JOC Article

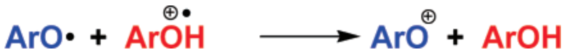
Electron Transfer between Protonated and Unprotonated Phenoxyl Radicals[1]

Kanji Omura*,†

College of Nutrition, Koshien University, Momijigaoka, Takarazuka, Hyogo 665-0006, Japan

k.omura@iris.eonet.ne.jp

Received September 5, 2007



$$ArO^{\bullet} + \overset{\oplus\bullet}{ArOH} \longrightarrow \overset{\oplus}{ArO} + ArOH$$

The reaction of phenoxyl radicals with acids is investigated. 2,4,6-Tri-*tert*-butylphenoxyl radical (**13**), a persistent radical, deteriorates in MeOH/PhH in the presence of an acid yielding 4-methoxycyclohexa-2,5-dienone **18a** and the parent phenol (**14**). The reaction is facilitated by a strong acid. Treatment of 2,6-di-*tert*-butyl-4-methylphenoxyl radical (**2**), a short-lived radical, generated by dissociation of its dimer, with an acid in MeOH provides 4-methoxycyclohexa-2,5-dienone **4** and the products from disproportionation of **2** including the parent phenol (**3**). A strong acid in a high concentration favors the formation of **4** while the yield of **3** is always kept high. Oxidation of the parent phenol (**33**) with PbO_2 to generate transient 2,6-di-*tert*-butylphenoxyl radical (**35**) in $AcOH/H_2O$ containing an added acid provides eventually *p*-benzoquinone **39** and 4,4′-diphenoquinone **42**, the product from dimerization of **35**. A strong acid in a high concentration favors the formation of **39**. These results suggest that a phenoxyl radical is protonated by an acid and electron transfer takes place from another phenoxyl radical to the protonated phenoxyl radical, thus generating the phenoxyl cation, which can add an oxygen nucleophile, and the phenol (eq 5). The electron transfer is a fast reaction.

Introduction

A large number of chemical and electrochemical syntheses and certain biosyntheses are based on phenol oxidation. Oxidative coupling and oxygenation are the main types of such oxidation.[2] The former is understood as involving intermediary formation of a phenoxyl radical. It has been observed that such reaction involving a phenoxyl radical is affected by an acid, and the results have been obtained which suggest intermediacy of a phenoxyl cation. The purpose of this article is to show the results from this laboratory on the effect of acid on the reaction of phenoxyl radicals and to present the interpretation for them. For this study, 2,4,6-tri-*tert*-butylphenoxyl (**13**), 2,6-di-*tert*-butyl-4-methylphenoxyl (**2**), and 2,6-di-*tert*-butylphenoxyl radicals (**35**) with different stabilities are employed as the substrates. Previous related studies are also discussed.

Results and Discussion

Phenoxyl radical **2** is short-lived as it rapidly undergoes irreversible disproportionation yielding the parent phenol (**3**) and reactive quinone methide **5**[3] which, in the absence[4] or presence[5] of a catalytic amount of an acid, can add MeOH to give 2,6-di-*tert*-butyl-4-methoxymethylphenol (**7**).[6] The present study started with reinvestigation of the reaction of **2** in MeOH (Table 1). Radical **2** can be conveniently generated by dissolving a solid of bis(cyclohexadienone) **1**, the dimer of **2**,[4a,c,5,7] in a solvent, as it readily dissociates reversibly to **2** in solution.[8] Dimer **1** was poorly soluble in MeOH at 30 °C but the dissolution progressed gradually as the decay of **2** progressed.

---

† Present address: 4-5-2, Matsuodai, Inagawa, Hyogo 666-0261, Japan.

[1] This article is dedicated to the memory of the late Professor Teruo Matsuura, Kyoto University.

[2] (a) Musso, H. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 723. (b) Scott, A. I. *Q. Rev.* **1965**, *19*, 1. (c) Altwicker, E. R. *Chem. Rev.* **1967**, *67*, 475. (d) Musso, H. In *Oxidative Coupling of Phenols*; Taylor, W. I., Battersby, A. R., Eds.; Marcell Dekker: New York, 1967; p 1. (e) Mihailović, M. L.; Čeković, Ž. In *The Chemistry of the Hydroxyl Group*; Patai, S., Ed.; Wiley: New York 1971; Part 1, p 505. (f) Forrester, A. R.; Hay, J. M.; Thomson, R. H. In *Organic Chemistry of Stable Free Radicals*; Academic Press: New York 1968; p 281. (g) Steenken, S.; Neta, P. In *The Chemistry of Phenols*; Rappoport, Z., Ed.; Wiley: Chichester, UK, 2003; Part 1, p 1107. (h) Yamamura, S. In *The Chemistry of Phenols*; Rappoport, Z., Ed.; Wiley: Chichester, UK, 2003; Part 1, p 1153.

[3] Stebbins, R.; Sicilio, F. *Tetrahedron* **1970**, *26*, 291 and references cited therein.

[4] (a) Orlando, C. M., Jr. *J. Org. Chem.* **1970**, *35*, 3714. (b) Macomber, R. S. *J. Org. Chem.* **1982**, *47*, 2481. (c) Omura, K. *J. Org. Chem.* **1984**, *49*, 3046.

[5] Becker, H.-D. *J. Org. Chem.* **1965**, *30*, 982.

[6] For the decay of **2** in aprotic solvents, see; Omura, K. *J. Am. Oil Chem. Soc.* **1992**, *69*, 461.

[7] For the structure of the dimer, see: Omura, K. *J. Org. Chem.* **1991**, *56*, 921.

[8] Dimer **1** is partially dissociated to **2** even in the solid state. See ref 5.

10.1021/jo701948a CCC: $40.75

SCHEME 1

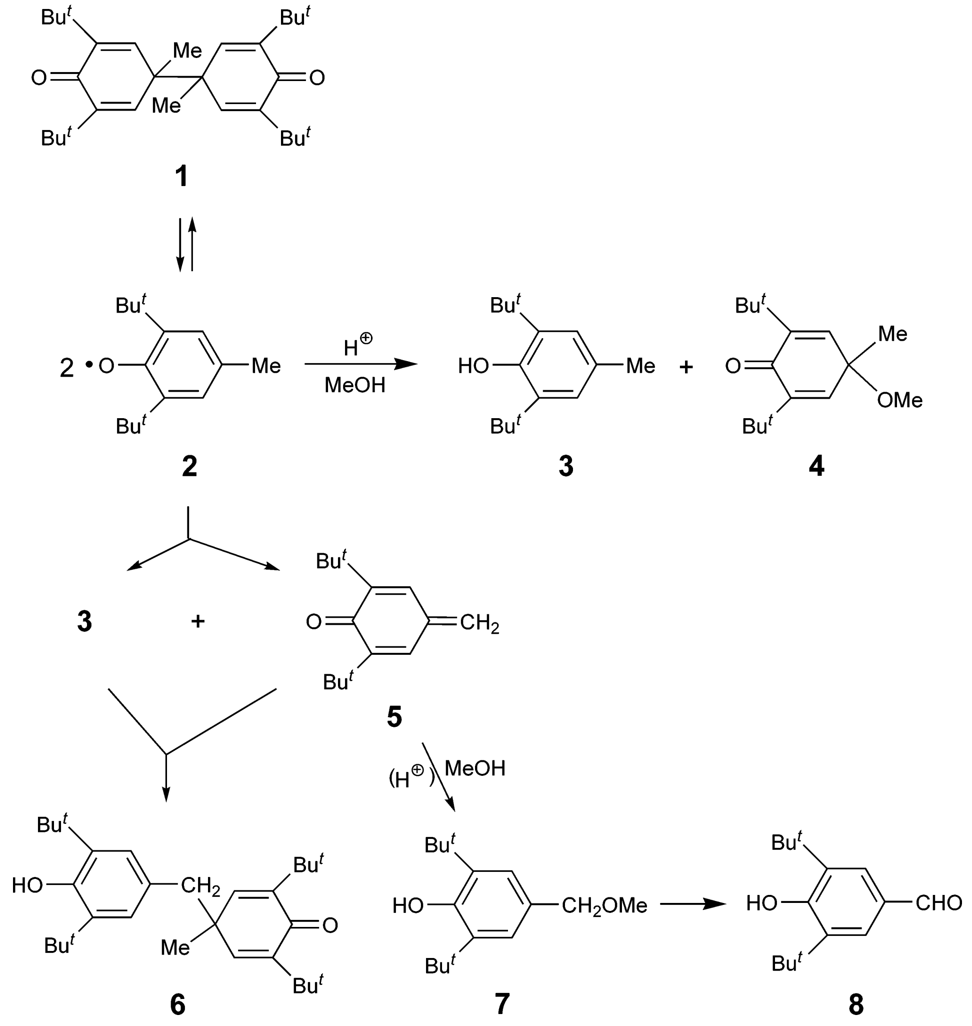


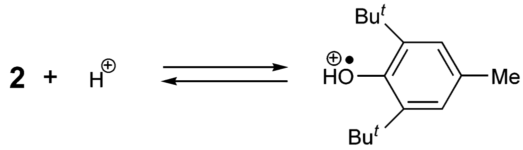
TABLE 1. Effect of Acid on Decay of Phenoxyl Radical 2 in MeOH[a]

run	acid (equiv[b])	time (min)	products (%[c]) 3	4	6	7	8
1		125	93	0	9	65	4
2	CF_3CO_2H (5)	111	101	3	0	73	5
3	CH_3SO_3H (1.25)	60	100	48	0	31	1
4	CH_3SO_3H (2.5)	46	103	60	0	19	tr
5	CH_3SO_3H (5)	36	105	67	0	13	tr
6	CF_3SO_3H (1.25)	45	106	53	0	25	tr
7	CF_3SO_3H (2.5)	29	102	68	0	12	tr
8	CF_3SO_3H (5)	21	104	75	0	7	0

