"Radical-Controlled" Oxidative Polymerization of 4-Phenoxyphenol by a Tyrosinase Model Complex Catalyst to Poly(1,4-phenylene oxide)

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ABSTRACT: A new concept, "radical-controlled" oxidative polymerization of phenols catalyzed by a tyrosinase model complex, has been proposed. A μ-η^2:η^2-peroxo dicopper(II) species formed by the reaction between the catalyst complex and dioxygen, reacted with phenol to give "controlled" phenoxy radical−copper(I) intermediate instead of "free" phenoxy radical. The polymerization of 4-phenoxyphenol was performed by the use of the tyrosinase model complexes, (hydrotris(3,5-diphenyl-1-pyrazolyl)borate)copper (Cu(Tpzb)) chloride complex and (1,4,7-R_3-1,4,7-triazacyclononane)copper (Cu(L^R): R = isopropyl (iPr), cyclohexyl (cHex), *n*-butyl (nBu)) dichloride complexes. The structures of these complexes were determined by X-ray crystallography, indicating that the order of steric repulsion of the substituents (R) in the Cu(L^R) complexes is cHex > iPr > nBu. Very little of C−C coupling dimers were afforded with the Cu(Tpzb) catalyst in toluene or THF, and with the Cu(L^{iPr}), Cu(L^{cHex}), or Cu(L^{nBu}) catalyst in toluene. The selectivity of para C−O coupling increased with an increase in the steric hindrance of R for the Cu(L^R) catalysts. On the other hand, the formation of C−C dimers was clearly observed in the polymerization catalyzed by a copper/diamine complex or horseradish peroxidase. The selective polymerization almost without the C−C dimer formation produced crystalline poly(1,4-phenylene oxide) having a melting point, although the polymer contained small amounts of 1,2,4-trioxybenzene units (ca. 1−5 unit %). However, the polymers obtained in the cases involving the C−C dimer formation showed no clear melting points. The reaction mechanism of catalytic cycle and oxidative polymerization is also discussed.

Introduction

Oxidative polymerization of phenols catalyzed by a metal complex[1−3] or an enzyme[4−7] provides an environmentally benign method to synthesize phenolic polymers, in which the reaction conditions are mild and the byproduct is only H_2O. Some 2,6-disubstituted phenols, where both the *o*-positions are protected, produced linear polymers having 1,4-oxyphenylene units. In particular, synthesis and properties of poly(2,6-dimethyl-1,4-phenylene oxide) have been investigated in detail, because this polymer is widely used as an engineering plastics in industrial fields.[8] On the other hand, catalytic oxidative polymerization of 2,6-unsubstituted phenols leading to poly(1,4-phenylene oxide) (PPO) has long been an attractive target in the field of polymer synthesis. Despite many efforts, no successful regioselective polymerization of 2,6-unsubstituted phenols has been reported so far,[2,6,9] since it was very difficult to control the regioselectivity of coupling of the phenoxy radical intermediates by the conventional catalysts, for example, a copper(I)/diamine complex[9] and horseradish peroxidase (HRP).[6]

It was reported that copper(I)/diamine complexes reacted with dioxygen to give bis(μ-oxo) dicopper(III) complexes.[10] In the reaction of HRP with hydrogen peroxide, Fe(IV)═O intermediates were formed.[11] These active oxygen complexes were subjected to the reaction with phenols to afford "free" phenoxy radical intermediates.[10,12] These data suggest that the regioselective coupling cannot be achieved by the catalysts generating "electrophilic" or "radical" active oxygen intermediates. On the basis of this view (Figure 1), we have paid much attention to a "nucleophilic" μ-η^2:η^2-peroxo dicopper(II) complex **1**,[13,14] a copper−dioxygen model complex for tyrosinase, and reached a working hypothesis as follows: complex **1** abstracts protons (not hydrogen atoms) from phenols to give phenoxo−copper(II) complex **2**, equivalent to phenoxy radical−copper(I) complex **3**. Intermediates **2** and/or **3** are not "free" radicals but "controlled" radicals. Thus, if a catalyst generates (and regenerates) only a nucleophilic active oxygen intermediate, followed by the reaction with phenols to give the "controlled" radical without formation of the "free" radical, this regioselectivity of the subsequent coupling

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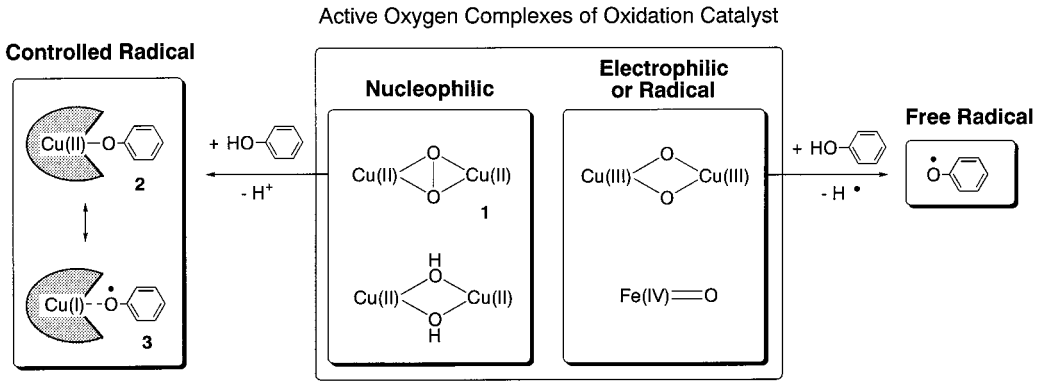
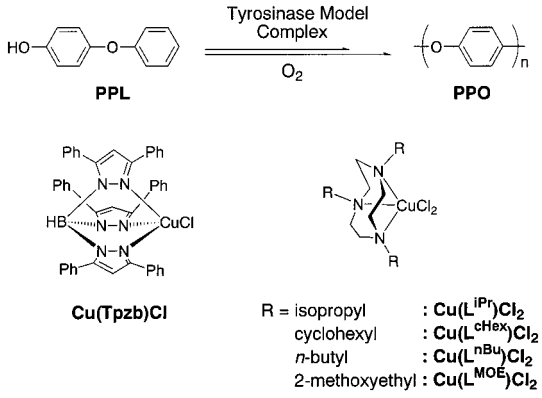


Figure 1. Working hypothesis for the control of phenoxy radical coupling by oxidation catalyst.

Scheme 1



may be entirely regulated. The concept of this "controlled" phenoxy radical in an attempt to avoid coupling at open *o*-position(s) of phenols has been already proposed, and in this direction, the oxidative polymerization of *o*-cresol using copper complexes with 2-alkylpyridines to give high molecular weight polymers has been reported.[15] Our concept is distinguished by the exclusive formation of "controlled" phenoxy radicals, and hence, we call this new concept "radical-controlled" oxidative polymerization.

Very recently we achieved the "radical-controlled" oxidative polymerization of 4-phenoxyphenol (PPL) catalyzed by tyrosinase model complexes (Scheme 1). This was the first synthesis of crystalline PPO having a melting point by the catalytic oxidative polymerization method,[16] although the synthesis by other tedious procedures has been reported.[17−19] The tyrosinase model complexes, (hydrotris(3,5-diphenyl-1-pyrazolyl)borate)-copper (Cu(Tpzb)) complex[14] and (1,4,7-triisopropyl-1,4,7-triazacyclononane)copper (Cu(L^{iPr})) complex[20] were employed. In this paper, (1,4,7-R_3-1,4,7-triazacyclononane)copper (Cu(L^R): R = cyclohexyl (cHex), *n*-butyl (nBu), and 2-methoxyethyl (MOE)) complexes were also examined as catalysts, compared with the copper(I)/diamine complex, HRP, and tyrosinase catalysts.

Experimental Section

Materials and Method. Dichloromethane and diethyl ether were carefully purified by refluxing/distilling under argon atmosphere from P_2O_5 and sodium benzophenone ketyl, respectively. THF was of commercial anhydrous grade. Horseradish peroxidase (activity: more than or equal to 100 units/mg) and tyrosinase from mushrooms (activity: about 500 units/mg) were purchased from Wako Pure Chemical Industries. Other reagents and solvents were commercially available and used without further purification. Preparation and handling of the copper complexes were performed under argon atmosphere using standard Schlenk techniques.

Caution! It is noted that perchlorate salts are potentially explosive and should be handled only in small quantities with appropriate precautions.

