peroxide, **4b** was also produced in some quantity if the reaction was not moisture free. The formation of **4b** in this reaction suggests the intermediacy of **3b**.

Oxide **9** was stable to moisture but, when allowed to react with aqueous sodium hydroxide, gave 2-carboxyphenyl phenyl selenone (**13**) in good yield. The formation of **13** from **9** also provides support for the selenurane oxide structure of **9**.

Experimental Section

^1H and ^{13}C NMR spectra were taken at an ambient temperature of 29 °C on a JEOL FX-60Q spectrometer operating at 60 and 15 MHz, respectively. ^{77}Se NMR spectra were obtained on a Varian FT-80A spectrometer at 15.2 MHz. IR spectra were determined for Nujol mulls with a Hitachi 295 infrared spectrophotometer.

Preparations of **4a,b**, **2a,b**, and **7** are described elsewhere.[8,13]

Reaction of 2a with *tert*-Butyl Hydroperoxide in the Presence of 1,1'-Carbonyldiimidazole. To a stirred solution of 1 g (4.7 mmol) of **2a** in 50 mL of THF was added 5.0 mmol of 1,1'-carbonyldiimidazole. After 30 min at 40 °C, 1.3 g (14 mmol) of *tert*-butyl hydroperoxide in 10 mL of THF was added at −10 °C, and the mixture was stirred for 30 h at −15 °C. The solvent was removed under reduced pressure at temperature below 0 °C. The residue contained **3a** and **4a** in a ratio of ca. 4:1 as judged by ^{13}C NMR: δ 37.0 for **3a** and δ 40.8 for **4a**. After attempted separation by fractional dissolution in ether, only **4a** [0.74 g (69%); mp 161–162 °C (lit.[13] mp 162–163 °C)] was obtained.

^{13}C NMR Monitoring of the Reaction of 2a with *tert*-Butyl Hydroperoxide. A solution of 100 mg of **2a** in 1.5 mL of THF was placed in a 10-mm-o.d. NMR tube fitted with a D_2O capillary for an external lock. The reaction was started by adding 70 mg of 1,1'-carbonyldiimidazole to the solution. ^{13}C NMR spectra were measured by using a 45° pulse of 3 s. A reasonable s/n ratio of higher than 5 of the methyl carbon signals was obtained by accumulating ca. 300 transients. Measurements were repeated every 20–40 min.

The reactions in chloroform were similarly monitored.

Reaction of 8 with *tert*-Butyl Hydroperoxide. To a solution of 5.0 g (55 mmol) of *tert*-butyl hydroperoxide and 5.9 g (75 mmol) of pyridine in 150 mL of ether was added dropwise 9.5 g (32 mmol) of 2-(phenylseleno)benzoyl chloride (**8**) in 200 mL of ether at −10 °C, and the mixture was stirred for 5 days at −15 °C. The reaction mixture was filtered, and the filtrate was concentrated to about 30 mL at a temperature below 0 °C. The residue was chromatographed on basic alumina (Merck, aluminum oxide 60, activity grade I) with ether at −15 °C. Two compounds **3b** and **9** were obtained. After recrystallization from ether, **9** was isolated as microcrystalline colorless solid: 0.96 g (8.2%); mp 153.5–155 °C. Anal. Calcd for $C_{17}H_{18}O_4Se$: C, 55.89; H, 4.96. Found: C, 55.59; H, 4.97. During the attempted purification of **3b** from the mother liquor, the ^1H NMR signal due to **3b** at δ 1.25 disappeared and **4b** [0.73 g (7.8%); mp 198–201 °C] was obtained instead. Anal. Calcd for $C_{13}H_{10}O_3Se$: C, 53.26; H, 3.44. Found: C, 53.04; H, 3.49.

The insoluble fraction from the reaction mixture gave, after washing with water and recrystallization from benzene, 3.2 g (37%) of 2-(phenylseleno)benzoic anhydride (**10**) as colorless needles, mp 162–163 °C. Anal. Calcd for $C_{26}H_{18}O_3Se_2$: C, 58.21; H, 3.36. Found: C, 58.05; H, 3.34.

Anhydride **10** was also obtained in good yield from the reaction of **8** with **2b** in ether in the presence of pyridine.

Reaction of 2b with *tert*-Butyl Hydroperoxide. To a solution of 1 g (3.6 mmol) of **2b** in 30 mL of chloroform was added 0.90 g (10 mmol) of *tert*-butyl hydroperoxide in 10 mL of chloroform, and the mixture was stirred for 5 h at an ambient temperature. The residue obtained after evaporation of the solvent in vacuo was washed with ether to give 1.2 g (91%) of **9** as microcrystalline solid.

2-Carboxyphenyl Phenyl Selenone (13). To a solution of 500 mg (1.4 mmol) of **9** in 5 mL of ethanol was added 500 mg of sodium hydroxide in 10 mL of 50% aqueous ethanol, and the mixture was stirred under reflux for 3 h. The solution was concentrated to ca. 5 mL, acidified by dilute hydrochloric acid, and treated with chloroform. Crystallization from hexane–chloroform gave **13**: 270 mg (64%); mp 194–196 °C. Anal. Calcd for $C_{13}H_{10}O_4Se$: C, 50.50; H, 3.26. Found: C, 50.24; H, 2.84.

Acknowledgment. This work was supported by the Grant-in-Aids for Scientific Research from the Ministry of Education, Science, and Culture (No. 374166 and 454160).

Registry No. 1a, 81408-03-9; **2a**, 6547-08-6; **2b**, 25562-42-9; **3a**, 81113-79-3; **3b**, 81113-82-8; **4a**, 40242-21-5; **4b**, 81113-85-1; **5a**, 81113-80-6; **8**, 81113-84-0; **9**, 81113-83-9; **10**, 81389-54-0; **13**, 81389-55-1; 1,1'-carbonyldiimidazole, 530-62-1; *tert*-butyl hydroperoxide, 75-91-2; 2-$MeSeC_6H_4COOMe$, 78377-06-7; 2-$PhSeC_6H_4COOMe$, 80014-45-5; 2-$MeSe(O)C_6H_4COOMe$, 80014-48-8; 2-$PhSC_6H_4COOH$, 1527-12-4; 2-$PhSO_2C_6H_4COOH$, 58844-73-8.

Oxygenation of 2,6-Di-*tert*-butylphenols Bearing an Electron-Withdrawing Group in the 4-Position[1]

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Co(Salpr), a five-coordinate cobalt(II) Schiff base complex, has been found to promote oxygenation of 2,6-di-*tert*-butylphenols bearing an electron-withdrawing group in the 4-position, leading to dioxygen incorporation exclusively into the ortho position of the phenols. 4-Acyl-2,6-di-*tert*-butylphenols (**1**) and their oxime *O*-methyl ethers (**2**) gave the corresponding 6-hydroperoxy-2,4-cyclohexadienone derivatives **3** and **4** quantitatively. Schiff bases **10** derived from 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde, on the other hand, gave unexpected products, 1,2-dihydropyridine derivatives **11**, cyclopentadienone **12**, and epoxy-*o*-quinol **13**. The structure of dihydropyridine **11a** was determined by X-ray analysis. 2,6-Di-*tert*-butyl-4-cyanophenol gave 2,5-di-*tert*-butyl-3-cyano-2,4-cyclopentadienone in good yield. The formation of these products can be understood to result from intramolecular decomposition of the corresponding *o*-peroxidic intermediate. Phenols **2** were readily oxygenated in *t*-BuOH containing *t*-BuOK to give epoxy-*o*-quinols **7** in excellent yield, although the other phenols examined were unsusceptible to oxygenation under various basic conditions.

In our previous works,[2] Co(Salpr), a five-coordinate cobalt(II)–Schiff base complex capable of binding dioxygen, has been demonstrated to mediate oxygenation of 4-alkyl- and 4-aryl-2,6-di-*tert*-butylphenols, leading to

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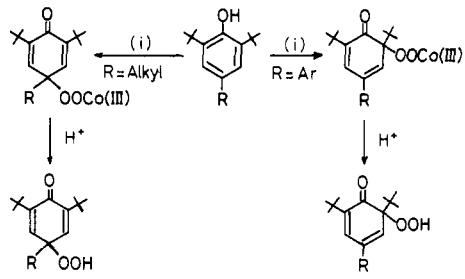
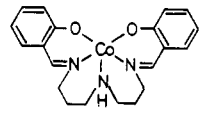
Scheme I

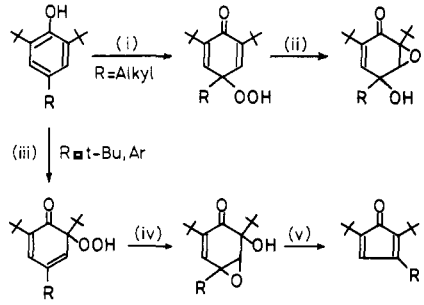


(i); O_2 / Co(Salpr) / CH_2Cl_2



Co(Salpr)

Scheme II



(i); O_2 / KOH / EtOH / 0°C or O_2 / t-BuOK / t-BuOH

(ii); O_2 / t-BuOK / DMF / r.t.

