Pergamon

Tetrahedron Vol. 51, No. 25, pp. 6901-6910, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00332-0

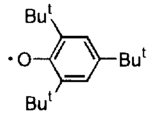
On the Structures of the Intermediates from Reversible Coupling between Hindered Phenoxy Radicals

Kanji Omura

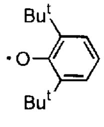
College of Nutrition, Koshien University, Momijigaoka, Takarazuka, Hyogo 665, Japan

***Abstract*:** Hindered phenoxy radicals **1** and **2** are found to undergo reversible, C-C rather than C-O cross-coupling, and give bis(cyclohexadienone)s **14** and **17**. These primary products are not isolable but are recovered as phenolic cyclohexadienones **15** and **18**, respectively, after treatment with Et_3N or as biphenols **16** and **12**, respectively, after treatment with TFA. The other products obtained after treating the reaction mixture with Et_3N or TFA are phenol **5** and 4,4'-diphenoquinone **13** alone. Dienones **14** and **17** are interconvertible with each other via dissociation into the parent radicals, and **14** appears to be thermodynamically more stable than **17**. Phenoxy radical **1** and other, less hindered 2,6-dialkylphenoxy radicals **24** also form intermediates of reversible cross-coupling. Treatment with TFA of the mixtures containing the intermediates provides 2,4'-biphenols **25** preferentially.

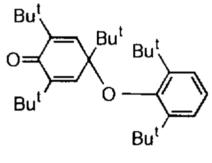
Phenoxy radicals undergo homo-(dimerization) or cross-coupling. Depending on their structures, quinol ethers (C-O coupling) or/and bis(cyclohexadienone)s (C-C coupling) are formed. These primary products are isolated as such or undergo further transformations. Coupling between sterically hindered phenoxy radicals is often reversible. The structures given to the products from coupling of such radicals have not been conclusive when their dissociation into the parent radicals in solution is extensive and adequate spectral informations thus are not available.[1-4] Müller and coworkers found that 2,4,6-tri-*tert*-buylphenoxy radical (**1**) and 2,6-di-*tert*-butyl-phenoxy radical (**2**) undergo cross-coupling.[5] The coupling product was not isolable due not only to reversibility of the coupling but also to irreversibility of dimerization of **2** regenerated by the dissociation of the product. Without firm evidence, they presumed it to be *p*-quinol ether **3**; for the stable products from coupling between **1** and a number of other phenoxy radicals, less hindered than **2**, are established to have *p*-quinol ether structures of type **6**.[6] An alternative *p*-quinol ether structure, **4**, also was reasonably considered for this particular product. We attempted to elucidate the structure of this intermediate from coupling between the hindered phenoxy radicals, **1** and **2**, by transforming it, generated *in situ*, into a more stable substance holding structural information regarding the original product. The reaction of **1** with other, less hindered 2,6-dialkyl-4-unsubstituted phenoxy radicals also was investigated.



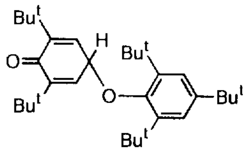
1



2



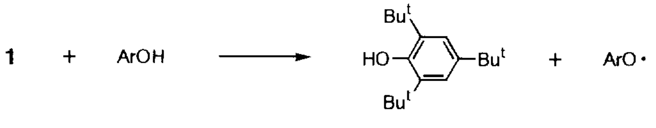
3



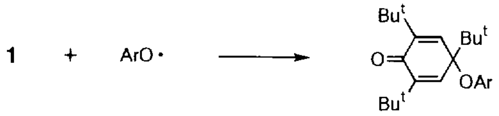
4

RESULTS AND DISCUSSION

The coupling reaction of **1** with an unstable phenoxy radical has often been conducted by adding a phenol to a benzene solution of **1** (2 mol equiv) generated by dehydrogenation of 2,4,6-tri-*tert*-butylphenol (**5**) with alkaline ferricyanide. The completion of the coupling is indicated by usually rapid and total discharge of a deep blue color due to **1**. Müller *et al.* carried out the reaction of **1** with **2** in this manner and we did it analogously.



