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Selective Oxidation of Phenols to Hydroxybenzaldehydes and Benzoquinones with Dioxygen Catalyzed by Polymer-Supported Copper

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Oxidation of 2,6-disubstituted 4-methylphenols with dioxygen by using a $CuCl_2$-poly(4-methyl-4′-vinyl-2,2′-bipyridine) catalyst gave the corresponding 4-hydroxybenzaldehydes in high yields. The activity of the catalyst and the selectivity of the products significantly depended on the reaction conditions and the composition of the catalyst. When the molar ratio of the bipyridine unit of the polymer ligand to Cu was unity, i.e., N/Cu = 2, the best results were obtained. Moreover, the reaction is likely to be promoted by coordination of the products to the catalyst. Similarly, 2,3,6-trimethylphenol and related compounds were converted to *p*-benzoquinones selectively with a $CuCl_2$-poly(4-vinylpyridine) catalyst. These polymer-supported catalysts were readily recovered and are reusable without noticeable decrease of their activity.

Hydroxybenzaldehyde and benzoquinone derivatives are important intermediates for the industrial synthesis of a wide variety of special chemicals, such as pharmaceuticals, flavors, dyes, polymers, and agricultural chemicals. Among their many synthetic methods, catalytic oxidation of the corresponding phenols with dioxygen could be most promising. In the last three decades, many polymer-supported copper-amine complexes, including pyridine, bipyridine, imidazole, benzylamine groups, have been explored for phenol oxidation with dioxygen, and their mechanism and various factors to control the reaction have been extensively investigated.[1] The majority of these studies are focused on the oxidation of 2,6-disubstituted phenols leading to poly(oxy-1,4-phenylene)s or diphenoquinones. However, polymer catalysts have been rarely applied to the oxidation of alkyl substituents of phenols to carbonyl groups. In contrast to the oxidation of catechols and hydroquinones,[2] selective preparation of *p*-benzoquinones from di- or tri-substituted phenols has been known to be difficult because of facile C–C and C–O couplings. Moreover, the potentially reusable property of the polymer catalysts has not been fully realized.[3]

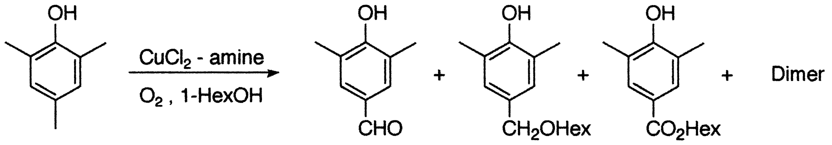
Previously, we succeeded in an efficient oxidation of 2,6-disubstituted 4-methylphenols to 4-formyl- and 4-alkoxymethylphenols with dioxygen by using copper-oxime or aliphatic amine catalysts.[4] We also reported the selective synthesis of trimethyl-*p*-benzoquinone from 2,3,6-trimethylphenol with an O_2/Cu-hydroxyamine hydrochloride system.[5] In the latter work, the oxidation could be repeated several times by recycling the catalyst in the two-phase reaction, but the amine hydrochloride had to be added at every run to make up for the loss. In an extension of our previous work, we studied an efficient recycling procedure for the synthesis of 4-hydroxybenzaldehydes and *p*-benzoquinones by the oxidation of the corresponding phenols with polymer-supported copper catalysts. We report herein these results.

Results and Discussion

Oxidation of 2,4,6-Trimethylphenol and Related Compounds. At first, various amine ligands for $CuCl_2$ were screened in order to achieve a selective oxidation of 2,4,6-trimethylphenol (**1a**) with dioxygen leading to 4-hydroxy-3,5-dimethylbenzaldehyde (**2a**) (Table 1). Generally, the reaction gave the aldehyde **2a**, ether **3a**, ester **4a**[6] and C–C coupling dimer **5a**, a mixture of 3,3′,5,5′-tetramethylbiphenyl-4,4′-diol and 3,3′,5,5′-tetramethyldiphenoquinone,[7] as detectable compounds by GC together with polymeric products. The effect of pyridine and 2,2′-bipyridine was comparable to that of previously reported acetone oxime and aliphatic secondary amines (Runs 1–3).[4] Thus, four polymer ligands carrying pyridine and 2,2′-bipyridine units were chosen, in which the aromatic rings were directly connected to each other or branched at the polyvinyl chain, as shown in Chart 1.[8,9] Poly(pyridine-2,5-diyl) (PPy) and poly(2,2′-bipyridine-5,5′-diyl) (PBPy) gave lower yields of the aldehyde **2a** than the corresponding monomeric amines, and the mass balance decreased, i.e., polymerization of the substrate **1a** took place readily (Runs 4 and 6). These results suggest that flexibility of the polymer ligands is important to form active complexes. In contrast to the high activity of the $CuCl_2$–pyridine complex, no reaction occurred with poly(4-vinylpyridine) (PVPy); this would be due to failure to complex with copper (Run 5).[10] Poly(4-methyl-4′-vinyl-2,2′-bipyridine) (PVBPy) exhibited the highest activity among the polymeric amines (Run 7).