Measurements. High-pressure liquid chromatography (HPLC) was performed on a Tosoh PD-8020 system connected to a Tosoh PD-8020 photodiode array set at 278 nm. Liquid chromatography−mass spectroscopy (LC-MS) was carried out on a Hewlett-Packard HP-1100 chromatography equipped with a Micromass Quattro II spectrometer. The mass spectrum was recorded by scanning in the mass range from *m*/*z* 50 to 500 with an atmosphere pressure chemical ionization interface in the negative mode at a cone voltage of 30 V. For HPLC and LC-MS analyses, a YMC ODS-AM/AM-304 column was used with methanol/water as eluent. Size exclusion chromatographic (SEC) analysis was performed on a Tosoh SC-8020 system connected to a Tosoh RI-8020 differential refractometer. Two Tosoh TSKGEL α-M columns were used with DMF containing 0.4 wt % LiCl as eluent at 60 °C. The calibration curves for SEC analysis were obtained by using standard polystyrenes. NMR spectra were recorded on a JEOL LA600 (600 MHz) spectrometer. FT-IR spectra were obtained by using KBr pellets on a JASCO FT/IR 550 or on a Perkin-Elmer Paragon 1000 instrument. Electronic spectra were recorded on a JASCO V-570 spectrometer. Differential scanning calorimetric (DSC) analysis was carried out under nitrogen on a Mac Science DSC 3200S calorimeter. The first heating was performed from room temperature to 300 °C at a rate of 10 °C/min, and the temperature was kept at 300 °C for 5 min, followed by cooling from 300 °C to room temperature at a rate of 10 °C/min. The procedure of the second heating was the same as that of the first one.

Synthesis of Cu(Tpzb)Cl. To a solution of $CuCl_2 \cdot 2H_2O$ (0.122 g, 0.716 mmol) in a mixture solvent of dichloromethane/acetone (15 mL/5 mL) was added K(Tpzb)[14] (0.539 g, 0.761 mmol) dissolved in dichloromethane (15 mL). The solution gradually turned red, and a small amount of white solid was precipitated. After the recation was stirred for 1 h, the solvent was removed under vacuum. The residue was extracted with dichloromethane and the part of organic solution was separated by filtration. The organic solvent was evaporated under reduced pressure to give a red solid. Recrystallization from dichloromethane/heptane at −30 °C gave a red powdery product (0.264 g, 48%). FT-IR (KBr, cm^{-1}): 3205, 1567 1486, 1469, 1256, 1189, 1082, 1060, 979, 760, 690, 548. UV−vis (dichloromethane, λ_{max} nm (ϵ $cm^{-1}M^{-1}$)): 342 (2610), 431 (1900), 863 (200). Anal. Calcd for $C_{45}H_{34}N_6BCuCl$: C, 70.32; H, 4.46; N, 10.93; Cl, 4.61. Found: C, 69.76; H, 4.42; N, 10.88; Cl, 4.34.

Synthesis of Cu(L^{iPr})Cl_2. In a 50 mL Schlenk tube, (L^{iPr})$HClO_4$[21] (0.320 g, 0.899 mmol) and powdered KOH (0.214 g, 3.81 mmol) were reacted in toluene (30 mL) overnight. The residue ($KClO_4$) was filtered off, and the solvent was removed under vacuum. To a solution of $CuCl_2 \cdot 2H_2O$ (0.142 g, 0.833 mmol) in methanol (20 mL) was added a solution containing free base ligand (L^{iPr}) in methanol (20 mL). The solution

immediately turned green. After this was stirred for 1 h, the solvent was removed under vacuum. Recrystallization from diethyl ether/methanol at −30 °C gave a pure product of green powder (0.200 g, 62%). FT-IR (KBr, cm^{-1}): 2971, 2866, 1495, 1458, 1384, 1366, 1148, 1075, 965, 762, 718, 604. UV−vis (dichloromethane, λ_{max} nm (ϵ cm^{-1} M^{-1})): 404 (1010), 752 (150). Anal. Calcd for $C_{15}H_{33}N_3CuCl_2$: C, 46.21; H, 8.53; N, 10.78; Cl, 18.19. Found: C, 45.93; H, 8.31; N, 10.62; Cl, 18.65.

Synthesis of Cu(L^{cHex})Cl_2. A solution of sodium hydroxide (1.07 g, 26.8 mmol) and 1,4,7-triazacyclononane trihydrochloride (2.04 g, 8.54 mmol) in ethanol (20 mL) was stirred for a few hours at room temperature, filtered, and evaporated. To the residue were added xylenes (20 mL), cyclohexyl bromide (11.4 g, 69.8 mmol), and potassium hydroxide (4.14 g, 73.9 mmol), and the solution was kept stirring at 120 °C under argon for 72 h. Then, the reaction mixture was filtered and evaporated, and a solution of sodium perchlorate monohydrate (1.27 g, 9.07 mmol) in methanol (20 mL) was added. To the solution was added distilled water dropwise with stirring, and then, a white solid precipitated. The solid was filtered and dried in vacuo, giving 1.27 g (2.66 mmol) of 1,4,7-tricyclohexyl-1,4,7-triazacyclononane hydrogen perchlorate ((L^{cHex})$HClO_4$) (31% yield). ^{1}H NMR (acetone-d_6): δ 1.06−1.22 (3H, m), 1.26−1.56 (12H, m), 1.65 (3H, d), 1.87 (12H, t), 2.78−2.94 (9H, m), 3.08−3.20 (6H, m). FT-IR (KBr, cm^{-1}): 2930, 2857, 2631, 1486, 1457, 1385, 1351, 1324, 1299, 1278, 1215, 1164, 1094, 955, 898, 845, 750, 622. Anal. Calcd for $C_{24}H_{46}N_3ClO_4$: C, 60.55; H, 9.74; N, 8.83; Cl, 7.45. Found: C, 60.42; H, 9.86; N, 8.64; Cl, 7.63.

Cu(L^{cHex})Cl_2 complex was obtained in a similar manner as the reaction used to obtain the Cu(L^{iPr})Cl_2 complex. Yield: 79%. FT-IR (KBr, cm^{-1}): 2957, 2931, 2872, 1500, 1457, 1284, 1084, 1005, 984, 789, 597. UV−vis (dichloromethane, λ_{max} nm (ϵ $cm^{-1}M^{-1}$)): 402 (830), 756 (120). Anal. Calcd for $C_{24}H_{45}N_3CuCl_2$: C, 56.51; H, 8.89; N, 8.24; Cl, 13.90. Found: C, 56.22; H, 8.93; N, 8.21; Cl, 14.58.

Synthesis of Cu(L^{nBu})Cl_2. A solution of sodium hydroxide (1.14 g, 28.5 mmol) and 1,4,7-triazacyclononane trihydrochloride (2.22 g, 9.29 mmol) in ethanol (20 mL) was stirred for a few hours at room temperature, filtered, and evaporated. To the residue, toluene (20 mL), *n*-butyl bromide (5.27 g, 38.5 mmol), and potassium hydroxide (2.21 g, 39.5 mmol) were added, and the solution was kept stirring at room temperature under argon for 72 h. Then, the reaction mixture was filtered and evaporated, and a solution of sodium perchlorate monohydrate (6.53 g, 46.6 mmol) in ethylene glycol (20 mL) was added. To the solution, distilled water was added dropwise with stirring, and then, a white solid precipitated. The solid was filtered and dried in vacuo, giving 1.53 g (3.84 mmol) of 1,4,7-tri-*n*-butyl-1,4,7-triazacyclononane hydrogen perchlorate ((L^{nBu})$HClO_4$) (41% yield). ^{1}H NMR (acetone-d_6): δ 0.96 (9H, t), 1.36−1.43 (6H, m), 1.62−1.67 (6H, m), 2.85 (1H, s), 2.97−3.06 (18H, m). ^{13}C NMR (acetone-d_6): δ 14.1, 20.9, 29.3, 50.2, 56.2. FT-IR (KBr, cm^{-1}): 2958, 2933, 2872, 2812, 1494, 1472, 1378, 1090, 753, 624. Anal. Calcd for $C_{18}H_{40}N_3ClO_4$: C, 54.32; H, 10.13; N, 10.56; Cl, 8.91. Found: C, 54.30; H, 9.97; N, 10.61; Cl, 8.82.

