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Notes

Serine-Based Helical Polyacetylenes. Effect of Hydroxyl Group on the Secondary Structure

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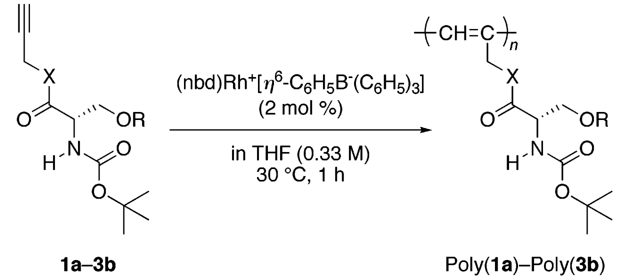
Hydroxyl group-containing polymers including poly(2-hydroxyethyl methacrylate) and poly(vinyl alcohol) are important as biomedical materials due to the high affinity and compatibility to living body. Peptides and proteins, naturally derived typical biopolymers, also carry hydroxyl groups at the serine moiety, in which hydroxyl groups largely affect the property and conformation.[1] This is due to the high polarity of hydroxyl group and formation of hydrogen bonding. We have recently reported that a serine-derived poly(*N*-propargylamide), poly(*N*-*tert*-butoxycarbonyl-L-serine *N*′-propargylamide) [poly(**1a**) in Scheme 1] forms a helical structure with predominantly one-handed screw sense.[2] It is considered that the pitch/diameter ratio[3] of poly(**1a**) helix is quite different from that of other amino acid-derived poly(*N*-propargylamides) without hydroxyl groups we have previously reported,[4] because they show completely different CD and UV−vis spectroscopic signal patterns. Since intramolecular hydrogen bonding between the amide groups in the side chains stabilizes the helical structure of poly(*N*-propargylamides),[5] they transform the structure from helix into random coil by the addition of MeOH, a solvent that disturbs hydrogen bonding. Unexpectedly, however, serine-based poly(**1**) can form a stable helical structure even in MeOH,[2] which is different from the poly(*N*-propargylamides) without hydroxyl groups. It seems that the hydroxyl groups bring about this unique behavior. In this note, we wish to report synthesis of a series of serine-based poly(*N*-propargylamides), poly(*N*-methyl-*N*-propargylamides), and poly(propargyl esters) carrying free and protected hydroxyl groups (Scheme 1) and elucidate the effect of hydroxyl groups on the secondary structure.

Table 1. Polymerization of 1a−3b[a]

monomer	yield[b] (%)	M_n[c]	M_w/M_n[c]	$[\alpha]_D$[d] (deg)
1a	91	9200	1.36	−455[e]
2a	99	6500	2.53	−109
3a	92	21000	1.73	−190
1b	83	9900	1.92	−188/+253[f]
2b	95	14100	1.87	+9.6
3b	92	21900	2.23	−9.7[f]

[a] Conditions: catalyst (nbd)$Rh^+[\eta^6\text{-}C_6H_5B^-(C_6H_5)_3]$, nbd = norbornadiene, $[M]_0/[Rh] = 50$, at 30 °C for 1 h under N_2. [b] Insoluble part in *n*-hexane. [c] Determined by GPC eluted with THF based on polystyrene standards. [d] Measured by polarimetry at room temperature, $c = 0.10$ g/dL in $CHCl_3$. [e] In MeOH. [f] In THF.

Scheme 1



1a: R = H, X = NH, **2a**: R = H, X = NCH_3, **3a**: R = H, X = O
1b: R = CH_3, X = NH, **2b**: R = CH_3, X = NCH_3, **3b**: R = CH_3, X = O

Table 1 summarizes the results of the polymerization of L-serine-derived *N*-propargylamide, *N*-methyl-*N*-propargylamide, and propargyl ester monomers **1a**−**3b** bearing free and methyl-etherated hydroxyl groups using (nbd)$Rh^+[\eta^6\text{-}C_6H_5B^-(C_6H_5)_3]$[6] as a catalyst in THF at 30 °C for 1 h. Polymers with M_n ranging from 6500 to 21 900 were obtained in good yields. The polymerization proceeded homogeneously throughout the reaction. As far as the yield and M_n of the polymers concern, we can say that the hydroxyl group of the monomers does not hamper the polymerization. The Rh zwitterion catalyst is highly tolerant to the hydroxyl group as well as amide and carbamate groups in acetylene polymerization.