The present reaction system essentially induces many competitive reactions, such as C–C and C–O coupling and peroxide formation from phenoxy radicals and dioxygen, and the product **2a** could be oxidized further (vide infra). Thus, the yield and selectivity of **2a** are very sensitive to the reaction conditions, particularly to the molar ratio of the bipyridine unit of PVBPy to $CuCl_2$, which was calculated based on elemental

Table 1. Effect of Amine Ligand on the Oxidation of 2,4,6-Trimethylphenol (**1a**)[a]



1a **2a** **3a** **4a** **5a**

Run	Amine/mg[b]	$CuCl_2$[c]	Temp	Time[d]	Conv.	Product and Yield/%				Mass balance[e]
		mol%	°C	h	%	**2a**	**3a**	**4a**	**5a**	%
1	$^{n}Pr_2NH$	10	40	7	100	92	6	—	—	98[f]
2	Pyridine	10	80	8	100	98	—	2	—	100
3	2,2′-Bipyridine	1	120	12	100	92	2	6	tr	100
4	PPy(9)	5	120	20	100	24	11	—	3	38
5	PVPy(11)	5	120	24	no reaction					
6	PBPy(18)	5	120	20	80	10	38	—	14	82
7	PVBPy(20)	5	120	14	100	92	2	6	tr	100
8	(2)	1	150	10	69	13	41	4	11	100
9	(4)	1	150	8	100	62	1	16	tr	79
10	(8)	1	150	20	100	34	2	11	tr	47

a) Conditions: **1a** (2 mmol), 1-hexanol (2 mL), O_2 (1 atm). b) Molar ratio of the monomeric amines and Py or BPy unit of the polymers to $CuCl_2$ is unity for Runs 1–7 and 9, 0.5 for Run 8, and 2 for Run 10. c) Based on **1a**. d) The time when the maximum yield of **2a** was attained. e) Total yield of **1a**–**5a**. f) 2,6-Dimethyl-*p*-benzoquinone was also formed in 2% yield.

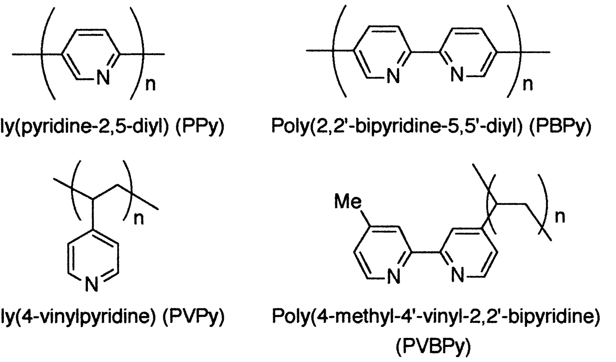


Chart 1.

analyses. When the ratio was unity, good results were obtained (Table 1, Run 9). Less loading of the ligand decreased the conversion of trimethylphenol **1a** and the selectivity of **2a** (Run 8); in contrast, polymerization of **1a** predominated with two molar amounts of the BPy unit (Run 10). Accordingly, a 1 : 1 complex of the BPy unit and Cu(II) would be an active catalyst for the reaction leading to **2a**.[11] On the other hand, the excess ligand was likely to accelerate the dissociation of the phenoxy species from copper to yield the polymer. Alternatively, another active species for the polymerization with the higher ratio would be generated.[12] With respect to the amounts of the catalyst (1 : 1), a maximum was observed at a given temperature. A higher concentration of the catalyst caused a decrease of the reaction rate, probably because of the aggregation of copper, to give the results similar to those of the reaction with half molar amount of BPy unit mentioned above; a lower concentration resulted in increase of the polymers.[13]

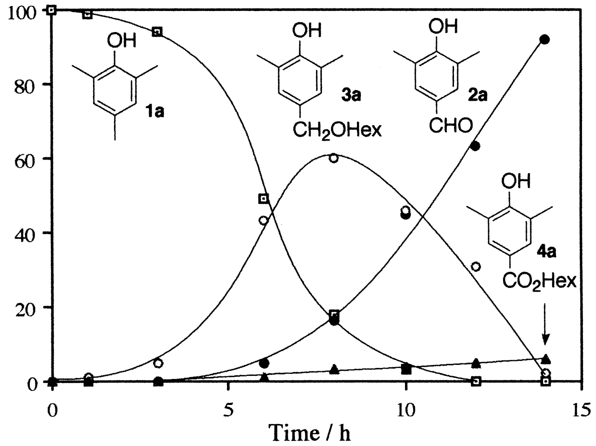
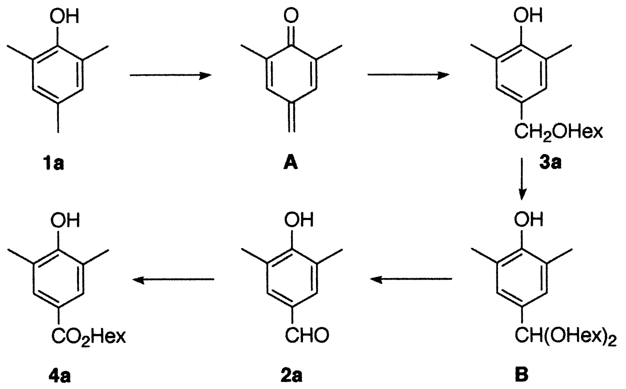


Fig. 1. Oxidation of 2,4,6-trimethylphenol with $CuCl_2$–PVBPy. Conditions, see: Run 7 in Table 1. Dimer **5a** is omitted for clarity.