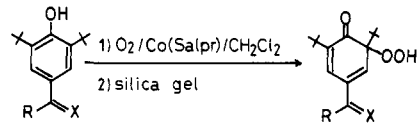
(iii); O_2 / t-BuOK / t-BuOH - PE / 0°C

(iv); O_2 / t-BuOK / t-BuOH / 40°C

(v); t-BuOK / t-BuOH / 70°C

regioselective dioxygen incorporation into the phenolic ring. The regioselectivity depends on the nature of substituent in the 4-position of the phenols. With 4-alkyl-2,6-di-*tert*-butylphenols, the oxygenation takes place in the *para* position to give peroxy-*p*-quinolato-Co^{III}(Salpr) complexes, whereas 4-aryl-2,6-di-*tert*-butylphenols are oxygenated exclusively in the ortho position, affording peroxy-*o*-quinolato-Co^{III}(Salpr) complexes. These peroxy complexes give the corresponding *p*- and *o*-hydroperoxides quantitatively upon treatment with silica gel (Scheme I). The same regioselective dioxygen incorporation has been observed in base-promoted oxygenation of these phenols, where the nature of the products depends on reaction conditions. For example, with 4-alkyl-2,6-di-*tert*-butylphenols, the oxygenation in alkaline ethanol gives peroxy-*p*-quinols, whereas in *N,N*-dimethylformamide (DMF) containing *t*-BuOK, epoxy-quinols are exclusively obtained. On the other hand, 4-aryl-2,6-di-*tert*-butylphenols can be oxygenated only when reaction conditions are selected so that phenolate anions are able to be associated with the countercation of the base used, where dioxygen is incorporated exclusively into the ortho position to give peroxy-*o*-quinols at low temperature, epoxy-*o*-quinols at 40 °C, and cyclopentadienones at 70 °C (Scheme II).[3]

Scheme III



1 (X = O) 3 (X = O)

2 (X = NOMe) 4 (X = NOMe)

a; R = H **b**; R = Me **c**; R = Et

d; R = i-Pr **e**; R = t-Bu **f**; R = Ph

e; R = OMe

These observations provide useful suggestions for understanding the mechanism of the oxygenation of phenolic compounds with metal complexes capable of binding dioxygen, which are of interest in both biological and synthetic systems.[2] In order to obtain further information on the highly regioselective phenolic oxygenation capabilities of Co(Salpr), we became interested in investigating the oxygenation of 2,6-di-*tert*-butylphenols bearing an electron-withdrawing group in the 4-position with Co(Salpr) as well as with bases.

Results

Co(Salpr)-Promoted Oxygenation of 4-Acyl-2,6-di-*tert*-butylphenols (1) and Their Oxime *O*-Methyl Ethers (2). The oxygenation of **1** with an equimolar amount of Co(Salpr) in dichloromethane at room temperature, although the reaction was slower than the Co(Salpr)-promoted oxygenation of 4-alkyl- and 4-aryl-2,6-di-*tert*-butylphenols, gave 2,6-di-*tert*-butyl-6-hydroperoxy-2,4-cyclohexadienone derivatives (**3**) quantitatively upon treatment of the reaction mixture with silica gel (Scheme III). The products were isolated as crystals in excelllent yield. Compounds **3** show IR absorption bands (ν_{OH}, 3370–3460 cm^{-1}; ν_{CO}, 1685, 1675 cm^{-1}) and ^1H NMR olefinic proton signals (δ 7.01–7.31 and 7.13–7.48, pair of doublets, J = 2.4 Hz), which are typical for 2,4-cyclohexadienones.[4,5] Similar results were obtained with phenols **2**, which afforded peroxy-*o*-quinols **4** quantitatively (Scheme III). The ν_{CO} of **4** appears around 1680 cm^{-1}, and the ^1H NMR of **4** shows characteristic olefinic proton signals for the 2,4-cyclohexadienone system (δ 6.20–6.62 and 7.02–7.38, pair of doublets, J = 2.3 Hz). The higher field shift for the olefinic proton signals in **4** compared with those for **3** may be due to a substituent effect, where the methoxyimino group is more electron-releasing than the carbonyl group, as expected. The substituent effect was also implicated in the fact that the oxygenation of oxime *O*-methyl ethers **2** proceeded faster than that of ketones **1**. For example, the conversion at room temperature of **1b** in 4.5 h was 65%, whereas that of **2b** in 2 h was 75%. The rate of oxygenation of **2** depended on the size of the group R: a bigger R group retarded the reaction. With **2e**, no appreciable oxygenation product was detected in the reaction mixture at room temperature in 9 h. This suggests that the conjugation of the C=N bond to the phenolic ring plays an important role in the oxygenation

(1) Preliminary communications: (a) Nishinaga, A.; Shimizu, T.; Matsuura, T. *J. Chem. Soc., Chem. Commun.* **1979**, 970. Nishinaga, A.; Shimizu, T.; Matsuura, T. *Tetrahedron Lett.* **1980**, *21*, 1265; **1981**, *22*, 5293.

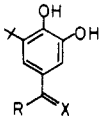
(2) Nishinaga, A.; Tomita, H.; Nishizawa, K.; Matsuura, T.; Ooi, S.; Hirotsu, K. *J. Chem. Soc., Dalton* Trans. **1981**, 1504.

(3) Nishinaga, A.; Itahara, T.; Shimizu, T.; Matsuura, T. *J. Am. Chem. Soc.* **1978**, *100*, 1820. (b) Nishinaga, A.; Itahara, T.; Matsuura, T.; Rieker, A.; Koch, D.; Albert, K.; Hitchcock, K. B. *Ibid.* **1978**, *100*, 1826. (c) Nishinaga, A.; Shimizu, T.; Matsuura, T. *J. Org. Chem.* **1979**, *44*, 2893. (d) Nishianga, A.; Shimizu, T.; Fujii, T.; Matsuura, T. *Ibid.* **1980**, *45*, 4997.

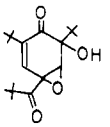
(4) Nishinaga, A.; Nishizawa, K.; Tomita, H.; Matsuura, T. *Synthesis* **1977**, 270.

(5) Rieker, A.; Rundel, W.; Kessler, H. *Z. Naturforsch. B, Anorg. Chem., Org. Chem.* **1969**, *B24*, 547.

of **2**. The structures **3** and **4** were further supported by their chemical reactions. The reduction of **3e** and **4b** with dimethyl sulfide at room temperature gave catechols **5a** and **5b** in quantitative yield, respectively. The treatment



5



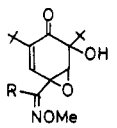
6

a; R = t-Bu, X = O

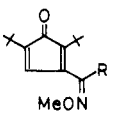
b; R = Me, X = NOMe

of **3e** with *t*-BuOK in *t*-BuOH or KOH in ethanol at room temperature afforded epoxy-*o*-quinol **6** quantitatively. Compound **6** was quite stable against *t*-BuOK in a hot *t*-BuOH solution, although epoxy-*o*-quinols of type **6** obtained from 4-aryl-2,6-di-*tert*-butylphenols readily undergo base-catalyzed decomposition in a hot *t*-BuOH solution containing *t*-BuOK to give 3-aryl-2,5-di-*tert*-butylcyclopentadienones.[6] Since peroxy-*o*-quinols of type **3** obtained from 4-aryl-2,6-di-*tert*-butylphenols are not converted to the corresponding epoxy-*o*-quinols in an ethanolic KOH solution,[3c] the electron-withdrawing nature of the 4-acyl group is responsible for the acceleration of the conversion of **3e** to epoxy-*o*-quinol **6**. 3,5-Di-*tert*-butyl-4-hydroxybenzaldehyde (**1a**), contrary to other phenols of type **1**, was not oxygenated with Co(Salpr). In this case, dark brown precipitates, $C_{35}H_{44}O_4N_3Co$ (mp >250 °C), were obtained in good yield. Since the precipitated complex gave the starting phenol **1a** quantitatively upon treatment with an acid, it should be a Co^{III}(Salpr) complex of the anion of this substrate, probably an enolate form, although no structural information was available because this complex is sparingly soluble in the usual solvents.