[a] The reaction was conducted with **1** (2 mmol), an acid (5−20 mmol), and MeOH (30 mL) at 30 °C until dissolution of **1** was complete. [b] Mol/2/mol **1** employed. [c] (Mol/mol **1** employed) × 100.

Workup after the reacting mixture became homogeneous afforded, in addition to **3** and **7**, small amounts of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde (**8**) and 2,6-di-*tert*-butyl-4-(3,5-di-*tert*-butyl-4-hydroxybenzyl)-4-methylcyclohexa-2,5-dienone (**6**) (run 1). Aldehyde **8** perhaps is derived from **7**, and **6** is the product of polar addition of **3** to **5**.[6] Dissolution of **1** was completed a little faster when it was treated with MeOH containing CF_3CO_2H (5 equiv, relative to **2**), a mild acid. In addition to **3**, **7**, and **8**, 4-methoxy-4-methyl-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**4**) was furnished albeit in a small quantity (run 2). The degradation of **1** in MeOH was carried out further with varying amounts (1.25−5 equiv) of a strong acid, CH_3SO_3H, and a very strong acid, CF_3SO_3H (runs 3−8). The results suggest that employment of a stronger acid in a larger amount makes the dissolution of **1** faster and gives **4** in a higher yield and **7** and **8** in lower yields. In contrast, the yield of **3** is maintained always very high or quantitative. The highest yield (75%) of **4** and only limited amounts of the products from **5** were obtained from the reaction under the most strongly acidic condition employed (run 8). Dienone **4** has been suggested to rearrange to **7** in MeOH in the presence of an acid,[9] but **4** was recovered intact when treated with CF_3CO_2H or CF_3SO_3H in MeOH for 2 h at 30 °C.

The above observations may be interpreted as follows. In acidic MeOH, there is, in addition to the disproportionation, a reaction of **2** leading to formation of **3** and **4** in equimolar amounts, which is predominant as the acidity of the medium is high (Scheme 1). A most rational account for the new reaction appears to be protonation of **2** giving protonated phenoxyl radical (i.e., phenol cation radical) **9** (eq 1) and subsequent



9

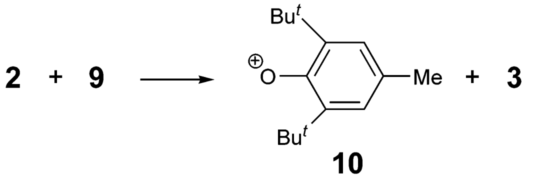
(1)

TABLE 2. **Effect of Acid on Decay of Phenoxyl Radical 13 in MeOH/PhH**[a]

run	acid	time (min)	recovery of **13**[b] (%)	products (%[c])		
				14	**18a**	others
1	AcOH	60	100	0	0	
2	CF_3CO_2H	60	41	104	63	N.E.[d]
3	36% HCl	60	8	108	61	**18b** (10), **19** (+[e]), **24** (10)
4	70% $HClO_4$	20	0	106	73	**18b** (+[e]), **19** (3)
5	CH_3SO_3H	11	0	107	70	N.E.[d]
6	CF_3SO_3H	3	0	107	73	N.E.[d]

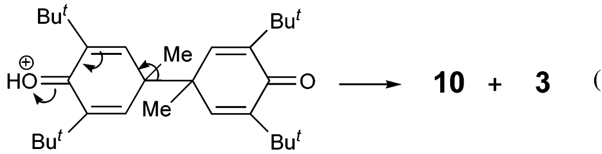
[a] The reaction was conducted with **13** (5 mmol), an acid (60 mmol), MeOH (100 mL), and PhH (70 mL) at 25 °C under N_2. [b] Recovered as **16** and **17**. [c] (Mol/mol **13** consumed) × 2 × 100. [d] Not examined. [e] Yield was not determined.

electron transfer from another **2** to **9** providing phenoxyl cation **10**, which can add MeOH giving **4**, and **3** (eq 2). Consumption



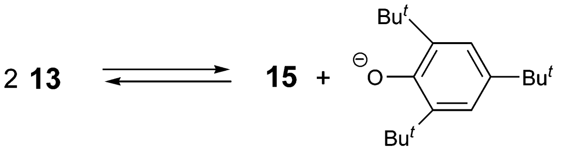
10 (2)

of **2** by the additional reaction may contribute to the acceleration of the dissolution of **1**. Equation 2 will be a quite fast reaction when it is considered that **2** is a poor base although in basicity **2** may be comparable to or stronger than the competitor, MeOH,[10] and that the process, eq 1 + eq 2, can compete well with the fast disproportionation of **2**; protonated phenoxyl radicals are strong acids with pK_a values of -1 to -2.[2g,11] A different account for the formation of **3** and **4** and for the accelerated dissolution of **1**, however, may not be excluded. Thus, **1** may be protonated giving cationic intermediate **11**, which may collapse heterolytically to give **10** and **3** (eq 3).



11 (3)

Phenoxyl radical **13** is a long-lived radical and essentially monomeric even in the solid state;[12] dimerization is prohibited due to steric repulsion and such disproportionation as **2** can undergo is not possible. This radical, therefore, was thought to be a more suitable substrate for the present study. A deep-blue benzene solution of **13**, prepared by oxidation of 2,4,6-tri-*tert*-butylphenol (**14**) with alkaline ferricyanide,[12] was treated under N_2 with an acid (12 equiv) in MeOH at 25 °C (Table 2). There was no effect of addition of AcOH on the decay of **13** in MeOH/PhH, as the treatment for 60 min resulted in no change of the blue color of the solution and gave nothing but **13**, which was recovered quantitatively as peroxides **16** and **17** after exposure of the solution to O_2 (run 1). With CF_3CO_2H, the reaction of **13** occurred slowly and yielded **14** quantitatively or more and 4-methoxy-2,4,6-tri-*tert*-butylcyclohexa-2,5-dienone (**18a**) in a good yield (run 2). The reaction of **13** to afford **14** and **18a** was remarkably enhanced when CH_3SO_3H was employed as the acid (run 5). The reaction with CF_3SO_3H was strikingly fast; the deep blue color of the solution was discharged within a few minutes (run 6). Evidently, the rate of the reaction of **13**, which will give equimolar amounts of **14** and **18a**, is dependent on the strength of an acid, and the formation of the products may be best accounted for as the result of protonation of **13** to give protonated phenoxyl radical **12** and subsequent electron transfer from another **13** to **12** giving phenoxyl cation **15** and **14** (Scheme 2). Another account for the product formation is possible. It is participation of disproportionation of **13** to **15** and phenoxyl anion **20**, another electron-transfer reaction of **13**, which will be reversible (eq 4).[13] If the mechanism is operative,



20 (4)

it may be expected, contradictory to the fact that all the reactions of **13** with the different acids are of equal order of rapidity, since subsequent protonation of **20**, the anion of **14** (pK_a = 10−11[14]), with AcOH (pK_a = 4.8) or with a stronger acid may be extremely fast equally.[15] First of all, since the intermediary cationic adduct between **15** and MeOH (the precursor of **18a**, a protonated ether) may facilely protonate **20**, it may also be expected that **13** in MeOH gives rise to **14** and **18a** even without an added acid. As a matter of fact, **13** in MeOH was persistent and gave none of the products (not shown in Table 2; cf. run 1). The result of the reaction of **13** may suggest that the formation of **3** and **4** from the reaction of **1**, described above, is the result of the process involving eq 2 rather than eq 3.

