# Unprecedented Regioregular Poly(1,4-arylene)s Prepared by Nickel(II)-Catalyzed Cross-Coupling Polymerization of 2,5-Disubstituted Bromo(chloro)arylene

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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

Yushin Shibuya,[a] Naoki Nakagawa,[a] Naoki Miyagawa,[a] Toyoko Suzuki,[a] Kentaro Okano,[a] and Atsunori Mori*[a]

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 $NiCl_2$(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 π-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 **1**, 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 **2** 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.
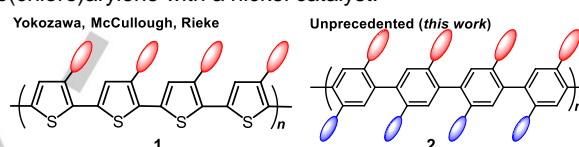


**Chart 1.** Regioregular HT-type poly(hetero)arylenes

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[6] 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 *t*BuLi and nickel catalyst $NiCl_2$(dppe) (1 mol%)[4d] to furnish the resulting poly(1,4-arylene) **2a** in 20% yield with the average molecular weight of $M_n = 5800$ ($M_w/M_n = 1.52$). (Scheme 1) The measurement of $^{13}C\{^1H\}$ NMR spectrum of **2a** suggested the formation of partly regioregular polymer but the regularity was suggested to be ca. 4:1[7] despite attempted metalation at –78 °C. The result shows that the halogen-metal exchange of **3a** preferencially takes place at the less hindered bromine atom of the 1-position adjacent to the methoxy substituent whereas the metallation reaction is also competitive at the alternative bromine atom.
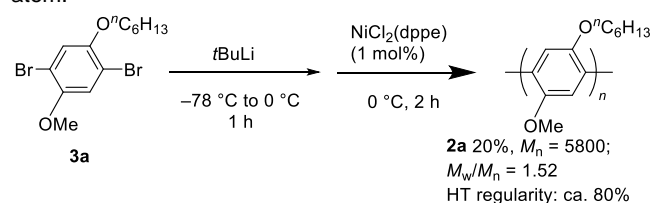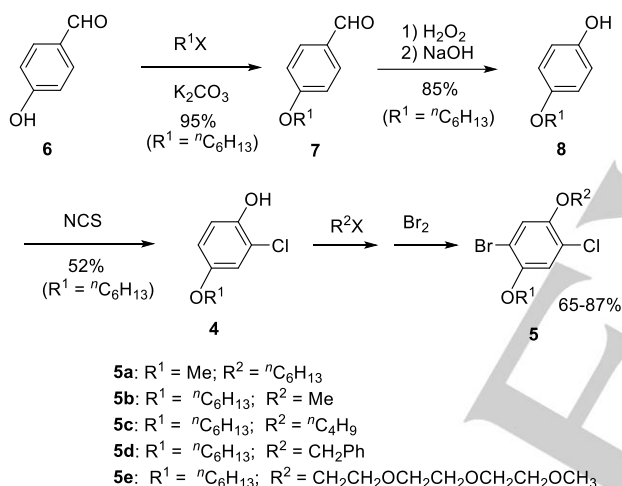


**Scheme 1.** Polymerization of 1,4-dibromoarylene **3a**

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We next envisaged that the use of bromo(chloro)-2,5-disubstituted arylene **5**, with which the halogen-metal exchange would occur at the bromine 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 chloroarene 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**[8] and the Dakin reaction to give 4-alkoxyphenol **8**[9,10] 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**.

**5a**: R$^1$ = Me; R$^2$ = $^n$C$_6$H$_{13}$
**5b**: R$^1$ = $^n$C$_6$H$_{13}$; R$^2$ = Me
**5c**: R$^1$ = $^n$C$_6$H$_{13}$; R$^2$ = $^n$C$_4$H$_9$
**5d**: R$^1$ = $^n$C$_6$H$_{13}$; R$^2$ = CH$_2$Ph
**5e**: R$^1$ = $^n$C$_6$H$_{13}$; R$^2$ = CH$_2$CH$_2$OCH$_2$CH$_2$OCH$_2$CH$_2$OCH$_3$

**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 dibromoarylene **3a**[4] and hardly to observe the metalation at the chlorine atom, polymerization of **5a** was carried out by the reaction of $^i$PrMgCl·LiCl at 60 °C for 1 h in THF followed by the addition of NiCl$_2$(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 $M_n$ =22000; $M_w/M_n$ = 2.01 as shown in Schme 3. Figure 1 shows $^{13}$C{$^1$H} 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** (R$^1$ =n-hexyl; R$^2$ = 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 polycondensation whereas a slightly broader $M_w/M_n$ value suggests that the polymerization proceeds in a less sufficient catalyst transfer-type[2a] manner probably because of difficulties of the intra-chain oxidative addition of the nickel complex to the carbon-chlorine atom at the polymer end.