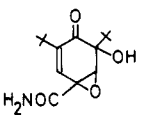
Base-Promoted Oxygenation of 2. Although phenols **1** were unsusceptible to base-promoted oxygenation under various basic conditions, their oxime *O*-methyl ethers (**2**) were oxygenated smoothly in *t*-BuOH containing *t*-BuOK. However, the oxygenation did not take place in DMF containing *t*-BuOK. The base-promoted oxygenation of **2** can be achieved only when their phenolate anions are associated with countercation K^+. This propensity is similar to that observed for base-promoted oxygenation of 4-aryl-2,6-di-*tert*-butylphenols.[3] The base-promoted oxygenation of **2** was affected remarkably by the nature of the group R in the 4-position. Thus, the oxygenation of **2b** at room temperature for 2 h gave epoxy-*o*-quinol **7b** (91%) and cyclopentadienone **8a** (9%) with a 93% con-



7



8



9

a; R = H

b; R = Me

c; R = i-Pr

d; R = t-Bu

a; R = Me

b; R = i-Pr

version. Similarly, **2d** gave **7c** (79%) and **8b** (9%), but the reaction was slower (94% conversion at room temperature in 15 h) than that of **2b**. Phenol **2e** was not dissolved at room temperature in the *t*-BuOH/*t*-BuOK system but dissolved at 50 °C. Therefore, the oxygenation of **2e** was carried out at 50 °C for 10 h to give **7d** (97%). In the oxygenation of **2a** with *t*-BuOK in *t*-BuOH at room temperature, on the other hand, unexpected product **9**[7] was obtained quantitatively (75% conversion in 6 h). However, normal product **7a** was obtained quantitatively when the oxygenation was carried out in dichloromethane at room temperature.

Table I. Oxygenation of 10 with Co(Salpr)[a]

compd	% conversion[b]	product yield,[b] % 11	12	13	15	others[c]
10a	72	70	trace	27		3
10b	89	81	trace	14		5
10c	85	65	15	15		5
10d	90	70	15	10		5
10e	85	*d*	40	15	20	15

[a] Oxygen was bubbled through a solution of **10** (1 mmol) of Co(Salpr) (1.1 mmol) in CH_2Cl_2 (20 mL) at 0 °C for 2 h. [b] Determined by ^1H NMR. [c] Not determined. [d] Compound **11e** seemed to be formed (ca. 10%) but was not confirmed.

The ^1H NMR spectra of **7** show two *t*-Bu signals (δ 0.92–1.0 and 1.21–1.24), a methine proton signal (δ 3.67–3.90, d, J = 0.3 Hz), an olefinic proton signal δ 6.42–7.29, d, J = 0.3 Hz), and an OH signal (δ 3.93–4.10). These signals are quite similar to those of epoxy-*o*-quinols obtained from 4-aryl-2,6-di-*tert*-butylphenols.[3b] Spectral and analytical data of cyclopentadienones **8** are in good agreement with the structure. Signals at δ 6.33 (C=CH), 1.14 (*t*-Bu), and 1.20 (*t*-Bu) for **8a**, and 6.21 (C=CH) 1.11 (*t*-Bu), and 1.18 (*t*-Bu) for **8b** are typical ones for 3-substituted 2,5-di-*tert*-butylcyclopentadienones.[6] The formation of epoxy-*o*-quinols **7** and cyclopentadienones **8** obviously results from dioxygen incorporation into the ortho position of **2**, taking into account the observations in the base-promoted oxygenation of 4-aryl-2,6-di-*tert*-butylphenols.[3b] The formation of cyclopentadienones of type **8** from 4-aryl-2,6-di-*tert*-butylphenols has been demonstrated to involve base-catalyzed decomposition (at an elevated temperature, 70 °C) of epoxy-*o*-quinols of type **7** which were intermediately formed.[8] On the contrary, treatment of **7b** with *t*-BuOK in *t*-BuOH at 70 °C or higher did not give **8a**. Therefore, the formation of **8** should involve another pathway, possibly a symmetric cleavage of a dioxetane intermediate formed by intramolecular addition of the peroxy anion of **4** to the dienone system as suggested for the oxygenation of phenols **10** (Scheme VII).

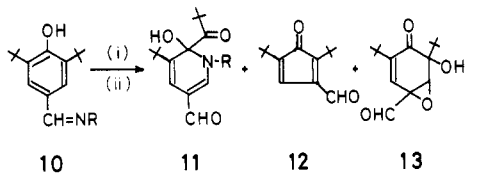
Co(Salpr)-Promoted Oxygenation of 4-[(*N*-Alkylimino)methyl]-2,6-di-*tert*-butylphenols (10). Phenols **10** were not oxygenated in the *t*-BuOH/*t*-BuOK system but underwent oxygenation readily in the presence of Co(Salpr) in dichloromethane at a low temperature. The oxygenation of **10** with Co(Salpr) was carried out at 0 °C for 2 h. Separation of the resulting products on a silica gel plate gave *N*-alkyl-3-*tert*-butyl-5-formyl-2-hydroxy-2-pivaloyl-1,2-dihydropyridines (**11**), 2,5-di-*tert*-butyl-3-formyl-2,4-cyclopentadienone (**12**), and 2,6-di-*tert*-butyl-4-formyl-6-hydroxy-4,5-epoxy-2-cyclohexenone (**13**) (Scheme IV). The results are summarized in Table I. In all cases except **10e**, the formation of **11** was predominant.

(6) Nishianga, A.; Itahara, T.; Matsuura, T.; Rieker, A.; Koch, D. *Angew. Chem.* **1976**, *88*, 154.

(7) The structure was tentatively assigned from its spectral and analytical data (see Experimental Section). This compound was also obtained when compound **7a** was treated with *t*-BuOK in *t*-BuOH under air.

(8) Nishinaga, A.; Rieker, A. *J. Am. Chem. Soc.* **1976**, *98*, 4667.

Scheme IV

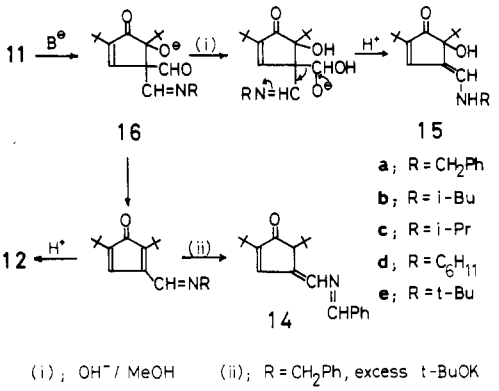


10 11 12 13

a; R = CH Ph **b**; R = i-Bu
c; R = i-Pr **d**; R = Cyclohexyl
e; R = t-Bu

(i); O_2 / Co(Salpr) / CH_2Cl_2 / 0°C
(ii); silica gel

Scheme V



16 15

a; R = CH_2Ph
b; R = i-Bu
c; R = i-Pr
d; R = C_6H_{11}
e; R = t-Bu

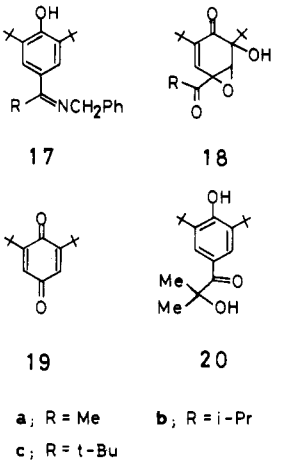
14

(i); OH^- / MeOH (ii); R = CH_2Ph, excess t-BuOK

Spectral data of **11** are all structurally well correlated to each other. The structure of **11a** was confirmed by X-ray analysis.[9] Although **11e** could not be isolated because of its instability under the chromatographic conditions, the ^1H NMR analysis of the reaction mixture showed the formation of **11e** (10%). Structures **12** and **13** were determined by their analytical and spectral data. The yield of **12** increases with an increase in bulkiness of the substituent R in **10**. With **10e**, compound **12** was the main product (Table I).

Treatment of **11a** with an equimolar amount of *t*-BuOK as well as treatment of **11b–d** with an excess of *t*-BuOK in *t*-BuOH at room temperature under a nitrogen atmosphere followed by an acidic treatment gave cyclopentadienone **12** quantitatively. Thus, the results provide a unique method for the preparation of **12** from 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (**1a**) via oxygenation. This is analogous to the base-promoted oxygenation of 4-aryl-2,6-di-*tert*-butylphenols, giving rise to the corresponding cyclopentadienones.[3b,c] When **11a** was treated with an excess of *t*-BuOK in *t*-BuOH, however, 4-(*N*-benzylideneamino)methylene-2,5-di-*tert*-butyl-2-cyclopentenone (**14**) was obtained in quantitative yield. Treatment of **11a–d** in methanol containing KOH at room temperature, on the other hand, resulted in deformylation to give 4-(*N*-alkylamino)methylene-2,5-di-*tert*-butyl-5-hydroxy-2-cyclopentenones **15a–d** quantitatively. These base-catalyzed reactions of **11** may be rationalized by assuming a key intermediate **16** as shown in Scheme V, which is analogous to the findings obtained for basic treatment of 2,5-di-*tert*-butyl-4-formyl-5-hydroxy-(4-methoxyphenyl)-2-cyclopentenone, confirmed as an intermediate in the oxygenation of 4-aryl-2,6-di-*tert*-butylphenols to 3-aryl-2,5-di-*tert*-butylcyclopentadienones.[8]