The time course of the oxidation of **1a** with $CuCl_2$–PVBPy is shown in Fig. 1. As the substrate **1a** was consumed, the ether **3a** appeared at first, increased up to ca. 60% yield, and then changed finally to the aldehyde **2a**. Small amounts of the ester **4a** were detected after the formation of **2a**. These results are in agreement with the previously proposed mechanism (Scheme 1): formation of **3a** from **1a** via quinonemethide **A**, repeated oxidation of **3a** to acetal **B**, hydrolysis to yield **2a**, and overoxidation of **2a** to **4a** through the corresponding benzoic acid. The most striking feature of the present system is the long induction period, as can be seen in Fig. 1, which was not attributed to the time for complexation of the catalyst.[14] Interestingly, this induction period almost disappeared on addition of a half molar amount of the aldehyde **2a** to the catalyst.

Since the $CuCl_2$–PVBPy catalyst is insoluble in 1-hexanol,



Scheme 1.

Table 2. Recycle of CuCl$_2$–PVBPy Catalyst in the Oxidation of 2,4,6-Trimethylphenol (**1a**)[a]

Recycle	Time[b]	Conv.	Product and Yield/%				Mass balance[c]
	h	%	**2a**	**3a**	**4a**	**5a**	%
First	22	100	90	4	6	tr	100
Second	12	100	82	tr	8	tr	90
Third	14	100	87	tr	11	tr	98

a) Conditions: **1a** (2 mmol), 1-hexanol (2 mL), O$_2$ (1 atm), 120 °C. CuCl$_2$ (5 mol%) and PVBPy (20 mg, BPy unit: 5 mol%) were used in the first reaction. b) The time when the maximum yield of **2a** was attained. c) Total yield of **1a**–**5a**.

its recovery by centrifuging and reuse can be readily performed at least three times with similar product yields and selectivities (Table 2). However, the second and third reaction brought about a considerable reduction in reaction time, which would be due to disappearance of the induction period by the coordination of the products, particularly the aldehyde **2a**. When the catalyst was recovered by filtration and thoroughly washed with 1-hexanol, the yield of **2a** decreased slightly (65–80%), but the catalyst activity was almost lost by washing with other insoluble solvents like methanol and benzene.

The catalyst activity is sharply dependent upon the preparation and recycling procedures as described above. Thus, in order to investigate the relation between activity of the catalysts and their composition, four samples were prepared from equimolar amounts of CuCl$_2$ and the BPy unit of PVBPy by different methods. The four were used in the oxidation of **1a** under standard conditions (Table 3). The catalyst 1, washed with methanol after complexation, showed very low activity, whereas the reaction with the catalyst 2, washed with 1-hexanol, gave the aldehyde **2a** in high yield. The catalysts 3 and 4, isolated after the first and second reactions, respectively, followed by 1-hexanol washing, also exhibited reasonable activities, but the yields of **2a** were slightly lower as compared with the results of the recycling test. With respect to the ratio of elements, which was determined by elemental analyses and represented based on N$_2$, the original N/Cu ratio of 2 was maintained in all catalysts, suggesting that copper was not eluted by the treatment.

Table 3. Relation between Activity of CuCl$_2$–PVBPy Catalysts and Their Composition[a]

Catalyst	Ratio of Element					Yield of **2a**
	C	H	N	Cu	Cl	%
(calcd)	13.0	12.0	2.0	1.0	2.0	
1[b]	13.3	15.7	2.0	0.9	2.9	4[c]
2[d]	14.7	17.0	2.0	1.1	1.7	83
3[e]	17.3	18.4	2.0	1.0	1.2	77
4[f]	20.2	21.3	2.0	1.1	0.9	70

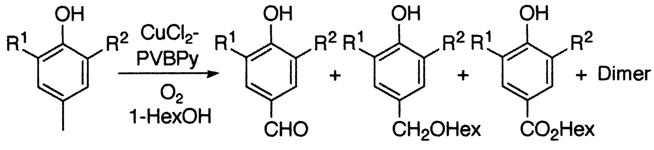
a) All catalysts were prepared from equimolar amounts of CuCl$_2$ and BPy unit of PVBPy. b) Heated at 120 °C in 1-hexanol under O$_2$, and then washed with methanol. c) **3a** was also formed in 26% yield with 30% conversion. d) Heated as above and washed with 1-hexanol. e) Recovered after the 1st reaction, followed by 1-hexanol washing. f) Recovered after the 2nd reaction, followed by 1-hexanol washing.

The Cl/Cu ratio was changed significantly and seemed to influence the catalyst activity. The good catalyst 2 nearly kept the original ratio of 2, whereas excess chloride was found for the catalyst 1, giving rise to a poor yield of **2a**. When the catalyst was prepared with two molar amounts or half molar amount of CuCl$_2$ to the BPy unit and washed with methanol, similar results were obtained, i.e., the N/Cu/Cl ratio was 2.0/1.0/3.3 and 2.0/0.5/1.9, respectively. Although the reason for the higher ratio of Cl to Cu caused by the methanol washing is not clear at present, it seems likely that the excess chloride hindered the oxidation of **1a** by forming some inactive complexes like Cl-bridged polynuclear species.[15] The Cl/Cu ratio reached unity for the recovered catalysts 3 and 4. Moreover, as the reaction was repeated, the ratio of carbon and hydrogen of the catalysts 3 and 4 increased, probably because of the formation of CuCl$_2$–PVBPy-product complexes, which would actually be responsible for the facile oxidation of **1a** to **2a**. Thus, the original complexes in 1-hexanol would be activated through the substitution of chloride for the product during the induction period.