**2a**, 56%
$M_n$ = 22000;
$M_w/M_n$ = 2.01
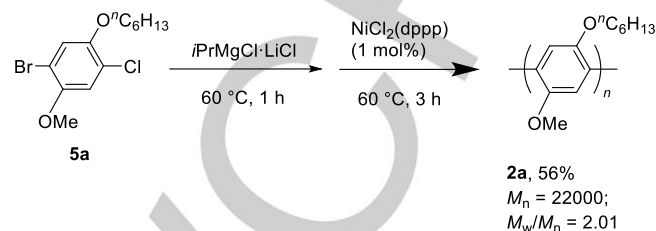
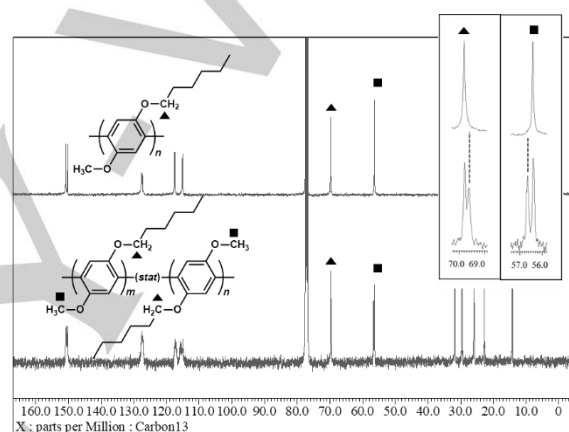**Scheme 3.** Polymerization of bromo(chloro)benzene with different substituents



**Figure 1.** $^{13}$C{$^1$H} NMR spectra of (a) regioregular poly(1,4-arylene) **2a** from **5a**; (b) polyarylene of statistical copolymer from **5a** and **5b**

It is remarkable that the polymerization protocol using bromo(chloro)arylene is applicable to the preparation of a wide range of differently substituted poly(1,4-arylene)s 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 dibromoarylene. 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 ºC) to afford **2d** in 67% yield with $M_n$ = 12700, $M_w/M_n$ = 2.20. Polymerization of **5e** with an oligoethereal substituent was also found to hardly take place under similar conditions (60 ºC), however, the reaction of **5e** was found to proceed when the temperature was elevated to 100 ºC to afford polyphenylene **2e** in 59% yield ($M_n$ = 17400, $M_w/M_n$ = 2.85).

**Table 1.** Polymerization of bromo(chloro)arylene 3 catalyzed by NiCl$_2$(dppp)[a]

| monomer precursor | R$^1$ | R$^2$ | temp (°C) [b] | yield of 1 (%)[c] | $M_n$[d] | $M_w/M_n$[d] |
|---|---|---|---|---|---|---|
| **5c** | $^nC_6H_{13}$ | $^nC_4H_9$ | 60 | 53 | 15500 | 2.28 |
| **5d** | $^nC_6H_{13}$ | $CH_2Ph$ | 60 | 26 | 6200 | 4.24 |
|  |  |  | 100 | 67 | 12700 | 2.20 |
| **5e** | $^nC_6H_{13}$ | $(CH_2)_2O(CH_2)_2O(CH_2)_2OCH_3$ | 60 | 0 |  |  |
|  |  |  | 100 | 59 | 17400 | 2.85 |