Müller and co-workers[16] earlier found that the deep blue color of the ethereal solution of **13** was discharged when it was agitated with concentrated HCl, and **14** and 4-chloro-2,4,6-tri-*tert*-butylcyclohexa-2,5-dienone (**24**) were obtained in 90% and 34% yields, respectively. To account for the products, they proposed canonical form **21** with a dipolar character for **13**,

---

(9) (a) Brunow, G.; Sumelius, S. *Acta Chem. Scand.* **1975**, *B29*, 499. (b) Homs, N.; Ramírez de la Piscina, P.; Borrull, F. *J. Chem. Soc., Chem. Commun.* **1988**, 1075.

(10) The pK_a for $MeOH_2^+$ is −2.2 to −2.5. See: (a) Deno, N. C.; Turner, J. O. *J. Org. Chem.* **1966**, *31*, 1969. (b) Levitt, L. S.; Levitt, B. W. *Tetrhedron* **1971**, *27*, 3777.

(11) (a) Dixon, W. T.; Murphy, D. *J. Chem. Soc., Faraday Trans. 2* **1976**, *72*, 1221. (b) Dixon, W. T.; Murphy, D. *J. Chem. Soc. Faraday Trans. 2* **1978**, *74*, 432. (c) Holton, D. M.; Murphy, D. *J. Chem. Soc., Faraday Trans. 2* **1979**, *75*, 1637.

(12) Müller, E.; Ley, K. *Chem. Ber.* **1954**, *87*, 922.

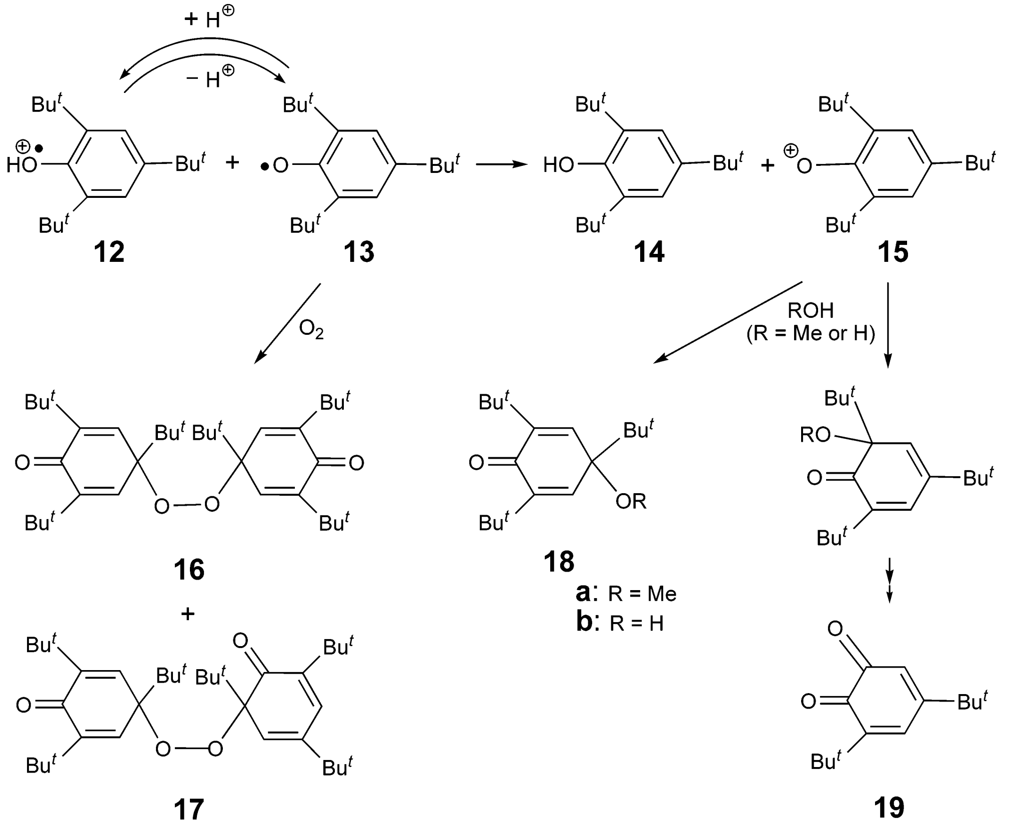
(13) (a) Disproportionation of a phenoxyl radical of the same type as eq 4 has been considered, and a numerical value of 10^{-10} has been proposed as the equilibrium constant. (b) Ready conproportionation between a phenoxyl cation and a phenoxyl anion to a phenoxyl radical has been shown. See: (a) Speiser, B.; Rieker, A. *J. Electroanal. Chem.* **1979**, *102*, 373. (b) Dimroth, K.; Umbach, W.; Thomas, H. *Chem. Ber.* **1967**, *100*, 132.

(14) By analogy with the pK_a values of polymethylphenols. See: Rochester, C. H. In *The Chemistry of the Hydroxyl Group*; Patai, S., Ed.; Wiley: New York, 1971; Part 1, p 327.

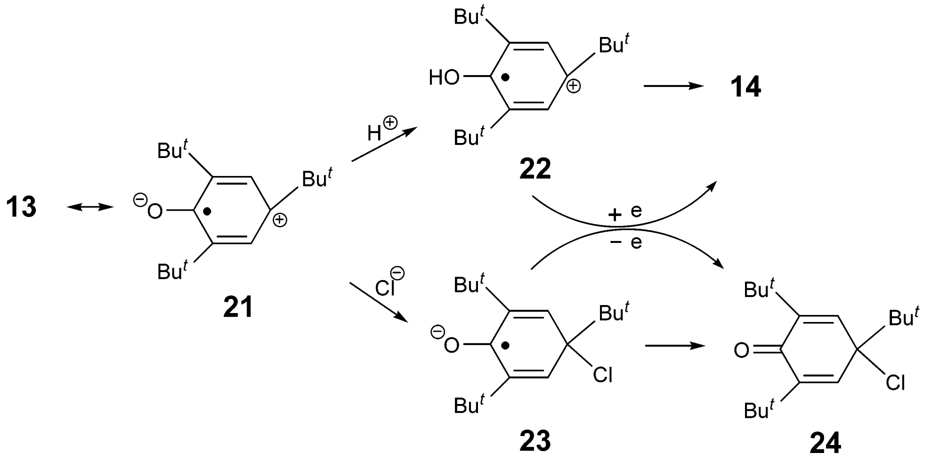
(15) As long as the difference between the pK_a of the conjugate acid of a base and that of an acid is greater than about 2 units, the proton transfer from the acid to the base is diffusion controlled (in water), and the rate is independent of that difference. See: (a) March, J. *Advanced Organic Chemistry*: *Reactions, Mechanisms, and Structure*; Wiley, New York, 1992; p 254. (b) Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1. (c) Decoursey, T. E. *Physiol. Rev.* **2003**, *83*, 475.

(16) Müller, E.; Ley, K.; Kiedaisch, W. *Chem. Ber.* **1955**, *88*, 1819.

