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Synthesis and Characterization of Dithia[3.3](2,6)pyridinophane-Containing Polymers: Application to the Palladium-Catalyzed Heck Reaction

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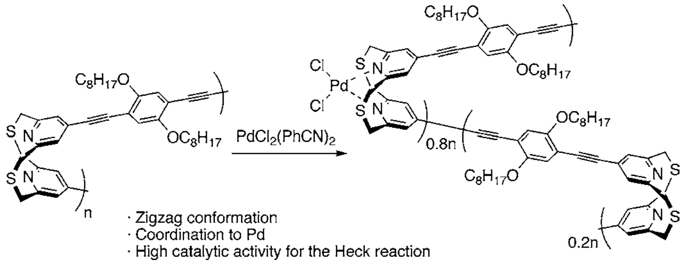
ABSTRACT



We synthesized zigzag polymers consisting of dithia[3.3](2,6)pyridinophane units that were flipped rapidly as a result of *syn-[anti]-syn* isomerization. Pyridinophane units were fixed in the *syn* form by complexation with palladium, and the resulting polymer complex exhibited a high catalytic activity for the Heck coupling reaction.

[3.3]Metacyclophane and its derivatives are well-known cyclophane compounds with two aromatic groups bridged by three atoms at each *meta* position. Furthermore, they are of great interest due to not only the interesting transannular $\pi-\pi$ interaction between two aromatic rings but also their conformational flexibility.[1] The structure of [3.3]metacyclophanes in solution reveals that two aromatic rings are flipped by a *syn-[anti]-syn* isomerization and bridged methylenes are wobbled by *chair-boat* isomerization,[2] whereas their general X-ray crystal structure shows a *syn* conformation.[1] Recently, we have focused on the construction of through-space π-conjugated systems where cyclophane derivatives are incorporated into a π-conjugated polymer backbone as a repeating unit.[3] In a series of our studies, we succeeded in the synthesis of poly(*p*-phenylene-ethynylene)s consisting of dithia[3.3]metacyclophane in a conjugated polymer main chain; this synthesis was performed by the coupling reaction of 6,15-dibromo-2,11-dithia[3.3]metacyclophane as the key monomer with 2,5-dialkoxy-1,4-diethynylbenzene.[3c] This polymer also showed flexible *syn-[anti]-syn* conformational changes of dithia[3.3]metacyclophane moieties in solution regardless of the polymer (M_n = 7500) and exhibited a delocalization of π-electrons via the through-space interaction.

The replacement of two benzene rings in [3.3]metacyclophane with two pyridine rings, i.e., [3.3](2,6)pyridinophane,

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[1] (a) *Modern Cyclophane Chemistry*; Cleiter, R., Hopf, H., Eds.; Wiley-VCH: Weinheim, Germany, 2004. (b) *Cyclophane Chemistry*; Vögtle, F.; Wiley & Sons: New York, 1993. (c) Shultz, J.; Vögtle, F. *Top. Curr. Chem.* **1994**, *172*, 42. (d) *Cyclophanes*; Diederich, F.; The Royal Society of Chemistry: Cambridge, 1989. (e) *Cyclophanes*; Keehn, P. M., Rosenfeld, S. M., Eds.; Academic Press: New York, 1983; Vols. I and II.

[2] (a) Mitchell, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 2352. (b) Semmelhack, M. F.; Harrison, J. J.; Young, D. C.; Gutiérrez, A.; Raffi, S.; Clardy, J. *J. Am. Chem.* Soc. **1985**, *107*, 7508.

[3] (a) Morisaki, Y.; Chujo, Y. *Macromolecules* **2002**, *35*, 587. (b) Morisaki, Y.; Ishida, T.; Chujo, Y. *Macromolecules* **2002**, *35*, 7872. (c) Morisaki, Y.; Ishida, T.; Chujo, Y. *Polym. J.* **2003**, *35*, 501. (d) Morisaki, Y.; Chujo, Y. *Macromolecules* **2003**, *36*, 9319. (e) Morisaki, Y.; Chujo, Y. *Macromolecules* **2004**, *37*, 4099. (f) Morisaki, Y.; Chujo, Y. *Tetrahedron Lett.* **2005**, *46*, 2533.