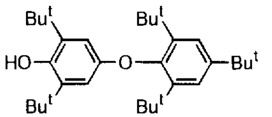
5

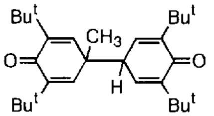


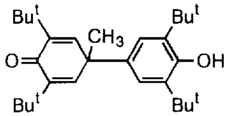
6

In accordance with their observation, addition of 2,6-di-*tert*-butylphenol (**10**) to a solution of **1** resulted only in rapid and serious reduction in intensity of the deep blue color.[7] They ascribed this fact to the formation of an intermediary product of reversible cross-coupling, the one proposed to be *p*-quinol ethers **3** or **4**. By allowing an analogous solution containing the intermediate to stand at ambient temperature for several hours or at 40 °C for a shorter period, they observed disappearance of the residual blue color, and obtained a reddish brown solution, from which they isolated **5** and 4,4'-diphenoquinone **13** as the exclusive end-products. Their formation has been accounted for by irreversible dimerization of **2**, regenerated by dissociation of the intermediate, giving bis(cyclohexadienone) **11**, and subsequent dehydrogenation by **1** (cf. Scheme 1). In our study, in contrast, this solution containing the intermediate was treated with Et_3N. This treatment was expected to convert **4**, provided that it indeed was the intermediate, into a possibly more stable substance, 4-hydroxydiphenyl ether **7**, or any other 4 (or 6)-hydrocyclohexa-2,5 (or 2,4)-dienone intermediates into their phenol isomers. Bases can facilely catalyze prototropic rearrangement of 4-hydrocyclohexa-2,5-dienones.[4,8,9] By this treatment, the residual blue color of the solution soon changed to reddish brown, suggesting that the intermediate was quenched. Subsequent evaporation of the reaction mixture below 30 °C under reduced pressure left a residue, which was suggested by TLC to consist almost exclusively of four products. Two of them were identified as **5** and **13**. The other two were new substances **15** and **18**, which were more or less unstable. Compound **15** was particularly labile, and careful workup was required for its isolation and purification. Subjecting the crude product to quick column chromatography on deactivated neutral Al_2O_3 (Activity III) separated **15** as a mixture with **13** from the rest of the products. Washing the mixture with cold MeOH removed most of the poorly soluble **13**. Evaporating the washing and recrystallizing the residue from hexane gave **15** as pale yellow crystals with mp 127-130 °C dec. These operations were all conducted below 30 °C. The ^1H NMR spectrum (C_6D_6) of this compound with molecular formula $C_{32}H_{50}O_2$ exhibited singlets at δ 7.45 (2 H), 4.87 (1 H), 1.38 (18 H), 1.25 (9 H), 1.23 (9 H) and 1.17 (9 H), and a pair of doublets at δ 6.90 (J = 2.6 Hz, 1 H) and 6.74 (J = 2.6 Hz, 1 H). The IR spectrum ($CHCl_3$) showed the presence of a hindered phenolic hydroxyl (3620 cm^{-1}) and a conjugated dienone (1660 and 1644 cm^{-1}). Hence the product was assigned 6-(4-hydroxyphenyl)cyclohexa-2,4-dienone structure **15**. The other, more stable product **18** was isolated facilely by the same chromatography. Microanalysis of this compound, obtained as pale yellow crystals with mp 161.5-165 °C dec, suggested it to be isomeric with **15**. The ^1H NMR spectrum (C_6D_6) showed singlets alone at δ 7.50 (2 H), 7.43 (2 H), 4.86 (1 H), 1.45 (18 H), 1.36 (18 H) and 1.01 (9 H). This compound had IR absorptions ($CHCl_3$) at 3620, and 1652 and 1628 cm^{-1}. These data were in accordance with 4-(4-hydroxyphenyl)cyclohexa-2,5-dienone structure **18** for the product. Structures **15** and **18** were also supported by ^{13}C NMR and UV spectroscopy (see Experimental).

