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Unprecedented regioregular poly(1,4-arylene)s prepared by nickel(II)-catalyzed cross-coupling polymerization of 2,5-disubstituted bromo(chloro)arylene


Dedication (optional)

Abstract: Unprecedented synthesis of regioregular head-to-tail (HT)-type poly(1,4-arylene) bearing different substituents at the 2- and 5-positions is described. The regioregular poly(1,4-arylene) was prepared by the polymerization of 2,5-disubstituted bromo(chloro)arylene by sequential selective halogen-metal exchange with a Grignard reagent followed by cross-coupling polymerization with a nickel catalyst NiCl2(dppp). Formation of the regioregular poly(1,4-arylene) was confirmed by measurement of NMR spectrum, which showed remarkable difference from that of the related polymer with uncontrolled regioregularity. Polymerization of bromo(chloro)arylene with a chiral alkoxy substituent under similar conditions also led to the regioregular HT-type polyarylene, which showed circular dichroism suggesting formation of a structure of a higher order regularity.

Synthesis and design of \( \pi \)-conjugated polymers attract much attention in materials science pursuing outstanding electronic properties. Conjugated polymers have been shown to be applicable to electron-conducting materials, organic semiconductors, photovoltaic cells, etc.[1] Concerning five-membered heteroaromatic compounds like polythiophenes, it is particularly important to possess high head-to-tail (HT) regioregularity to exhibit remarkable properties as materials.[2] Much efforts have been devoted for the development of preparative methodologies for the regioregular polythiophenes, in which the cross-coupling strategy has been a powerful tool for the designed synthesis of 1.[3] By a marked contrast to polythiophene synthesis, much less attention has been paid to the study on the design of poly(1,4-arylene)s of controlled regioregularity. In poly(1,4-arylene) synthesis, it is also effective to undergo Kumada-Tamao-type catalyst transfer polymerization (KCTP), which has been developed by Yokozawa and McNeil, by the catalysis of a transition metal complex.[4] However, poly(2,5-disubstituted-1,4-arylene) bearing the same substituent at the 2- and 5-positions do not show regioregularity, while such an issue appears in the case of 2,5-differently substituted polyarylene. Nevertheless, synthesis of head-to-tail-type regioregular poly(1,4-arylene) has not been attempted so far, to the best of our knowledge,[5] albeit involving potential constitution of higher order orientation. It is therefore challenging to prepare and characterize such unprecedented regioregular poly(1,4-arylene). Herein, we describe synthesis of head-to-tail-type regioregular poly(1,4-arylene) bearing different alkoxy substituents at the 2- and 5-positions through the cross-coupling polymerization of bromo(chloro)arylene with a nickel catalyst.

Yokozawa, McCullough, Rieke Unprecedented (this work)

Chart 1. Regioregular HT-type poly(hetero)arylenes

We first examined the polymerization of a 1,4-dibromobenzene derivative 3a bearing different alkoxy substituents at the 2- and 5-positions, which may distinguish steric bulkiness of each substituent, to undergo regioselective bromine-metal exchange at the bromine atom adjacent to the less sterically congested substituent followed by a transition metal-catalyzed cross-coupling polymerization[5] leading to the regioregular poly(1,4-arylene). Synthesis of 1,4-dibromobenzene 3a was carried out employing 4-methoxyphenol (8a) as a starting material. Introduction of the hexyl substituent by the Williamson ether synthesis followed by dibromination at the 2,5-positions afforded 3a. Polymerization of the thus obtained 3a was carried out by Kumada-Tamao-type catalyst-transfer polymerization with \( \text{BuLi} \) and nickel catalyst NiCl2(dppp) (1 mol%)[6] to furnish the resulting poly(1,4-arylene) 2a in 20% yield with the average molecular weight of \( M_w = 5800 \) (\( M_w/M_n = 1.52 \)). (Scheme 1) The measurement of \( ^{13} \text{C}(1^\text{H}) \) NMR spectrum of 2a suggested the formation of partly regioregular polymer but the regularity was suggested to be ca. 4:1[7] despite attempted metatation at \(-78^\circ \text{C}\). The result shows that the halogen-metal exchange of 3a preferentially takes place at the less hindered bromine atom of the 1-position adjacent to the methoxy substituent whereas the metatation reaction is also competitive at the alternative bromine atom.