Co(Salpr)-Promoted Oxygenation of 4-[Alkyl(*N*-benzylimino)methyl]-2,6-di-*tert*-butylphenols (17). In order to examine substituent effect on the unusual oxygenation of **10** mentioned above, the oxygenation of phenols **17** with Co(Salpr) was investigated. Phenols **17** were

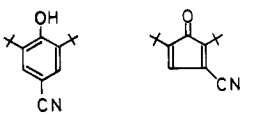


17 18 19 20

a; R = Me **b**; R = i-Pr
c; R = t-Bu

also unsusceptible to base-promoted oxygenation. In contrast with the oxygenation of **10**, the oxygenation of **17** with Co(Salpr) in dichloromethane gave a complex mixture. From **17a** were obtained epoxy-*o*-quinol **18a** (35%) and benzoquinone **19** (25%), and **17b** gave **18b** (50%), **19** (5%), and a phenolic alcohol (**20**, 20%). The oxygenation of **17c**, on the other hand, gave peroxy-*o*-quinol **3e** in 90% yield. All the products isolated were ones which underwent hydrolysis of the imino group probably during silica gel workup of the reaction mixture. The bulkiness of the substituent R in **17** also influenced the rate of the oxygenation, which was similar to the effect observed for the oxygenation of **2**. The formation of benzoquinone **19** seems to result from dioxygen incorporation into the para position of the phenols, and compound **20** arises evidently from the oxygenation on the side chain. These results indicate that selectivity in the dioxygen incorporation into Schiff bases of 4-acylphenols **1** strongly depends on the nature of the para substituent.

Co(Salpr)-Promoted Oxygenation of 4-Cyano-2,6-di-*tert*-butylphenol (21). Phenol **21** was not oxygenated



21 22

in the *t*-BuOH/*t*-BuOK system but underwent oxygenation in dichloromethane in the presence of Co(Salpr), although the reaction was very slow (1 week was required to obtain a 50% conversion). Silica gel chromatographic separation of the reaction mixture gave 3-cyano-2,5-di-*tert*-butylcycloheptadienone (**22**) in 60% yield.

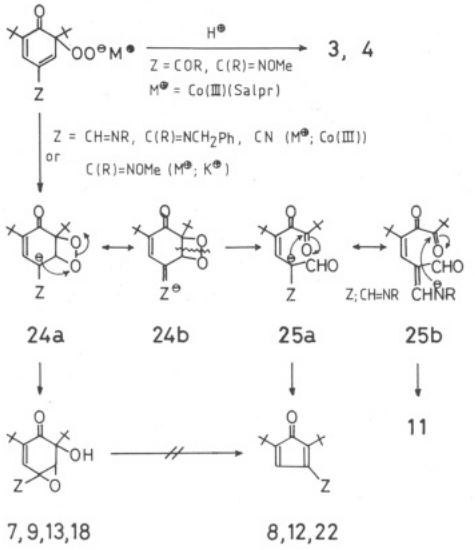
Discussion

In general, 2,6-di-*tert*-butylphenols bearing an electron-withdrawing group in the 4-position, except for phenols **2**, are unsusceptible to base-promoted oxygenation. The reason why only phenols **2** among other phenols examined in this work can undergo the base-promoted oxygenation is not clear, although the electron-releasing effect of the methoxy group may be responsible.

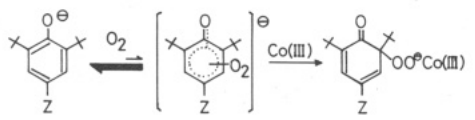
The formation of all the products except **19** and **20** apparently involves *o*-peroxidic intermediates as illustrated

(9) The dihydropyridine ring of **11a** is planar within 0.035 Å. An sp^2 hybridization is therefore assumed for the nitrogen atom since sum of the valence angles around this atom is 359.2°. All X-ray data are in the supplementary material.

Scheme VI



Scheme VII



in Scheme VII. It is therefore noted that Co(Salpr) has the ability of mediating the oxygenation of 2,6-di-*tert*-butylphenols bearing an electron-withdrawing group in the 4-position, leading to the dioxygen incorporation into the ortho position of the substrate.

Oxygenation of phenolate anions has been shown to be a reversible process.[3c,d,10] Therefore, the apparent unsusceptibility of phenols **1**, **10**, **17**, and **21** to base-promoted oxygenation may be rationalized by assuming an equilibrium between phenolate and oxygenated peroxidic anions that shifts extremely to the phenolate anion, and the observed acceleration of the oxygenation by Co(Salpr) may be due to stabilization of the peroxidic anion by complexation, giving rise to peroxy-*o*-quinolato–Co^{III}(Salpr) complex **23** as shown in Scheme VI. Analogous peroxyquinolato–Co^{III}(Salpr) complexes have been isolated in the oxygenation of 4-alkyl- and 4-aryl-2,6-di-*tert*-butylphenols with Co(Salpr).[2] Reactivity of the peroxy-*o*-quinolate species depends on the nature of the substituent Z and the countercation in **23**. With Z = COR and C(R) = NOMe, Co^{III}(Salpr) complex **23** is so stable that the corresponding peroxy-*o*-quinol is obtained quantitatively by silica gel workup, whereas potassium salts of **4** readily undergo decomposition.[3] The instability of **23** derived from **10**, **17**, and **21** is remarkable. With these phenols, no characteristic signals for **23** were observed in the ^1H NMR spectra of the oxygenation mixture before silica gel workup. The unusual instability of these peroxy Co^{III} complexes may be attributable to the nitrogen atom in Z which would accelerate ionic cleavage of the Co–O bond, leading to dioxetane intermediate **24** (Scheme VIII).[11] Assymetric cleavage of the peroxy bond (**24a**) is the normal case as seen in base-promoted oxygenation of 2,6-di-*tert*-butylphenols, and cyclopentadienones are usually derived from

Scheme VIII[a]

$$Co(Salpr) + O_2 \longrightarrow \underset{[Co^{II}]}{Co^{III}(Salpr)(O_2^-)} \quad (1)$$
$$\underset{[Co^{III}(O_2^-)]}{Co^{III}(O_2^-)} + PH \longrightarrow P\cdot + Co^{III}(OOH^-) \quad (2)$$
$$P\cdot + Co^{II} \longrightarrow P^-Co^{III} \quad (3)$$
$$Co^{III}(OOH^-) \longrightarrow Co^{III}(OH^-) + {}^1/_2O_2 \quad (4)$$
$$Co^{III}(OH^-) + PH \longrightarrow P^-Co^{III} + H_2O \quad (5)$$

or

$$Co^{III}(O_2^-) + PH \longrightarrow P^-Co^{III} + HOO\cdot \quad (6)$$
$$HOO\cdot \longrightarrow {}^1/_2H_2O + {}^3/_4O_2 \quad (7)$$
$$P^-Co^{III} + O_2 \longrightarrow POO^-Co^{III} \quad (8)$$

[a] PH = phenol substrate; POO^-Co^{III} = peroxy-*o*-quinolato-Co^{III}(Salpr) complex.

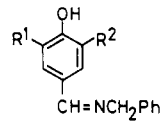
the resulting epoxy-*o*-quinols.[3] However, in the oxygenation of **10**, the product ratios **13**/**11** and **13**/**12** were not changed with changing reaction time. It is therefore clear that the formation of **11** and **12** results from symmetric cleavage of the dioxetane intermediate (**24b**) but not from the assymetric one (**24a**). This is the first example that demonstrates such a symmetric cleavage of the dioxetane intermediate derived from peroxyquinols, providing a model for the mechanism postulated for the meta-pyrocatechase reaction.[12] The formation of all products derived from **23** may be rationalized by the diagram depicted in Scheme VII. Epoxy-*o*-quinols **7**, **9**, **13**, and **18** are formed by the normal assymetric decomposition of dioxetane intermediate **24a**. When the dioxetane intermediate is stabilized by the substituent Z through resonance, on the other hand, **24b** may have a chance to undergo a symmetric cleavage of the peroxy bond to give **25a**, which finally gives cyclopentadienenones **8**, **12**, and **22** via key intermediates of type **16**. With Z = CH=NR, **25b** is stabilized and gives **11**.