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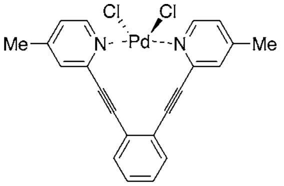
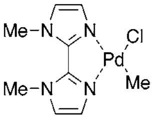
is an interesting feature in addition to conformational flexibility and the transannular $\pi-\pi$ interaction. [3.3](2,6)-Pyridinophane can act as a bidentate nitrogen ligand for transition metals. Tsuge and co-workers reported the preparation of Pt(II) and Pd(II) complexes by the reaction of dithia[3.3](2,6)pyridinophane with $PtCl_2(PhCN)_2$ and $PdCl_2(PhCN)_2$, respectively.[4] An X-ray crystallographic investigation of these complexes revealed that two pyridine rings were fixed into the *syn* geometry with a dihedral angle of about 90°.



1,2-bis(2-pyridylethynyl)benzene[5a]



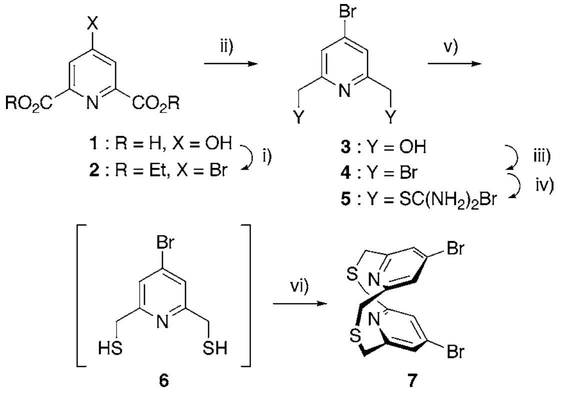
bis-*N*-methylimidazole[5b]

On the other hand, the catalytic activity of palladium complexes with regard to the phosphine-free Heck reaction in air was affected by the bidentate nitrogen ligands such as 1,2-bis(2-pyridylethynyl)benzene[5a] and bis-*N*-methylimidazole.[5b] Therefore, the polymers bearing a pyridinophane−palladium complex are potentially applicable in the polymer-supported catalysts in air, which are used for palladium-catalyzed coupling reactions, as well as recyclable polymer catalysts. In the present study, we synthesized a novel poly(*p*-phenylene-ethynylene)-type polymer[6] with dithia[3.3](2,6)pyridinophane in the main chain as a repeating unit and investigated the stereochemistry of the resulting polymer. Moreover, we studied the complexation of this polymer with the palladium complex and its catalytic performance and the recycling aspect for the Heck coupling reaction.

The key monomer 6,15-dibromo-2,11-dithia[3.3](2,6)-pyridinophane **7** was synthesized according to Scheme 1.[3c,7] Commercially available chelidamic acid monohydrate **1** was converted into 2,5-bisbromomethyl-3-bromopyridine **4** with a good yield.[8] Both the bromomethyl groups of **4** were reacted with thiourea in EtOH to give compound **5** with a yield of 91%. Finally, the target monomer **7** was synthesized with a yield of 34% by the reduction of **5** via intermediate dithiol followed by a treatment with **4**.

