, 1 H), 6.41 (d, J = 15.6 Hz, 1 H), 6.43 (d, J = 15.6 Hz, 1 H), 6.56 (d, J = 8.4 Hz, 2 H), 6.59 (d, J = 8.4 Hz, 2 H), 7.11−7.36 (m, 14 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.38, 36.46, 45.5, 45.7, 45.90, 45.96, 46.8, 46.9, 47.01, 47.05, 50.82, 50.87, 50.91, 50.96, 59.8, 70.2, 70.6, 71.01, 71.03, 71.11, 113.33, 113.34, 126.2, 127.2, 128.7, 130.05, 130.08, 130.6. 131.3, 131.76, 131.9, 137.65, 137.67, 147.86, 147.90; IR (KBr) ν 3024, 2918, 1613, 1518, 1479, 1354, 1280, 1197, 1107, 952, 821 cm^{-1}. HRMS (FAB) m/z: calcd for $C_{70}H_{96}N_4O_{10}$, (M^+ + H), 1152.7167; found, 1152.7158.

Preparation of L-Ala Solution and Helicity Induction of Polymer 7a. A stock solution of **7a** in CH_2Cl_2 (2 mg/mL (4.1 mM, 10 mL) and a stock solution of L-Ala (7.3 mg/mL, 82 mM, 10 mL) in aqueous $HClO_4$ (0.1 M) were prepared. To a flask was added an equal volume (10 mL) of the above two solutions and the resulting mixture was thoroughly stirred for 18 h, then allowed to stand for 8 h and the organic phase was separated for the CD measurement (Figures 1 and S1 (Supporting Information)).

CD Titration Experiment. Stock solutions of **7a** (4 mg/mL, 20 mL) in CF_3CH_2OH and D-alanine-$HClO_4$ in CF_3CH_2OH (19.4 mg/mL, 5 mL) were prepared. To a flask a stock solution of **7a** (1 mL) were added different volumes of the solution of D-alanine−$HClO_4$ and the resulting solutions were diluted with CF_3CH_2OH to keep the concentration of **7a** at 2 mg/mL. The CD spectra are shown in Figure S-2 (Supporting Information). The Hill plot analysis[33] of the data gave the binding constant of 6.6×10^2 M^{-1} with D-alanine. In a similar manner, a stock solution of D-valine was employed for a similar measurements and CD spectra were recorded. The binding constant with D-valine was 6.4×10^2 M^{-1} (see Figure S3 (Supporting Information) for the Hill plot analysis).

^{1}H NMR Experiments for the Complex Formation between 7 and Protonated D-Alanine. A stock solution of **7a** in CD_2Cl_2 (2 mg/mL, 4.1 mM, 8 mL) and D-Ala (7.3 mg/mL (82 mM), 25 mL) in aqueous $HClO_4$ (0.1 M) were prepared. To a flask were mixed equal volumes of **7a** in CD_2Cl_2 (4 mL) and D-Ala solution (4 mL), and the mixture was thoroughly stirred for 15 h then stand for 8 h. The organic phase was separated for ^{1}H NMR measurement. A similar procedure was used for the complexation of **7b** with protonated D-Ala. The results are shown in Figure S21 (Supporting Information).

DFT Calculations. DFT calculations were based on the GGA/BLYP/DNP level and implemented with the DMol^3 program package.[34] The electronic configuration of molecular systems was described by a double-numerical plus polarization (DNP) basis set−comparable to the Gaussian 6-31G** basis sets.[34] The local exchange-correlation potential[35] was augmented in a self-consistent manner with Becke exchange[36] and Lee−Yang−Parr correlation[37] gradient corrections, giving a generalized gradient approximation (GGA/BLYP) for the evaluation of energies and geometries. Convergence criteria for geometry optimizations were based on the threshold values: 2×10^{-5} hartree, 0.004 hartree/Å, 0.005 Å, and 1×10^{-5} hartree for energy, force, displacement, and self-consistent field (SCF) density, respectively. In order to obtain precise results, neither direct inversion of iterative subspace (DIIS) to accelerate convergence of the SCF algorithm nor smearing techniques were used.

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Supporting Information Available: Figures showing ^{1}H and ^{13}C NMR spectra of all new compounds, the CD profiles of the complexes, and titration curves. This material is available free of charge via the Internet at http://pubs.acs.org.

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