Cu(L^{nBu})Cl_2 complex was obtained in a similar manner as the reaction used to obtain the Cu(L^{iPr})Cl_2 complex. Yield 92%. FT-IR (KBr, cm^{-1}): 2939, 2856, 1490, 1456, 1375, 1270, 1121, 1099, 1033, 968, 900, 811, 762, 640, 630. UV−vis (dichloromethane, λ_{max} nm (ϵ $cm^{-1}M^{-1}$)): 392(1060), 714(90). Anal. Calcd for $C_{18}H_{39}N_3CuCl_2$: C, 50.05; H, 9.10; N, 9.73; Cl, 16.41. Found: C, 49.71; H, 8.93; N, 9.65; Cl, 16.65.

Synthesis of Cu(L^{MOE})Cl_2. To a solution of 1,4,7-triazacyclononane (1.00 g, 7.75 mmol) in toluene (40 mL) were added 2-methoxyethyl bromide (4.31 g, 31.0 mmol) and potassium hydroxide (1.74 g, 31.0 mmol), and the solution was stirred at 80 °C under argon for 6 h. Then, the reaction mixture was filtered, evaporated, and distilled. As the distillate (about 185 °C/0.2 mmHg), 1.98 g (6.35 mmol) of 1,4,7-tris(2-methoxyethyl)-1,4,7-triazacyclononane−hemihydrate (L^{MOE}·0.5 H_2O) (82% yield). ^{1}H NMR (chloroform-d_1): δ 2.73 (6H, t), 2.79 (12H, s), 3.34 (9H, s), 3.46 (6H, t). ^{13}C NMR (chloroform-d_1): δ 56.7, 58.1, 58.9, 71.7. FT-IR (KBr, cm^{-1}): 3480, 2925, 2874, 2814, 1652, 1456, 1359, 1120. Anal. Calcd for $C_{15}H_{34}N_3O_{3.5}$: C, 57.66; H, 10.97; N, 13.45. Found: C, 57.97; H, 11.45; N, 13.57.

To a solution of $CuCl_2$·$2H_2O$ (0.193 g, 1.13 mmol) in methanol (20 mL) was added a solution containing free base ligand (HL^{MOE}) (0.364 g, 1.20 mmol) in methanol (10 mL). The solution immediately turned green. After the reaction was stirred for 2 h, the solvent was removed under vacuum. Crystallization from diethyl ether/methanol at −30 °C yielded a pure product as a green powder, Cu(L^{MOE})Cl_2·CH_3OH (0.393 g, 75%). FT-IR (KBr, cm^{-1}): 2888, 1622, 1458, 1350, 1262, 1198, 927, 824, 772, 726, 539. UV−vis (dichloromethane, λ_{max} nm (ϵ cm^{-1} M^{-1})): 387 (1700), 717 (200). Anal. Calcd for $C_{16}H_{37}N_3CuCl_2O_4$: C, 40.89; H, 7.94; N, 8.94; Cl, 15.09. Found: C, 40.38; H, 7.36; N, 9.42; Cl, 15.6.

X-ray Structure Determination of Cu(Tpzb)Cl, Cu(L^{iPr})Cl_2, Cu(L^{cHex})Cl_2 and Cu(L^{nBu})Cl_2. The structures of Cu(Tpzb)Cl, Cu(L^{iPr})Cl_2, Cu(L^{cHex})Cl_2, and Cu(L^{nBu})Cl_2 were determined by means of X-ray crystallography. The detail of measurement, the ORTEP presentations of these complexes, and their structural information are available in the Supporting Information.

Synthesis of 4-[4-(4-Phenoxyphenoxy)phenoxy]phenol (p-4) and 2-(4-phenoxyphenoxy)-4-phenoxyphenol (o-4). Compounds p-4 and o-4 were prepared and characterized according to the literature.[9]

Synthesis of 4,4′-Diphenoxy-2,2′-diphenol (oo-22). To a mixture of magnesium (0.546 g, 22.5 mmol) and 1,2-dibromoethane (0.1 mL) in anhydrous diethyl ether (50 mL) was added 2-bromo-4-phenoxyanisole[9] (5.61 g, 20.1 mmol) in anhydrous diethyl ether (50 mL). The mixture was refluxed with stirring for 23 h, followed by the addition of 2-bromo-4-phenoxyanisole (5.54 g, 19.9 mmol) and $CoCl_2$ (0.20 g, 1.5 mmol) to the mixture. Subsequently, the mixture was kept at room temperature under stirring for 94 h and refluxed for 6 h. Water (100 mL) and aqueous 3 M HCl (6.7 mL) were added to the mixture, and the layer of diethyl ether was separated off. The organic solution was washed twice with saturated NaCl solution (100 mL), dried over Na_2SO_4, and evaporated under reduced pressure. The product, 2,2′-dimethoxy-5,5′-diphenoxydiphenyl (2.45 g, 6.15 mmol), was separated by silica gel column chromatography (hexanes−ethyl acetate) (yield 31%).

A mixture of 2,2′-dimethoxy-5,5′-diphenoxydiphenyl (2.45 g, 6.15 mmol) and 57% HI solution (13.5 g) in acetic acid (34 mL) was refluxed for 34 h and cooled to room temperature. To the reaction mixture was added a small amount of $Na_2S_2O_3$ aqueous solution to decolorize the mixture. Then, toluene−ethyl acetate (100 mL) was added, and the mixture was neutralized by $NaHCO_3$ solution. The parts containing the organic solution were washed with saturated NaCl solution and dried over Na_2SO_4, followed by concentration of the organic solvents under reduced pressure. The residue was subjected to purification by silica gel column chromatography (hexanes−ethyl acetate), giving 1.08 g (2.93 mmol) of oo-22 (yield 48%). Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.81; H, 4.91. Found: C, 78.01; H, 4.81. ^{1}H NMR (acetone-d_6): δ 6.93−7.05 (12H, m), 7.31 (4H, t), 8.36 (2H, bs). ^{13}C NMR (acetone-d_6): δ 118.3, 118.5, 121.1, 123.3, 123.4, 127.5, 130.5, 150.5, 151.2, 159.5. FT-IR (KBr, cm^{-1}): 3346, 3064, 3039, 1589, 1487, 1416, 1353, 1214, 1072, 957, 874, 818, 752, 690.

Synthesis of 4-(4-Phenoxyphenoxy)-2,2′-diphenol (oo-13). *N*-Bromosuccinimide (24.8 g, 0.139 mol) dissolved in DMF (50 mL) was added dropwise to a solution of 2,2′-diphenol (25.9 g, 0.139 mol) and DMF (100 mL) at 0 °C for 3 h, and the mixture was stirred at 1−13 °C for 11 h. To the reaction mixture was added water (600 mL), and it was extracted by toluene (150 mL × 2). The organic layer and the extracts were combined, washed with water, and dried over Na_2SO_4. After concentration of the organic solution, the residue was subjected to distillation under reduced pressure to produce 26.1 g (0.0741 mmol) of crude 4-bromo-2,2′-diphenol (75% purity, yield 53%) as the distillate of 128−152 °C/0.1−0.3 mmHg.

The crude 4-bromo-2,2′-diphenol (26.1 g) in anhydrous THF (100 mL) was added to a mixture of 60% NaH (8.58 g, 0.215 mol) and anhydrous THF (50 mL) under stirring. To the

mixture was added dimethyl sulfate (30.2 g, 0.240 mol) dissolved in anhydrous THF (30 mL), and the mixture was stirred at room temperature for 11 h. Water (500 mL), aqueous 3 M HCl (6 mL), and toluene (100 mL) were added to the reaction mixture, which was extracted with toluene (100 mL × 2). The organic layer and the extracts were combined and washed with water, followed by drying over Na_2SO_4. The organic solution was evaporated under reduced pressure, and the crude product was separated by distillation under reduced pressure. The distillate (13.3 g) obtained at 130−140 °C/0.6 mmHg was subjected to silica gel column chromatography (hexane−chloroform) and subsequent recrystallization (hexane−chloroform), giving 9.51 g (98% purity, 0.0317 mmol) of 5-bromo-2,2′-dimethoxydiphenyl (yield 43%).