Comonomers 2,5-dialkoxy-1,4-diethynylbenzenes **8a**−**c** were prepared according to the established procedures.[9] Flexible alkoxy side chains were attached to momomers **8a**−**c** to increase the solubility of the resulting conjugated polymers.[10]

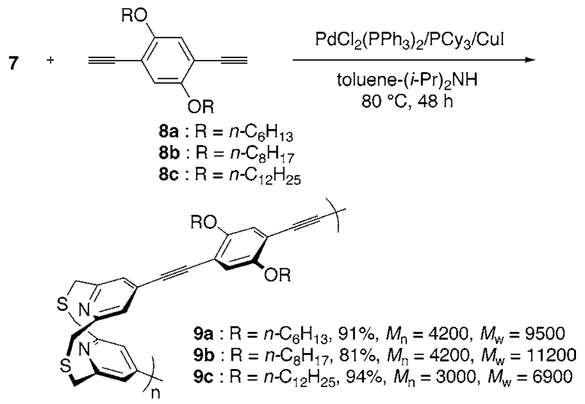
Scheme 1[a]



[a] Reagents and conditions: (i) (1) PBr_3, Br_2, rt, (2) EtOH, 0 °C, 87%; (ii) $NaBH_4$, EtOH, rt to reflux, 70%; (iii) HBr, AcOH, reflux, 87%; (iv) thiourea, EtOH, reflux, 91%; (v) $NaBH_4$, MeOH, rt; (vi) **4**, NaOH, EtOH−benzene, reflux, 34%.

The polymerizations of monomer **7** with **8a**−**c** were carried out in toluene−diisopropylamine solution in the presence of a catalytic amount of $PdCl_2(PPh_3)_2/PCy_3/CuI$ (Cy = cyclohexyl) at 80 °C for 48 h (Scheme 2). After the reaction was completed, inorganic byproducts were removed by washing with aqueous NH_3, and the filtrate was dried in vacuo. The THF-soluble portion of the crude polymer was purified by reprecipitation from a large amount of MeOH to yield target polymers **9a**−**c** in the form of a yellowish brown powder. Molecular weight measurements were performed by gel permeation chromatography (GPC) in eluent $CHCl_3$ using a calibration curve of polystyrene standards.

Scheme 2



The structures of monomer **7** and polymers **9a**−**c** were confirmed by the ^1H and ^{13}C NMR spectra. The ^1H NMR spectra of [3.3]metacyclophane and [3.3]metapyridinophane

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[4] Moriguchi, T.; Kitamura, S.; Sakata, K.; Tsuge, A. *Polyhedron* **2001**, *20*, 2315.

[5] (a) Kawano, T.; Shinomaru, T.; Ueda, I. *Org. Lett.* **2002**, *4*, 2545. (b) Park, S. B.; Alper, H. *Org. Lett.* **2003**, *5*, 3209.

[6] Bunz, U. H. F. *Chem. Rev.* **2000**, *100*, 1605.

[7] Kawashima, T.; Kurioka, S.; Tohda, Y.; Ariga, M.; Mori, Y.; Misumi, S. *Chem. Lett.* **1985**, 1289.

[8] (a) Takalo, H.; Kankare, J. *Acta Chem. Scand.* **1987**, *B41*, 219. (b) Takalo, H.; Kankare, J. *Acta Chem. Scand.* **1988**, *B42*, 373.

[9] (a) Moroni, M.; Moigne, J. L. *Macromolecules* **1994**, *27*, 562. (b) Li, H.; Powell, D. R.; Hayashi, R. K.; West, R. *Macromolecules* **1998**, *31*, 52.

[10] (a) Le Moignem, J.; Moroni, M.; Coles, H.; Thierry, A.; Kajzar, F. *Mater. Res. Soc. Symp. Proc.* **1992**, *247*, 65. (b) Rutherford, D.; Stille, J. K.; Elliott, C. K.; Reichert, V. R. *Macromolecules* **1992**, *25*, 2294. (c) Sasabe, H.; Wada, T.; Hosoda, H.; Ohkawa, H.; Yamada, A.; Garito, A. F. *Mol. Cryst. Liq. Cryst.* **1990**, *189*, 155.