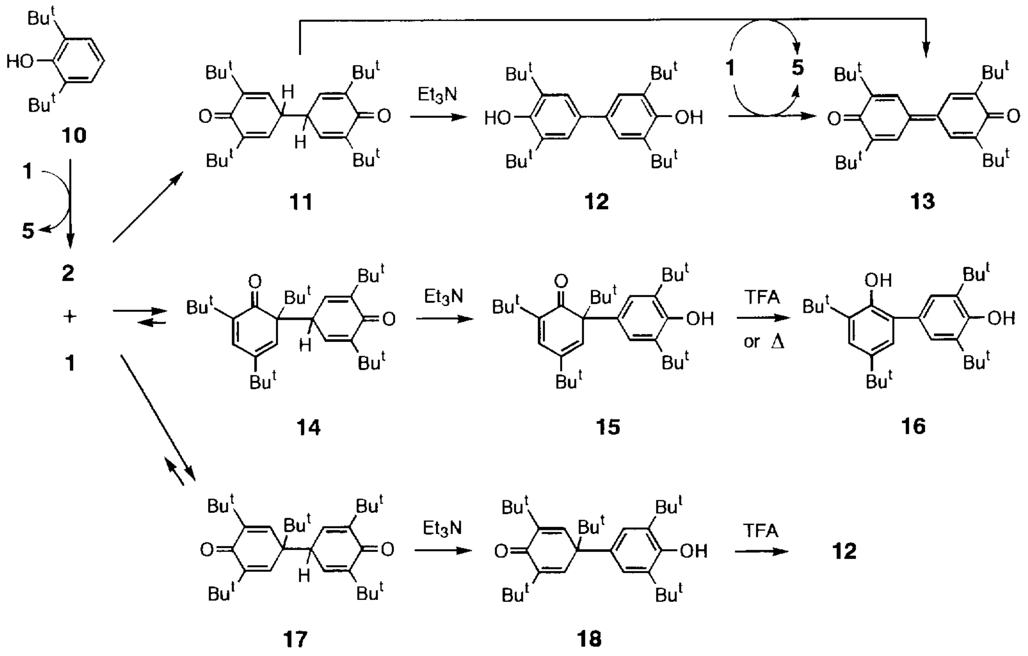
The obtention of **15** and **18** after quenching with Et_3N suggests strongly that the structures of the primary products of coupling between **1** and **2** are bis(cyclohexadienone)s **14** and **17**, the products of C-C coupling. The Et_3N-catalyzed prototropic rearrangement of **14** and **17** is in close analogy with the ready rearrangement by the same base of bis(cyclohexadienone)s **11** or **8** into 4,4'-biphenol **12** or phenolic dienone **9**, respectively.[4]


7


8


9

Both of **14** and **17** may dissociate into the parent radicals, since the ultimate products of the reaction (without added Et_3N) are, as described by Müller *et al.*, **5** and **13** alone. Hence **14** and **17** are interconvertible. The remarkable reduction in intensity of the deep blue color due to **1** after adding **10** suggests that the equilibriums



Scheme 1

between the phenoxy radicals and the coupling products lie over in favor of the products (see also note 7). We are not aware of other instances of *ortho-para* coupling of 2,6-di-*tert*-butylphenoxy radicals, or of 2,6-disubstituted phenoxy radicals in general. Diphenoquinone **13** (as well as **5**) may arise before addition of Et_3N according to the path shown by Müller *et al.*, who also suggested that the dehydrogenation of **11** with **1** is sluggish. Compound **13** may be formed additionally after addition of the base by rapid dehydrogenation of **12** with **1** (Scheme 1). However, these are not the sole paths for the formation of **13** (and **5**), as mentioned later.

The instability of **15** and **18** turned out to be ascribable to their propensity to lose the *tert*-butyl group bound to sp^3-C, giving 2,4'-biphenol **16** and **12**, respectively. Thus, quantitative conversion of **15** into **16** was brought about by exposing to TFA (trifluoroacetic acid) for a short period at 0 °C, or by heating in MeOH at 60 °C for 3 hours. The decay of **15** in hot benzene (60 °C) also gave **16** in high yield, but it was relatively slow. The de-*tert*-butylation of **15** upon column chromatography on SiO_2 was also substantial. The de-*tert*-butylation of a small fraction of **15** could not be avoided even during quick column chromatography on the deactivated neutral Al_2O_3 described above. Quantitative de-*tert*-butylation of **18** giving **12** by the treatment with TFA was also facile. The de-*tert*-butylation of **18** in benzene containing a small quantity of TFA, however, was significantly slower than that of **15**. Dienone **18** was recovered intact upon the heating in MeOH, or upon column chromatography on SiO_2 or the deactivated neutral Al_2O_3. It decayed slowly in heated benzene (60 °C), but the product was **13**. No thermal interconversion in solution (up to 60 °C) was observed between **15** and **18**.