The present method was applied to the oxidation of various 2,6-disubstituted 4-methylphenol; the results are summarized in Table 4. The reaction of **1b** and **1c** gave the corresponding aldehyde **2b** and **2c** in moderate yields, though the radical stabilizing effect of Ph and ^{t}Bu substituents would induce many side reactions. Similarly, phenols carrying alkoxy substituents, **1d** and **1e**, were converted to the aldehyde **2d** and **2e** in 94% and 47% yields, respectively, wherein the undesirable methanol solvent instead of 1-hexanol should be used in the latter reaction; otherwise, the methoxy group of **1e** could be substituted by 1-hexanol.

Oxidation of 2,3,6-Trimethylphenol and Related Compounds. Next, selective oxidation of 2,3,6-trimethylphenol (**6a**) to *p*-benzoquinone **7a** was investigated. As a result of screening of monomeric amine ligands, pyridine was found to be suitable for this transformation, whereas hydrochloric acid additive showed an inhibitory effect, in contrast to the reaction with aliphatic amines.[5] No reaction took place with 2,2′-bipyridine.[16] Thus, the reaction with CuCl$_2$–pyridine was carried out under various conditions (Table 5). Alcoholic solvents such as ^{t}BuOH and ^{i}PrOH–toluene, which were the choice for

Table 4. Oxidation of 2,6-Disubstituted 4-Methylphenol **1**[a)]

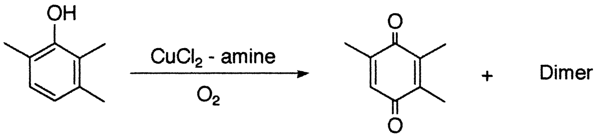


1 **2** **3** **4** **5**

Run	Phenol	R^1	R^2	Time	Conv.	Product and Yield/%				Mass balance[b)]
				h	%	**2**	**3**	**4**	**5**	%
1	**1a**	Me	Me	14	100	92	2	6	tr	100
2	**1b**	Me	^{t}Bu	19	100	66	7	6	—	79
3	**1c**	Me	Ph	24	100	54	17	19	—	90
4[c)]	**1d**	Me	OHex	12	100	94	1	5	—	100
5[c),d)]	**1e**	OMe	OMe	8	97	47	47	—	3	100

a) Conditions: **1** (2 mmol), 1-hexanol (2 mL), O_2 (1 atm), $CuCl_2$ (5 mol%), PVBPy (20 mg, BPy unit: 5 mol%), 120 °C. b) Total yield of **1**–**5**. c) O_2 (4 atm). d) Methanol was used as a solvent, and thus, **3e** was methyl ether instead of hexyl ether.

Table 5. Oxidation of 2,3,6-Trimethylphenol (**6a**) with $CuCl_2$–Amine[a)]



6a **7a** **8a**

Run	Solvent	Amine[b)]	$CuCl_2$[c)]	Temp.	Conv.	Product and Yield/%		Mass balance[d)]
		(mg)	mol%	°C	%	**7a**	**8a**	%
1[e)]	CH_3CN	Pyridine	10	40	100	68	32	100
2	DMF		10	100	100	29	26	55
3	DMSO		10	100	100	78	20	98
4			20	80	100	94	6	100
5		PVPy(45)[f)]	20	80	100	95	tr	95
6	DMSO–C_6H_6(1/3)	PVPy(66)[g)]	20	80	100	92	tr	92
7		(2nd reaction)		80	100	88	4	92
8		(3rd reaction)		80	98	88	10	100

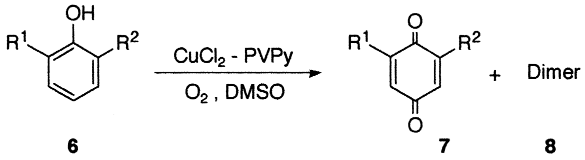
a) Conditions: **6a** (2 mmol), solvent (2 mL), O_2 (1 atm for Runs 1–4 and 10 atm for Runs 5–8), reaction time (24 h). b) Ratio of pyridine and Py unit of PVPy to $CuCl_2$ is unity. c) Based on **6a**. d) Total yield of **6a**–**8a**. e) Reaction time (9 h). f) 2% cross-linked. g) 25% cross-linked.

the reaction with $CuCl_2$–hydroxyamine hydrochloride,[5] inhibited the oxidation. Instead, aprotic polar solvents, particularly dimethyl sulfoxide, gave good results for the synthesis of **7a** (Runs 1–3). The molar ratio of the pyridine ligand to $CuCl_2$ affected the catalyst activities as significantly as that of bipyridine–$CuCl_2$ catalyst mentioned above. With a 1 : 1 catalyst, much better yield and selectivity of **7a** were obtained than with a 0.5 : 1 complex. However, excess use of pyridine (2 mol amt.) slightly decreased the activity, contrary to the bipyridine catalyst. The reaction with more loading of the catalyst at lower temperature improved the selectivity of the quinone **7a** (Runs 3 and 4).