A mixture of 4-phenoxyphenol (2.75 g, 14.8 mmol) and sodium methoxide solution from Na (0.343 g, 14.8 mmol) and methanol (55 mL) was evaporated under reduced pressure. After toluene (100 mL) was added to the mixture, the solvent was again removed by evaporation until the residue became viscous. 5-Bromo-2,2′-dimethoxydiphenyl in 98% purity (4.15 g, 13.8 mmol) and CuCl (0.202 g, 2.04 mmol) were added to the mixture, which was stirred at 150−200 °C under nitrogen for 20 h. Aqueous 3 M HCl (50 mL), water (100 mL), and chloroform (100 mL) were poured into the mixture under vigorous stirring, and the formed precipitates were removed by filtration. The organic layer and the extract of chloroform (100 mL) were washed twice by water (100 mL), dried over Na_2SO_4, and concentrated by evaporation under reduced pressure. The residue was subjected to silica gel column chromatography (hexane−chloroform), giving 3.30 g (8.29 mmol) of 2,2′-dimethoxy-5-(4-phenoxyphenoxy)diphenyl (yield 60%).

A mixture of 2,2′-dimethoxy-5-(4-phenoxyphenoxy)diphenyl (3.30 g, 8.29 mmol) and 57% HI (25 g, 111 mmol) in acetic acid (60 mL) was refluxed for 14 h. After cooling to room temperature, water (200 mL) was added to the reaction mixture. The organic layer and the extract (toluene−ethyl acetate, 100 mL × 2) were decolorized by a small amount of $Na_2S_2O_3$ aqueous solution, washed with water (100 mL × 2), dried over Na_2SO_4, and concentrated by evaporation under reduced pressure. The product (oo-13) was separated by using silica gel column chromatography (toluene-ethyl acetate). Yield: 1.30 g (3.49 mmol, 42%). Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.81; H, 4.91. Found: C, 77.72; H, 4.81. ^{1}H NMR (acetone-d_6): δ 6.94−7.05 (11H, m), 7.09 (1H, t), 7.24 (1H, t), 7.29 (1H, d), 7.35 (2H, t), 8.39 (2H, bs). ^{13}C NMR (acetone- d_6), δ 117.4, 118.5, 118.8, 120.0, 120.4, 121.3, 121.4, 123.1, 123.7, 126.4, 128.3, 129.9, 130.7, 132.5, 151.15, 151.17, 152.9, 154.8, 155.3, 159.0. FT-IR (KBr, cm^{-1}): 3256, 3062, 3040, 1589, 1498, 1448, 1414, 1352, 1209, 1097, 913, 872, 832, 756, 691.

Typical Procedure of Polymerization of PPL Catalyzed by Copper Complexes. Under dioxygen (1 atm), PPL (112 mg, 0.60 mmol), Cu(L^{iPr})Cl_2 (12 mg, 0.030 mmol), 2,6-diphenylpyridine (69 mg, 0.30 mmol), and diphenyl ether (80 mg, internal standard) in toluene (1.2 g) were kept at 40 °C with vigorous stirring. At 0.20 h, a small portion (10 mg) of the reaction mixture was sampled for determination of the conversion of PPL (9%) and the total yield of the dimers (8%) by HPLC. After 19 h (conversion 98%), a few drops of concentrated aqueous HCl was added, and a large amount of methanol was poured into the reaction mixture to precipitate the polymeric materials, which were collected by filtration, washed with methanol, and dried under vacuum to give 99 mg of the white polymer (yield 89%).

Typical Procedure of Polymerization of PPL Oxidized by 2,2′-Azobis(isobutyronitrile) (AIBN). A mixture of PPL (112 mg, 0.60 mmol), AIBN (98 mg, 0.60 mmol), and diphenyl ether (80 mg, internal standard) in toluene (1.2 g) was evacuated at liquid nitrogen temperature, thawed, and filled with nitrogen. The same procedure was repeated three times. The reaction was performed at 40 °C under stirring. After 120 h, a small portion (10 mg) of the reaction mixture was sampled and used for HPLC analysis to determine the conversion of PPL (27%) and the total yield of the dimers (15%). After 380 h (conversion 69%), a large amount of methanol was poured into the reaction mixture to precipitate the polymeric materials, which were collected by filtration, washed with methanol, and dried under vacuum to give 9 mg of the brownish polymer (yield 8%).

Polymerization of PPL Catalyzed by HRP. To HRP (2.4 mg) in phosphate buffer solution (pH 6.86, 1.2 mL) was added a mixture of PPL (112 mg, 0.60 mmol) and nitrobenzene (5 mg, internal standard) in dioxane (4.8 mL). Then 30% H_2O_2 (3.4 μL, 0.03 mmol) was added to the mixture every 0.25 h for 20 times at 25 °C under vigorous stirring. After 0.25 h, a small portion (10 mg) of the reaction mixture was sampled for determination of the conversion of PPL (11%) and the total yield of the dimers (7%) by HPLC. After 24 h (conversion 99%), a large amount of methanol was poured into the reaction mixture to precipitate the polymeric materials, which were collected by filtration, washed with methanol, and dried under vacuum to give 48 mg of the brownish polymer (yield 43%).

Oxidation of PPL Catalyzed by Tyrosinase. A mixture of PPL (112 mg, 0.60 mmol) and nitrobenzene (5 mg, internal standard) in acetone (3 mL) was added to tyrosinase (2.4 mg) in phosphate buffer solution (pH 6.86, 3 mL). The mixture was kept at 25 °C with vigorous stirring under air (1 atm). After 1 h, a small portion (10 mg) of the reaction mixture was sampled for HPLC analysis to determine the conversion of PPL (14%) and the yield of the dimers (<0.1%). Afterward, the reaction did not proceed any more. The reaction mixture was concentrated by evaporation under reduced pressure. The residue was separated by filtration and washed with water and subsequently diethyl ether to give 3 mg of dark brown products (yield 3%), which was insoluble in any organic solvents.

Results and Discussion

X-ray Structure Determination. The structures of Cu(Tpzb)Cl, Cu(L^{iPr})Cl_2, Cu(L^{cHex})Cl_2, and Cu(L^{nBu})Cl_2 were determined by X-ray crystallography (see Supporting Information). In the case of Cu(Tpzb)Cl, the structure consists of a discrete monomeric copper unit containing a N_3Cl ligand donor set, and the CuN_3 core is analogous to those of tyrosinase and hemocyanin.[14] The coordination environment about the copper centers is trigonally distorted tetrahedral, and the structural details of the ligand coordination are similar to those reported for the (hydrotris(3,5-diisopropyl-1-pyrazolyl)-borate)copper complex.[22]

The structures of Cu(L^{iPr})Cl_2, Cu(L^{cHex})Cl_2, and Cu(L^{nBu})Cl_2 contain discrete copper monomers with approximately square-pyramidal N_3Cl_2 ligand donor sets. In each of the complexes, the macrocyclic triamine is coordinated facially with two N atoms occupying equatorial positions and another N atom apically situated; chloride ions occupy the two remaining equatorial positions, and the copper(II) atom is displaced ca. 0.20 Å from this basal plane. These structural details of the ligand coordination are similar to those reported for (1,4,7-triazacyclononane)copper dichloride complex (Cu(L^H)Cl_2).[23] All the complexes have almost the same Cu−Cl bond lengths, which are nonequivalent and are typical for equatorial Cu−Cl bonding.[24] However, the order of average lengths of three Cu−N bonds is Cu(L^H)Cl_2 (2.12 Å) < Cu(L^{nBu})Cl_2 (2.16 Å) < Cu(L^{iPr})Cl_2 (2.18 Å) < Cu(L^{cHex})Cl_2 (2.20 Å), showing the effect of steric repulsion of substituted groups.