Interestingly, the ortho regioselectivity observed in the present oxygenation is in contrast to that observed in the reaction of phenoxy radicals derived from **1b**, **1g**, and **21** with a superoxo Co(III) complex, where radical coupling takes place selectively at the para position of the phenoxy radicals, giving rise to the corresponding peroxy-*p*-quinols.[13] It is therefore evident that such a radical-coupling mechanism is not involved in the present oxygenation, although Co^{III}(Salpr) ($O_2^-\cdot$), a superoxo complex, is obviously the initial reactive species in the Co(Salpr)-promoted oxygenation.[2] A mechanism involving direct incorporation of dioxygen into a (phenolato)cobalt(III) complex intermediate (Scheme VIII, eq 8) may be acceptable as suggested for the Co(Salpr)-promoted oxygenation of 4-alkyl- and 4-aryl-2,6-di-*tert*-butylphenols.[2] Involvement of hydrogen abstraction by $Co^{III}(O_2^-\cdot)$ from the phenol substrate giving rise to the corresponding phenoxy radical followed by reduction of the resulting phenoxy radical by Co(Salpr) to give a (phenolato)cobalt(III) complex intermediate (Scheme VIII, eq 2–5) has been demonstrated for the oxygenation of 4-alkyl- and 4-aryl-2,6-di-*tert*-butylphenols.[2,14,15] However, it is not clear in the present case whether Co^{III}(Salpr) ($O_2^-\cdot$) abstracts hydrogen from the phenols bearing an electron-

(10) Nishinaga, A.; Shimizu, T.; Matsuura, T. *Chem. Lett.* **1977**, 547.
(11) The stability of **23** obtained from **2** which has a nitrogen atom in the side chain is rather exceptional. The reason is obscure.
(12) Nozaki, M. "Molecular Mechanism of Oxygen Activation"; Hayaishi, O., Ed.; Academic Press: New York and London, 1974; p 144.
(13) Nishinaga, A.; Tomita, H.; Matsuura, T. *Tetrahedron Lett.* **1980**, 3407.
(14) Nishinaga, A.; Tomita, H. *J. Mol. Catal.* **1980**, *7*, 179.
(15) Nishinaga, A.; Itahara, T.; Shimizu, T.; Tomita, H.; Nishizawa, K.; Matsuura, T. *Photochem. Photobiol.* **1978**, *28*, 687.

withdrawing group in the 4-position or acts as a base to accept a proton from the substrate (Scheme VIII, eq 6, 7).

The oxygenation of phenols **26** ($R^1 = R^2 = OMe$; $R^1 = R^2 = Me$; $R^1 = OMe$, $R^2 = H$) with *t*-BuOK and/or Co-



26

(Salpr) was also examined, but no reaction took place. The results may be attributed to the nature of the anionic species of these phenols, which exist in stable phenoxide forms and do not produce the carbanion in the phenolic ring required for oxygenation.

Experimental Section

All melting points are uncorrected. Elemental analyses were performed by the Analytical Center of Pharmaceutical Department, Kyoto University. Infrared spectra were recorded on a JASCO IR-1 spectrophotometer. Ultraviolet spectra were recorded on a Shimazu UV-200 spectrophotometer. Proton magnetic resonance spectra were determined with a Varian T-60 spectrometer. Solvents were dried and distilled before use. Co(Salpr) was prepared according to the reported method.[16]

Preparation of 4-Acyl-2,6-di-*tert*-butylphenols (1). 2,6-Di-*tert*-butylphenol (60 mmol) was added to a solution of an appropriate carboxylic acid (80 mmol) in trifluoroacetic anhydride (13 mL) at 0 °C. After being allowed to stand at room temperature for 3 h, the mixture was poured into an ice-cooled aqueous bicarbonate solution and extracted with dichloromethane. The extract was dried (Na_2SO_4) and evaporated to give a semicrystalline residue. Trituration of the residue with petroleum ether gave **1** as crystals. 4-(Methoxycarbonyl)-2,6-di-*tert*-butylphenol (**1g**) was prepared according to the reported method.[17]

1b: yield 87%; mp 147–148 °C (lit.[18] mp 150–151 °C); ^1H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 2.53 (s, 3 H), 5.68 (s, 1 H, OH), 7.83 (s, 2 H). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.43; H, 9.80.

1d: yield 92%; mp 145–147 °C; ^1H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 1.21 (d, J = 7 Hz, 6 H), 3.53 (septet, J = 7 Hz, 1 H), 5.66 (s, 1 H, OH), 7.86 (s, 2 H); IR (Nujol) 3580, 1675 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.23; H, 10.04.

1e: yield 54%; mp 137–139 °C (lit.[19] mp 133–134 °C); ^1H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 1.38 (s, 9 H), 5.58 (s, 1 H, OH), 7.77 (s, 2 H). Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.66; H, 10.68.

1f: yield 65%; mp 132–134 °C (lit.[19] mp 124–125 °C); ^1H NMR ($CDCl_3$) δ 1.45 (s, 18 H), 5.70 (s, 1 H, OH), 7.73 (s, 2 H), 7.4–7.9 (m, 5 H). Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.52; H, 8.52.

Co(Salpr)-Promoted Oxygenation of 1. Oxygen was bubbled through a solution of **1** (1 mmol) in dichloromethane (20 mL) containing Co(Salpr) (1.1 mmol) at room temperature for 4.5 h. The mixture was filtered through a short column of silica gel (5 g) to remove the metal complex. The filtrate was chromatographed on a silica gel plate developed with dichloromethane to give 4-acyl-2,6-di-*tert*-butyl-6-hydroperoxy-2,4-cyclohexadienone (**3**) as yellow crystals. The conversions of **1b,d–g** were 65%, 75%, 60%, 60%, and 53%, respectively, as determined by ^1H NMR. The IR and ^1H NMR spectra of **3** are available as supplementary material.

3b: yield 96%; mp 105 °C dec. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.64; H, 8.87.

3d: yield 98%; mp 115 °C dec. Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.34. Found: C, 70.08; H, 9.34.

3e: yield 98%; mp 112 °C dec. Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.52; H, 9.34.

3f: yield 92%; mp 107 °C dec. Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.66. Found: C, 73.81; H, 7.77.

3g: yield 93%; mp 92 °C dec. Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.66; H, 7.96.

Reduction of 3e with Dimethyl Sulfide. Dimethyl sulfide (1 mL) was added dropwise to a solution of **3e** (1 mmol) in dichloromethane (5 mL) at 0 °C. After being allowed to stand at room temperature for 30 min, the mixture was evaporated in vacuo to give catechol **5a** (100% yield) as colorless crystals: mp 144–146 °C; ^1H NMR ($CDCl_3$) δ 1.38 (s, 9 H), 1.42 (s, 9 H), 6.38 (s, 1 H, OH), 7.54 (d, J = 2.2 Hz, 1 H), 7.60 (d, J = 2.2 Hz, 1 H), 7.97 (s, 1 H, OH); IR (Nujol) 3550, 3430, 1660 cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.17; H, 8.89.

Base-Catalyzed Reaction of 3e. Compound **3e** (1 mmol) was added to a mixture of *t*-BuOH and petroleum ether (1:1, 10 mL) containing *t*-BuOK (3 mmol) of alkaline ethanol (KOH, 3 mmol; EtOH; 10 mL) at 0 °C. After being allowed to stand at room temperature for 30 min, the mixture was poured into an ice-cooled aqueous NH_4Cl solution and extracted with ether. The extract was dried (Na_2SO_4) and evaporated to leave epoxy-*o*-quinol **6** (100% yield) as colorless needles: mp 151–152 °C; ^1H NMR ($CDCl_3$) δ 0.98 (s, 9 H), 1.21 (s, 9 H), 1.23 (s, 9 H), 3.80 (d, J = 0.8 Hz, 1 H), 4.03 (s, 1 H, OH), 6.76 (d, J = 0.8 Hz, 1 H); IR (Nujol) 3530, 1710, 1690 cm^{-1}. Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.80; H, 9.51.

Preparation of 4-Acyl-2,6-di-*tert*-butylphenol Oxime *O*-Methyl Ethers (2). Compounds **2** were prepared according to the reported method.[19,21] Among compounds **2**, **2c** and **2d** are new.

2c: bp 107–109 °C (2 mmHg); ^1H NMR ($CDCl_3$) δ 1.15 (t, J = 7 Hz, 3 H), 1.46 (s, 18 H), 2.73 (q, J = 7 Hz, 2 H), 3.94 (s, 3 H), 5.32 (s, 1 H, OH), 7.45 (s, 2 H); IR (Nujol) 3718 cm^{-1}. Anal. Calcd for $C_{18}H_{29}NO_2$: C, 74.18; H, 10.03; H, 4.87. Found: C, 73.97; H, 9.89; N, 4.71.

2d: mp 101–103 °C; ^1H NMR ($CDCl_3$) δ 1.14 (d, J = 7 Hz, 6 H), 1.43 (s, 18 H), 3.91 (s, 3 H), 5.21 (s, 1 H, OH), 7.14 (s, 2 H); IR (Nujol) 3729 cm^{-1}. Anal. Calcd for $C_{19}H_{31}NO_2$: C, 74.64; H, 10.23; N, 4.59. Found: C, 74.71; H, 10.30; N, 4.60.