To get further insight into the nature of the reaction with Et_3N, it was carried out under various conditions and the results were compared (Table 1). In every run, almost all of the products were accounted for, as suggested by the yields of the products shown in the table. A standard reaction was carried out by adding **10** to a benzene solution of **1** (2 mol equiv) at 6-8 °C and letting the resulting solution wait for 1 min at that temperature for subsequent addition in one portion of a relatively large amount of Et_3N (run 3). The treatment with Et_3N changed the residual blue color of the solution into reddish brown almost instantly. Of the two cross-coupling products, **15** was formed preferentially. The product distribution was found to be affected markedly

Table 1. Et_3N-Interruption of Reaction between Phenoxy Radicals **1** and **2**[a]

run	time[b] (min)	Et_3N	products (%[c])			
			5	**13**	**15**[d]	**18**
1	1	1 drop	91	82	0	14
2	1	1.5 mL	76	55	21	23
3	1	5 mL	66	29	44	25
4	10	5 mL	69	37	47	17
5	30	5 mL	69	39	52	11

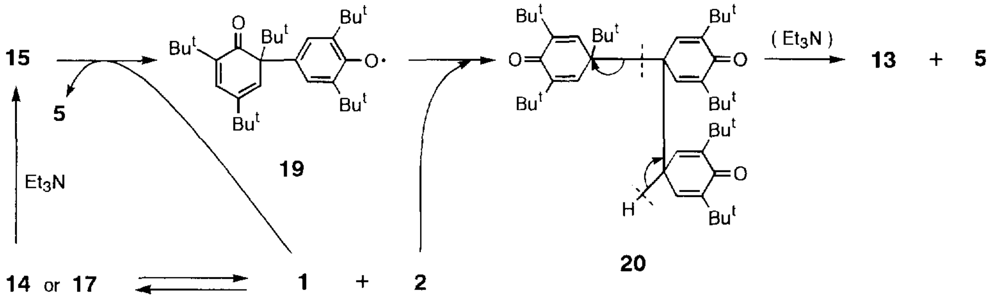
[a] Conducted with **1** (9 mmol) and **10** (4.5 mmol).

[b] Time-interval between additions of **10** and of Et_3N.

[c] Proposed yields of **5**, **13**, **15**, and **18** are 9, 2.25, 4.5, and 4.5 mmol, respectively. The proposed yield of **5** includes that (4.5 mmol) from the primary reaction of **1** with **10**.

[d] Total yield of **15** itself and **16** (0-4%). The crude product (before chromatography) did not contain **16**.

by the quantity of Et_3N. Thus, employment of a smaller quantity of the base resulted in sharp and slight reduction in yield of **15** and **18**, respectively (run 2, compare with run 3). With a catalytic amount of the base, the reaction no longer afforded **15**. Instead, **13** and **5** were furnished in high yields, although some **18** was still obtained (run 1). In this particular run, the discharge of the blue color after adding Et_3N was not quite fast, yet it survived only for several minutes at 6-8 °C. Such dependence of the product distribution on quantity of Et_3N may not be expected from the paths shown in Scheme 1 alone. An additional path must, therefore, be assumed which can account for that dependence. It may be as follows. When Et_3N is added, dienones **14** and **17** and phenols **15** and **18** coexist, either momentarily or for a longer period depending upon the quantity of Et_3N employed. These dienones are, as described above, equilibrated with phenoxy radicals **1** and **2**. Radical **1** abstracts hydrogen, for example, from **15** by a rapid process generating **5** and a new phenoxy radical **19**.[10] Radical **19** combines with **2** to form tris(cyclohexadienone) **20**, which undergoes collapse into **13** and **5** intiatated by Et_3N-catalyzed deprotonation (arrow) or homolytic fission of a weak C-C bond (dotted line) (Scheme 2).



Scheme 2

The breakdown of isomeric phenol **18** by **1** and **2** into **13** and **5** takes place similarly. The net reaction is

$$15\ (\text{or}\ 18) + 14\ (\text{or}\ 17) \longrightarrow 2\ 5 + 13$$

If the concentration of added Et_3N is high, most of **14** and **17** has been rearranged prototropically, and the quantities of residual **14** and **17** available for the reaction shown above are limited. If that concentration is quite low, on the other hand, slowly generating **15** and **18** are largely destroyed by the action of **1** and **2** supplied from **14** and **17** remaining amply. Accordingly, it is highly probable that quantitative recovery of **14** and **17** as **15** and **18**, respectively was not attained even in the run with the large quantitiy of Et_3N (run 3). That **15** experienced severer reduction in yield than **18** upon lowering the concentration of Et_3N, may suggest that **15** is dehydrogenated faster than **18**, by **1**, although further investigation is needed for the details. The rate of dehydrogenation of a phenol by **1** is significantly dependent on the nature of substituent on the benzene ring.[6,11] In other runs, the time-interval between the additions of **10** and of Et_3N (the large amount) was expanded (runs 4 and 5). By the expansion, yield of **15** was found to improve while that of **18** to decline, although the total yield of **15** and **18** suffered only gradual decrease (compare with run 3). This may mean the following. Firstly, **17** is gradually converted into **14** via dissociation into **1** and **2** until an equilibrium is