Dimer Formation from PPL. Table 1 summarizes the ratio of oxidative coupling dimers formed at the initial stage of polymerization of PPL using various catalysts. In entries 1−7, the polymerization catalyzed by Cu(Tpzb)Cl, Cu(L^{iPr})Cl_2, Cu(L^{cHex})Cl_2, Cu(L^{nBu})Cl_2, and Cu(L^{MOE})Cl_2 (5 mol % based on PPL) was performed under dioxygen (1 atm) in toluene or THF at 40 °C. For

Table 1. Dimer Formation at Initial Stage of Oxidative Polymerization of PPL[a]

							dimer ratio (%)[b]			
entry	catalyst	oxidant	solvent	time (h)	convn[b,c] (%)	dimer[b,d] (%)	p-4	o-4	oo-22	oo-13
1	Cu(Tpzb)Cl[e]	O_2[h]	toluene[l]	0.25	13	9	91	9	0	0
2	Cu(Tpzb)Cl[e]	O_2[h]	THF[l]	1.7	11	7	91	9	0	0
3	Cu(L^{iPr})Cl_2[e]	O_2[h]	toluene[l]	0.2	9	8	93	7	0	0
4	Cu(L^{iPr})Cl_2[e]	O_2[h]	THF[l]	7.5	12	9	89	7	1	3
5	Cu(L^{cHex})Cl_2[e]	O_2[h]	toluene[l]	0.2	7	7	95	5	0	0
6	Cu(L^{nBu})Cl_2[e]	O_2[h]	toluene[l]	0.2	12	12	90	9	0	1
7	Cu(L^{MOE})Cl_2[e]	O_2[h]	toluene[l]	24	12	10	88	9	0	3
8	CuCl/teed[f]	O_2[h]	toluene[l]	0.02	17	12	79	6	2	13
9		AIBN[i]	toluene[l]	120	27	15	82	4	2	12
10	HRP[g]	H_2O_2[j]	dioxane/buffer(8/2)[m]	0.25	11	7	37	17	8	38
11		AIBN[i]	dioxane/buffer(8/2)[m]	96	8	6	54	12	4	30
12	tyrosinase[g]	air[k]	acetone/buffer(5/5)[n]	1	14	<0.1				
13	-	AIBN[i]	acetone/buffer(5/5)[n]	96	13	6	22	9	10	59

[a] PPL (0.60 mmol). [b] Determined by HPLC. [c] Conversion of PPL. [d] Total yield of dimers. [e] Cu complex (0.030 mmol); 2,6-diphenylpyridine (0.30 mmol). [f] CuCl (0.030 mmol); teed (0.015 mmol). [g] Enzyme (2.4 mg). [h] Under dioxygen (1 atm) at 40 °C. [i] Oxidized by AIBN (0.60 mmol) under nitrogen at 40 °C. [j] 30% H_2O_2 (0.030 mmol) at 25 °C. [k] Under air (1 atm) at 25 °C. [l] Solvent (1.2 g). [m] Dioxane (4.8 mL), buffer of pH = 7 (1.2 mL). [n] Acetone (3 mL), buffer of pH = 7 (3 mL).

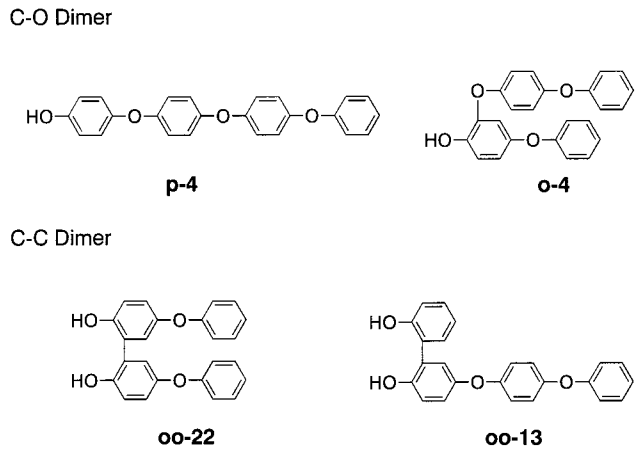


Figure 2. Oxidative coupling dimers of PPL.

comparison with the polymerization by using these catalysts, the polymerization catalyzed by CuCl/*N*,*N*′,*N*′,*N*′-tetraethylethylenediamine (teed), which was the sole catalyst reported for oxidative coupling of PPL,[9] HRP, and tyrosinase, was examined. The Cu/teed complex was used under dioxygen in toluene at 40 °C (entry 8). HRP catalyst with hydrogen peroxide in dioxane/buffer (8/2) (entry 10) and tyrosinase catalyst under air in acetone/buffer (5/5) (entry 12) were employed at 25 °C. As a model system of free phenoxy radical coupling, the polymerization of PPL oxidized by an equimolar amount of 2,2′-azobis(isobutyronitrile) (AIBN) was performed at 40 °C in the same solvent used for the above catalyst (entries 9, 11, and 13).

A small portion of the reaction mixture was taken out at the initial stage of the polymerization for HPLC analysis. In the case of CuCl/teed (entry 8), four dimers were detected by LC-MS spectroscopy. The structures of the dimers were identified as p-4, o-4, oo-22, and oo-13 (Figure 2) on the basis of the comparison of their NMR and absorption spectra with those of the authentic samples. Products p-4 and o-4 are formed by the C−O coupling, and formation of oo-22 and oo-13 is based on the C−C coupling. Almost no phenol and 4-(4-phenoxyphenoxy)phenol were detected. In the range of the PPL conversion less than 30%, the PPL conversion was fairly close to the total yield of these four dimers, and thereby, the dimer ratio can be taken as a good measure of the coupling regioselectivity.

For the CuCl/teed catalyst (entry 8), considerable amounts of the two C−C coupling dimers of oo-22 and oo-13 were detected, and p-4 selectivity was consequently low (79%). These dimer ratios were very similar to those obtained via free radical coupling by AIBN oxidation (entry 9), in which the formation of the C−C coupling dimers is characteristic. However, for Cu(Tpzb) in toluene (entry 1) and in THF (entry 2), and for Cu(L^{iPr}) (entry 3), Cu(L^{cHex}) (entry 5), and Cu(L^{nBu}) (entry 6) in toluene, no or very little C−C coupling dimers were detected, and high regioselectivity of p-4 was achieved (maximum 95%). In entries 3, 5, and 6, the order of p-4 selectivity was Cu(L^{nBu}) (90%) < Cu(L^{iPr}) (93%) < Cu(L^{cHex}) (95%) in good agreement with that of steric hindrance of the substituents from the X-ray analysis (vide supra). These data show that the regioselectivity of phenoxy radical coupling can be controlled by these catalysts. On the other hand, the dimerization catalyzed by Cu(L^{iPr}) in THF (entry 4) and Cu(L^{MOE}) in toluene (entry 7) gave the C−C coupling dimers to some extent.

In oxidative polymerization of phenols catalyzed by enzymes, an aqueous organic solvent is often used.[4−7] We first examined the oxidative coupling in the free radical model systems in dioxane/buffer (8/2) (entry 11) and acetone/buffer (5/5) (entry 13). The ratio of p-4 decreased and those of oo-22 and oo-13 increased with increasing water content of the solvent (entries 9, 11, and 13). These data indicate that the C−O/C−C selectivity can be drastically changed by the solvent polarity, but complete C−O selectivity could not be achieved. In the case of the HRP catalyst (entry 10), the dimer composition was close to that by AIBN in the same solvent (entry 11), suggesting that HRP catalyzed the oxidative coupling of free radical intermediates. The oxidation catalyzed by tyrosinase (entry 12) gave almost none of the dimers and insoluble dark-brown powdery materials (yield 3%) at 14% of PPL conversion, whereas AIBN oxidation (entry 13) produced the dimers in 6% yield at 13% of PPL conversion. In entries 11−13, all the reactions scarcely proceeded further conversion of PPL under these reaction conditions.

Polymerization of PPL. The oxidative polymerization of PPL was performed until PPL was not consumed any more. Then, the resulting polymer was isolated as the methanol-insoluble part (Table 2). In the case of the Cu(L^{MOE}) catalyst (entry 7), the consumption of PPL was extremely slow and did not increase beyond 29%, and

Table 2. Oxidative Polymerization of PPL[a]

entry	catalyst	oxidant	solvent	time (h)	convn[b] (%)	yield[c] (%)	M_n[d]	M_w[d]	1,2,4-unit[e] (unit%)	T_m[f] (°C)
1	Cu(Tpzb)Cl[g]	O_2[j]	toluene[m]	14	55	4	700	1100	1.2	186
2	Cu(Tpzb)Cl[g]	O_2[j]	THF[m]	70	91	54	1500	2900	4.8	194
3	$Cu(L^{iPr})Cl_2$[g]	O_2[j]	toluene[m]	19	98	89	1200	4700	5.1	171
4	$Cu(L^{iPr})Cl_2$[g]	O_2[j]	THF[m]	81	86	52	3800	13700	(8.0)[p]	nd[q]
5	$Cu(L^{cHex})Cl_2$[g]	O_2[j]	toluene[m]	210	76	28	600	700	0.8	186
6	$Cu(L^{nBu})Cl_2$[g]	O_2[j]	toluene[m]	23	87	40	800	1100	(2.6)[p]	184
7	$Cu(L^{MOE})Cl_2$[g]	O_2[j]	toluene[m]	168	29	0				
8	CuCl/teed[h]	O_2[j]	toluene[m]	24	100	77	5400	29100	(7.3)[p]	nd[q]
9		AIBN[k]	toluene[m]	380	69	8	1600	3100	(6.5)[p]	nd[q]
10	HRP[i]	H_2O_2[l]	dioxane/buffer(8/2)[n]	24	99	43	*o*	*o*	(8.3)[p]	nd[q]