analogues are very useful for observing their conformational flexibility. Figure 1a shows the ^{1}H NMR spectrum of monomer **7** in a $CDCl_3$ solution at 25 °C. The chemical shift of the bridge methylene protons (-CH_2-S-CH_2-) of **7** was 3.9 ppm and appeared as a sharp singlet peak. This result indicates the occurrence of rapid bridge *chair-boat* wobbling and rapid ring *syn-[anti]-syn* flipping of monomer **7** in solution.[11] In the ^{1}H NMR spectrum of **9b** in $CDCl_3$ (Figure 1b), the signals of the octyloxy chains were observed at 0.87 ppm for -CH_3, at 1.2−1.9 ppm for -CH_2-, and at 3.8 ppm for -OCH_2- as a shoulder peak. The signals of the aromatic protons ranged between 6.7 and 7.2 ppm. The chemical shifts of the bridged methylene protons (-CH_2-S-CH_2-) did not vary between polymer **9b** (δ = 4.0 ppm) and monomer **7** (δ = 3.9 ppm). It is implied that the dithia[3.3](2,6)pyridinophane units of polymer **9b** are also flexible, and the rapid *syn-[anti]-syn* interconversion of pyridine rings occurs in solution at room temperature, albeit in the conjugated polymer main chain.[12]

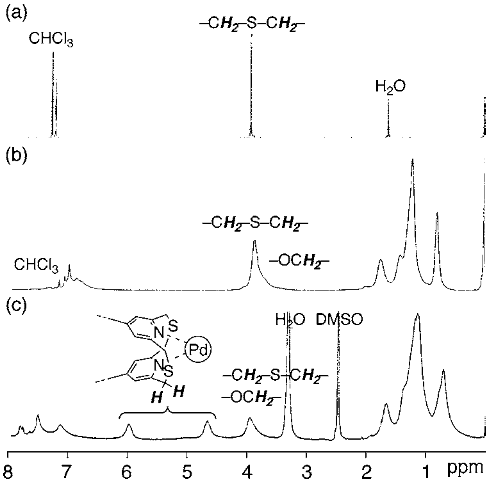
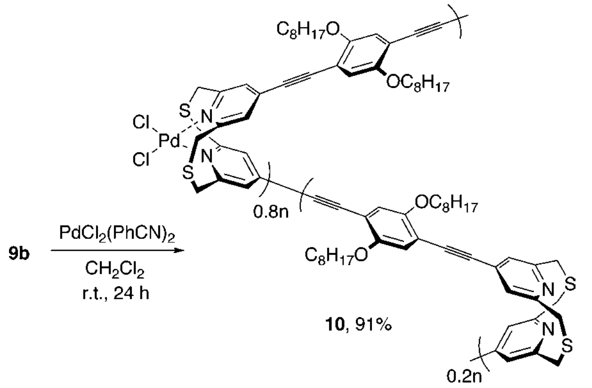
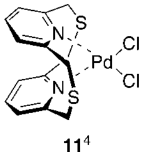


Figure 1. ^{1}H NMR spectra of (a) monomer **7** in $CDCl_3$, (b) polymer **9b** in $CDCl_3$, and (c) polymer complex **10** in DMSO-d_6 at room temperature.