SCHEME 2

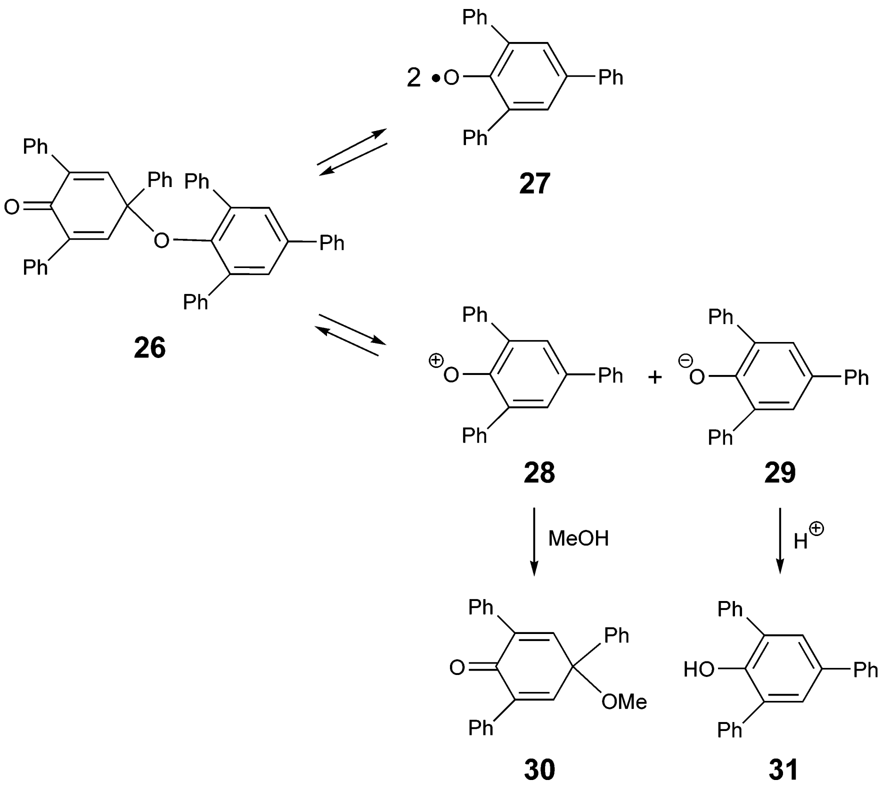


SCHEME 3



and assumed attacks by proton at the negative site of **21** yielding intermediate **22**, another form of **12**, and by chloride ion at the positive site of another **21** yielding intermediate **23**, and subsequent electron transfer from **23** to **22**, thus furnishing **24** and **14** (Scheme 3). The failure of isolation of **24** in the stoichiometrically anticipated amount was ascribed to its partial decomposition during manipulation of the product. Keeping their proposal in mind, we also conducted the reaction of **13** in the presence of 36% HCl in MeOH/PhH (run 3, Table 2). The major products were again **14** and **18a**. On this occasion, the minor products were also investigated and found to be **24**, 4-hydroxy-2,4,6-tri-*tert*-butylcyclohexa-2,5-dienone (**18b**), and 3,5-di-*tert*-butyl-*o*-benzoquinone (**19**). Allowing a solution of **24** in MeOH/PhH containing 36% HCl to sit for 60 min at 25 °C resulted in practically quantitative recovery of **24**, and only a trace amount of **18a** was detectable. Therefore, the probability of the formation of most of **18a** (and **18b**) by methanolysis (and hydrolysis) of product **24** during the reaction of **13** may be excluded. To account for our results by Müller's mechanism, it may have to be assumed that **21**, i.e., **13**, is so electrophilic as to accept nucleophilic attack not only by the chloride ion but also by MeOH (and H_2O). In other words, **13** may be expected to react with MeOH (or H_2O) to afford **14** and **18a** (or **18b**) without assistance by an acid, contrary to the fact. It seems possible that the product of Müller's reaction in fact contained **18b** in a significant quantity, and the reaction appears to be as well accounted for as that involving the electron transfer between **12** and **13**, shown above. The homogeneous reaction of **13** with 36% HCl as well as that with 70% $HClO_4$ (run 4, Table 2) was not quite as fast as might be anticipated when the high acidity

SCHEME 4

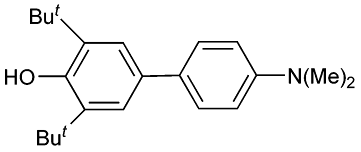


of the acid is taken into consideration. The reason for this is not clearly understood although H_2O is more basic than MeOH.

Phenoxyl radicals other than **2** and **13** may undergo the electron-transfer reaction similarly (eq 5). There is indeed a

$$\mathrm{ArO}\bullet \;+\; \overset{\oplus\bullet}{\mathrm{ArOH}} \longrightarrow \mathrm{Ar}\overset{\oplus}{\mathrm{O}} \;+\; \mathrm{ArOH} \qquad (5)$$

precedent for such a reaction. Thus, Speiser and Rieker[17]analyzed cautiously the cyclic voltammograms of 2,6-di-*tert*-butyl-4-(4-dimethylaminophenyl)phenol (**25**) in MeCN containing varied



25

amounts of 2,6-dimethylpyridine as base, and, taking into account additional data as well obtained by other workers, concluded that the generation of the phenoxyl cation is the result of electron transfer from the long-lived phenoxyl radical to the protonated phenoxyl radical. Here, the protonated phenoxyl radical is one generated by one-electron oxidation of **25** in the primary electrochemical stage. They showed that the formal potential for the oxidation of **25** to the protonated phenoxyl radical is greater than that of the phenoxyl radical to the phenoxyl cation and the equilibrium constant for the electron-transfer reaction thus is greater than 1.[18] Operation of an ECE mechanism, by which the results of anodic phenol oxygenations have often been explained,[2h,19] was excluded. Another mechanistic possibility, reversible disproportionation of the phenoxyl radical yielding the phenoxyl cation and the phenoxyl anion (cf. eq 4), was also excluded. The amino group in **25** played a key role in their analysis of the reaction of **25**.

Dimroth and co-workers investigated the reaction of another long-lived phenoxyl radical, 2,4,6-triphenylphenoxyl radical (**27**), with a strong acid. They found that a red solution of **27** in an inert solvent such as CS_2, in which it is equilibrated with dimer **26**, transiently turned dark blue when mixed with 70% $HClO_4$ or concentrated H_2SO_4.[20] They assumed the short-lived blue species to be protonated phenoxyl radical **32**. However, they were led to doubt the assumption when they succeeded in isolation of some salts of related 2,4,6-triarylphenoxyl cations as deep blue crystals; their solutions also exhibited dark blue colors close to the transient color observed in the above experiment. The transient species now was reasonably thought to be phenoxyl cation **28** rather than **32**.[13b] To account for their additional finding that treatment of **27** in a mixture of MeOH and CCl_4 with 70% $HClO_4$ readily afforded phenol **31** and 4-methoxycyclohexa-2,5-dienone **30** in good yields, they assumed that under the acidic conditions, **26** can dissociate heterolytically to give **28** and phenoxyl anion **29** (Scheme 4).[21] However, it is not that intermediacy of **32** in this reaction was disproved, and there appears no reason to exclude a different possibility that the products are formed by the process involving the electron-transfer reaction between **27** and **32** (eq 6).

---

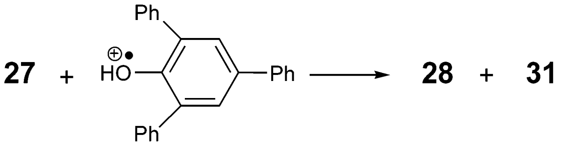
[17] Speiser, B.; Rieker, A. *J. Electroanal. Chem.* **1980**, *110*, 231.

[18] The redox potentials of phenols have been shown to be pH dependent. See: (a) Reference 2g. (b) Steenken, S.; Neta, P. *J. Phys. Chem.* **1982**, *86*, 3661. (c) Li, C.; Hoffman, M. Z. *J. Phys. Chem. B* **1999**, *103*, 6653.

[19] For a few examples, see: (a) Suttie, A. B. *Tetrahedron Lett.* **1969**, 953. (b) Ronlán, A.; Parker, V. D. *J. Chem. Soc. C* **1971**, 3214. (c) Nilsson, A.; Palmquist, U.; Petterson, T.; Ronlán, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 696. (d) Webster, R. D. *Acc. Chem. Res.* **2007**, *40*, 251.

[20] Dimroth, K.; Kalk, F.; Neubauer, G. *Chem. Ber.* **1957**, *90*, 2058.

[21] Dimroth, K.; Perst, H.; Schlömer, K.; Worschech, K.; Müller, K.-H. *Chem. Ber.* **1967**, *100*, 629.



32

(6)