The structures of the polymers were examined by IR and ^1H NMR spectroscopies.[7] The polymers exhibited absorption peaks and signals reasonably assignable to the polyacetylene structures illustrated in Scheme 1. Poly(**1a**), poly(**2a**), and poly(**3a**) showed specific rotations much larger than the corresponding monomers (maximum 46 times). This suggests that these polymers form a helical structure with one-handed screw sense. Parts A and B of Figure 1 depict the CD spectra of poly(**1a**), poly(**2a**), and poly(**3a**) measured in MeOH and $CHCl_3$, respectively. Poly(**1a**) exhibited an intense Cotton effect in MeOH, while it did not in $CHCl_3$. On the other hand, poly(**2a**) and poly(**3a**) exhibited a Cotton effect in $CHCl_3$, while they did not in MeOH. These results indicate that poly(**1a**) forms a helical structure in MeOH while it does not in $CHCl_3$, and poly(**2a**) and poly(**3a**) form a helix in $CHCl_3$ while they do not in MeOH. It is considered that the different way of hydrogen bonding caused this dramatic difference depending on the structures. In all cases, the presence of intramolecular hydrogen bonding was confirmed by liquid-state IR spectroscopy.[8] The reason why poly(**1a**) could form a helix in MeOH, a solvent that disturbs the hydrogen bonding, may be explained by the shielding effect. Namely, the hydroxyl groups form intermolecular

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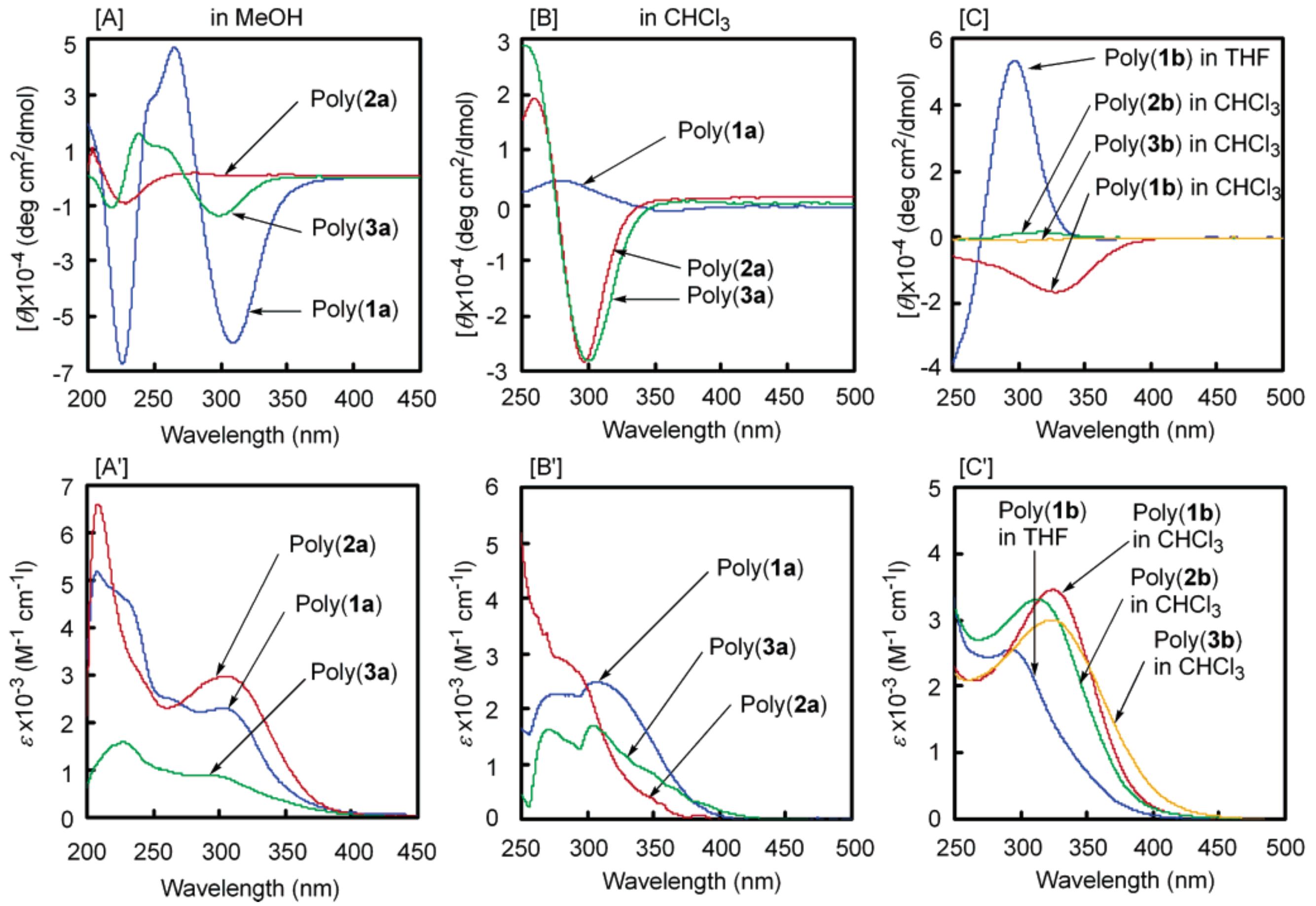
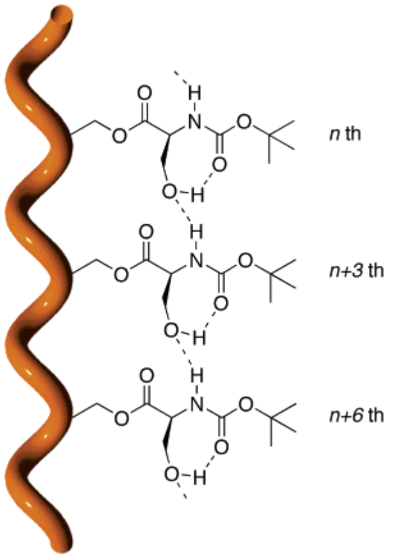