Table 2. TFA-Interruption of Reaction between Phenoxy Radicals **1** and **2**[a]

run	time[b] (min)	products (%[c])			
		5	**13**	**16**	**12**
1	2	56	17	56	24
2	30	58	18	66	15

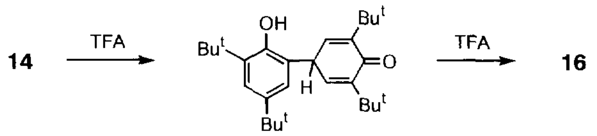
[a] Conducted with **1** (9 mmol), **10** (4.5 mmol), and TFA (3 mL).

[b] Time-interval between additions of **10** and of TFA.

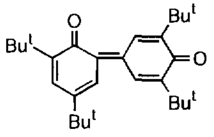
[c] Proposed yields of **5**, **13**, **16**, and **12** are 9, 2.25, 4.5, and 4.5 mmol, respectively. The proposed yield of **5** includes that (4.5 mmol) from the primary reaction of **1** with **10**.

reached. In other words, **14** is thermodynamically more stable than **17**. Secondly, the loss in total of **14** and **17** due to the reactions including the irreversible dimerization of **2** generated by their dissociation, progresses only slowly (in the absence of Et_3N). Moreover, the decrease in the total quantity of **15** and **18** by postponing the Et_3N treatment need not be ascribed only to the decrease in the total quantity of **14** and **17**. It may also be ascribable to the increased proportion of **14** to **17**: the efficiency of the conversion by Et_3N of **14** into **15** is poorer than that of **17** into **18** (see above).

It has been shown that prototropic rearrangement of 4-hydrocylohexa-2,5-dienones is catalyzed by acid as well.[4,12] Besides, **15** and **18** can be de-*tert*-butylated by the action of TFA, as described above. It was, therefore, expected that treatment of the mixture containing intermediates **14** and **17** with TFA (in place of Et_3N) would provide **16** and **12** directly (cf. Scheme 1). Rapid quenching of **14** and **17** by adding a relatively large quantity of TFA in one portion at 6-8 °C, was indicated by quick replacement of the blue color of the solution with reddish brown. After workup, **16** and **12** were isolated, the former having been predominant. The other products were **13** and **5** alone (Table 2, run 1). The reaction was complete quite fast: in 2 minutes after the TFA-addition, the solution contained these four products alone as indicated by TLC. It is noted that alternative paths for the formation of **16** and **12** may not be excluded in which de-*tert*-butylation precedes and prototropic rearrangement follows, e. g.;

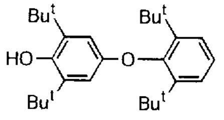


It is presumed that **12** was formed also by TFA-catalyzed isomerization of **11** but that the **12** was dehydrogenated by **1** to give **13** (cf. Scheme 1). There is no knowing whether or not a fraction of **12** formed by the other path(s) shown above similarly suffered dehydrogenation, but it is noteworthy that 2,4'-diphenoquinone **21**, the expected product of dehydrogenation of **16**, was not obtained from run 1.[13] Delaying the addition of TFA resulted in increase and decrease in yield of **16** and **12**, respectively (run 2), as would be anticipated from the result of the reaction with Et_3N.



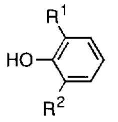
21

Lack of indication of formation of 4-phenoxyphenol **7** from the reaction with Et_3N or TFA, may exclude the possibility that *p*-quinol ether **4** was among the primary coupling products. Failure to obtain 4-phenoxyphenol **22** from the reaction with TFA might suggest that *p*-quinol ether **3** was not included either in the primary products. 4-Phenoxy-2,4,6-tri-*tert*-butylcyclohexa-2,5-dienones reportedly are facilely de-*tert*-butylated by TFA under mild conditions giving the corresponding 4-phenoxy-2,6-di-*tert*-butylphenols.[14] The coupling of **1** and **2** to form highly congested ether **3** is far less likely than that to form much less congested ether **4**. There appears to be no explicit examples of obtaining products whose structures have been unequivocally established to be *p*-quinol ethers, from homo- or cross-coupling between 2,6-di-*tert*-butylphenoxy radicals.[4]

