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A new method of using supercritical carbon dioxide as a green solvent for synthesis and purification of 5,5‴-bis(tridecafluorohexyl)-2,2′:5′,2″:5″,2‴-quaterthiophene, which is one of n-type organic semiconducting materials

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ABSTRACT

We have investigated synthesis as well as purification of 5,5‴-bis(tridecafluorohexyl)-2,2′:5′,2″:5″,2‴-quaterthiophene (BFH-4 T, n-type organic semiconducting material) using supercritical carbon dioxide (scCO$_2$) as a green solvent. BFH-4T was obtained in good selectivity and high yield by TDAE/PdCl$_2$-catalyzed reductive coupling reaction of 5-bromo-5′-(tridecafluorohexyl)-2,2′-bithiophene in scCO$_2$. We have also successfully established purification of the reaction mixture by passing scCO$_2$ in the reaction vessel. The product was yellow powder of BFH-4T with purity of more than 99% and Pd catalyst was not contained.

Organic semiconducting materials have attracted much attention for large and flexible electronic applications because their fabrication processes are easier and more cost effective than silicon technologies. Among their applications, field effect transistors are especially interesting since they can be used as low-cost, large-area, flexible, and light-weight electronic devices such as active-matrix flat displays, electronic papers, radio frequency identification tags and sensors.[1–4] In recent years, as application to complementary circuits has been proceeded,[5,6] not only p-type but also n-type organic semiconductors play an important role in electronic devices. However, the synthesis of organic semiconducting materials generally require a large amount of organic solvents that are noxious and harmful to the environment. Supercritical carbon dioxide (scCO$_2$) has been widely considered as an environmentally benign medium instead of volatile organic solvents. In addition, scCO$_2$ has several advantages such as low viscosity, liquid-like density, high diffusivity, nearly zero surface tension, and mild critical data (critical temperature of 31.1 °C and critical pressure of 7.38 MPa).[7] Furthermore, it can be easily removed without leaving any residues in the reaction mixture.[7] To date, several researchers have been made metal-catalyzed C—C bond formation reactions (Suzuki-Miyaura, Mizoroki-Heck, and Ullmann coupling)[8–13] and polymerization of polyheterocycles[14,15] in scCO$_2$. In this paper, we will describe synthesis as well as purification of organic semiconducting materials (quaterthiophene derivatives) in scCO$_2$ which is used as a green solvent.

We used palladium-catalyzed reductive coupling (Scheme 1) that is quite suitable to synthesize symmetrical compounds. In contrast to alkylation, relatively few synthetic methods for introducing fluoroalkyl groups on a quaterthiophene core are reported.[16] ScCO$_2$ is known to have a high affinity with fluorine compounds,[15,17,18] so we focused on 5,5‴-bis(tridecafluorohexyl)-2,2′:5′,2″:5″,2‴-quaterthiophene (BFH-4T) **2a**[19,20] (n-type organic semiconducting material) that contains fluoroalkyl groups. This is the first attempt to synthesize as well as purify organic semiconducting material using scCO$_2$.

Route A in Fig. 1 shows a conceivable mechanism for the palladium-catalyzed reductive coupling of aryl bromides.[21] On the other hand, a parallel reduction reaction (debromination) occurs under same reaction conditions (Route B in Fig. 1).[22,23] The selectivity of these reactions (Route A/B) highly depends on components of the system, e.g., solvent, palladium reagent (electron-transfer catalyst), and reductant that is required to regenerate active palladium in the reduction state.[21,24,25] Many combinations of catalyst and reductant have been developed.[21–32] In this paper, we selected several systems from them and examined palladium-catalyzed reductive coupling of 5-bromo-5′-(tridecafluorohexyl)-2,2′-bithio-

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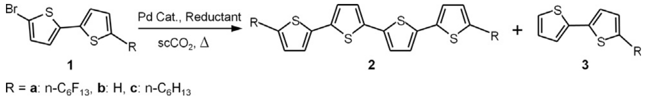

Scheme 1. Palladium-catalyzed reductive coupling reaction of aryl bromide (**1a**–**1c**) in $scCO_2$.