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Supporting information for this article is given via a link at the end of the document. (Please delete this text if not appropriate)
We next envisaged that the use of bromo(chloro)-2,5-disubstituted areylene 5, with which the halogen-metal exchange would occur at the proximate atom predominantly to the chlorine atom, to afford the regioregular poly(1,4-arylene) although a transition metal-catalyzed synthesis of poly(1,4-arylene) through metalated chloroarylamine as a monomer from 5 as well as any preparation pathways to 5 also have not yet been reported so far. Preparation of 4-chloro-5-hexyloxy-2-methoxy-bromobenzene (5a) was found to be performed with commercially available 2-chloro-4-methoxyphenol (4a). Etherification of the phenol moiety followed by bromination led to 5a in excellent yields. It should also be pointed out that a broad range of differently substituted bromo(chloro)benzene 5 can be, in general, synthesized as outlined in Scheme 2 employing 4-hydroxy-benzaldehyde 6. Etherification of phenol to give 4-alkoxybenzaldehyde 7 and the Dakin reaction to give 4-alkoxymethylphenol 8 and following chlorination at the ortho-position of phenol afforded 4. The second phenol was then transformed into the alkoxy group and the bromination led to the differently substituted 2,5-dialkoxy-bromo(chloro)benzene 5.

Scheme 2. Preparation of bromo(chloro)benzene 5

As the synthetic pathway of the monomer precursor 5 in hand, polymerization of 5a was performed. After examination of the conditions of halogen-metal exchange of bromo(chloro)benzene, which was found to take place under similar conditions to those of dibrornoareylene 3a4) and hardly to observe the metatlation at the chlorine atom, polymerization of 5a was carried out by the reaction of PrMgCl-LiCl at 60 °C for 1 h in THF followed by the addition of NiCl2(dppp) (1 mol%) as a catalyst. The polymerization proceeded to afford the 1,4-polyphenylene 2a in 56% yield. SEC analysis of 2a revealed to exhibit Mw = 22000; Mw/Mn = 2.01 as shown in Scheme 3. Figure 1 shows 13C{1H} NMR spectra of poly(1,4-arylene) 2a obtained by the reaction of bromo(chloro)benzene 5a (a) and the corresponding statistical copolymer (b) employing 5a and the oppositely substituted 5b (R1 = n-hexyl, R2 = Me). Characteristic signals of methylene (red) and methyl (blue) clearly show the formation of regioregular 2a by the reaction of 5a while the statistical polymer 2a indicated two signals of different chemical shifts suggesting formation of non-regioregular 2a. Considering the high regioregularity polymerization proceeds in a chain growth manner despite copolycondensation whereas a slightly broader Mw/Mn value suggests that the polymerization proceeds in a less sufficient catalyst transfer-type manner probably because of difficulties of the intra-chain oxidative addition of the nickel complex to the carbon-chlorine atom at the polymer end.

Scheme 3. Polymerization of bromo(chloro)benzene with different substituents

It is remarkable that the polymerization protocol using bromo(chloro)areylene is applicable to the preparation of a wide range of differently substituted poly(1,4-arylenes) with alkoxy groups. The results are summarized in Table 1. Although the regioregularity can be hardly confirmed by a spectroscopic or chromatographic analysis, the reaction of 5c bearing n-butyl and n-hexyl substituents proceeded under similar conditions and afforded the regioregular polymer 2c, which control would not be possible by the polymerization with corresponding dibromomonomere. Attempted polymerization of 5d bearing n-hexyl and benzyl groups was found to proceed with much less efficiency to afford the corresponding polymer 2d in an inferior yield. It was found that polymerization took place at the elevated temperature (100 °C) to afford 2d in 67% yield with Mw = 12700, Mw/Mn = 2.20. Polymerization of 5e with an oligoetheral substituent was also found to hardly take place under similar conditions (60 °C), however, the reaction of 5e was found to proceed when the temperature was elevated to 100 °C to afford polyphenylene 2e in 59% yield (Mw = 17400, Mw/Mn = 2.85).
Table 1. Polymerization of bromo(chloro)arylene 3 catalyzed by NiCl₂(dppp)\[a\]

<table>
<thead>
<tr>
<th>monomer precursor</th>
<th>R¹</th>
<th>R²</th>
<th>temp (°C) [b]</th>
<th>yield of 1 (%) [c]</th>
<th>$M_n$/M₅ [d]</th>
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<tr>
<td>5c</td>
<td>°C₆H₅</td>
<td>°C₆H₅</td>
<td>60</td>
<td>53</td>
<td>15500</td>
</tr>
<tr>
<td>5d</td>
<td>°C₆H₅</td>
<td>CH₆Ph</td>
<td>60</td>
<td>26</td>
<td>6200</td>
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[a] The reaction was carried out with 3 (0.3 mmol) and a metallating agent (1.0 eq) in 0.6 mL of THF at 60 °C for 1 h to form the corresponding metallated monomer followed by addition of NiCl₂(dppp) (1 mol %). [b] The reaction temperature in the polymerization. [c] Isolated yield. [d] Determined by SEC analysis on the basis of 6 polystyrene standards.