[a] PPL (0.60 mmol). [b] Conversion of PPL, determined by HPLC. [c] Methanol-insoluble part. [d] Determined by SEC. [e] Estimated from the peak at 970 cm^{-1} based on the 1,2,4-trioxybenzene units by FT-IR spectra. [f] Temperature of the largest endothermic peak in the second scan of DSC measurement under nitrogen. [g] Cu complex (0.030 mmol), 2,6-diphenylpyridine (0.30 mmol). [h] CuCl (0.030 mmol), teed (0.015 mmol). [i] Enzyme (2.4 mg). [j] Under dioxygen (1 atm) at 40 °C. [k] Oxidized by AIBN (0.60 mmol) under nitrogen at 40 °C. [l] 30% H_2O_2 (0.060 mmol) at 25 °C. [m] Solvent (1.2 g). [n] Dioxane (4.8 mL), buffer of pH = 7 (1.2 mL). [o] Insoluble in the eluent (DMF) for SEC analysis. [p] These values may be inaccurate, because the phenylene units are neglected. [q] Not detected.

no methanol-insoluble polymer was obtained. The polymerizations catalyzed by the $Cu(L^{cHex})$ complex (entry 5) and that oxidized by AIBN (entry 9) were also very slow, but the conversions reached 76 and 69%, respectively, at the final stages. For the Cu(Tpzb) in toluene (entry 1), the consumption proceeded rapidly but no more than 55%. This complex seemed to be decomposed during the polymerization in toluene from the FT-IR analysis of the reaction mixture. In other cases (entries 2−4, 6, 8, 10), the conversions reached 86−100%, and the polymers were obtained in 40−89% yields.

In the systems with little or no C−C dimer formation (entries 1−3, 5, 6), white powdery polymers were obtained, which were almost soluble in DMF and partially soluble in chloroform. Number- and weight-average molecular weights (M_n and M_w) measured by size exclusion chromatography (SEC) in DMF at 60 °C were 600−1500 and 700−4700, respectively.

The polymer structure was primarily determined by NMR spectroscopy in DMF-d_7 at 80 °C. From the ^1H NMR spectrum of the typical polymer for the $Cu(L^{iPr})$ catalyst (entry 3), a main singlet peak at 6.93 ppm due to four hydrogen atoms of the 1,4-oxyphenylene unit, a small triplet peak at 7.24 ppm ascribed to two hydrogens at 3-positions of phenoxy group (tail unit), and small complicated multiplet peaks in 6.71−6.97 ppm were detected. The ^{13}C NMR spectrum of the polymer (entry 3) showed a major set (120.5 and 153.7 ppm) due to the 1,4-oxyphenylene unit, a minor set (116.8, 119.5, 150.0, and 158.5 ppm) ascribed to the 4-hydroxyphenyl group (head unit), another minor set (118.7, 123.6, 130.4, and 158.5 ppm) attributed to the phenoxy group (tail unit), and several unclear small peaks.

The further estimation of polymer structure was made by FT-IR spectroscopy. The spectrum patterns of the resulting polymers (entries 1−3, 5, 6) were very similar to that of PPO synthesized by Ullmann condensation.[17] However, the polymer from PPL showed a small peak at 970 cm^{-1}, which was not observed in the spectrum of PPO by the Ullmann synthesis. 2,4-Diphenoxyphenol[17] and o-4 each have a peak at 970 cm^{-1}, but neither 4-(4-phenoxyphenoxy)phenol[17] nor p-4 has this peak at 970 cm^{-1}. These spectral data indicate that the 970 cm^{-1} peak is based on the 1,2,4-trioxybenzenes (1,2,4-unit). The amount of the 1,2,4-unit was determined from the area ratio of the peak at 970 cm^{-1} against a peak at ca. 1500 cm^{-1} (C═C vibrations) on the basis of 25 unit % of o-4. With almost no formation of the C−C dimers (entries 1−3, 5, 6), the 1,2,4-unit ratios of these PPO obtained were 0.8−5.1 unit %. These data support the structure of these polymers containing 1,4-oxyphenylene linkage as the major unit.

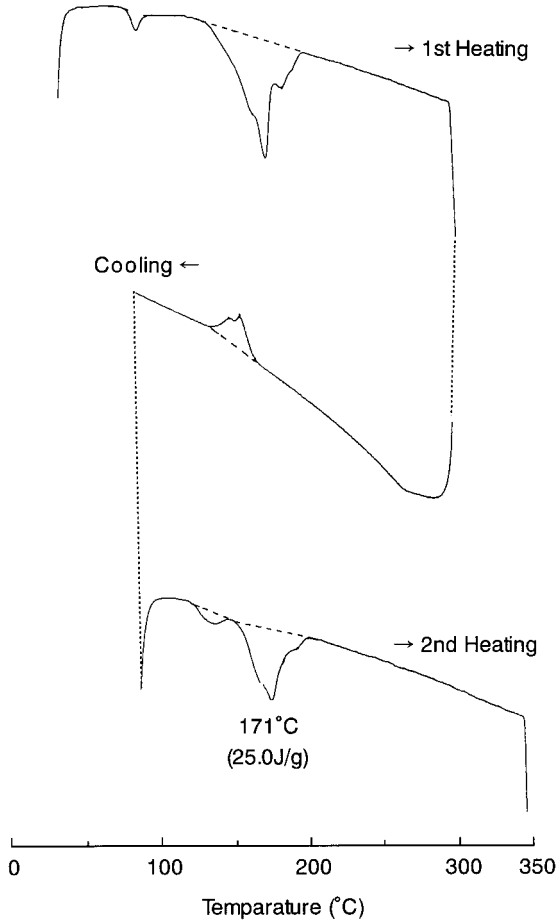


Figure 3. DSC chart of the polymer of entry 3.

The DSC traces of the polymer (entry 3) are shown in Figure 3. There were endothermic peaks in the first and second heating and exothermic peaks in the cooling. The peak-top temperature of the endothermic peak in the second was defined as melting point (T_m). The polymerization which had almost no C−C dimer formation at the initial stage produced polymer having T_m at 171−194 °C. The T_m values were lower than that of the PPO obtained by the Ullmann synthesis (298 °C),[17] which is ascribed to the presence of the ortho C−O linkages and/or the lower molecular weight.

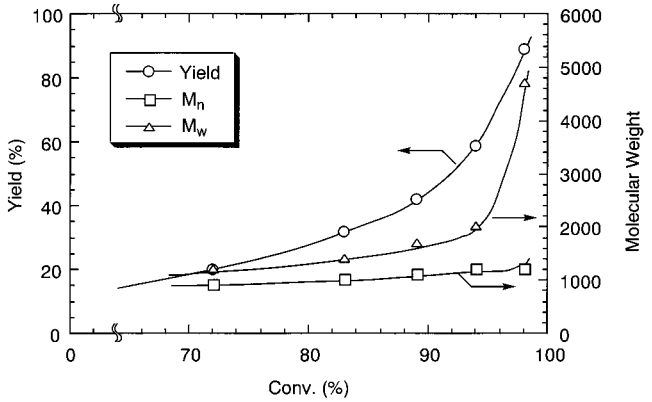


Figure 4. PPL conversion versus yield and molecular weight of the polymer. The polymerization was carried out by Cu(L^{iPr}) catalyst in toluene at 40 °C under dioxygen.

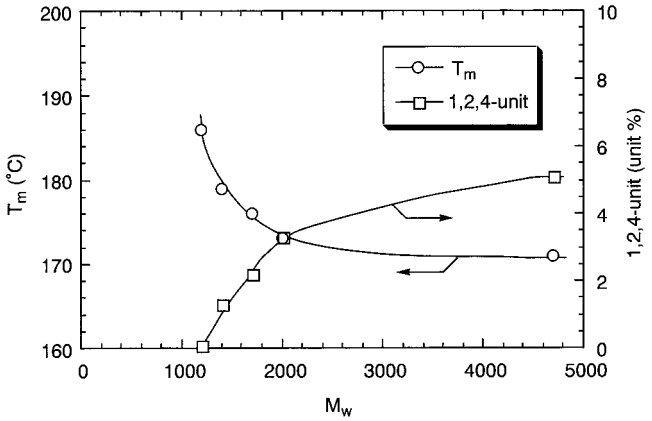


Figure 5. M_w versus T_m and 1,2,4-unit values of the polymer obtained by Cu(L^{iPr}) catalyst in toluene at 40 °C under dioxygen.