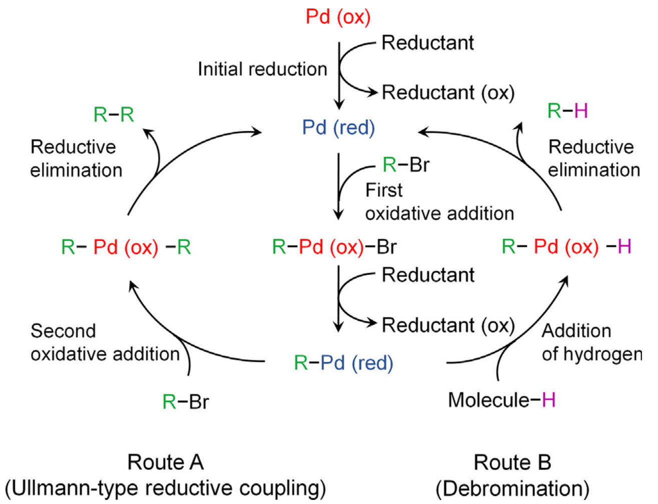

Fig. 1. Possible mechanism for the palladium-catalyzed reductive coupling reaction of aryl bromide.

phene **1a** with various reductants at 120 °C for 4 h using $scCO_2$ (14 MPa) as reaction solvent (Table 1).

Firstly, coupling reaction with a Pd/C and zinc combination was carried out (Table 1, entry 1). Li et al. reported that the combination is suitable for reductive coupling reaction containing CO_2 in water.[28] However, selectivity toward **2a** was found to be as low as 24.0%. Next, we examined palladium catalysts containing ligands such as $Pd(bpy)Cl_2$ and $Pd(dppf)Cl_2$ in combination with isopropyl alcohol (IPA), because primary and secondary alcohols have been reported to be an effective reductant for palladium catalyst.[22,25] The conversion of **1a** was greatly affected by the type of ligands and decreased compared to the Pd/C and zinc combination, while the selectivity was greatly improved (Table 1, entry 2 and 3). A use of L-ascorbic acid[27] as a reductant resulted in a lower conversion (Table 1, entry 4). This result is probably derived from poor solubility of L-ascorbic acid in $scCO_2$. Therefore, we examined concomitant use of L-ascorbic acid and IPA. However, the concomitant use of reductants resulted in a lowering of the selectivity (Table 1, entry 5). Moreover, the selectivity significantly decreased by further addition of IPA (Table 1, entry 6) indicating that IPA preferentially acts as a hydrogen-donor (Route B Addition of hydrogen Step in Fig. 1) in the $scCO_2$ system. At the same time, further IPA addition greatly increased the conversion, which can be attributed to improved solubility of the base (Cs_2CO_3) in $scCO_2$ due to IPA which acts as a cosolvent. This result suggests that the use of a base with good solubility will improve the conversion. Hence, we employed liquid organic bases that are presumed to be more soluble in $scCO_2$ than inorganic bases. By the use of triethylamine, the selectivity was approximately doubled while maintaining the conversion almost 30% (Table 1, entry 7). In addition, we tried to use tetrakis (dimethylamino)ethylene (TDAE),[21,29] since TDAE is expected to act not only as a base but also as a reductant and ligand for palladium catalyst.[21] We have found that coupling reaction has been achieved by the TDAE/$PdCl_2$ system and obtained best results in conversion and selectivity (Table 1, entry 8). We have also found that debrominated product **3a** was generated (19.2%), regardless of hydrogen-donor free system. We assumed that the result was caused by water contained in the reagents and the medium. In practice, the addition of water to the reaction system significantly reduced the selectivity (Table 1, entry 9). However, despite the sufficient addition of water into the reaction system, the selectivity was still higher than we expected. This result suggests existence of other hydrogen-donors which are not specified yet. The identification of them is a remaining problem and will be carried out in our future study. It is also noted that a use of organic solvent as a reaction medium instead of $scCO_2$ resulted in a lower conversion (Table 1, entry 10). From these results, we consider that a TDAE/$PdCl_2$ system is the most suitable for reductive coupling reaction in $scCO_2$. Therefore, we chose a TDAE/$PdCl_2$ system for the following experiments.