Then, the oxidation of **6a** with $CuCl_2$–PVPy (2% cross-linked, Py unit/Cu = 1) was carried out under similar conditions to those above. Although the quinone **7a** was obtained in over 90% yields, it took a long time to complete the reaction (ca. 72 h). Bubbled or pressurized oxygen reduced the time to 24 h with 80% and 95% yields of **7a**, respectively (Table 5, Run 5). The reaction could be repeated twice, but the catalyst did not precipitate after that, probably because of its mechanical degradation and/or elution of the catalyst. This limitation was overcome by use of 25% cross-linked PVPy and substitution of the solvent for DMSO–benzene (1/3) or DMSO–chloroform (1/1), though some increase of the dimer **8a** was observed as the reaction was repeated (Runs 6–8).

Finally, oxidation of 2,6-disubstituted phenols **6** to the corresponding *p*-benzoquinones **7** was investigated by using the $CuCl_2$–PVPy catalyst (Table 6). These phenols are predicted to give C–C coupling products **8** and C–O coupling polymers more readily than did 2,3,6-trimethylphenol (**6a**) due to the less steric environment. In fact, the reaction of 2,6-dimethylphenol (**6b**) gave the quinone **7b** in low yield together with large amounts of polymer (Run 1). On the other hand, quinones **7c** and **7d** were produced in moderate to good yields from

Table 6. Oxidation of 2,6-Disubstituted Phenol **6**[a)]



Run	Phenol	R^1	R^2	O$_2$	Time	Conv.	Product and Yield/%		Mass balance[b)]
				atm	h	%	**7**	**8**	%
1	**6b**	Me	Me	10	24	83	43	tr	60
2	**6c**	Me	^{t}Bu	1	72	100	67	22	89
3	**6c**			10	24	100	68	5	73
4	**6d**	^{t}Bu	^{t}Bu	1	24	100	57	43	100
5	**6d**			10	24	100	93	7	100

a) Conditions: **6** (2 mmol), DMSO (2 mL), CuCl$_2$ (20 mol%), PVPy (2% cross-linked, 45 mg, Py unit: 20 mol%), 60° C. b) Total yield of **6**–**8**.

the substrates **6c** and **6d** carrying the ^{t}Bu substituent, respectively, wherein the product selectivity was much improved by the pressurized oxygen (Runs 2–5).

In summary, effective oxidation of 2,6-disubstituted 4-methylphenols **1** with dioxygen has been achieved by using a CuCl$_2$–PVBPy catalyst, giving rise to the corresponding 4-hydroxybenzaldehydes **2** selectively. Similar oxidation of 2,3,6-trimethylphenol and related compounds **6** with CuCl$_2$–PVPy gave the *p*-benzoquinones **7** in good yields. Efficiency of the present method is comparable with that of our previous reaction catalyzed by Cu(II)-oxime or hydroxyamine hydrochloride catalysts. In addition, the polymer-supported copper catalysts can be reused in a simple procedure without noticeable decrease of their activity.

Experimental

General. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 99 MHz, respectively. IR spectra were taken on an FT-IR spectrophotometer. Mass spectra were obtained at 70 eV on a GC-MS apparatus. Elemental analyses were performed at our analytical laboratory with a CHN corder, ion chromatography, and ICP. Melting points are uncorrected. GC analyses were carried out on a 30 m × 0.25 mm i.d. column of (5% phenyl)-methylpolysiloxane.