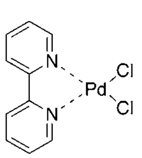
It is established that dithia[3.3](2,6)pyridinophane acts as a bidentate nitrogen ligand with the palladium complex $PdCl_2(PhCN)_2$ to give $PdCl_2$(dithia[3.3](2,6)pyridinophane).[4] To investigate the stereochemistry as well as coordination ability of polymer **9b** with regard to the palladium complex, the complexation reaction of polymer **9b** with $PdCl_2(PhCN)_2$ was examined. This polymer was treated with an equimolar amount of $PdCl_2(PhCN)_2$ in CH_2Cl_2 at room temperature for 24 h to give a brown polymer complex **10** in 91% yield (Scheme 3). The obtained polymer complex **10** was insoluble in CH_2Cl_2, $CHCl_3$, and THF and slightly soluble in polar aprotic solvents such as DMF and DMSO. The ^{1}H NMR chemical shifts of polymer complex **10** (Figure 1c) in DMSO-d_6 were compared with those of monomer **7** (Figure 1a) and polymer **9b** (Figure 1b). The general trends of the chemical shift at 4.0 ppm of the bridged methylene protons (-CH_2-S-CH_2-) were similar between **7**, **9b**, and polymer complex **10**. Signals at 4.7 and 6.0 ppm of **10** (Figure 1c) were consistent with those of complex **11** (at 4.72 and 6.07 ppm) reported by Tsuge and co-workers.[4] This ^{1}H NMR spectrum of polymer complex **10** assumes that the dithia[3.3](2,6)pyridinophane units have a fixed *syn* geometry; these units are obtained by the coordination of nitrogen atoms to the palladium complex. The introduction of the palladium species with the dithia[3.3](2,6)pyridinophane skeleton was calculated to be 80% by comparing with the integral ratio of the bridged methylene protons of the unreacted pyridinophane unit (4.0 ppm, Figure 1c). The isolated yield of **10** was found to be 91%. Because of a decrease in the solubility of polymer complex **10** in CH_2Cl_2 by complexation and the immobility of the polymer main chain, **10** was precipitated during the complexation process.

Scheme 3





11[4]



12

We also examined the catalytic activity of the obtained pyridinophane−palladium polymer complex **10**, pyridinophane−palladium complex **11**,[4] and (2,2′-bipyridine)-

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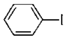
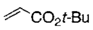
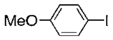
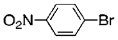
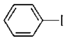
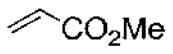
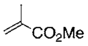
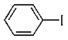
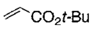
(11) Ring flipping and bridge wobbling systems of [3.3]phanes were studied in detail. For 2,11-dithia[3.3]metacyclophane: ref 2a. For dithia[3.3]metacyclophane derivatives: (a) Laali, K. K.; Okazaki, T.; Mitchell, R. H. *J. Chem. Soc., Perkin Trans. 2* **2001**, 745. For 2,11-diaza[3.3](3,5)-pyridinophane: (b) Satou, T.; Shinmyouzu, T. *J. Chem. Soc., Perkin Trans. 2* **2002**, 393. For 9-nitro- and 9-amino-2,11-dithia[3.3]metacyclophane: (c) Moriguchi, T.; Sakata, K.; Tsuge, A. *Chem. Lett.* **1999**, 167. (d) Moriguchi, T.; Sakata, K.; Tsuge, A. *J. Chem. Soc., Perkin Trans. 2* **2001**, 934. For [3.3]metacyclophane-2,11-dione derivatives: (e) Yamato, T.; Tsuchihashi, K.; Nakamura, N.; Hirahara, M.; Tanaka, K. *Can. J. Chem.* **2002**, *80*, 510. (f) Isaji, H.; Yasutake, M.; Takemura, H.; Sako, K.; Tatemitsu, H.; Inazu, T.; Shinmyozu, T. *Eur. J. Org. Chem.* **2001**, 2487. For 2,11-dithia[3.3]-(2,6)pyridinophane and 1,3,10,12-tetrathia[3.3](2,6)pyridinopahne: (g) Newkome, G. R.; Pappalardo, S.; Fronczek, F. R. *J. Am. Chem. Soc.* **1983**, *105*, 5152.