Table 2 lists the effects of various reaction parameters (reaction time, temperature, catalyst loading, and kinds of aryl bromide) on the reaction selectivity and the coupling product (compound **2**)

Table 1

Reductive coupling reaction of 5-bromo-5′-(tridecafluorohexyl)-2,2′-bithiophene **1a** catalyzed by various systems.[a]

Entry	Solvent	Catalyst	Base	Reductant	Yield[b] (%)		Conversion[c] (%)	Selectivity (%)
					2a	**3a**		
1	CO_2/H_2O = 14/1	5% Pd/C	–	Zinc[d]	18.5	58.7	79.3	24.0
2	CO_2	$Pd(bpy)Cl_2$	Cs_2CO_3	IPA[e]	0.4	0	0.5	100
3	CO_2	$Pd(dppf)Cl_2$	Cs_2CO_3	IPA[e]	18.5	7.9	26.5	70.1
4	CO_2	$Pd(dppf)Cl_2$	Cs_2CO_3	Ascorbic acid[f]	9.3	3.7	13.1	71.7
5	CO_2	$Pd(dppf)Cl_2$	Cs_2CO_3	Ascorbic acid[f] + IPA[e]	11.6	11.4	23.8	50.4
6	CO_2	$Pd(dppf)Cl_2$	Cs_2CO_3	Ascorbic acid[f] + IPA[g]	21.8	75.0	98.4	22.5
7	CO_2	$Pd(dppf)Cl_2$	Triethylamine	Ascorbic acid[f]	18.9	10.6	29.5	64.1
8	CO_2	$PdCl_2$	(TDAE)	TDAE[h]	78.3	19.2	97.5	80.3
9[i]	CO_2	$PdCl_2$	(TDAE)	TDAE[h]	22.1	53.7	75.9	29.1
10[j]	Dioxane	$PdCl_2$	(TDAE)	TDAE[h]	3.5	0.6	4.2	86.4

[a] Reaction conditions: **1a** (0.1 mmol), catalyst (0.01 mmol), base (0.075 mmol), solvent (3 mL), 14 MPa, 120 °C, 4 h.
[b] HPLC yield.
[c] Conversion = 100 – unreacted starting material **1a**.
[d] Zinc was 0.13 mmol.
[e] Isopropyl alcohol (IPA) was 0.17 mmol.
[f] Ascorbic acid was 0.1 mmol.
[g] IPA was 4 mmol.
[h] Tetrakis(dimethylamino)ethylene (TDAE) was 0.2 mmol.
[i] 1 mmol of H_2O was added.
[j] The reaction mixture was refluxed under atmospheric pressure.

Table 2
Reductive coupling reaction of various conditions and aryl bromides catalyzed by TDAE/$PdCl_2$ system.[a]

Entry	Starting material	$PdCl_2$ (mmol)	Temperature (°C)	Time (h)	Yield[b] (%)		Conversion[c] (%)	Selectivity (%)
					2	**3**		
1	**1a**	0.01	120	1	35.9	7.0	43.4	83.6
2	**1a**	0.01	180	1	75.8	18.5	94.3	80.4
3	**1a**	0.025	120	1	63.0	22.5	90.4	73.7
4	**1a**	0.01	120	4	78.3	19.2	97.5	80.3
5	**1a**	0.0025	120	4	62.7	25.0	88.4	71.5
6	**1b**	0.01	120	1	13.1	11.2	25.6	53.9
7	**1b**	0.01	120	4	39.4	39.8	80.5	49.7
8	**1c**	0.01	120	1	17.3	14.5	32.4	54.4
9	**1c**	0.01	120	4	55.1	41.1	96.2	57.2

[a] Reaction conditions: aryl bromide (0.1 mmol), TDAE (0.2 mmol), CO_2 (3 mL), 14 MPa.
[b] HPLC yield.
[c] Conversion = 100 − unreacted starting material **1**.

yield. It was found that the reaction time of at least 4 h at 120 °C was required for completion of the reaction (Table 2, entries 4, 7, 9). When the reaction time was 1 h at 120 °C, a large amount of starting material was recovered (Table 2, entries 1, 6, 8). The coupling product yield was raised in accordance with the reaction temperature and the catalyst loading, whereas the reaction selectivity was kept high regardless of reaction parameters (Table 2, entries 1, 2, 3). A decrease in the amount of catalyst had slightly negative effect on the reaction selectivity (Table 2, entry 4, 5). Next, we investigated the influence of substituent groups of aryl bromides on the coupling product yield. While there was a small difference in the conversion of compound **1**, the reaction selectivity was greatly different (Table 2, entries 4, 7, 9). The best selectivity was obtained with compound **1a** having a tridecafluorohexyl group (Table 2, entry 4). We supposed that this phenomenon is attributed to high compatibility between fluorine compounds and $scCO_2$.[15,17,18]

To facilitate the product isolation is another interesting possibility in replacing organic solvents with $scCO_2$.[7] Then, we tried to purify the crude product obtained by a reductive coupling. The adopted purification process utilizes a difference in the solubilities of reaction mixture components in $scCO_2$. Thus we connected the second vessel (empty vessel) to the reaction vessel, and carried out the purification by passing $scCO_2$ through the reaction mixture from the reaction vessel to the second vessel (Fig. 2). We considered that purification would be achieved as follows. The unreacted starting material, the side (debromination) product and the excess base can be readily stripped off together with $scCO_2$, because those compounds are readily dissolved in $scCO_2$. The target compound **2a** having a lower solubility slowly migrates to the second vessel together with $scCO_2$ and deposits in the second vessel with relatively low temperature. The palladium catalyst remains in the reaction vessel since its solubility in $scCO_2$ is very low.