Bromo(chloro)benzene 5f bearing a chiral substituent was also prepared in a similar manner employing a chiral alkyl bromide derived from natural terpene (S)-(-)-β-citronellol. The monomer precursor 5f (R¹ = Me, R² = (CH₂)₅CH(CH₃)₂CH(CH₂)₅CH(CH₃)₂) was prepared from 2-chloro-4-methoxyphenol (4a) in 2 steps as shown in Scheme 4. Although attempted polymerization at 60 °C catalyzed by NiCl₂(dppp) was unsuccessful at all, the reaction proceeded at 100 °C to afford 2f in 64% yield ($M_n = 13200$; $M_w$/$M_n = 2.39$).

Scheme 4. Preparation of regioregular poly(1,4-arylene) 2f bearing a chiral side chain

Optical rotation of the obtained 2f bearing a chiral side chain showed $[\alpha]_D^{25} = +25.0$ (c 0.5, CHCl₃) and measurement of the CD spectrum of 2f was also carried out. The results are shown in Figure 2. Although the CD peak was hardly observed in a 1,2-dichlorethane solution, it was found to exhibit the Cotton effect by the addition of methanol at the wavelength corresponding to the absorption maximum of the polyphenylene moiety at the polymer main chain (ca. 340 nm). A weak CD peak emerged in a mixed solution of 1,2-dichlorethane/methanol = 9:1. The remarkably strong Cotton effect was observed in a solution of 1,2-dichlorethane/methanol = 7:3 (ca. 300 mdeg). The CD spectrum of non-regioregular polyphenylene 2f prepared by the polymerization of the related dibromoarylene 3f (R¹ = Me, R² = (CH₂)₅CH(CH₃)₂CH(CH₂)₅CH(CH₃)₂) was also measured to observe a much smaller CD (less than 5 mdeg) value (See Supporting Information). The results suggested that the chirality of the regioregular side chain induced a higher order regularity such as helix structure\[11,12\] based on a specific interaction of the phenylene moiety and such characteristics was only observed in the poly(1,4-arylene) bearing a head-to-tail-type regioregularity, while CD of the related non-regioregular analog was much weaker\[13\].

![Figure 2](image-url)
In summary, we have shown that synthesis of unprecedented regioregular poly(1,4-arylene) bearing different alkoxy substituents at the 2- and 5-positions was achieved by the nickel-catalyzed cross-coupling polymerization. Control of the head-to-tail regioregularity was found to be successful by the use of bromo(chloro)benzene derivatives, while such regularity has not been realized by the related polymerization of 1,4-dibromobenzene. Poly(1,4-arylene) prepared by bromo(chloro)benzene bearing a chiral substituent was found to exhibit circular dichroism suggesting chirality-driven aggregation-oriented orientation of the polyphenylene main chain. Further studies on the characterization of polymer properties are in progress.

Experimental Section

General procedure for the polymerisation of 1 hexoxybenzen-2 5-diyi (2a): To 20 ml Schlenk tube equipped with a magnetic stirring bar were added 4-chloro-2-hexoxy-5-methoxybromobenzene (5a, 96 mg, 0.3 mmol), PPh3/PtCl2 (1.1 M in THF, 273 µL, 0.3 mmol) and THF (0.33 mL) at room temperature under a nitrogen atmosphere. The mixture was warmed to 60 °C and stirring was continued for 1 h. NiCl2(dppp) (1.6 mg, 3.0 µmol) was added and further stirring was continued at 60 °C for 3 h. The reaction mixture was poured into a mixture of hydrochloric acid (1.0 M, 2 mL) and methanol (10 mL) to form a precipitate, which was filtered off to leave a solid. After washing with methanol repeatedly, the solid was dried under reduced pressure to afford 36.0 mg of 2a (56% isolated yield). Mw = 22000, Mw/Mn = 2.01. 1H NMR (400 MHz, CDCl3) δ 7.10 (s, 1H), 7.07 (s, 1H), 3.98 (s, 2H), 3.82 (s, 3H), 1.81-1.59 (m, 2H), 1.42-1.22 (m, 6H), 0.89 (t, J = 6.4 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 150.80, 150.26, 127.65, 127.39, 117.50, 115.12, 69.80, 56.41, 31.79, 29.64, 25.92, 22.78, 14.21; IR (ATR) 2951, 2931, 2859, 2935, 1528, 1400, 1375, 1207, 1043, 928 cm–1

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Keywords: regioregular poly(1,4-arylene) • bromo(chloro)arylene • halogen-metal exchange • nickel catalyst • Cotton effect


See Supporting Information.
Polymerization of differently substituted 1,4-bromo(chloro)benzene afforded unprecedented head-to-tail (HT) regioregular poly(1,4-arylene), while the regio-controlled synthesis from the 1,4-dibromoarylene is unsuccessful. Regioregular HT poly(1,4-arylene) bearing a chiral substituent showed the Cotton effect in a CD spectrum with a mixed solvent system of 1,2-dichloroethane/methanol suggesting a helix structure.

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