Materials. 3,5-Dimethylbiphenyl-2-ol (**1c**) was prepared by [Pd(PPh$_3$)$_4$]-catalyzed coupling reaction of 2-bromo-4,6-dimethylphenol with PhMgBr:[17] [180680-60-8]; IR (neat) 3556 cm^{-1}; MS *m*/*z* 198 (M$^+$), 183, 165, 128; ^{1}H NMR (CDCl$_3$) δ 2.25 (6H, s), 5.13 (1H, s), 6.89 (1H, s), 6.95 (1H, s), 7.42 (5H, br s); ^{13}C NMR (CDCl$_3$) δ 16.0, 20.3, 124.3, 127.4, 127.5, 128.0, 129.0, 129.06, 129.12, 131.0, 137.5, 148.2. 2-Hexyloxy-4,6-dimethylphenol (**1d**) was synthesized by the reaction of 2-bromo-4,6-dimethylphenol with sodium hexoxide:[18] mp 31–32 °C; IR (Nujol) 3562 cm^{-1}; MS *m*/*z* 222 (M$^+$), 138; ^{1}H NMR (CDCl$_3$) δ 0.91 (3H, t, J = 7.0 Hz), 1.31–1.36 (4H, m), 1.41–1.48 (2H, m), 1.75–1.82 (2H, m), 2.22 (3H, s), 2.24 (3H, s), 3.99 (2H, t, J = 6.6 Hz), 5.55 (1H, s), 6.52 (1H, s), 6.54 (1H, s); ^{13}C NMR (CDCl$_3$) δ 14.0, 15.4, 21.0, 22.6, 29.3, 25.7, 31.5, 68.9, 109.9, 110.0, 123.3, 128.4, 141.5, 145.3. HRMS calcd for $C_{14}H_{22}O_2$ (M$^+$) 222.1620, found 222.1605. 2,6-Dimethoxy-4-methylphenol (**1e**) was prepared from 2,6-dibromo-4-methylphenol and sodium methoxide:[18] [6638-05-7]; ^{1}H NMR (CDCl$_3$) δ 2.29 (3H, s), 3.86 (6H, s), 5.36 (1H, br s), 6.39 (2H, s); ^{13}C NMR (CDCl$_3$) δ 21.5, 56.2, 105.5, 128.7, 132.4, 146.8. Poly(pyridine-2,5-diyl) (PPy), poly(2,2′-bipyridine-5,5′-diyl) (PBPy), and poly(4-methyl-4′-vinyl-2,2′-bipyridine) (PVBPy) were a gift from Dr. Y. Sato, who prepared these polymers by the literature methods[19] and used them as ligands of the CuCl$_2$ catalyst in the oxidative carbonylation of methanol leading to dimethyl carbonate.[20] Anal of PPy. Calcd for $(C_5H_3N)_n$: C, 77.91; H, 3.92; N, 18.17%. Found: C, 75.72; H, 4.09; N, 14.95%. Anal of PBPy. Calcd for $(C_{10}H_6N_2)_n$: C, 77.91; H, 3.92; N, 18.17%. Found: C, 68.79; H, 3.68; N, 15.37%. Anal of PVBPy. Calcd for $(C_{13}H_{12}N_2)_n$: C, 79.56; H, 6.16, N, 14.28%. Found: C, 77.50; H, 5.99; N, 13.94%. 2% and 25% cross-linked poly(4-vinylpyridine) (PVPy) were purchased from Aldrich. Anal of PVPy. Found: C, 77.18; H, 6.72; N, 12.43% (2% cross-linked) and C, 80.03; H, 7.24; N, 8.47% (25% cross-linked). Other materials were commercially available and were used as received.

General Procedure for the Oxidation of 2,4,6-Trimethylphenol and Related Compounds 1. CuCl$_2$•2H$_2$O and tridecane, an internal standard, were dissolved in 1-hexanol (2 mL). In the reaction with low molecular amine ligands, equimolar amounts of the amine were added to the green solution, and the homogeneous mixture was stirred for a while at room temperature under O$_2$ (1 atm). In the case with polymer ligands, appropriate amounts of the polymer, whose molar quantities of the amine unit were calculated based on the elemental analyses, were added to the solution of CuCl$_2$•2H$_2$O and tridecane in 1-hexanol. After stirring for 3 h at 120 °C under O$_2$, white precipitate of the polymer ligand changed to green and the green solution changed to colorless. Then the phenol (2 mmol) was added to the mixture and stirring was continued under the conditions indicated in Tables 1 and 4 with monitoring by GC. If necessary, the mixture was concentrated in vacuo and the residue was chromatographed on silica gel with hexane–EtOAc eluent to isolate the products.

Recycle of CuCl$_2$–PVBPy Catalyst in the Oxidation of 2,4,6-Trimethylphenol (1a). In a centrifuge tube equipped with a reflux condenser attached to the O$_2$ inlet are placed CuCl$_2$•2H$_2$O (17 mg, 0.1 mmol), PVBPy (20 mg, 0.1 mmol of BPy unit), tridecane, and 1-hexanol (2 mL). The mixture was stirred for 3 h at 120 °C under O$_2$. Then, the phenol **1a** (272 mg, 2 mmol) was added to the suspension, and the mixture was stirred at 120 °C. Monitored by GC, the reaction was completed after 22 h. After cooling to room temperature, the reaction mixture was centrifuged and the solution was taken out of the tube with a syringe. Only a trace amount of the products was detected in the wet precipitate by GC. Fresh 1-hexanol (2 mL), tridecane, and **1a** (272 mg, 2 mmol) were added to the residue without the pretreatment, and the reaction was repeated similarly (Table 2).

General Procedure for the Oxidation of 2,3,6-Trimethylphenol and Related Compounds 6. $CuCl_2 \cdot 2H_2O$ and pyridine were dissolved in an appropriate solvent (2 mL) containing mesitylene as an internal standard, and the stirring was continued for a while at room temperature under O_2 (1 atm). The phenol **6a** (272 mg, 2 mmol) was added to the homogeneous green solution and the mixture was stirred under the conditions indicated in Table 5 with monitoring by GC. In the reaction using PVPy under pressurized O_2 (Table 6), a centrifuge glass tube equipped with a Teflon-covered magnetic stirring bar was charged with $CuCl_2 \cdot 2H_2O$ (68 mg, 0.4 mmol), PVPy (45 mg, 2% cross-linked, 0.4 mmol of Py unit), mesitylene and DMSO (2 mL). The mixture was stirred for 5 h at 60 °C under O_2 (1 atm) to afford green precipitate in the colorless solution. After addition of the phenol **6** (2 mmol) to the mixture, a rubber septum with a glass needle was fitted to the tube, which was placed in a stainless autoclave. The autoclave was closed and pressurized to 10 atm with O_2. The mixture was heated at 60 °C for 24 h with stirring. After cooling and venting of the residual gas, the autoclave was opened and the mixture was analyzed by GC. The products were isolated by column chromatography, if necessary.