The polymerization catalyzed by the Cu(L^{iPr}) complex in toluene (entry 3) was followed (Figure 4). When the PPL conversion arrived at more than 50%, white solid precipitated and was identified as PPO. The reason that M_n of the methanol-insoluble polymer increased a little and did not reach 2000 seemed to be due to the precipitation of the polymer in the reaction solvent. The profiles of polymer yield and M_w indicate that this polymerization proceeds as a stepwise-growth polymerization. The T_m and 1,2,4-unit content against the M_w of polymers are plotted in Figure 5. As the M_w value increased, the 1,2,4-unit content increased, and then, the T_m value decreased. From these data, it seems that the ortho C−O linkages are more influential on the T_m than the molecular weight.

In the polymerization giving considerable amounts of the C−C dimers (entries 4, 8−10), brownish polymeric materials were formed. The polymers had high 1,2,4-trioxybenzene unit contents (6.5−8.3%), although the values may be inaccurate because of neglecting phenylene units (C−C coupling structures), and showed no clear melting points in the DSC traces.

Reaction Mechanism of Catalytic Cycle and Oxidative Polymerization. On the basis of the above data, the reaction mechanism of catalytic cycles for the copper complexes are postulated as follows (Scheme 2). First, copper(II) chloride complexes **6** of the Cu(Tpzb)-Cl, Cu(L^{iPr})Cl_2, Cu(L^{cHex})Cl_2, Cu(L^{nBu})Cl_2, and Cu(L^{MOE})-Cl_2 complexes (entries 1−7) react with PPL or oligomers of PPL to give phenoxo−copper(II) complexes **2**, equivalent to phenoxy radical−copper(I) complexes **3**. Although we have not tried to detect the complex **2** from PPL, similar ones (**2**) from 4-fluorophenol, 2,6-dimethylphenol, and 2,6-di-*tert*-butylphenol were analyzed.[25] Complex **2** of 4-fluorophenol was stable, and its structure was determined by means of X-ray crystallography. For the 2,6-disubstituted phenols, **2** gave the oxidative coupling products at room temperature, indicating that **2** possesses radical resonance structure **3**. These previous data support the structure and reactivity of "controlled" phenoxy radical species **2** and **3**. 2,6-Diphenylpyridine having no coordination ability to copper atom neutralizes the generated hydrogen chloride. Regioselective coupling takes place between two molecules of **2** and/or **3** to produce copper(I) complexes **7** as well as the phenylene oxide products having *p*-linkage selectively, because the steric hindrance of the catalysts blocks the coupling at *o*-positions.

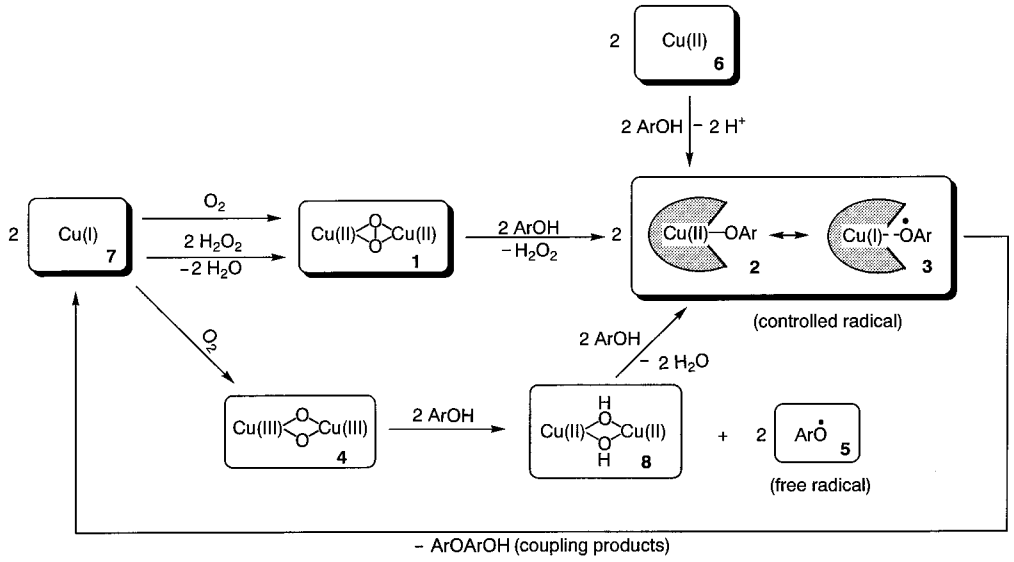
In the case of the Cu(Tpzb) complex, formation of μ-η^2:η^2-peroxo dicopper(II) complex **1** from **7** was confirmed under dioxygen[14] in both toluene (entry 1) and THF (entry 2). For the Cu(L^{iPr}) complex, it was reported that **7** afforded complex **1** in nonpolar solvents such as toluene (entry 3),[26] and **1** reacted with HBF_4 to yield hydrogen peroxide.[20] A similar complex **1** of (hydrotris-(3,5-diisopropyl-1-pyrazolyl)borate)copper reacted with 4-fluorophenol to give complex **2**,[25,27] and complex **7** was proved to react not only with dioxygen, but also with hydrogen peroxide to form complex **1**.[16] These data strongly indicate that, for entries 1−3, μ-η^2:η^2-peroxo dicopper(II) complexes **1** are formed and reacted with phenols to regenerate **2** and hydrogen peroxide. Hence, this catalytic system would allow only the regioselective coupling process from **2** and/or **3** and completely exclude free radical coupling reactions; the present system is recognized as "radical-controlled" oxidative polymerization.

For the Cu(L^{iPr}) complex under dioxygen in THF (entry 4), **7** gave bis(μ-oxo) dicopper(III) complex **4**,[26] and **4** did not react with HBF_4.[28] A similar (1,4,7-tribenzyl-1,4,7-triazacyclononane)copper complex, **4**, abstracted hydrogen atoms from its benzyl group to give the bis-(μ-hydroxo) copper(II) complex **8**.[29] These previous data indicate that, in the case of entry 4, the bis(μ-oxo) dicopper(III) complex **4** is formed, followed by abstraction of hydrogen atoms from phenols to give free phenoxy radical **5**. Therefore, this catalytic cycle should involve the free radical coupling with the formation of C−C linkages, although production of **2** from complex **8** also takes place.[25]

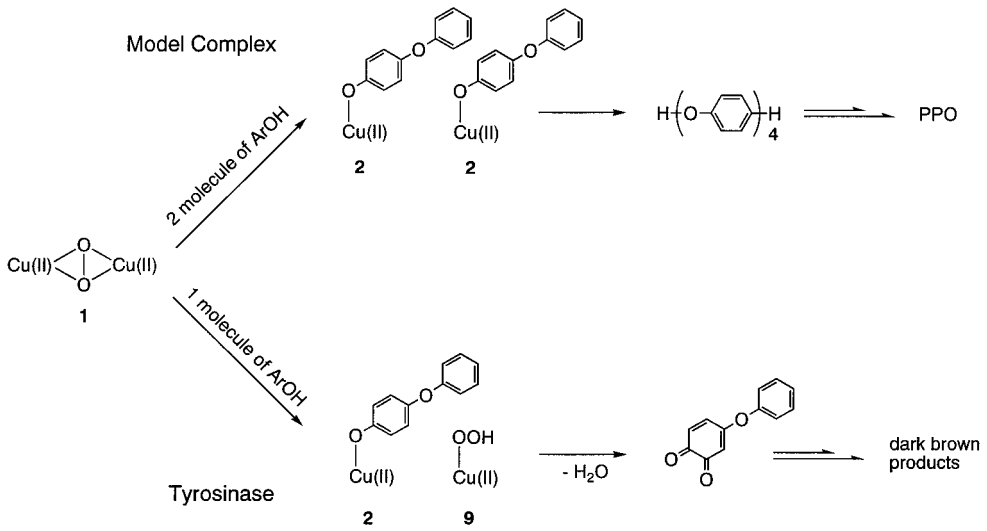
The Cu(L^{cHex}) complex **7** in toluene (entry 5) was ascertained to form μ-η^2:η^2-peroxo dicopper(II) complex **1**, which will give **2** similarly to the Cu(L^{iPr}) complex in toluene (entry 3). The Cu(L^{nBu}) complex in toluene (entry 6) would generate not only **1** but also the bis(μ-oxo) dicopper(III) complex **4**, from the fact that the (1,4,7-tribenzyl-1,4,7-triazacyclononane)copper complex afforded **4** in dichrolomethane.[26] This seems to be the reason that the dimerization catalyzed by Cu(L^{nBu}) gave a very slight amount of the C−C dimer. These findings that, in entries 3, 5, and 6, the regioselectivity to p-4 increased with an increase in the steric hindrance of catalyst substituent, strongly support the "radical-controlled" coupling mechanism.