Most of phenoxyl radicals are short-lived, even more so than **2**; they decay rapidly owing to dimerization.[3,22] The reaction of such a phenoxyl radical with or without an added acid can be studied only under the influence of an oxidant responsible for its generation from the parent phenol. Phenoxyl radical **35** is among such transient radicals.[22,23] Previously, we reported on the preparation of *p*-benzoquinones by oxidation of various phenols including 2,6-di-*tert*-butylphenol (**33**) with PbO_2, a one-electron oxidant, in AcOH or acetone containing 70% $HClO_4$.[24] The solvent was chosen after investigating the solvent effect on the oxidation of **33** to furnish 2,6-di-*tert*-butyl-*p*-benzoquinone (**39**) and 3,5,3′,5′-tetra-*tert*-butyl-4,4′-diphenoquinone (**42**), the product from dimerization of **35**, in a high total yield. It appears that the yield of **39** is sensitive to solvent basicity; it tends to be high from the oxidation in a poorly basic solvent such as AcOH and relatively low from that in a more basic solvent such as MeOH. In other words, high acidity of the medium seems to favor the formation of **39**. This is what is anticipated when **39** is the end product of the reaction of phenoxyl cation **37** and when **37** is generated by the electron-transfer reaction (eq 5) between **35** and protonated phenoxyl radical **34**. The effect of the acidity of the medium on the reaction was studied in a different way. Thus, **33** was treated with excess PbO_2 in the absence or presence of CF_3CO_2H, CH_3SO_3H, CF_3SO_3H, or $HClO_4$ in varying amounts (4−15 equiv) in a mixture of AcOH and a small amount of H_2O, and the results were compared (Table 3). In every run, almost all of the products were accounted for. The reaction without an added acid, which proceeded relatively slowly at 25 °C, gave principally 3,5,3′,5′-tetra-*tert*-butylbis(cyclohexa-2,5-diene)-4,4′-dione (**36**), the primary product of dimerization of **35** (run 1). Enolization of **36** to 3,5,3′,5′-tetra-*tert*-butyl-4,4′-dihydroxybiphenyl (**38**) appears to be sluggish in the solvent. The reactions with the added acids were mildly exothermic and were discontinued in a short time. The ^1H NMR spectrum in $CDCl_3$ of the crude product obtained from the reaction with 8 equiv of CF_3CO_2H (run 2) exhibited, in addition to the singlets due to **39** and **42**, relatively small, new signals at δ 6.53 (d, $J = 3.1$ Hz), 5.87 (t, $J = 3.1$ Hz), 2.17 (s), and 1.24 (s), although a part of the doublet overlapped with one of the singlets due to **39**. The new signals coincided with those included in the ^1H NMR spectrum of the product obtained from treatment of 4-bromo-2,6-di-*tert*-butylcyclohexa-2,5-dienone with $AgClO_4$ in AcOH containing AcONa.[25] The spectrum of the product mixture from the debromination also contained the singlets due to 4-acetoxy-2,6-di-*tert*-butylphenol (**40a**). Upon addition of pyridine-d_5 to the $CDCl_3$ solution, the new signals disappeared from the spectrum of the product from run 2 and fresh singlets ascribable to **40a** appeared. Column chromatography of the crude product on SiO_2 gave **40a** as well as **39** and **42** but did not afford the product responsible for the new NMR signals. These facts may imply that the crude product contained labile 4-acetoxy-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**41a**) and that **41a** underwent prototropic rearrangement to give **40a** upon catalysis with pyridine-d_5 or SiO_2; the NMR signals at δ 6.53, 5.87, 2.17, and 1.24 are assignable to vinyl, methine, acetoxy, and *tert*-butyl protons, respectively. Catalysis by CF_3CO_2H of the enolization of **41a** under the conditions seems slow, and **41a** in run 2 may have been converted eventually into **39** via **40a** upon extending the reaction time. Rapid and quantitative oxidation of **40a** to **39** by PbO_2/CF_3CO_2H in $AcOH/H_2O$ was experimentally substantiated. 4-Hydroxycyclohexa-2,5-dienone **41b** may have been also formed in run 2, but signals assignable to **41b** or hydroquinone **40b**[25] were not observed in the ^1H NMR spectrum of the crude product. Dienone **41b** is assumed to have been readily converted into **39** possibly via **40b**. Dienone **41** can be assumed to be the primary product of the reaction of **37** with the nucleophile. The reactions of **33** with CH_3SO_3H, CF_3SO_3H, and $HClO_4$ gave **39** and **42** almost exclusively (runs 4−9). It will be seen that, as anticipated, employment of a strong acid in a high concentration favors the formation of **39**, i.e., of **41**. The reaction of **33** including the proposed electron-transfer reaction may be summarized as shown in Scheme 5. That **36** was quantitatively isomerized to **38** by CF_3CO_2H or CF_3SO_3H in $AcOH/H_2O$ may suggest that the generation of **37** is not the result of protonation of **36** (cf. eq 3).

TABLE 3. Effect of Acid on Oxidation of Phenol 33 with PbO_2 in $AcOH/H_2O$[a]

run	added acid (equiv[b])	recovery of **33** (%)	products (%[c]) **39**	**42**	others
1		14	1	6	**36** (79), **41a** (1)
2	CF_3CO_2H (8)	0	24	65	**41a** (11)
3	CF_3CO_2H (15)	0	38	51	**41a** (9)
4	CH_3SO_3H (4)	0	49	46	
5	CH_3SO_3H (8)	0	80	16	
6	CF_3SO_3H (4)	0	55	43	
7	CF_3SO_3H (8)	0	95	2	
8	$HClO_4$ (4)	0	75	21	
9	$HClO_4$ (8)	0	97	0	

[a] The reaction was conducted with **33** (4 mmol), PbO_2 (10 mmol), an added acid (16−60 mmol), AcOH (30 mL), and H_2O (2.5 mL) for 10 min. The initial reaction temperature was 25 °C. [b] Mol/mol **33** employed. [c] (Mol/mol **33** employed) × 100 for **39** and **41a**, and (mol/mol **33** employed) × 2 × 100 for **36** and **42**.

The above discussion on the involvement of the electron transfer in the reaction of **33** is based on the assumption that **39** is formed exclusively by way of **41**. Unfortunately, the validity of such assumption is questioned by the following observations. First, as anticipated from our previous work,[26] treatment of **42** with PbO_2 and $HClO_4$ in $AcOH/H_2O$ gave **39** relatively slowly in selectivity not exceeding 60%. Second, treatment of **38** with PbO_2 and $HClO_4$ in $AcOH/H_2O$ gave, in addition to **42**, **39**, which may have been formed not only via **42** but also possibly via the phenoxyl cation of **38**. Hence, a part of **39** obtained from runs 8 and 9 and possibly runs 4−7 could have arisen by way of **42** and/or **38**. In contrast, treatment of **38** with PbO_2 and CF_3CO_2H in $AcOH/H_2O$ gave **42** quantitatively, which proved to remain totally intact under the reaction conditions. Hence, **39** obtained from runs 2 and 3 can be assumed to have arisen exclusively from **41**. From run 9 with 8 equiv of $HClO_4$, **39** was obtained in a high yield and no **42**. The lack of intermediary formation of **38** as well as **42** was

---

[22] Weiner, S. A. *J. Am. Chem. Soc.* **1972**, *94*, 581.

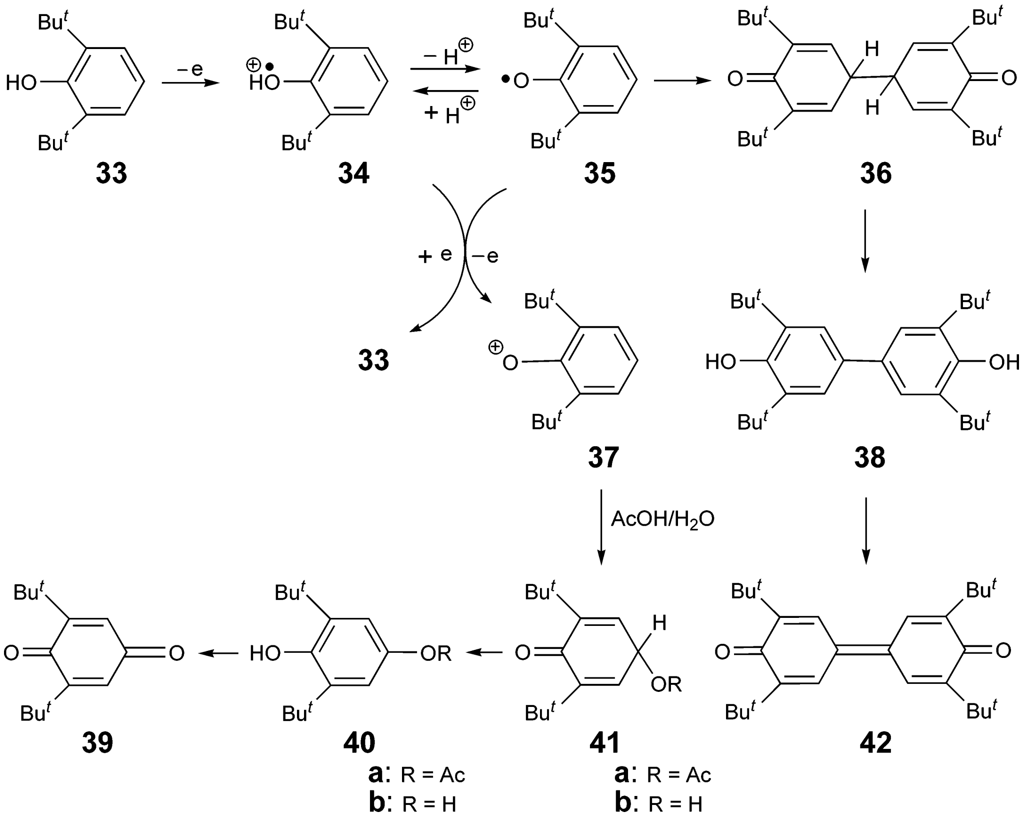
[23] Ley, K.; Müller, E.; Mayer, R.; Scheffler, K. *Chem. Ber.* **1958**, *91*, 2670.

[24] Omura, K. *Synthesis* **1998**, 1145.