Recycle of $CuCl_2$–PVPy Catalyst in the Oxidation of 2,3,6-Trimethylphenol (6a). A mixture of $CuCl_2 \cdot 2H_2O$ (68 mg, 0.4 mmol), PVPy (66 mg, 25% cross-linked, 0.4 mmol of Py unit) and mesitylene in DMSO-benzene (1/3, 2 mL) was stirred for 5 h at 60 °C under O_2 (1 atm). The phenol **6a** (272 mg, 2 mmol) was added to the mixture, and the reaction was carried out at 80 °C for 24 h under pressurized O_2 (10 atm) in a similar manner to that described above. The precipitated catalyst was recovered by decantation and used directly in the next reaction with the same quantities of the substrate **6a** and solvent (Table 5).

Identification of Products and Determination of Their Yields. All products were identified by GC and GC-MS, and additionally by IR, NMR, and microanalyses for the isolated ones, since most of them are commercially available or known compounds. Their yields were determined by GC using an internal standard such as tridecane and mesitylene. 4-Hydroxy-3,5-dimethylbenzaldehyde (**2a**): [2233-18-3]; MS *m/z* 150 (M^+), 121. 3-t-Butyl-4-hydroxy-5-methylbenzaldehyde (**2b**): MS *m/z* 192 (M^+), 177, 149; IR (neat) 3179, 1666 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (9H, s), 2.31 (3H, s), 5.73 (1H, s), 7.57 (1H, s), 7.71 (1H, s), 9.83 (1H, s). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39%. Found: C, 74.85; H, 8.48%. 4-Hydroxy-3-methyl-5-phenylbenzaldehyde (**2c**): MS *m/z* 212 (M^+), 183, 153. 3-Hexyloxy-4-hydroxy-5-methylbenzaldehyde (**2d**): MS *m/z* 236 (M^+), 152. 4-Hydroxy-3,5-dimethoxybenzaldehyde (**2e**): [134-96-3]; mp 110–112 °C; MS *m/z* 182 (M^+), 167; IR (Nujol) 3255, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.96 (6H, s), 6.16 (1H, s), 7.15 (2H, s), 9.82 (1H, s); ^{13}C NMR ($CDCl_3$) δ 59.4, 106.7, 128.3, 140.8, 147.3, 190.7. Anal. Calcd for $C_9H_{10}O_4$: C, 59.34; H, 5.53%. Found: C, 59.33; H, 5.50%. 4-(Hexyloxymethyl)-2,6-dimethylphenol (**3a**): [134778-31-7]; MS *m/z* 236 (M^+), 135, 121; IR (neat) 3398 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.7–0.9 (3H, m), 1.2–1.8 (8H, m), 2.17 (6H, s), 3.43 (2H, t, J = 7.0 Hz), 4.33 (2H, s), 4.84 (1H, s), 6.91 (2H, s). Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.22; H, 10.24%. Found: C, 76.12; H, 10.27%. 2-*t*-Butyl-4-hexyloxymethyl-6-methylphenol (**3b**): MS *m/z* 278 (M^+), 191; IR (neat) 3224 cm^{-1}. 5-Hexyloxymethyl-3-methylbiphenyl-2-ol (**3c**): MS *m/z* 298 (M^+), 214, 168. 2-Hexyloxy-4-hexyloxymethyl-6-methylphenol (**3d**): MS *m/z* 322 (M^+), 222, 137. 2,6-Dimethoxy-4-(methoxymethyl)phenol (**3e**): MS *m/z* 198 (M^+), 167; IR (neat) 3143 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.38 (3H, s), 3.89 (6H, s), 4.38 (2H, s) 5.56 (1H, s), 6.58 (2H, s); ^{13}C NMR ($CDCl_3$) δ 56.2, 57.9, 75.0, 104.5, 129.6, 134.2, 147.0. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12%. Found: C, 60.60; H, 7.12%. Hexyl 4-hydroxy-3,5-dimethylbenzoate (**4a**): MS *m/z* 250 (M^+), 165, 150, 120; IR (neat) 3433, 1689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (3H, t, J = 6.9 Hz), 1.31–1.45 (6H, m), 1.75 (2H, tt, J = 7.4 and 6.9 Hz), 2.28 (6H, s), 4.27 (2H, t, J = 6.9 Hz), 5.25 (1H, s), 7.70 (2H, s); ^{13}C NMR ($CDCl_3$) δ 14.0, 15.7, 22.5, 25.7, 28.7, 31.5, 64.8, 122.2, 122.8, 130.4, 156.4, 166.8. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%. Found: C, 72.34; H, 8.66%. Hexyl 3-*t*-butyl-4-hydroxy-5-methylbenzoate (**4b**): MS *m/z* 292 (M^+), 277, 208, 193. Hexyl 4-hydroxy-3-methyl-5-phenylbenzoate (**4c**): MS *m/z* 312 (M^+), 228, 211. Hexyl 3-hexyloxy-4-hydroxy-5-methylbenzoate (**4d**): MS *m/z* 336 (M^+), 252, 235, 168, 151. 3,3′,5,5′-Tetramethylbiphenyl-4,4′-diol (**5a**) and (**8b**): MS *m/z* 242 (M^+), 121; IR (neat) 3461 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.07 (12H, s), 6.67 (4H, s), 7.97 (2H, s); ^{13}C NMR (DMSO-d_6) δ 16.9, 124.3, 128.6, 132.8, 151.4. 2,3,5-Trimethyl-1,4-benzoquinone (**7a**): [935-92-2]; MS *m/z* 150 (M^+), 123, 107; ^1H NMR ($CDCl_3$) δ 2.01 (3H, s), 2.04 (6H, two s), 6.56 (1H, s); ^{13}C NMR ($CDCl_3$) δ 12.0, 12.3, 15.8, 133.0, 140.7, 140.8, 145.3, 187.4, 187.8. 2,6-Dimethyl-1,4-benzoquinone (**7b**): [527-61-7]; MS *m/z* 136 (M^+), 120. 2-*t*-Butyl-6-methyl-1,4-benzoquinone (**7c**): [25543-57-1]; MS *m/z* 178 (M^+), 163, 150, 135. 2,6-Di-*t*-butyl-1,4-benzoquinone (**7d**): [719-22-2]; MS *m/z* 220 (M^+), 163; IR (Nujol) 1659, 1601 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (18H, s), 6.48 (2H, s); ^{13}C NMR ($CDCl_3$) δ 29.4, 35.6, 130.2, 157.9, 187.8, 189.1. 2,2′,3,3′,5,5′-Hexamethylbiphenyl-4,4′-diol (**8a**): MS *m/z* 270 (M^+), 239, 224, 135; ^1H NMR ($CDCl_3$) δ 1.93 (6H, s), 2.22 (6H, s), 2.23 (6H, s), 4.58 (2H, s), 6.56 (2H, s); ^{13}C NMR ($CDCl_3$) δ 12.2, 15.8, 16.9, 119.4, 121.6, 129.3, 133.8, 134.7, 150.7. 3,3′-Di-*t*-butyl-5,5′-dimethylbiphenyl-4,4′-diol (**8c**): MS *m/z* 326 (M^+), 311, 283. 3,3′,5,5′-Tetra-*t*-butyldiphenoquinone (**8d**): mp 125–126 °C; MS *m/z* 408 (M^+), 393, 351; ^1H NMR ($CDCl_3$) δ 1.35 (36H, s), 7.69 (4H, s); ^{13}C NMR ($CDCl_3$) δ 29.6, 36.0, 126.0, 136.2, 150.5, 180.5. HRMS calcd for $C_{28}H_{40}O_2$ (M^+) 408.3025, found 408.3014.