The dimer ratio for the Cu(L^{MOE}) complex in toluene (entry 7) was nearly equal to that for the Cu(L^{iPr}) complex in THF (entry 4). In the case of entry 7, the bis(μ-oxo) dicopper(III) complex **4** may be also generated.

Scheme 2



Scheme 3



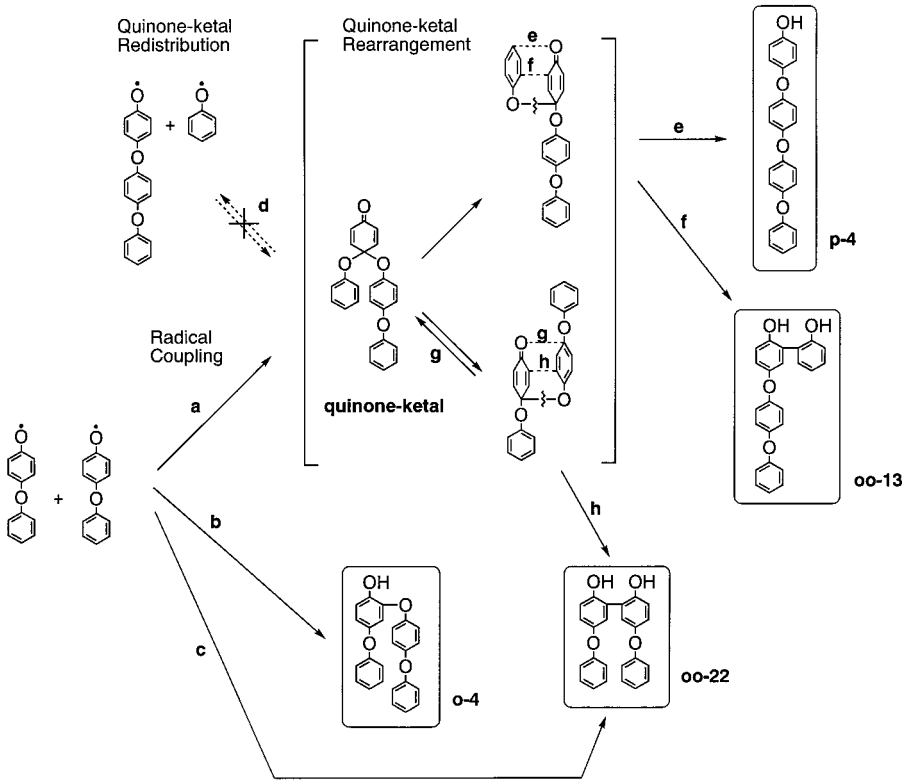
For the CuCl/teed complex (entry 8), it was reported that copper(I)/peralkylated ethylenediamine complexes reacted with dioxygen to give **4**.[10] The slight disagreement between the dimer ratio in entry 8 and that in entry 4 might be due to the difference of copper valence of the starting complexes, that of reactivity of the corresponding complexes **2** and/or **3**, or that of solvent of the reactions.

The reaction mechanism of HRP-catalyzed oxidation has been studied in detail,[30,31] and from the previous studies, the polymerization catalyzed by HRP (entry 10) would proceed via the free-radical coupling as we reported already.[32]

The difference of the reaction behavior between tyrosinase (entry 12) and the tyrosinase model complexes (entries 1−3, 5, 6) can be explained below (Scheme 3). In the case of tyrosinase **1** reacts with only one molecule of PPL to give **2** and the hydroperoxo−copper(II) complex **9** (one molecule each), followed by ortho oxygenation to produce an *o*-quinone,[27] which will lead to the dark-brown product. It was reported that the oxidation of *p*-substituted phenols catalyzed by tyrosinase in the presence of water gave *o*-quinone intermediates resulting in the subsequent rapid polymerization.[33] For the model complexes, on the other hand, **1** reacts with two molecules of PPL to give two molecules of **2**, leading to PPO via the "radical-controlled" coupling. Tyrosinase possesses two functions: the formation of μ-η^2:η^2-peroxo dicopper(II) complex and the oxygenation of phenols. For the present "radical-controlled" polymerization, only the former is required.

The reaction mechanism of oxidative coupling of PPL to produce dimers is speculated as follows (Scheme 4). For simplicity, the mechanism is argued here by expressing intermediate structures in the form of not "controlled radical" but free radical. First, two molecules of PPL are oxidized, and the two generating radicals are coupled to each other (radical coupling). Since radical coupling does not occur in the 4-phenoxy group of PPL,[34] only three reaction routes (**a**, **b**, and **c**) can take place, giving rise to a quinone−ketal intermediate, o-4, and oo-22, respectively. From the quinone−ketal, the redistribution path (quinone−ketal redistribution, **d**) was ruled out owing to no detection of phenol and 4-(4-phenoxyphenoxy)phenol, and therefore, the rearrangement path (quinone−ketal rearrangement) was proposed in the oxidative coupling of PPL.[9] On cleavage of the ketal C−O bond, synchronous bond formation of **e** to p-4, that of **f** to oo-13, and that of **h** to oo-22 occur,

Scheme 4



although that of **g** regenerates the quinone−ketal.

In the "radical-controlled" oxidative coupling of PPL, the radical coupling takes place from the controlled phenoxy radical−copper(I) intermediate. Therefore, the steric effect of the catalyst would suppress o-4 formation (route **b**) and inhibits oo-22 formation (route **c**), mainly giving the quinone−ketal intermediate (route **a**). Moreover, almost no detection of oo-13 as well as oo-22 shows that the catalyst must be kept interacting with the quinone−ketal intermediate in the rearrangement. Probably, the carbonyl group of the quinone−ketal will coordinate to the copper(I) atom of the catalyst. Thereby, the protection of bond formation at the *o*-position to oo-13 and oo-22 via routes **f** and **h**, respectively, would give p-4 predominately via route **e**.

In a similar manner of dimerization, oxidative coupling of controlled radicals from PPL and p-4 will give a trimeric quinone−ketal intermediate, from which corresponding rearrangements will afford linear C−O trimer (six oxyphenylene units). Further oxidative couplings between controlled radicals generated from PPL, dimer, trimer, and higher oligomers will lead to a linear PPO.

Conclusion

In this paper, we described "radical-controlled" oxidative polymerization of phenols catalyzed by tyrosinase model complexes, in which nucleophilic μ-η^2:η^2-peroxo dicopper(II) complexes are formed as the active dioxygen intermediates and react with phenols to give controlled phenoxy radical−copper(I) complexes exclusively, without generating free phenoxy radicals. The finding that the selectivity for p-4 in dimer formation increased with an increase in the steric hindrance of substituents of catalyst complexes strongly supports the "radical-controlled" mechanism for this polymerization. It is essential to use the model complexes, since tyrosinase itself did not show the polymerization activity. On the basis of the present method, highly regioselective polymerization of PPL to synthesize crystalline PPO showing a melting point has been achieved for the first time by the catalytic oxidative polymerization. This method of polymer synthesis would be a clean, low-loading process, because the catalyst efficiency is high and the solvent can be recycled, and thus it may provide an example of green polymer chemistry. Further polymerization of other phenolic monomers will be published[32,35] and related studies including detailed mechanistic aspects are also under progress.

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Supporting Information Available: Text giving details of the X-ray structural measurements, figures showing ORTEP presentations, and tables giving detailed structural information for the X-ray crystallography structure determination of Cu(Tpzb)Cl, Cu(L^{iPr})Cl_2, Cu(L^{cHex})Cl_2, and Cu(L^{nBu})Cl_2. This material is available free of charge via the Internet at http://pubs.acs.org.

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