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Highly Regioselective Oxidative Polymerization of 4-Phenoxyphenol to Poly(1,4-phenylene oxide) Catalyzed by Tyrosinase Model Complexes

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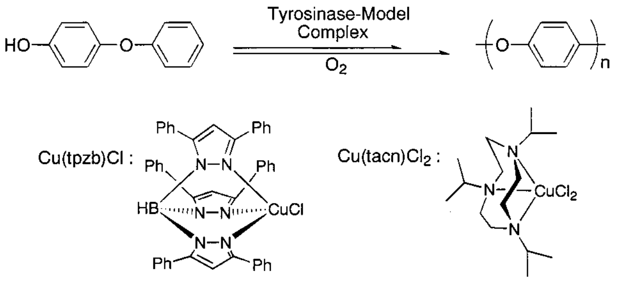
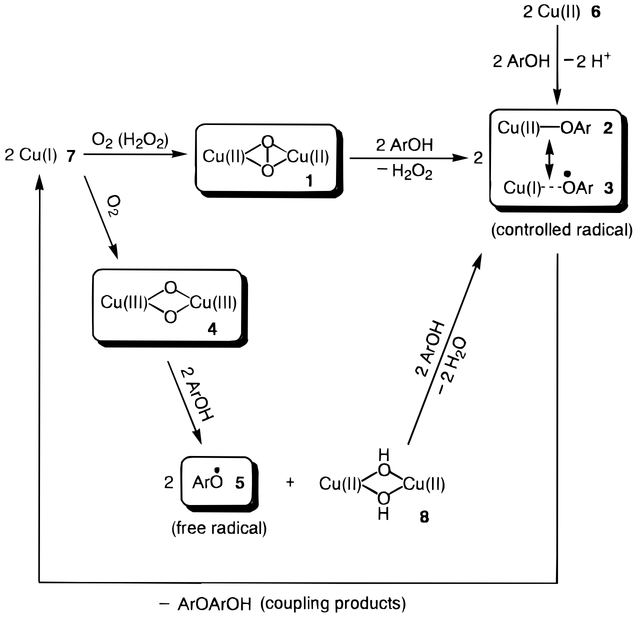
Regioselective oxidative polymerization of phenols leading to *2,6-unsubstituted* poly(1,4-phenylene oxide) (PPO) has long been a target of research activities in the field of polymer synthesis. Despite many attempts, no successful regioselective polymerization of 2,6-unsubstituted phenols has been reported so far,[1] although that of 2,6-disubstituted phenols, where the *o*-positions are protected, produces useful linear polymers.[2] In this paper, we report highly regioselective oxidative coupling of 4-phenoxyphenol (PPL) catalyzed by tyrosinase model complexes. This is the first example to synthesize PPO showing crystallinity with a melting point by oxidative polymerization (Scheme 1).

Scheme 1



A CuCl/*N*,*N*,*N*′,*N*′-tetraethylethylenediamine (teed) catalyst under dioxygen was the only example reported as catalyst for oxidative coupling of PPL.[3] However, this catalyst could not control regioselectivity of the phenoxy radical coupling. The main reason might be that the CuCl/teed catalyst generates "electrophilic" bis(μ-oxo) dicopper(III) complex **4**,[4,5] which abstracts hydrogen atoms from PPL to give "free" phenoxy radical **5** (Scheme 2). On the basis of this view, we have paid much attention to "nucleophilic" μ-η^2:η^2-peroxo dicopper(II) complex **1**,[6] a copper−dioxygen model complex for tyrosinase, and reached a working hypothesis as follows: complex **1** will abstract protons (not hydrogen atoms) from PPL 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, and hence, regioselectivity of the subsequent coupling may be regulated.[7] In this study, two copper(II) chloride complexes, (hydrotris(3,5-diphenyl-1-pyrazolyl)borate)copper(II) chloride (Cu(tpzb)Cl)[8a,c] and (1,4,7-triisopropyl-1,4,7-triazacyclononane)copper(II) dichloride (Cu(tacn)Cl_2)[8b,c] were selected as catalysts for the oxidative polymerization of PPL.