[25] Omura, K. *J. Org. Chem.* **1996**, *61*, 7156.

[26] Omura, K. *Tetrahedron Lett.* **2000**, *41*, 685.

SCHEME 5



suggested by following the progress of the reaction by TLC. Consequently, it may be assumed that the dimerization of **35** to **36** took place to a minimum extent, if at all, and that **39** was formed exclusively or almost exclusively by way of **41**. From run 2 with 8 equiv of CF_3CO_2H, **42** was principally afforded, the formation of **41** being the minor course. It is now rational to conclude that high acidity of the medium indeed favors the formation of **41** and thus to propose the electron-transfer mechanism, when the results from run 2 with the modest acid and run 9 with the very strong acid are compared with each other. The same conclusion can be drawn simply by making a comparison between the product distributions obtained from runs 2 and 3 carried out using different amounts of CF_3CO_2H. The results further suggest that, despite poor basicity of short-lived **35**,[2g,11] the process for generating **37** (protonation of **35** and the subsequent electron transfer) can be so efficient as to overwhelm the rapid competing dimerization of **35** provided that the acidity of the medium is sufficiently high, or that the electron transfer is a quite fast reaction. The obtention from run 1 of **40a** (artifact of product **41a**) and **39** after chromatography of the crude product albeit in minute quantities may suggest that even AcOH, a weak acid, can participate in that process under appropriate reaction conditions. Oxidation of **3**, **14**, and **33** with excess PbO_2 and 70% $HClO_4$ (2.9 equiv) in MeOH under the identical conditions readily afforded **4** (90%), **18a** (87%), and only 5% of **39** together with **42** (91%), respectively. The results may reflect the difference in lifetime between **35** and **2** or **13**.

A similar effect of addition of an acid is expected for reactions of **33** with other oxidants which can generate **35**. Oxidation of **33** with activated MnO_2, $K_3Fe(CN)_6$, and $Ce(NH_4)_2(NO_3)_6$ (CAN), which are classified as one-electron oxidants, CrO_3, or HIO_3 was attempted in a hydroxylic solvent mixture or H_2O/acetone, containing or not containing a strong acid, and the results were compared (Table 4). For every reaction, the optimal conditions were not looked for. Treatment of **33** with activated MnO_2 in $AcOH/H_2O$ containing $HClO_4$ at 80 °C for a short period gave **39** in an excellent yield (run 2), while that in the absence of $HClO_4$ afforded only a small amount of **39**, the rest of the product being **42** (run 1). Oxidation of 2,6-dimethylphenol with MnO_2 in H_2O in the presence of H_2SO_4 gives the *p*-benzoquinone in low yield, whereas the same oxidation in $CHCl_3$ without an added acid provides the 4,4′-diphenoquinone.[27] Oxidation of **33** with CrO_3 in $AcOH/H_2O$ containing 96% H_2SO_4 for a short time provided a good yield of **39** (run 4), while that in the absence of 96% H_2SO_4 gave **39**, **42**, and

TABLE 4. Effect of Acid on Oxidation of Phenol 33 with Various Oxidants in a Hydroxylic Solvent Mixture or H_2O/Acetone[a]

run	oxidant	acid	solvent	recovery of **33** (%)	products (%[b]) **39**	**42**
1	activated MnO_2		$AcOH/H_2O$	0	1	99
2	activated MnO_2	$HClO_4$	$AcOH/H_2O$	0	89	0
3	CrO_3		$AcOH/H_2O$	36	40	19
4	CrO_3	96% H_2SO_4	$AcOH/H_2O$	0	80	0
5	$K_3Fe(CN)_6$		acetone/H_2O	100	0	0[c]
6	$K_3Fe(CN)_6$	$HClO_4$	acetone/H_2O	0	39	47
7	CAN		$MeOH/H_2O$	0	28	71
8	CAN	HNO_3	$MeOH/H_2O$	0	68	15
9	HIO_3[d]		$MeOH/H_2O$	0	25	28[e]
10	HIO_3[f]	$HClO_4$	$MeOH/H_2O$	0	73	0[g]

[a] See the Experimental Section for experimental details. [b] (Mol/mol **33** employed) × 100 for **39**, and (mol/mol **33** employed) × 2 × 100 for **38** and **42**. [c] A trace amount of **36** or **38** was detectable by TLC. [d] Reaction for 7.5 h. [e] In addition, **38** (22%) was obtained. [f] Reaction for 30 min. [g] In addition, **38** (7%) was obtained.

recovery of **33** (run 3). *p*-Benzoquinones can be prepared by a modified Jones oxidation of phenols including **33**.[28] Oxidation of 2,6-disubstituted phenols with CrO_3 in AcOH has been reported to give the corresponding 4,4′-diphenoquinones in unspecified yields.[29] Vigorous shaking of a solution of **33** in acetone/H_2O with $K_3Fe(CN)_6$ and $HClO_4$ consumed all of **33** shortly, and **39** and **42** were obtained in comparable yields (run 6). Omission of $HClO_4$ resulted in almost complete recovery of **33** (run 5). Ferricyanide oxidation of a phenol is usually carried out under alkaline conditions. However, oxidation of phenols with relatively low redox potentials under acidic conditions has been reported. For example, homogeneous oxidation of **3** with $H_3Fe(CN)_6$, a strong acid, in MeOH gives **4** in a small yield and **7** in a smaller yield.[30] For the formation of **4**, one-electron oxidation of intermediary **2** by $H_3Fe(CN)_6$ generating **10** has been considered. Homogeneous oxidation of **3** with $(Bu_4N)_3Fe(CN)_6$ in MeOH containing *p*-toluenesulfonic acid affords **4** as a minor product and **7**.[9a] To explain the formation of **4**, the Waters' mechanism described below has been considered. For comparison, we also carried out a heterogeneous reaction of **3** with $K_3Fe(CN)_6$ and $HClO_4$ in MeOH/H_2O in a manner analogous to that described above for run 6, and obtained **4** (65%) and **7** (7%). Dropwise addition of a solution of **33** in MeOH to a stirred solution of CAN in MeOH/H_2O containing added HNO_3 gave **39** principally in addition to **42** (run 8). The same products were obtainable from the reaction without added HNO_3, although **42** was the predominant one (run 7). Oxidation of monohydric phenols with Ce(IV) ion in H_2O or H_2O/CH_3CN, containing a strong acid, gives *p*-benzoquinones and/or coupling products.[31] Addition of HIO_3, a modest acid, to a stirred solution of **33** in MeOH/H_2O containing $HClO_4$ gave **39** mainly and **38** (run 10), while the coupling reaction took place principally at a slow rate if $HClO_4$ was omitted (run 9). 2,6-Disubstituted phenols including **33** have been reported to give the corresponding 4,4′-diphenoquinones upon treatment with HIO_3 in MeOH/H_2O at elevated temperature.[32] In all the instances, the anticipated effect of an acid on the oxidation of **33** thus was observable. A part of **39** obtained from the runs with the added acids could have arisen through **42** (and/or **38**) (see above). The reactions of **42** with the activated $MnO_2/HClO_4$ and CAN/HNO_3 systems indeed afforded **39**, although the selectivities were only fair. On the other hand, no or little reaction of **42** took place with the CrO_3/96% H_2SO_4, $K_3Fe(CN)_6/HClO_4$, or $HIO_3/HClO_4$ system.

Finally, a comment will be noted on one-electron oxidation of phenols under acidic conditions. Waters[33] argued that at a pH below 4 to 5, conversion of a phenoxyl radical to a phenoxyl cation is favored energetically over that of a phenol to a phenoxyl radical and that as a consequence the radical will be further oxidized and not dimerize. In a few studies on phenol oxidation, the results were interpreted in favor of the argument.[9a,34] On the other hand, it was questioned because oxidation of phenols with PbO_2 or $FeCl_3$ even in 1 M H_2SO_4 gave dimerized products predominantly.[35] In our oxidation of **33** with PbO_2, the formation of **39** is preferential and that of **42** insignificant only under strongly acidic conditions, as described above, although the Waters' results are strict only for aqueous solutions.

Summary

Long- and short-lived phenoxyl radicals are shown to undergo electron-transfer reaction with the protonated phenoxyl radicals yielding the phenoxyl cations and the phenols (eq 5). It is such a fast reaction that despite poor basicity of a phenoxyl radical, the process of its protonation and the subsequent electron transfer may cope with or even overwhelm its rapid dimerization provided that the acidity of the medium is sufficiently high. The present results may suggest a principle of modifying the nature of oxidation of a phenol from oxidative coupling to oxygenation. It is added that the electron-transfer reaction can in principle take place even under nonacidic conditions during one-electron oxidation of a phenol, as has been exemplified in the electrochemical study. In closing, it is hoped that our study will contribute to the progress of the chemistry of phenoxyl radicals and of phenol oxidation.