Figure 1. CD and UV−vis spectra of poly(**1a**)−poly(**3a**) measured in MeOH ([A], [A′]) and in $CHCl_3$ ([B], [B′]) at 0 °C. CD and UV−vis spectra of poly(**1b**)−poly(**3b**) measured in $CHCl_3$ and THF ([C], [C′]) at 0 °C. $c = (1.69{-}4.55) \times 10^{-4}$ M.

Chart 1



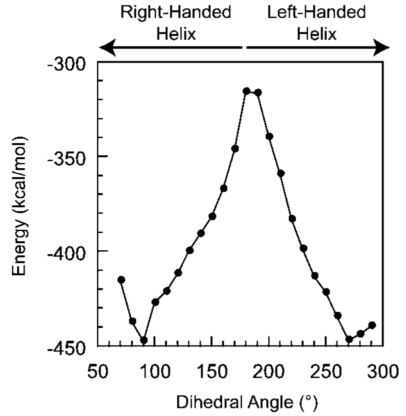


Figure 2. Relationship between the dihedral angle at the single bond of the main chain of poly(**3a**) (20-mer) and the energy calculated by MMFF94.

hydrogen bonding with solvent MeOH molecules to shield the inner amide groups. As a result, the amide groups can form intramolecular hydrogen bonding to stabilize the helical structure. On the contrary, *N*-methylamide and propargyl ester polymers, poly(**2a**) and poly(**3a**), cannot form this amide−amide hydrogen bonding. In $CHCl_3$, poly(**2a**) and poly(**3a**) possibly form hydrogen-bonding strands between the hydroxyl groups and carbamate, and amide or ester groups, which stabilize the helical structure. This assumption is supported by the behavior of the CD spectra of poly(**1b**), poly(**2b**), and poly(**3b**) with protected hydroxyl groups, as shown in Figure 1C. Poly(**2b**) and poly(**3b**) exhibited no apparent Cotton effect in $CHCl_3$. This result means that their counterparts, poly(**2a**) and poly(**3a**), form a helix utilizing the hydroxyl groups. Poly(**1b**) showed a Cotton in $CHCl_3$, indicating that it forms a helical structure presumably stabilized by intramolecular hydrogen bonding between the amide groups. In THF, poly(**1b**) showed a Cotton effect different from that in $CHCl_3$. As shown in Figure 1C′, the λ_{max} values of poly(**1b**) agreed with the wavelength values of $[\theta]_{max}$ in THF and $CHCl_3$, and the λ_{max} was shorter in THF than in $CHCl_3$. This indicates that the main-chain conjugation