First, the reaction vessel containing the reaction mixture which is listed in Table 2, entry 2 was heated at 200 °C, and liquid CO_2 was pressurized by a pump up to 14 MPa and controlled successively with 2 mL/min flow for 1 h. The target compound **2a** recovered from the second vessel was 8 mg (16%). Next, the purification was carried out with increasing the pressure to 25 MPa. Liquid CO_2 was passed into the vessel with 2 mL/min flow for 0.5 h. Yellow powder was deposited on the inner wall and the top of the second vessel (Fig. 3a). Purity of the obtained yellow powder (target compound **2a**), which was measured by HPLC, was more than 99% and the yield was 17 mg (35%). It is thought that an increase in the yield results from an increase in solubility of **2a** with increasing CO_2 density. Yield of the purified product **2a** using $scCO_2$ was considerably lower than the reaction yield (75.8%). It is thought that the recovery losses were large due to a small scale synthesis. The black residue remained in the reaction vessel (Fig. 3b), which were analyzed by energy dispersive spectroscopy (EDS). Results for the yellow powder and the black residue are shown in Fig. 4a and b, respectively. The yellow powder contained expected elements (C, F, S), and palladium was not detected (Fig. 4a). The black residue consisted of palladium catalyst, ligand (TDAE), bromine compound, and a small amount of **2a**. Fig. 5 shows a differential scanning calorimetric analysis (DSC) thermogram of the yellow powder. This is identical with the thermogram of BFH-4T reported by Facchetti et al.[19] The sharpness of the observed transition peaks suggest high purity of the yellow powder, which was achieved by the afore-described procedure.

In conclusion, the TDAE/$PdCl_2$ system was the most suitable for reductive coupling of aryl bromides in $scCO_2$. A use of the fluorine-

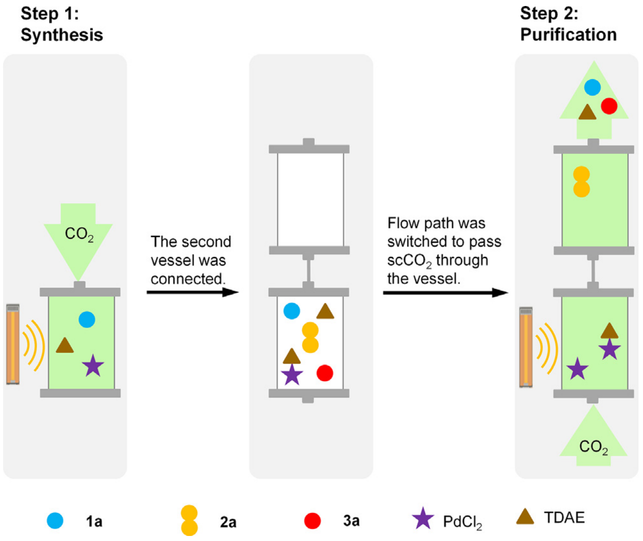

Fig. 2. Schematic illustration for the synthesis and purification of 5,5‴-bis(tridecafluorohexyl)-2,2′:5′,2″:5″,2‴-quaterthiophene **2a**.

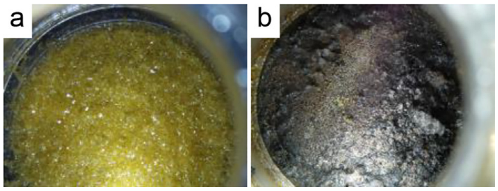

Fig. 3. Micrographs of (a) the top of second and (b) the bottom of reaction vessel (7.5 mm i.d.) after the purification process.