Experimental Section

^1H (90 MHz) NMR spectra were taken in $CDCl_3$. Column chromatography was conducted on SiO_2 using gradient elution (100% petroleum ether to 100% benzene) unless otherwise specified. TLC was run on SiO_2 or Al_2O_3. Product identification by comparison with authentic samples was carried out with ^1H NMR spectroscopy, melting point measurement, and TLC.

Effect of Acid on Decay of Phenoxyl Radical 2 in MeOH (Table 1): General Procedure. A mixture of a powdery solid of **1**[4c] (876 mg, 2 mmol) and MeOH (30 mL) containing or not containing an acid (5−20 mmol) was stirred in a stoppered bottle at 30 °C for the time indicated in the table until it became homogeneous. The mixture was poured into water, and extractive workup with ether gave a residue. Column chromatography of the residue afforded successively **3**, **6**, **4**, **7**, and **8**.

Compound **3**: colorless crystals; identical with a commercially available sample (Wako) of **3** (^1H NMR and TLC).

Compound **4**: colorless crystals from MeOH, identical with an authentic sample;[36] mp 93−94 °C (lit.[36] mp 94 °C).

Compound **6**: pale yellow crystals from diisopropyl ether, identical with an authentic sample;[6] mp 108−109 °C (lit.[37] mp 115−117 °C).

Compound **7**: colorless crystals from diisopropyl ether, identical with an authentic sample;[4c] mp 100−101 °C (lit.[38] mp 99.5 °C).

Compound **8**: colorless crystals from ethyl acetate, identical with an authentic sample;[4c] mp 192−193 °C (lit.[36] mp 189 °C).

A solution of **4**[36] (500 mg, 2 mmol) in MeOH (30 mL) containing CF_3CO_2H (1.49 mL, 20 mmol) or CF_3SO_3H (1.80 mL, 20 mmol) was let stand at 30 °C for 2 h. The reaction mixture was poured into water, and extractive workup with ether gave **4** quantitatively. No **7** was detectable.

Effect of Acid on Decay of Phenoxyl Radical 13 in MeOH/PhH (Table 2): General Procedure. The following preparation and reaction of **13** were conducted in a flask, and N_2 was bubbled through its contents all the time until the reaction was discontinued. At the bottom of the flask, a tube with a two-way stopcock was

---

[27] Bacon, R. G. R.; Izzat, A. R. *J. Chem. Soc. C* **1966**, 791.

[28] Liotta, D.; Arbiser, J.; Short, J. W.; Saindane, M. *J. Org. Chem.* **1983**, *48*, 2932.

[29] Stroh, R.; Seydel, R.; Hahn, W. *Angew. Chem.* **1957**, *69*, 699.

[30] Taimr, L.; Pospíšil, J. *Tetrahedron Lett.* **1971**, 2809.

[31] (a) Periasamy, M.; Bhatt, M. V. *Tetrahedron Lett.* **1977**, 2357. (b) Gopinathan, M. B.; Bhatt, M. V. *Indian J. Chem.* **1981**, *20B*, 71. (c) Ignaczak, M.; Dziegieć, J. *Pol. J. Appl. Chem.* **1992**, *36*, 183. (d) Domagała, S.; Steglińska, V.; Dziegieć, J. *Monatsh. Chem.* **1998**, *129*, 761.

[32] Fatiadi, A. J. *Synthesis* **1973**, 357.

[33] Waters, W. A. *J. Chem. Soc. B* **1971**, 2026.

[34] Swenton, J. S.; Carpenter, K.; Chen, Y.; Kerns, M. L.; Morrow, G. W. *J. Org. Chem.* **1993**, *58*, 3308.

[35] Nilsson, A.; Ronlán, A. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2337.

[36] Coppinger, G. M.; Campbell, T. W. *J. Am. Chem. Soc.* **1953**, *75*, 734.

[37] Magnusson, R. *Acta Chem. Scand.* **1966**, *20*, 2211.

[38] Kharasch, M. S.; Joshi, B. S. *J. Org. Chem.* **1957**, *22*, 1435.

joined. To a magnetically stirred solution of $K_3Fe(CN)_6$ (6.59 g, 20 mmol) and KOH (2.24 g, 40 mmol) in H_2O (50 mL) in the flask was added a N_2-purged solution of **14** (1.310 g, 5 mmol) in PhH (70 mL). The mixture was stirred for 40 min until the PhH solution no longer contained **14** as suggested by TLC. The aqueous layer was removed through the tube, and the deep-blue organic layer was washed 5 times with N_2-purged water (500 mL in total). Each washing was removed through the tube. The third washing was neutral. A N_2-purged solution of an acid or aqueous acid (60 mmol) in MeOH (100 mL) was added to the stirred PhH solution. The resulting homogeneous mixture was kept stirring at 25 °C for the time shown in the table until its deep-blue color was totally discharged (runs 4−6). In runs 1−3, after the stirring of the mixture was carried out for 60 min, O_2 was bubbled through the blue mixture until the color was discharged. The mixture was washed with water, dried (anhyd Na_2SO_4), and evaporated to give a residue.

Run 1: Comparison of the residue (1.382 g) with authentic samples of **16** and **17**[4c] by ^{1}H NMR spectroscopy and TLC suggested that it consisted exclusively of the peroxides (100%).

Runs 2 and 4−6: Column chromatography of the residue gave successively **14**, **18a**, and a mixture of **16** and **17**.[39] In run 4, continued elution gave a mixture (28 mg) containing **18b** and elution with CH_2Cl_2 gave **19** (17 mg, 3%).

Compound **18a**: colorless crystals from MeOH; mp 56−57.5 °C (lit.[40] mp 58−59 °C).

Compound **19**: red crystals from hexane; mp 115−117 °C (lit.[41] mp 113−114 °C).

Run 3: The residue was chromatographed on deactivated neutral Al_2O_3 (Merck, activity grade III). Elution with petroleum ether gave a colorless solid, which consisted exclusively of **14** (0.65 g, 108%), **18a** (0.41 g, 61%), and **24** (69 mg, 10%) as analyzed by ^{1}H NMR spectroscopy as well as TLC.[42] Compound **24** was synthesized according to the reported method[43] and used as an authentic sample for the analysis. Further elution provided a mixture of **16** and **17** (112 mg, 8%). Elution with CH_2Cl_2 gave **18b** (62 mg, 10%).

Compound **18b**: colorless crystals from hexane; mp 82−124 °C (lit. mp 129−130[44] and 80.9−82.1 °C[45]). Repeated recrystallization did not reduce the mp range. Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.37; H, 10.96. The ^{1}H NMR spectrum was consistent with that reported for **18b**.[44]

Duplication of each run gave essentially the identical results.

A solution of **24**[43] (371 mg, 1.25 mmol) in a mixture of MeOH (50 mL) and PhH (35 mL) containing 36% HCl[46] (2.55 mL, 30 mmol) was stirred at 25 °C for 60 min. The mixture was washed with water, dried, and evaporated to give a residue (368 mg), which consisted almost exclusively of recovery of **24** (99%) (^{1}H NMR). A trace amount of **18a** was detectable by TLC.

Effect of Acid on Oxidation of Phenol 33 with PbO_2 in AcOH/H_2O (Table 3): General Procedure. To a stirred mixture of PbO_2 (Aldrich) (2.39 g, 10 mmol), an acid (16−60 mmol), AcOH (15 mL), and H_2O (2.5 mL) was added at 25 °C a solution of **33** (824 mg, 4 mmol) in AcOH (15 mL) dropwise over a period of 5 min. In run 1, the added acid was omitted. In runs 8 and 9, 70% $HClO_4$[46] (1.38 mL, 16 mmol) and H_2O (1.81 mL), and 70% $HClO_4$ (2.76 mL, 32 mmol) and H_2O (1.12 mL) were substituted for the added acid and the H_2O, respectively. The resulting mixture was kept stirring for 5 min. The temperature of the reacting mixture rose to 33−38 °C (runs 2−9). The mixture was filtered into a flask containing water. The filter cake was washed with CH_2Cl_2 into the flask containing the filtrate. Extractive workup of the contents of the flask with CH_2Cl_2 gave a residue.

Run 2: See the text for the ^{1}H NMR spectrum of the residue. Column chromatography of the residue gave successively **42** (527 mg, 65%), **39** (211 mg, 24%), and **40a** (113 mg, 11%).

Compound **39**: orange crystals from MeOH, identical with an authentic sample;[24] mp 67−68.5 °C (lit.[47] mp 67−68 °C).