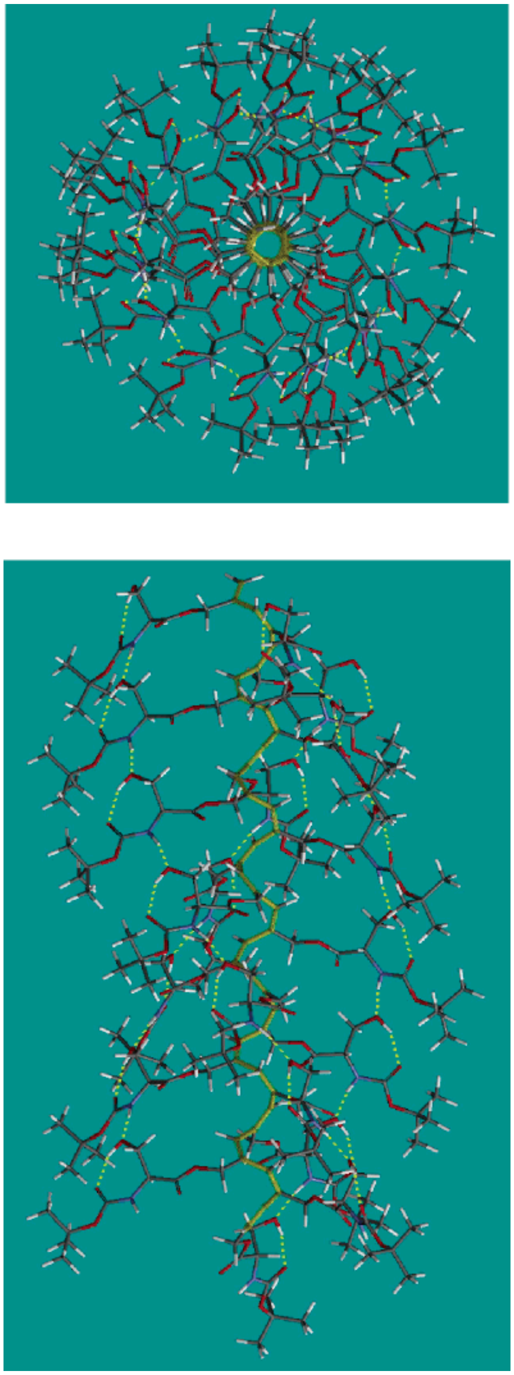


Figure 3. Top and side views of a possible conformer of poly(**3a**) (20-mer) optimized by MMFF94. The dihedral angles at the single bonds of the main chain are fixed at +270° (= −90°). The gold line and the green dotted line represent the polyacetylene main chain and hydrogen bonding, respectively. The hydrogen bonds are formed between −OH [nth unit] and ⟩C=O (carbamate) [nth unit] and −OH [nth unit] and −NH [($n + 3$)th unit].

of poly(**1b**) is shorter in THF than that in CHCl$_3$. Consequently, it is considered that the helix of poly(**1b**) in THF is tight compared with that in CHCl$_3$,[3] and the senses are opposite each other in these solvents judging from the signs of the Cotton effects.[9] The oppositely signed specific rotations of poly(**1b**) in CHCl$_3$ and THF (Table 1) support the opposite helical sense in these solvents. In the case of poly(**1a**) in CHCl$_3$, the hydroxyl groups may participate in the hydrogen bonding between the amide groups. As a result, it is likely that the hydroxyl groups disturb the formation of regulated hydrogen-bonding strands between the amide groups, which brings about the collapse of a helical structure.