Scheme 2



The oxidative polymerization of PPL was performed in the presence of the catalyst (5 mol % based on PPL) in toluene or THF under dioxygen (1 atm) at 40 °C. As a model system of free phenoxy radical coupling, polymerization of PPL oxidized by an equimolar of 2,2′-azobisisobutyronitrile (AIBN) was examined in toluene under nitrogen at 40 °C. During these polymerization reactions, small portions of the reaction mixtures were taken out and dimers of the initial polymerization stages were analyzed. With the CuCl/teed catalyzed polymerization, major products detected were four dimers and identified as p-4, o-4, oo-22, and oo-13 (Table 1) by using liquid chromatography−

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(1) (a) Hay, A. S. *J. Polym. Sci.* **1962**, *58*, 581−591. (b) Uyama, H.; Kurioka, H.; Kaneko, I.; Kobayashi, S. *Chem. Lett.* **1994**, 423−426.

(2) (a) Hay, A. S.; Blanchard, H. S.; Endres, G. F.; Eustance, J. W. *J. Am. Chem. Soc.* **1959**, *81*, 6335−6336. (b) Hay, A. S. *Macromolecules* **1969**, *2*, 107−108. (c) Ikeda, R.; Sugihara, J.; Uyama, H.; Kobayashi, S. *Macromolecules* **1996**, *29*, 8702−8705.

(3) Mijs, W. J.; van Lohuizen, O. E.; Bussink, J.; Vollbracht, L. *Tetrahedron* **1967**, *23*, 2253−2264.

(4) Mahadevan, V.; Hou, Z.; Cole, A. P.; Root, D. E.; Lal, T. K.; Solomon, E. I.; Stack, T. D. P. *J. Am. Chem. Soc.* **1997**, *119*, 11996−11997. In this paper, the reaction of copper(I)/peralkylated-1,2-cyclohexanediamine complexes with dioxygen generated bis(μ-oxo) dicopper(III) complexes, which reacted with 2,4,6-tri-*tert*-butylphenol to yield the phenoxy radical and bis-(μ-OH) dicopper(II) complexes.

(5) (a) Halfen, J. A.; Mahapatra, S.; Wilkinson, E. C.; Kaderli, S.; Young, V. G., Jr.; Que, L., Jr.; Zuberbühler, A. D.; Tolman, W. B. *Science* **1996**, *271*, 1397−1400. (b) Tolman, W. B. *Acc. Chem. Res.* **1997**, *30*, 227−237.

(6) (a) Kitajima, N.; Fujisawa, K.; Moro-oka, Y.; Toriumi, K. *J. Am. Chem. Soc.* **1989**, *111*, 8975−8976. (b) Kitajima, N.; Moro-oka, Y. *Chem. Rev.* **1994**, *94*, 737−757.

(7) Hay, A. S. *Polym. Eng. Sci.* **1976**, *16*, 1−10. In this paper, the concept of using copper complexes with bulky ligands and "controlled" radicals in an attempt to avoid coupling at open *o*-position(s) in phenols was proposed, and in this direction, the oxidation of *o*-cresol using copper complexes with 2-alkylpyridines to give high molecular weight polymers was found.

(8) (a) Kitajima, N.; Fujisawa, K.; Fujimoto, C.; Moro-oka, Y.; Hashimoto, S.; Kitagawa, T.; Toriumi, K.; Tatsumi, K., Nakamura, A. *J. Am. Chem. Soc.* **1992**, *114*, 1277−1291. (b) Mahapatra, S.; Halfen, J. A.; Wilkinson, E. C.; Que, L., Jr.; Tolman, W. B. *J. Am. Chem. Soc.* **1994**, *116*, 9785−9786. (c) We determined the structures of Cu(tpzb)Cl and Cu(tacn)Cl_2 by using X-ray crystallography.