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6 In the reaction with $CuCl_2$–oxime or aliphatic amine, 2,6-dimethyl-*p*-benzoquinone (**7b**), instead of **4a**, was formed as an overoxidation product, see: Ref. 4.

7 The biphenyldiols were obtained in preference to the diphenoquinones under the reaction conditions, except for the dimer **8d**.

8 PVPy used in this work was 2% cross-linked with divinylbenzene unless otherwise noted.

9 In contrast, aliphatic polyamines seemed to be unsuitable for the present reaction because TMEDA and diethylenetriamine showed much less activity than ^{n}Pr$_2$NH.

10 White precipitate of PVPy remained unchanged in 1-hexanol solvent, see: Experimental.

11 In the oxidation of **1a** to **2a** with $CuCl_2$–diethylamine in ethanol, the active species was suggested to be $[Cu(Et_2NH)(EtOH)Cl_2]$, and $[Cu(Et_2NH)_2Cl_2]$, formed with the excess amine, caused the predominant polymerization, see: Ref. 4a.

12 It has been known that $[Cu(DMAP)_4Cl(OH)]$ was the most active species for the oxidation of 2,6-dimethylphenol to poly(oxy-1,4-phenylene) with Cu(II)-4-(dimethylamino)pyridine catalyst, see: C. E. Koning, G. Challa, F. B. Hulsbergen, and J. Reedijk, *J. Mol. Catal.*, **34**, 355 (1986). Moreover, a very high ratio of the Py unit of PVPy to $CuCl_2$ (ca. 40) was reported to give the maximum turnover number in the oxidation of 3,5-di-*t*-butylcatechol to *o*-benzoquinone, see: Ref. 2c.

13 For example, under similar conditions as Run 7 in Table 1, use of 10 and 3 mol% of the catalyst (1 : 1) gave **2a** (12%), **3a** (53%), **4a** (2%), and **5a** (8%) with 75% conversion and quantitative mass balance, and **2a** (80%), **3a** (1%), **4a** (9%), and **5a** (tr) with 100% conversion and 90% mass balance, respectively.

14 Shorter induction period (ca. 1 h) was also observed for the reaction with $CuCl_2$–bipyridine. However, these phenomena were not found with ^{n}Pr$_2$NH and pyridine.

15 Decrease of the catalyst activity with increase of the Cl/Cu ratio over unity has been often observed in the oxidation of phenols, for example, see: Ref. 12.

16 In addition, the reaction with TMEDA and diethylenetriamine predominantly gave the dimer **8a** along with polymeric products.

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