Co(Salpr)-Promoted Oxygenation of 2. Oxygen was bubbled through a solution of **2** (2 mmol) and Co(Salpr) (2.2 mmol) in dichloromethane (10 mL). Reaction conditions (temperature, time, and conversion) were as follows: **2a**, 0 °C, 6 h, 87%; **2b**, 20 °C, 2 h, 75%; **2c**, 0 °C, 6 h, 55%; **2d**, 0 °C, 10 h, 66%; **2e**, 20 °C, 9 h, or 70 °C, 10 h, 0% (no reaction). The mixture was filtered through a short column of silica gel (10 g) to remove the metal complex. The filtrate was evaporated to leave a crystalline residue, which was recrystallized from petroleum ether to give *o*-hydroperoxide **4** as pale yellow prisms. The IR and ^1H NMR spectra of **4** are available as supplementary material. The yield of **4** was quantitative on the basis of the conversion.

4a, mp 114–116 °C. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74. Found: C, 65.02; H, 8.67; N, 4.68.

4b, mp 127–128 °C. Anal. Calcd for $C_{17}H_{27}NO_4$: C, 65.99; H, 8.80; N, 4.53. Found: C, 65.90; H, 8.97; N, 4.59.

4c, mp 122–124 °C. Anal. Calcd for $C_{18}H_{29}NO_4$: C, 66.85; H, 9.04; N, 4.33. Found: C, 66.92; H, 9.14; N, 4.57.

4d, mp 125–127 °C. Anal. Calcd for $C_{19}H_{31}NO_4$: C, 67.63; H, 9.26; N, 4.15. Found: C, 67.49; H, 9.34; N, 4.07.

Base-Promoted Oxygenation of 2. Oxygen was bubbled through a solution of **2** (1 mmol) and *t*-BuOK (4 mmol) in *t*-BuOH (10 mL) containing petroleum ether (5 mL) at room temperature for an appropriate time: 4, 2, 15, and 10 h for **2a**, **2b**, **2d**, and **2e**, respectively. With **2e**, the reaction was carried out at 50 °C, because no clear solution was obtained at room temperature. The mixture was poured into an ice-cooled dilute HCl solution (60 mL) and extracted with petroleum ether. The extract was dried (Na_2SO_4) and evaporated to leave an oily residue, which was chromatographed on a silica gel plate developed with a mixture of dichloromethane and petroleum ether (1:1). Epoxy-*o*-quinols, **7a,b,d** were crystallized and recrystallized from methanol to give

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(17) Müller, E.; Rieker, A.; Mayer, R.; Scheffler, K. *Justus Liebigs Ann. Chem.* **1961**, *645*, 36.
(18) Matsuura, T.; Nishinaga, A.; Cahnmann, H. J. *J. Org. Chem.* **1962**, *27*, 3620.
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(20) Cook, C. D.; Gilmour, N. D. *J. Org. Chem.* **1960**, *25*, 1429.
(21) Müller, E.; Mayer, R.; Narr, B.; Rieker, A.; Scheffler, K. *Justus Liebigs Ann. Chem.* **1961**, *645*, 19.

colorless prisms. Compound **7c** and cyclopentadinones **8a,b** were purified by distillation. The conversion of **2** was determined by the ^1H NMR of the reaction mixture: 70%, 93%, 94% and 86% for **2a**, **2b**, **2d**, and **2e**, respectively.

7a: CH_2Cl_2 was used as solvent instead of *t*-BuOH; yield 100%; mp 110–113 °C; ^1H NMR ($CDCl_3$) δ 0.92 (s, 9 H), 1.21 (s, 9 H), 3.80 (d, J = 0.3 Hz, 1 H), 3.93 (s, 3 H), 4.04 (s, 1 H, OH), 7.06 (s, 1 H), 7.20 (d, J = 0.3 Hz, 1 H); IR (Nujol) 3550, 1690 cm^{-1}. Anal. Calcd for $C_{16}H_{25}NO_4$: C, 65.06: H, 8.53; N, 4.74. Found: C, 65.02; H, 8.64; N, 4.70.

7b: yield 91%; mp 78–79 °C; ^1H NMR ($CDCl_3$) δ 0.98 (s, 9 H), 1.24 (s, 9 H), 1.75 (s, 3 H), 3.80 (d, J = 0.3 Hz, 1 H), 3.95 (s, 3 H), 4.10 (s, 1 H, OH), 7.29 (d, J = 0.3 Hz, 1 H); IR (Nujol) 3560, 1690 cm^{-1}. Anal. Calcd for $C_{17}H_{27}NO_4$: C, 65.99; H, 8.80; N, 4.53. Found: C, 67.49; H, 9.34; N, 4.07.

7c: yield 79%; bp 100–102 °C (2 mmHg); ^1H NMR ($CDCl_3$) δ 1.00 (s, 9 H), 1.22 (s, 9 H), 1.20 (d, J = 7 Hz, 6 H), 2.72 (septet, J = 7 Hz, 1 H), 3.82 (d, J = 0.3 Hz, 1 H), 3.89 (s, 3 H), 4.04 (s, 1 H, OH), 7.05 (d, J = 0.3 Hz, 1 H); IR (Nujol) 3550, 1690 cm^{-1}. Anal. Calcd for $C_{19}H_{31}NO_4$: C, 67.62; H, 9.26; N, 4.15. Found: C, 67.73; H, 9.46; N, 4.23.

7d: yield 97%; mp 88–90 °C; ^1H NMR ($CDCl_3$) δ 1.03 (s, 9 H), 1.20 (s, 9 H), 1.22 (s, 9 H), 3.67 (d, J = 0.1 Hz, 1 H), 3.80 (s, 3 H), 3.93 (s, 1 H, OH), 6.42 (d, J = 0.1 Hz, 1 H); IR (Nujol) 3550 1690 cm^{-1}. Anal. Calcd for $C_{20}H_{33}NO_4$: C, 68.34; H, 9.46; N, 3.99. Found: C, 68.33; H, 9.70; N, 4.18.

8a: yield 9%; bp 65–68 °C (2 mmHg); ^1H NMR ($CDCl_3$) δ 1.14 (s, 9 H), 1.20 (s, 9 H), 1.98 (s, 3 H), 3.93 (s, 3 H), 6.33 (s, 1 H); IR (neat) 1718 cm^{-1}; UV (C_6H_{12}) λ_{max} 412 nm (ϵ 457). Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57; N, 5.32. Found: C, 72.88; H, 9.79; N, 5.07.

8b: yield 9%; bp 62–65 °C (2 mmHg); ^1H NMR ($CDCl_3$) δ 1.11 (s, 9 H), 1.18 (s, 9 H), 1.22 (d, J = 7 Hz, 6 H), 3.16 (septet, J = 7 Hz, 1 H), 3.87 (s, 3 H), 6.21 (s, 1 H); IR (neat) 1720 cm^{-1}; UV (C_6H_{12}) λ_{max} 412 nm (ϵ 451). Anal. Calcd for $C_{18}H_{29}NO_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 73.93; H, 10.24; N, 4.71.

Phenol **2a** (0.26 g, 1 mmol) was oxygenated in the *t*-BuOK/*t*-BuOH system for 6 h, and the mixture was acidified in the same way as described above. The resulting mixture was extracted with ether. The extract was dried (Na_2SO_4) and evaporated to leave an oily residue (0.2 g), whose ^1H NMR spectrum showed only signals for **2a** (75% conversion) and product **9**. The residue was chromatographed on a silica gel plate developed with a mixture of dichloromethane and ethyl acetate (1:1). Elution of a band near the original point with methanol gave **9** as crystals. Recrystallization from a mixture of dichloromethane and petroleum ether (1:2) gave colorless prisms: mp 191–193 °C; ^1H NMR ($CDCl_3$) δ 1.00 (s, 9 H), 1.24 (s, 9 H), 3.89 (s, 1 H), 4.09 (s, 1 H, OH), 5.91 (br s, 1 H), 6.31 (br s, 1 H), 7.10 (s, 1 H); IR (nujol) 3470, 3250, 1720, 1685 cm^{-1}. Anal. Calcd for $C_{15}H_{23}NO_4$: C, 64.03; H, 8.24; N, 4.98. Found: C, 64.35; H, 8.31; N, 4.94.

Preparation of 4-[(*N*-Alkylimino)methyl]-2,6-di-*tert*-butylphenols (10). Phenols **10** were prepared by the condensation of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (**1a**)[22] with alkylamines. A solution of **1** (R = H, 10 mmol) and an appropriate alkylamine (11 mmol) in absolute ethanol (30 mL) was refluxed for 3 h. The solution was evaporated to give a semicrystalline residue. Trituration of the residue with petroleum ether gave **10** as crystals in nearly quantitative yield.

10a: mp 140–142 °C; ^1H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 4.77 (s, 2 H), 5.45 (s, 1 H, OH), 7.27 (s, 5 H), 7.58 (s, 2 H), 8.29 (s, 1 H); IR (nujol) 3120, 1635 cm^{-1}. Anal. Calcd for $C_{22}H_{29}NO$: C, 81.69; H, 9.04; N, 4.33. Found: C, 81.65; H, 9.12; N, 4.20.