(12) VT ^{1}H NMR measurements (down to −80 °C) for **9a** produced almost no distinct change in the spectrum; see Supporting Information, Figure S1.

dichloropalladium complex **12** for a typical Heck reaction.[13] The results are summarized in Table 1. The reaction of phenyl iodide with *tert*-butyl acrylate in the presence of a catalytic amount of the palladium–pyridinophane units of polymer complex **10** proceeded smoothly to give a corresponding *tert*-butyl cinnamate with high yield. The best result was obtained when 1.0 mol % of palladium–pyridinophane units was used (run 1, 98% yield); however, only 0.01 mol % of the palladium–pyridinophane units showed a high catalytic activity to yield a coupling compound with a yield of 86% (run 7). Note that the present polymer complex **10** gave a good result when the reaction was performed in air (run 4). Other aryl halides (runs 8 and 9) and terminal alkenes (runs 10–12) were available in the present system, and the coupling products were obtained with a high isolated yield. The effect of the bidentate nitrogen ligands was also examined (runs 13–16). Although complexes **11** (runs 13 and 14) and **12** (runs 15 and 16) exhibited a good catalytic activity, further reaction time was needed to complete the reaction, while the reaction time for polymer complex **10** was only 1 h. We speculate that the conjugation effect of polymer complex **10** from electron-rich phenylene units with alkoxy chains to pyridinophane units enhances the oxidative addition of aryl iodide to the palladium center in comparison with the normal pyridinophane–palladium complex **11** and (2,2′-bipyridine)dichloropalladium complex **12**.[14] Additionally, active sites of palladium centers in polymer complex **10** appear at the corner of the zigzag conformation without being embedded in the polymer chain.

Table 1. Heck Reaction of Haloarenes with Alkenes[a]

run	catalyst, mol %[b]	ArX	alkene	time (h)	yield (%)[c]
1	**10**, 1.0			1	98
2	**10**, 0.05			1	90
3	**10**, 0.05			24	93
4[d]	**10**, 0.05			1	91
5[e]	**10**, 0.05			1	85
6[f]	**10**, 0.05			1	81
7	**10**, 0.01			24	86
8	**10**, 0.05			24	94[g]
9	**10**, 0.05			24	95[g]
10	**10**, 0.20			2	97[g]
11	**10**, 0.20			2	91[g]
12	**10**, 0.20			2	95[g]
13	**11**, 0.05			1	trace
14	**11**, 0.05			24	90
15	**12**, 0.05			1	8
16	**12**, 0.05			24	73

[a] Reaction conditions: DMF (4.0 mL), NEt_3 (1.0 mL), ArX (5.0 mmol), and alkene (7.0 mmol), 100 °C, nitrogen atmosphere. [b] Mol % of palladium–pyridinophane units for catalyst **10**. [c] Determined by GLC based on the amount of ArX charged. [d] The reaction was performed in air. [e] Second cycle. [f] Third cycle. [g] Isolated yield.

The present polymer catalyst **10** was purified by reprecipitation from an excess amount of $CHCl_3$ after the Heck coupling reaction. The polymer precipitates were washed with $CHCl_3$, dried in vacuo, and used for the next reaction. The results of this recycling study are also listed in Table 1, runs 5 and 6. Polymer complex **10** maintained the catalytic activity in the third cycle and correspondingly yielded a *tert*-butyl cinnamate with a yield of 81% (run 6).

In conclusion, we developed zigzag polymers using a dithia[3.3](2,6)pyridinophane skeleton in the conjugated polymer main chain. It was found that the obtained polymer was flipped rapidly as the result of *syn-[anti]-syn* isomerization and was fixed in the *syn* form by complexation with a transition metal such as palladium. With regard to the resulting polymer complex, the phosphine-free Heck coupling reaction in air exhibited a high catalytic activity. The scope of application of dithia[3.3](2,6)pyridinophane-containing polymers to recyclable polymer catalysts and their optical aspects are currently under investigation.

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Supporting Information Available: Experimental procedures and spectroscopic data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[13] (a) Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, *37*, 2320. (b) Heck, R. F. *Org. React.* **1982**, *27*, 345. (c) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: London, 1990.

[14] This hypothesis would be worth considering. The effort to clarify this question on the high catalytic activity of **10** is currently underway.