As described above, poly(**2a**) and poly(**3a**) formed a helix that should be stabilized by hydrogen bonding involving the hydroxyl groups. We have examined thepossible conformation of poly(**3a**) considering hydrogen bonding. Among the many possible conformers examined, we have found that the conformer illustrated in Chart 1 is stable. This conformer forms regulated hydrogen-bonding strands between the hydroxyl and carbamate groups at the nth and ($n + 3$)th units. Figure 2 depicts the relationship between the twisted angle and energy of the 20-mer of **3a**.[10] The conformers with $\phi = +90^\circ$ (right-handed helix) and +270° (= −90°, left-hand helix) were the most stable. Considering the energies of the neighboring conformers, the one with $\phi = +270^\circ$ (Figure 3) seems to be more likely. Deviating from these two conformers, the distance between the pendent groups becomes longer. In the meantime, the hydrogen-bonding strands gradually get collapsed, which results in an energetically unfavorable state. The conformers accompanying hydrogen-bonding strands between the hydroxyl and carbamate moieties at the nth and ($n + 2$)th units were also possible, but the strands partly defected due to insufficient length between the side chains. A conformer with $\phi = +90^\circ$ could also form hydrogen bonding between the hydroxyl group at the nth unit and carbamate carbonyl group at the ($n + 3$)-th unit without defect of the hydrogen-bonding strands, but the energy was 28 kcal/mol unstable compared to the one illustrated in Figure 3. In this case, bulky *tert*-butoxy groups were twisted from trans zigzag form, which should be responsible for the unfavorableness. The conformers with hydrogen bonding between the hydroxyl group at the nth unit and ester carbonyl group at the ($n + 3$)th unit were further unfavorable because the twist of the side chains was very large.

In summary, we demonstrated the synthesis and chiroptical properties of serine-derived poly(*N*-propargylamides), poly(*N*-methyl-*N*-propargylamides), and poly(propargyl esters) with free and protected hydroxyl groups. It was confirmed that the hydroxyl groups greatly affected the secondary structures of the polymers, which was supported by liquid-state IR and molecular modeling studies. As far as we know, this is the first finding concerning the helix formation of poly(*N*-methyl-*N*-propargylamide) and poly(propargyl ester), which is stabilized by hydrogen bonding involving hydroxyl groups.

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Supporting Information Available: Experimental procedure for the synthesis and polymerization of monomers **1a**−**3b**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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(3) A pitch/diameter ratio represents the tightness of helical polyacetylene derivatives, and the wavelength of UV−vis absorption based on the polyacetylene backbone depends on

the tightness. See: Percec, V.; Obata, M.; Rudick, J. G.; De, B. B.; Glodde, M.; Bera, T. K.; Magonov, S. N.; Balagurusamy, V. S. K.; Heiney, P. A. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 3509.

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(5) Nomura, R.; Tabei, J.; Masuda, T. *J. Am. Chem. Soc.* **2001**, *123*, 8430.

(6) This Rh zwitterionic catalyst efficiently polymerizes monosubstituted acetylene monomers to give the polymers with highly *cis*-stereoregulated structure. See: Kishimoto, Y.; Itou, M.; Miyatake, T.; Ikariya, T.; Noyori, R. *Macromolecules* **1995**, *28*, 6662.

(7) See Supporting Information.

(8) The presence of intramolecular hydrogen bonding in poly(**1a**), poly(**2a**), and poly(**3a**) was confirmed by liquid-state IR spectra of the monomers and polymers measured in $CHCl_3$ (c = 27−67 mM). Data of amide or ester carbonyl $\nu_{C=O}$ (cm^{-1}): **1a** 1680, poly(**1a**) 1655, **2a** 1646, poly(**2a**) 1640, **3a** 1753, poly(**3a**) 1745. Data of carbamate carbonyl $\nu_{C=O}$ (cm^{-1}): **1a**−(overlapped with amide C=O), poly(**1a**) 1701, **2a** 1705, poly(**2a**) 1701, **3a** 1711, poly(**3a**) 1698. In every case, the $\nu_{C=O}$ of the polymer shifted to lower field compared to that of the corresponding monomer.

(9) The large difference between these solvents is basicity. It is likely that THF molecules strongly interact with the polymer compared with $CHCl_3$ because the oxygen atom has lone pair electrons directing outside of the molecule. This may affect the conformation of the chiral side chains, which results in the change of the helical sense and tightness. We are now attempting to simulate the solvent effect on the conformation and helical structure, but it still requires further investigation.

(10) All the calculations were carried out with MMFF94 force field, using Wavefunction, Inc. Spartan ’04 Windows version 1.01. Halgren, T. A. *J. Comput. Chem.* **1996**, *17*, 490.

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