10b: mp 147–148 °C; ^1H NMR ($CDCl_3$) δ 1.45 (s, 18 H), 0.95 (d, J = 6.5 Hz, 6 H), 1.77 (dd, J = 7, 6.5 Hz, 1 H), 3.37 (d, J = 7 Hz, 2 H), 5.48 (s, 1 H, OH), 7.57 (s, 2 H), 8.13 (s, 1 H); IR (Nujol) 3130, 1625 cm^{-1}. Anal. Calcd for $C_{19}H_{31}NO$: C, 78.84; H, 10.80; N, 4.84. Found: C, 79.45; H, 11.17; N, 4.79.

10c: mp 186–187 °C; ^1H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 1.25 (d, J = 6.5 Hz, 6 H), 3.50 (septet, J = 6.5 Hz, 1 H), 5.42 (s, 1 H, OH), 7.52 (s, 2 H), 8.20 (s, 1 H); IR (nujol) 3150, 1625 cm^{-1}. Anal. Calcd for $C_{18}H_{29}NO$: C, 78.49; H, 10.61; N, 5.09. Found: C, 78.38; H, 10.76; N, 4.89.

10d: mp 118–119 °C; ^1H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 1.0–2.0 (m, 10 H), 3.13 (m, 1 H), 5.37 (s, 1 H, OH), 7.55 (s, 2 H), 8.22 (s, 1 H); IR (nujol) 3130, 1625 cm^{-1}. Anal. Calcd for $C_{21}H_{33}NO$: C, 79.94; H, 10.54; N, 4.44. Found: C, 80.07; H, 10.81; N, 4.22.

10e: mp 202–204 °C; ^1H NMR ($CDCl_3$) δ 1.29 (s, 9 H), 1.47 (s, 18 H), 5.42 (s, 1 H, OH), 7.55 (s, 2 H), 8.18 (s, 1 H); IR (nujol) 3180, 1620 cm^{-1}. Anal. Calcd for $C_{19}H_{31}NO$: C, 78.84; H, 10.80; N, 4.84. Found: C, 78.99; H, 11.08; N, 4.71.

Co(Salpr)-Promoted Oxygenation of 10. The oxygenation of **10** was carried out at 0 °C for 2 h by the same method as described for that of **1**. The resulting residue was chromatographed on a silica gel plate developed with dichloromethane to give dihydropyridine **11**, cyclopentadienone **12**, and epoxy-*o*-quinol **13**. The results are given in Table I. The spectral data of **11b–d** are available as supplementary material.

11a: mp 117–118 °C; ^1H NMR ($CDCl_3$) δ 1.18 (s, 9 H), 1.32 (s, 9 H), 4.07 (d, 1 H, J = 15 Hz), 4.18 (d, 1 H, J = 15 Hz), 6.08 (s, 1 H, OH), 6.80 (d, 1 H, J = 1 Hz), 6.87 (d, 1 H, J = 1 Hz), 7.33 (s, 5 H), 8.97 (s, 1 H); IR (nujol) 3370, 1690, 1630 cm^{-1}; UV (C_6H_{12}) λ_{max} 387 nm (log ϵ 3.39). Anal. Calcd for $C_{22}H_{29}NO_3$: C, 74.33; H, 8.22; H, 3.94. Found: C, 74.26; H, 8.25; N, 3.88.

11b, mp 131–133 °C. Anal. Calcd for $C_{19}H_{31}NO_3$: C, 70.99; H, 9.72; N, 4.36. Found: C, 70.90; H, 10.01; N, 4.16.

11c, mp 99–101 °C. Anal. Calcd for $C_{18}H_{29}NO_3$: C, 70.32; H, 9.51; N, 4.56. Found: C, 70.16; H, 9.27; N, 4.44.

11d, mp 96–98 °C. Anal. Calcd for $C_{21}H_{33}NO_3$: C, 72.58; H, 9.57; N, 4.03. Found: C, 72.81; H, 9.68; N, 4.04.

12: mp 28–29 °C; ^1H NMR ($CDCl_3$) δ 1.15 (s, 9 H), 1.40 (s, 9 H), 7.16 (s, 1 H), 10.48 (s, 1 H); IR (Nujol) 1715, 1665 cm^{-1}; UV (C_6H_{12}) λ_{max} 416 nm (ϵ 570). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.15; H, 9.32.

13: bp 75–77 °C (10^{-2} mmHg); ^1H NMR ($CDCl_3$) 0.95 (s, 9 H), 1.23 (s, 9 H), 4.08 (d, 1 H, J = 0.7 Hz), 4.13 (s, 1 H, OH), 7.13 (d, 1 H, J = 0.7 Hz), 8.97 (s, 1 H); IR (nujol) 3500, 1725, 1675 cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.47; H, 8.83.

Crystallographic Determination of 11a. Preliminary X-ray photographs of crystals of dihydropyridine **11a** grown from a pentane solution revealed monoclinic symmetry. A least-squares fitting of 37 reflections ($30° \leq 2\theta \leq 40°$) gave a = 22.858 (9) Å, b = 8.579 (3) Å, c = 21.812 (8) Å, and β = 107.12 (5)°. Systematic extinctions conformed to the monoclinic space group $C2/c$, and an observed density of 1.14 g cm^{-3} indicated Z = 8. All unique reflections with $2\theta \leq 45°$ were measured on a computer-controlled four-circle diffractometer by using graphite monochromated Mo Kα (0.7107 Å) X-rays. Three reference reflections monitored every 180 min displayed neither systematic nor significant deviations from their initial values. Of the 2994 reflections surveyed, 1757 were judged observed ($I > 3\sigma(I)$). The data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by a multisolution, weighted sign determining procedure.[23] Full-matrix, least-squares refinement with anisotropic temperature factors for all nonhydrogen atoms and isotropic temperature factors for all hydrogens converged to a standard crystallographic residual of 0.054 for the observed reflections.[24] There were no significant residual peaks in a final difference electron density synthesis, and the length of N1–C2 (1.330 (5) Å) corresponds to an N(sp^2)–C(sp^2) bond. Further crystallographic details are available in the supplementary material.

Base-Catalyzed Reaction of Dihydropyridines 11. Each of compounds **11b–d** (1 mmol) was added to a mixture of *t*-BuOH and petroleum ether (1:1, 10 mL) containing *t*-BuOK (3 mmol) at 0 °C. With **11a** (1 mmol), *t*-BuOK (1 mmol) was used. After being allowed to stand at room temperature for 1 h, the mixture was poured into an ice-cooled aqueous NH_4Cl solution and extracted with ether. The extract was dried (Na_2SO_4) and evaporated in vacuo to give cyclopentadienone **12** in quantitative yield. The same treatment of **11a** (1 mmol) with *t*-BuOK (3 mmol) gave 4-[(*N*-benzylideneamino)methylene]-2,5-di-*tert*-butyl-2-cyclopentenone (**14**) quantitatively. When the base-catalyzed reaction of **11** was carried out in alkaline methanol (KOH, 3 mmol; MeOH,

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10 mL) by the same procedure, 4-[(*N*-alkylamino)methylene]-2,5-di-*tert*-butyl-5-hydroxy-2-cyclopentenones (**15**) were obtained in quantitative yield.

14: bp 134–135 °C (10^{-2} mmHg); ^{1}H NMR ($CDCl_3$) δ 1.04 (s, 9 H), 1.28 (s, 9 H), 2.60 (s, 1 H), 6.88 (s, 1 H), 7.3–8.0 (m. 5 H), 8.23 (s, 1 H), 8.37 (s, 1 H); IR (neat) 1695 cm^{-1}. Anal. Calcd for $C_{21}H_{27}NO$: C, 81.51; H, 8.80; N, 4.53. Found: C, 81.27; H, 9.05; N, 4.38.

15a: mp 135–137 °C; ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 9 H), 1.17 (s, 9 H), 2.62 (s, 1 H, OH), 4.26 (d, J = 6 Hz, 2 H), 5.04 (1 H, NH), 6.23 (br d, 1 H), 7.32 (s, 5 H), 7.35 (s, 1 H); IR (nujol) 3440, 3370, 1650 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_2$: C, 77.02; H, 8.93; N, 4.28. Found: C, 76.92; H, 9.16; N, 4.16.

15b: bp 120–122 °C (10^{-2} mmHg); ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 9 H), 1.17 (s, 9 H), 0.92 (d, J = 6 Hz, 6 H), 1.80 (m, 1 H), 2.86 (m, 2 H), 2.60 (s, 1 H, OH), 4.85 (1 H, NH), 6.13 (br d, 1 H), 7.33 (s, 1 H); IR (neat) 3420, 3350, 1640 cm^{-1}. Anal. Calcd for $C_{18}H_1NO_2$: C, 73.67; H, 10.65; N, 4.77. Found: C, 73.83; H, 10.90; N, 4.48.