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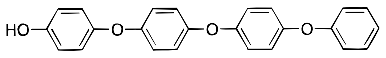
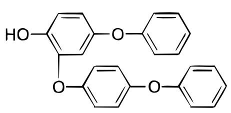
Table 1. Oxidative Polymerization of 4-Phenoxyphenol[a]

				dimers at the initial stage of polymerization							polymers					
							dimer ratio (%)									
entry	catalyst	oxidant	solvent	time (h)	conv.[b] (%)	yield[c] (%)	p-4[d]	o-4[d]	oo-22[d]	oo-13[d]	time (h)	conv.[b] (%)	yield[e] (%)	M_n[f]	M_w[f]	T_m[g] (°C)
1	Cu(tpzb)Cl[h]	O_2[i]	toluene	0.25	13	9	91	9	0	0	14	55	4	700	1100	186
2	Cu(tpzb)Cl[h]	O_2[i]	THF	1.7	11	7	91	9	0	0	70	91	54	1500	2900	194
3	Cu(tacn)Cl_2[h]	O_2[i]	toluene	0.20	9	8	93	7	0	0	19	98	89	1200	4700	171
4	Cu(tacn)Cl_2[h]	O_2[i]	THF	7.5	12	9	89	7	1	3	81	86	52	3800	13700	nd[j]
5	CuCl/teed[k]	O_2[i]	toluene	0.02	17	12	79	6	2	13	24	100	77	5400	29100	nd[j]
6		AIBN[l]	toluene	120	27	15	82	4	2	12	380	69	8	1600	3100	nd[j]

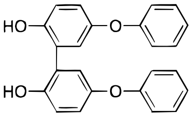
[a] Polymerization of PPL (0.60 mmol) in solvent (1.2 g) at 40 °C. [b] Conversion of PPL. [c] Total yield of dimers. [d] Dimers shown below. [e] Methanol-insoluble part. [f] Determined by size exclusion chromatography. [g] Temperature of the largest endothermic peak in the second scan of DSC measurement under nitrogen. [h] Cu complex (0.030 mmol) and 2,6-diphenylpyridine (0.30 mmol). [i] Under dioxygen (1 atm). [j] Not detected. [k] CuCl (0.030 mmol) and teed (0.015 mmol). [l] Oxidized by AIBN (0.60 mmol) under nitrogen.



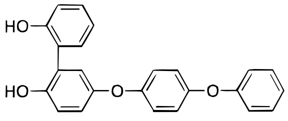
p-4



o-4



oo-22



oo-13

mass spectroscopy and NMR spectroscopy.[9] Products p-4 and o-4 are formed by the C−O coupling. Formation of oo-22 and oo-13 is based on the C−C coupling. In the range of PPL conversion less than 30%, the conversion of PPL was fairly close to the total yield of the four dimers, and therefore, the ratio of the dimers can be taken as a strong measure of the regioselectivity of the coupling.

In the oxidative polymerization of PPL catalyzed by CuCl/teed catalyst (entry 5), considerable amounts of two C−C coupling dimers of oo-2 and oo-13 were detected, and p-4 selectivity was consequently low (79%). These values were almost the same as those oxidized by AIBN (entry 6), in which the formation of the C−C coupling dimers is characteristic. However, for Cu(tpzb) catalyst in toluene (entry 1) and in THF (entry 2), and for Cu(tacn) catalyst in toluene (entry 3), none of the C−C coupling dimers were detected and high regioselectivity of p-4 (maximum 93%) was achieved. These data strongly indicate that the regioselectivity of phenoxy radical coupling can be controlled by these catalysts. The Cu(tacn) catalyst in THF (entry 4), however, yielded the C−C coupling dimers to some extent.

In the polymerization without the C−C dimer formation at the initial reaction stage (entries 1−3), the polymers (methanol-insoluble part) showed the same IR spectra as crystalline PPO,[10a] and their melting points (171−194 °C) were detected by differential scanning calorimetric (DSC) analysis.[10b] In the polymerization involving the formation of the C−C dimers (entries 4−6), no clear melting points of the polymers were detected.