Compound **40a**: colorless crystals from petroleum ether, identical with an authentic sample;[25] mp 90−91 °C (lit.[48] mp 87−88 °C).

Compound **42**: reddish brown crystals from PhH, identical with an authentic sample;[4c] mp 248−250 °C (lit.[49] mp 246 °C).

Run 1: The ^{1}H NMR spectrum of the residue indicated that it contained **36** principally and no or little **38**. Recrystallization of the residue from hexane provided **36** (158 mg) as colorless crystals, identical with an authentic sample;[7] mp 140−150 °C (lit.[23] mp 140−150 °C). The filtrate from the recrystallization was evaporated and the residue was chromatographed. Elution afforded **33** (112 mg, 14% recovery). Further elution provided **38** (486 mg): pale yellow crystals from hexane, identical with an authentic sample;[7] mp 187−189 °C (lit.[49] mp 185 °C). Biphenol **38** isolated is assumed to be an artifact formed from **36** during the chromatography.[7] The total yield of **36** thus is estimated to be 644 mg (79%). Further elution gave successively **42** (49 mg, 6%), **39** (10 mg, 1%), and **40a** (12 mg, 1%).

The reaction of **40a**[25] (1.056 g, 4 mmol) in place of **33** with PbO_2, CF_3CO_2H (2.38 mL, 32 mmol), AcOH, and H_2O gave **39** (888 mg, 100%).

To a stirred homogeneous mixture of CF_3CO_2H (2.38 mL, 32 mmol), AcOH (30 mL), and H_2O (2.5 mL) was added **36**[49] (103 mg, 0.25 mmol) in one portion at 25 °C, and the mixture was kept stirring for 10 min. Pouring the reaction mixture into water and extractive workup with CH_2Cl_2 afforded **38** (101 mg, 98% or quantitative) alone. The reaction with CF_3SO_3H (2.82 mL, 32 mmol) in place of CF_3CO_2H gave a similar result.

To a stirred mixture of PbO_2 (2.39 g, 10 mmol), 70% $HClO_4$ (2.76 mL, 32 mmol), H_2O (1.12 mL), and AcOH (30 mL) was added at 25 °C a pulverized solid of **42** (408 mg, 1 mmol) in one portion, and the resulting mixture was kept stirring for 10 min. Compound **42** was poorly soluble in the medium. The mixture was worked up by a procedure similar to the general procedure described above for the effect of acid on the oxidation of phenol **33** with PbO_2 in AcOH/H_2O. Column chromatography of the residue provided successively **42** (160 mg, 39% recovery) and **39** (155 mg, 35% or 58% based on reacted **42**). The reaction using CF_3CO_2H (2.38 mL, 32 mmol) and H_2O (2.5 mL) in place of 70% $HClO_4$ and the H_2O gave recovery of **42** quantitatively. No **39** was obtained. The reaction using more CF_3CO_2H (60 mmol) gave the same result.

The reaction of **38** (410 mg, 1 mmol) in place of **42** with PbO_2 and 70% $HClO_4$ in AcOH/H_2O gave **38** (84 mg, 20% recovery), **39** (181 mg, 41%), and **42** (95 mg, 23%). Compound **38** was not sufficiently soluble in the reaction medium. The reaction using CF_3CO_2H (2.38 mL, 32 mmol) and H_2O (2.5 mL) in place of 70% $HClO_4$ and the H_2O gave **38** (90 mg, 22% recovery) and **42** (320

---

(39) Up to 1% of a mixture of **16** and **17** was obtained from runs 4−6. They are compounds formed before the discontinuation of the reaction of **13**; unintentional contamination of the contents of the flask by air could not be totally avoided during the operation. The small amount of **13** lost due to the undesired reaction is disregarded and not considered in calculating the yields of the products as well as the recovery of **13**. A small fraction of the peroxides obtained from runs 1−3 may also be those which arose before interrupting the reaction.

(40) Müller, E.; Ley, K.; Kiedaisch, W. *Chem. Ber.* **1954**, *87*, 1605.

(41) Ley, K.; Müller, E. *Chem. Ber.* **1956**, *89*, 1402.

(42) Compound **24** suffered decomposition upon chromatography on SiO_2.

(43) Pearson, D. E.; Venkataramu, S. D.; Childers, W. E., Jr. *Synth. Commun.* **1979**, *9*, 5.

(44) Rieker, A.; Rundel, W.; Kessler, H. *Z. Naturforsch.* **1969**, *24b*, 547.

(45) Futamura, S.; Yamazaki, K.; Ohta, H.; Kamiya, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3852.

(46) One milliliter each of commercially available 36% HCl, 70% $HClO_4$, and 60% HNO_3 were determined by titration to consist of HCl (11.8 mmol) and H_2O (0.76 mL), $HClO_4$ (11.6 mmol) and H_2O (0.50 mL), and HNO_3 (13.5 mmol) and H_2O (0.53 mL), respectively.

(47) Müller, E.; Ley, K. *Chem. Ber.* **1955**, *88*, 601.

(48) Müller, E.; Rieker, A.; Mayer, R.; Scheffler, K. *Liebigs Ann. Chem.* **1961**, *645*, 36.

(49) Kharasch, M. S.; Joshi, B. S. *J. Org. Chem.* **1957**, *22*, 1439.

mg, 78%). No **39** was obtained. The reaction using more CF_3CO_2H (60 mmol) also gave **42** and recovery of **38** alone.

Effect of Acid on Oxidation of Phenol 33 with Various Oxidants in a Hydroxylic Solvent Mixture or H_2O/Acetone (Table 4). (a) With activated MnO_2 (Runs 1 and 2). To a stirred mixture of activated MnO_2 (Aldrich) (4.35 g, 50 mmol) and AcOH (100 mL) containing H_2O (5 mL) (run 1) or 70% $HClO_4$ (10 mL, 0.12 mol) (run 2) was added dropwise at 80 °C a solution of **33** (2.06 g, 10 mmol) in AcOH (10 mL) over a period of 5 min. The mixture was kept stirring for 5 min at 80 °C. The reaction mixture was filtered, and the filter cake was washed with CH_2Cl_2 into the flask containing the filtrate. The contents of the flask were poured into water.

(b) With CrO_3 (Runs 3 and 4). To a stirred mixture of CrO_3 (302 mg, 3 mmol), AcOH (30 mL), and H_2O (3 mL), containing (run 4) or not containing (run 3) 96% H_2SO_4 (4 mL, 72 mmol), was added at 20 °C a solution of **33** (206 mg, 1 mmol) in AcOH (6 mL) dropwise over a period of 5 min. The mixture was kept stirring for 5 min. The reaction mixture was poured into water.

(c) With $K_3Fe(CN)_6$ (Runs 5 and 6). To a solution of **33** (826 mg, 4 mmol) in acetone (30 mL) containing H_2O (5 mL) (run 5) or 70% $HClO_4$ (10 mL, 0.12 mol) (run 6) was added at 25 °C pulverized crystals of $K_3Fe(CN)_6$ (7.93 g, 24 mmol) in one portion, and the resulting heterogeneous mixture in a stoppered bottle was mechanically shaken vigorously for 10 min. The reaction mixture was poured into water.

(d) With CAN (Runs 7 and 8). To a stirred solution of CAN (5.48 g, 10 mmol) in MeOH (20 mL) containing H_2O (1.6 mL) (run 7) or 60% HNO_3[46] (3 mL, 40 mmol) (run 8) was added dropwise at 20 °C a solution of **33** (412 mg, 2 mmol) in MeOH (10 mL) over a period of 5 min. The resulting mixture was kept stirring for 10 min. The reaction mixture was pored into water.

(e) With HIO_3 (Runs 9 and 10). To a stirred solution of **33** (412 mg, 2 mmol) in MeOH (30 mL) containing H_2O (1 mL) (run 9) or 70% $HClO_4$ (2 mL, 23 mmol) (run 10) was added at 20 °C a pulverized solid of HIO_3 (887 mg, 5 mmol) in one portion, and the resulting mixture was kept stirring for 7.5 h (run 9) or 30 min (run 10). The reaction mixture was poured into water containing excess $NaHSO_3$.

The resulting mixture from each reaction was subjected to extractive workup with CH_2Cl_2 or ether, and the residue was chromatographed.

Acknowledgment. The author thanks Yuhko Ikeda, Chisato Nohara, and Rie Arioka (students) for experimental contributions.

Supporting Information Available: Experimental procedures for the additional reactions of **33** and **42** and the reactions of **3**, **14**, and 4-bromo-2,6-di-*tert*-butylcyclohexa-2,5-dienone. This material is available free of charge via the Internet at http://pubs.acs.org.

JO701948A