[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 NiCl$_2$(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** (R$^1$ = Me, R$^2$ =(CH$_3$)$_2$CH(CH$_2$)$_3$CH(CH$_3$)(CH$_2$)$_2$) was prepared from 2-chloro-4-methoxyphenol (**4a**) in 2-steps as shown in Scheme 4. Although attempted polymerization at 60 ºC catalyzed by NiCl$_2$(dppp) was unsuccessful at all, the reaction proceeded at 100 ºC to afford **2f** in 64% yield ($M_n$ = 13200; $M_w/M_n$ = 2.39).
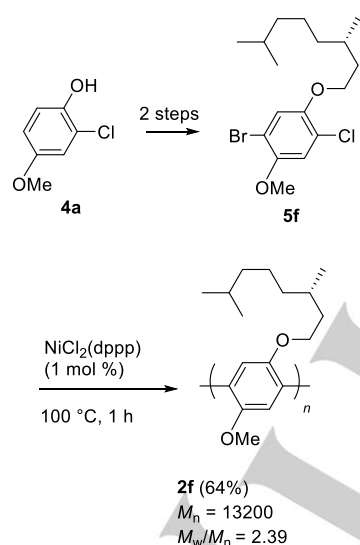


**Scheme 4.** Preparation of regioregular poly(1,4-arylene) **2f** bearing a chiral side chain

Optical rotation of the obtained **2f** bearing a chiral side chain showed [α]$_D^{32}$ = +25.0 (c 0.5, ClCH$_2$CH$_2$Cl) 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-dichloroethane/methanol = 9:1. The remarkably strong Cotton effect was observed in a solution of 1,2-dichloroethane/methanol = 7:3 (ca. 300 mdeg). The CD spectrum of non-regioregular polyphenylene **2f** prepared by the polymerization of the related dibromoarylene **3f** (R$^1$ = Me, R$^2$ =(CH$_3$)$_2$CH(CH$_2$)$_3$CH(CH$_3$)(CH$_2$)$_2$) 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]
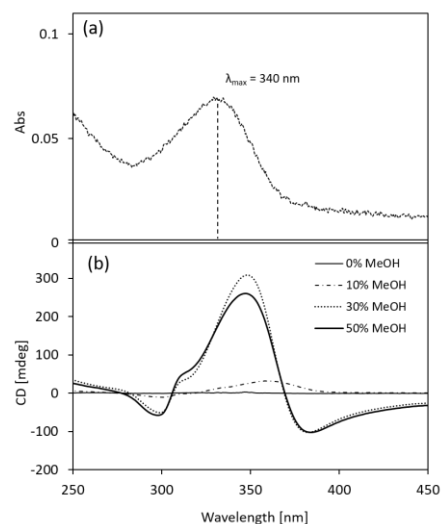


**Figure 2.** UV-vis (a) and CD (b) spectra of polymer **2f** as 1.0 x 10$^{-5}$ M 1,2-dichloroethane solution (UV-vis) and 3.0 x 10$^{-4}$ M mixed solution of 1,2-dichloroethane/methanol (CD)

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-dibomobenzene. Poly(1,4-arylene) prepared by bromo(chloro)benzene bearing a chiral substituent was found to exhibit circular dichroism suggesting chirality-induced aggregation-driven orientation of the polyphenylene main chain. Further studies on the characterization of polymer properties are in progress.

## Experimental Section

**General procedure for the preparation of poly(1-hexyloxy-4-methoxybenzen-2,5-diyl) (2a):** To 20 mL Schlenk tube equipped with a magnetic stirring bar were added 4-chloro-2-hexyloxy-5-methoxy-bromobenzene (**5a**, 96 mg, 0.3 mmol), $^i$PrMgCl·LiCl (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 ºC and stirring was continued for 1 h. NiCl$_2$(dppp) (1.6 mg, 3.0 μmol) was added and further stirring was continued at 60 ºC 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). $M_n$ = 22000, $M_w/M_n$ = 2.01; $^1$H NMR (400 MHz, CDCl$_3$) 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); $^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$) 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, 2932, 2859, 2835, 1528, 1490, 1407, 1375, 1207, 1043, 928 cm$^{-1}$.
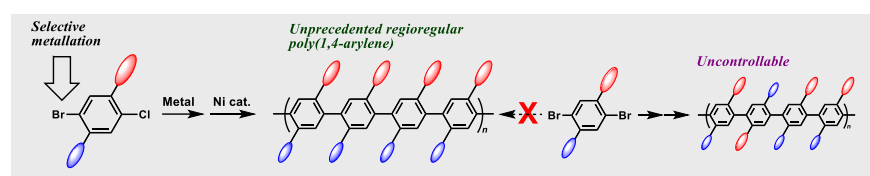
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[13] See Supporting Information.

**Entry for the Table of Contents** (Please choose one layout)

Layout 2:

## COMMUNICATION



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