On the basis of the above data, the polymerization mechanism is postulated as follows (Scheme 2). First, copper(II) chloride complexes **6** of Cu(tpzb)Cl and Cu(tacn)Cl_2 react with PPL or oligomers of PPL to give phenoxo−copper(II) complexes **2**,[11] equivalent to phenoxy radical−copper(I) complexes **3**. Regioselective coupling takes place via **2** and/or **3** to produce copper(I) complexes **7** of Cu(tpzb) and Cu(tacn)Cl. In case of the Cu(tpzb) complex, formation of μ-η^2:η^2-peroxo dicopper(II) complex **1** from **7** was confirmed under dioxygen[8a] in both toluene and THF. For the Cu(tacn) complex, **7** was also known to afford complex **1** in nonpolar solvents such as toluene.[5a] It was reported that complex **1** reacted with HBF_4 to yield hydrogen peroxide,[8b] and the reaction of another complex **1** with 4-fluorophenol gave complex **2**.[6b] These previous studies indicate that, for entries 1−3, μ-η^2:η^2-peroxo dicopper(II) complexes **1** are formed and react with phenols to regenerate intermediates **2** or **3** and hydrogen peroxide,[12] and thus, the free radical coupling processes would be completely excluded.

For the Cu(tacn) complex under dioxygen in THF, it was reported that **7** gave bis(μ-oxo) dicopper(III) complex **4**;[5a] **4** did not react with HBF_4,[13a] and a similar complex of **4** abstracted hydrogen atoms of its substituents to give bis(μ-OH) copper(II) complex **8**.[13b] These data show that, in case of entry 4, bis(μ-oxo) dicopper(III) complex **4** is formed, followed by abstraction of hydrogen atoms from phenols to give free phenoxy radical **5**, in the radical coupling of which the regioselectivity cannot be regulated, and complex **8** producing intermediates **2** or **3**. For entry 5, the polymerization catalyzed by the CuCl/teed is seemed to be almost governed via the free radical coupling.[14]

In conclusion, we have first achieved synthesis of crystalline PPO showing a melting point by highly regioselective oxidative polymerization of 4-phenoxyphenol using tyrosinase model complex catalysts, from which nucleophilic μ-η^2:η^2-peroxo dicopper(II) complexes were formed in situ as the active dioxygen intermediates. The present study is very significant not only in the fields of polymer chemistry and polymeric materials but also in that of bioinorganic chemistry, because only few examples have been reported that enzyme model complexes are really advantageous to functional material productions.

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Supporting Information Available: Text describing the characterization data for Cu(tpzb)Cl and Cu(tacn)Cl_2, the synthetic procedures and characterization data for p-4, o-4, oo-22, and oo-13, and the typical procedure for polymerization (5 pages, print/PDF). See any current masthead pages for ordering information and Web access instructions.

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[9] The authentic samples of p-4, o-4, oo-22, and oo-13 were synthesized and characterized by the method reported in the Supporting Information.

[10] (a) van Dort, H. M.; Hoefs, C. A. M.; Magré, E. P.; Schöpf, A. J.; Yntema, K. *Eur. Polym. J.* **1968**, *4*, 275−287. (b) The melting points of the resulting polymers were lower than that of linear high molecular weight PPO (298 °C),[10a] which may be because the polymers contained a small amount of ortho C−O linkage and/or had lower molecular weight.

[11] When the copper(II) complexes of Cu(tpzb)Cl and Cu(tacn)Cl_2 were reacted with phenols, giving the phenoxo−copper(II) complexes, hydrogen chloride was generated. To neutralize generated hydrogen chloride, an excess of 2,6-diphenylpyridine, having no coordination ability to copper atom, was added to the complexes.

[12] We proved that a similar copper(I) complex was reacted not only with dioxygen but also with hydrogen peroxide to form the μ-η^2:η^2-peroxo dicopper(II) complex.

[13] (a) Mahapatra, S.; Halfen, J. A.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11575−11586. (b) Mahapatra, S.; Halfen, J. A.; Wilkinson, E. C.; Pan, G.; Cramer, C. J.; Que, L., Jr.; Tolman, W. B. *J. Am. Chem. Soc.* **1995**, *117*, 8865−8866.

[14] The dimer ratio by the Cu(tacn) in THF was slightly different from that by the CuCl/teed in toluene. This might be due to the difference in copper valences of the starting complexes, reactivity of the phenoxo−copper complexes, or solvents of the reaction.