15c: mp 110–111 °C; ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 9 H), 1.18 (s, 9 H), 1.18 (d, J = 6.5 Hz, 6 H), 3.35 (m, J = 6.5 Hz, 1 H), 2.62 (s, 1 H, OH), 4.67 (1 H, NH), 6.18 (br d, 1 H), 7.33 (s, 1 H); IR (nujol) 3480, 3440, 1645 cm^{-1}. Anal. Calcd for $C_{17}H_{29}NO_2$: C, 73.07; H, 10.46; N, 5.01. Found: C, 72.93; H, 10.66; N, 4.81.

15d: mp 122–124 °C; ^{1}H NMR ($CDCl_3$) δ 0.96 (s, 9 H), 1.17 (s, 9 H), 0.8–2.0 (m, 10 H), 2.92 (m, 1 H), 2.60 (s, 1 H, OH), 4.74 (1 H, NH), 6.28 (br d, 1 H), 7.40 (s, 1 H); IR (nujol) 3350, 3240, 1655 cm^{-1}. Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; H, 4.38. Found: C, 74.92; H, 10.48; N, 4.21.

15e: unstable oil; ^{1}H NMR ($CDCl_3$) δ 0.97 (s, 9 H), 1.17 (s, 9 H), 1.23 (s, 9 H), 2.67 (s, 1 H, OH), 4.88 (1 H, NH), 6.32 (br d, 1 H), 7.34 (s, 1 H); IR (neat) 3450, 3420, 1635 cm^{-1}. This compound could not be purified because of its instability, but the spectral data are in good agreement with the structure.

Preparation of 4-[Alkyl(*N*-benzylimino)methyl]-2,6-di-*tert*-butylphenols (17). A solution of titanium tetrachloride (0.66 mL) in dry benzene (10 mL) was added dropwise to a solution of **1** (10 mmol) and benzylamine (100 mmol) in dry benzene (50 mL) under nitrogen atmosphere at 0 °C. The mixture was stirred under a nitrogen atmosphere at room temperature for 2 days and filtered through a Celite layer. The filtrate was evaporated in vacuo to give **17** in nearly quantitative yield. Phenols **17** thus obtained were purified by vaccum distillation (1 mmHg). Products **17a** and **17c** were crystallized after the distillation.

17a: mp 103–105 °C; ^{1}H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 2.27 (s, 3 H), 3.83 (s, 1 H, OH), 4.67 (s, 2 H), 7.32 (br s, 5 H), 7.72 (s, 2 H); IR (nujol) 3650 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO$: C, 81.85; H, 9.26; H, 4.15. Found: C, 81.90; H, 9.23; N, 4.33.

17b: bp 160–163 °C (1 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.20 (d, J = 7 Hz, 6 H), 1.47 (s, 18 H), 3.27 (septet J = 7 Hz, 1 H), 3.85 (s, 1 H, OH), 4.68 (s, 2 H), 7.32 (br s, 5 H), 7.76 (s, 2 H); IR (neat) 3650 cm^{-1}. Anal. Calcd for $C_{25}H_{35}NO$: C, 82.14; H, 9.65; N, 3.83. Found: C, 82.32; H, 9.69; N, 3.71.

17c: mp 57–59 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 9 H), 1.37 (s, 18 H), 4.19 (s, 2 H), 5.10 (s, 1 H, OH), 6.70 (s, 2 H), 7.27 (s, 5 H); IR (nujol) 3700 cm^{-1}. Anal. Calcd for $C_{26}H_{37}NO$: C, 82.27; H, 9.83; N, 3.69. Found: C, 82.12; H, 9.97; N, 3.58.

Co(Salpr)-Promoted Oxygenation of 17. The oxygenation of **17** was carried out at room temperature by the same method as that described for **1**. The percent conversion (**17a**, 74%; **17b**, 50%; **17c**, 45%) and yield of the products were determined from the ^{1}H NMR of the reaction mixture. Products were isolated by chromatographic separation on a silica gel plate developed with CH_2Cl_2. From **17a**, epoxy-*o*-quinol **18a** (35%) and benzoquinone **19** (25%) were obtained, and **18b** (50%), **19** (5%), and phenolic alcohol **20** (20%) were obtained from **17b**. Phenol **17c** gave *o*-hydroperoxide **3e** in 90% yield. Benzoquinone **19** was identical with an authentic sample.

18a: mp 102–103 °C; ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 9 H), 1.22 (s, 9 H), 2.15 (s, 3 H), 3.95 (s, 1 H, OH), 3.97 (d, J = 1 Hz, 1 H), 7.15 (d, J = 1 Hz, 1 H); IR (nujol) 3500, 1715, 1680 cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.53; H, 8.63. Found: C, 68.76; H, 8.83.

18b: mp 57–59 °C; ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 9 H), 1.20 (d, J = 7 Hz, 6 H), 1.23 (s, 9 H), 2.83 (septet, J = 7 Hz, 1 H), 3.86 (d, J = 0.8 Hz, 1 H), 4.10 (s, 1 H, OH), 7.09 (d, J = 0.8 Hz, 1 H); IR (nujol) 3550, 1720, 1685 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.36; H, 9.45.

20: mp 168–169 °C; ^{1}H NMR ($CDCl_3$) δ 1.47 (s, 18 H), 1.63 (s, 6 H), 4.40 (s, 1 H, OH), 5.72 (s, 1 H, OH), 7.95 (s, 2 H); IR (nujol) 3680, 3500, 1655 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.83; H, 9.77.

Co(Salpr)-Promoted Oxygenation of 2,6-Di-*tert*-butyl-4-cyanophenol (21). A solution of **21**[25] (1 mmol) and Co(Salpr) (1.1 mmol) in dichloromethane (20 mL) was stirred under an oxygen atmosphere at room temperature for 6 days. The solution was filtered through a short column of silica gel (10 g) to remove the metal complex. The filtrate was evaporated to give an oily residue, which was chromatographed on a silica gel plate developed with a mixture of dichloromethane and petroleum ether (1:2) to give the starting phenol **21** (0.5 mmol; conversion 50%) and cyclopentadienone **22** (60% yield based on the conversion) as orange crystals: mp 61–62 °C; ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 9 H), 1.33 (s, 9 H), 6.48 (s, 1 H); IR (nujol) 2230, 1735 cm^{-1}; UV (C_6H_{12}) λ_{max} 421 nm (ϵ 510). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.10; H, 8.85; N, 6.23.

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Registry No. **1a**, 1620-98-0; **1b**, 14035-33-7; **1d**, 14035-36-0; **1e**, 14035-38-2; **1f**, 7175-89-5; **1g**, 2511-22-0; **2a**, 14446-64-1; **2b**, 14446-94-7; **2c**, 81389-56-2; **2d**, 81389-57-3; **2e**, 14446-95-8; **3b**, 81389-58-4; **3d**, 81389-59-5; **3e**, 81389-60-8; **3f**, 81389-61-9; **3g**, 81389-62-0; **4a**, 81389-63-1; **4b**, 81389-64-2; **4c**, 81389-65-3; **4d**, 81389-66-4; **5a**, 81389-67-5; **6**, 81389-68-6; **7a**, 81389-69-7; **7b**, 81389-70-0; **7c**, 81389-71-1; **7d**, 81389-72-2; **8a**, 81389-73-3; **8b**, 81389-74-4; **9**, 81389-75-5; **10a**, 38209-90-4; **10b**, 77149-47-4; **10c**, 30829-34-6; **10d**, 30957-84-7; **10e**, 71530-29-5; **11a**, 77149-48-5; **11b**, 81389-76-6; **11c**, 77149-50-9; **11d**, 77149-51-0; **11e**, 81389-76-6; **12**, 77149-52-1; **13**, 77149-53-2; **14**, 77149-55-4; **15a**, 77149-56-5; **15b**, 77149-57-6; **15c**, 77149-58-7; **15d**, 77149-59-8; **15e**, 77149-54-3; **17a**, 81389-77-7; **17b**, 81389-78-8; **17c**, 81408-04-0; **18a**, 81389-79-9; **18b**, 81389-80-2; **19**, 719-22-2; **20**, 81389-81-3; **21**, 1988-88-1; **22**, 81389-82-4; Co(Salpr), 15306-22-6; 2,6-di-*tert*-butylphenol, 128-39-2; acetic acid, 64-19-7; 2-methylpropanoic acid, 79-31-2; 2,2-dimethylpropanoic acid, 75-98-9; benzoic acid, 65-85-0; monomethyl carbonate, 7456-87-3; 2-methyl-2-propanamine, 75-64-9; cyclohexanamine, 108-91-8; 2-propanamine, 75-31-0; 2-methyl-1-propanamine, 78-81-9; benzenemethanamine, 100-46-9.

Supplementary Material Available: X-ray data for compound **11a**, including fractional coordinates and temperature factors (Table I), bond distances (Table II), bond angles (Table III), observed and calculated structure factors (Table IV), a computer-generated perspective drawing of the final X-ray model. IR and ^{1}H NMR spectral data for compounds **3**, **4** (Table V), and **11** (Table VI) (10 pages). Ordering information is given on any current masthead page.

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