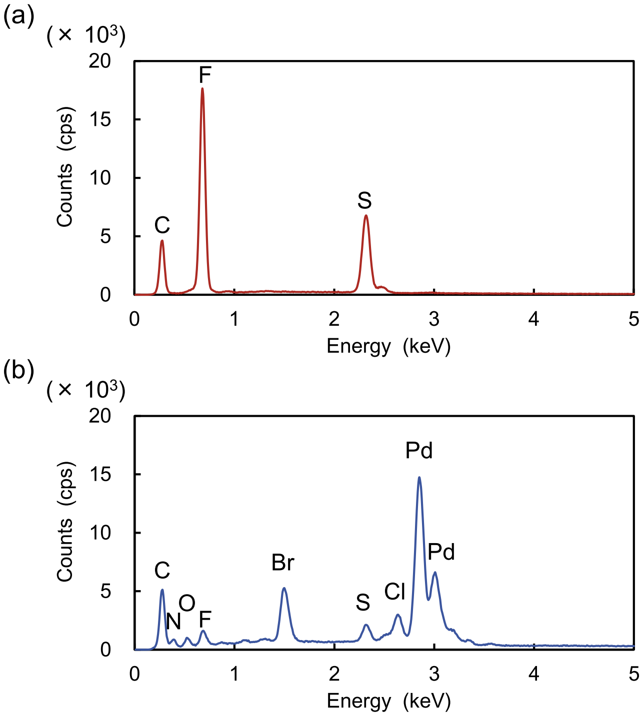

Fig. 4. EDS spectra for (a) the yellow powder and (b) the black residue shown in Fig. 3a and b, respectively.

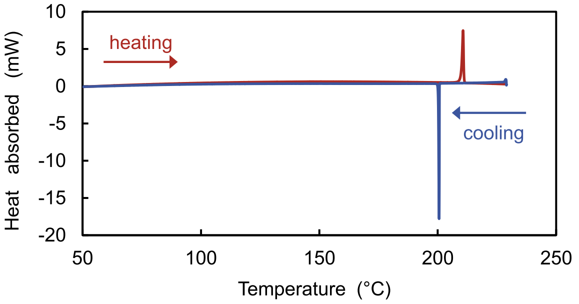

Fig. 5. DSC trace of the yellow powder shown in Fig. 3a indicating reversible thermal transitions (under nitrogen at a scanning rate of 5 °C min^{-1}).

containing aryl bromide (5-bromo-5′-(tridecafluorohexyl)-2,2′-bithiophene) provided the coupling product (BFH-4T: n-type organic semiconducting material) in good reaction selectivity and high product yield, which is attributed to high compatibility between fluorine compounds and $scCO_2$. We could easily purify BFH-4T from the reaction mixture by sweeping $scCO_2$. This is the first attempt at synthesis as well as purification of an organic semiconducting material using $scCO_2$. This strongly indicates that the procedure described above is applicable to a wide range of organic semiconducting materials.

Typical procedure for reductive coupling reactions

0.1 mmol of 5-bromo-5′-(tridecafluorohexyl)-2,2′-bithiophene **1a**, 0.01 mmol of $PdCl_2$, and 0.2 mmol of TDAE were placed in a 3 mL high-pressure stainless steel vessel with the sintered stainless steel filter at both ends (75 mm × 7.5 mm i.d. empty column) charged with a stirring bar. Liquid CO_2 was added to a pressure of 7 MPa using a high-pressure liquid plunger pump. A pressure of CO_2 was regulated using an automatic back pressure regulator. The vessel was heated at 180 °C to a stabilized pressure of 10 MPa, then more CO_2 was added to obtain a pressure of 14 MPa. The reaction was carried out under the above conditions with the stirring speed of 1200 rpm for 1 h. Then, the stirrer and temperature controls were switched off and CO_2 was carefully vented as gas to the atmospheric pressure. The resulting reaction mixture was extracted with tetrahydrofuran and extract was analyzed by HPLC to determine reaction selectivity and yield.

Procedure for product purification

After the reaction was completed, the second vessel (empty vessel) was connected to the reaction vessel, and flow path was switched to pass $scCO_2$ through the reaction mixture from the reaction vessel to the second vessel. Liquid CO_2 was pressurized by a pump up to 25 MPa and controlled successively with 2 mL/min flow at 200 °C (only reaction vessel) for 0.5 h. Then, the vessel was cooled to room temperature and the remaining CO_2 was slowly vented out from the vessel. The resulting powder in the second vessel was collected. 17 mg (35%) of **2a** was obtained as a yellow powder; mp: 211 °C, IR (KBr): 3056, 1460, 1439, 1365, 1293, 1202, 1142, 1085, 807, 791, 710, 663 cm^{-1}.

Reproducibility of the most experimental data have been confirmed.

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