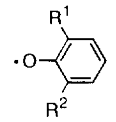


22

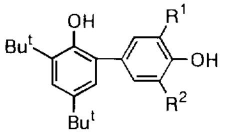
Literature survey suggested to us that the reaction of **1** with 2,6-disubstituted-4-unsubstituted phenoxy radicals other than **2** has been scarcely studied.[15] Finally, therefore, the reaction of **1** was carried out with some, less hindered 2,6-dialkyl-4-unsubstituted phenoxy radicals, in the manner described above for the reaction with **2**. Addition of 2-*tert*-butyl-6-methyl- (**23a**), 2,6-diisopropyl- (**23b**) or 2,6-dimethylphenol (**23c**) again resulted only in abrupt reduction in intensity of the deep blue color of **1**, suggesting that cross-coupling of **1** and phenoxy radicals **24a**, **24b** or **24c** is also reversible. Addition of TFA to the mixtures containing the intermediary products readily discharged the residual blue color. The principal products of cross-coupling obtained after the TFA treatment were found to be those of *ortho-para* coupling, 2,4'-biphenols **25a** (70%), **25b** (66%) and **25c** (39%). They were isolated easily. Analyses of other coupling products were not detailed, and the possibility was not excluded that products of C-O cross-coupling were among them. However, the obtention of **25c** in a significant quantity may indicate at least that C-O coupling of **1** giving a quinol ether of type **26** is not a sterically very favorable process as compared with C-C coupling, even with the least hindered 2,6-dialkylphenoxy radical, **24c**. Our procedure may serve as a convenient method for preparation of 2,4'-biphenols of type **25** (R^1, R^2 = alkyl) which are not easily accessible otherwise. The coupling reaction of sterically hindered, stable phenoxy radicals other than **1** with 2,6-dialkyl-4-unsubstituted phenoxy radicals may deserve investigation.



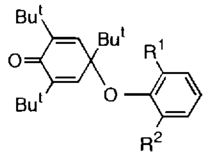
23



24



25



26

a: $R^1 = CH_3$, R^2 = *t*-Bu

b: $R^1 = R^2$ = i-Pr

c: $R^1 = R^2 = CH_3$

ACKNOWLEDGMENTS The author is grateful to Dr. Masahiro Sakaitani and Mr. Tsuyoshi Fujita (Suntory Institute for Bioorganic Research) for a HRMS. He also thanks Emiko Yamada and Junko Kawarada for experimental contribution.

EXPERIMENTAL

Unless specifically stated, ^1H (90 MHz) and ^{13}C (22.6 MHz) NMR, IR, and UV spectra were taken in $CDCl_3$, $CHCl_3$, and cyclohexane, respectively. TLC was run on SiO_2.

Et_3N-Interruption of Reaction between Phenoxy Radicals 1 and 2 (Table 1). A mixture of a benzene (100 mL) solution of 2,4,6-tri-*tert*-butylphenol (**5**) (2.358 g, 9 mmol) and an aqueous (50 mL) solution of $K_3Fe(CN)_6$ (11.85 g, 36 mmol) and KOH (4.5 g, 80 mmol), was vigorously stirred magnetically for 40 min, until the benzene solution no longer contained **5** as indicated by TLC. The aqueous layer was removed, and the deep blue benzene solution was washed repeatedly with water. The solution (wet) was cooled to 6-8 °C, and maintained at that temperarure until addition of Et_3N (described below) was complete. To the stirred solution was added at one time a solution of 2,6-di-*tert*-butylphenol (**10**) (927 mg, 4.5 mmol) in benzene (15 mL). The deep blue color was rapidly reduced in intensity but was not discharged totally. After 1-30 min, Et_3N (1 drop-5 mL) was added at one time to the resulting solution while the vigorous stirring was maintained. The blue color of the solution was replaced by reddish brown in about 4 min (1 drop of Et_3N) or instantly (1.5-5 mL of Et_3N). All these operations were conducted under N_2. The mixture was dried over anhydrous Na_2SO_4, and evaporated under reduced pressure below 30 °C. Half of the crystalline residue was quickly chromatographed on deactivated neutral Al_2O_3 (Merck, Activity III, 200 g) with petroleum ether as eluent. A typical chromatographic procedure is described for run 3. The first fraction gave **5** (778 mg, 66%). The second fraction was evaporated under reduced pressure below 30 °C. To the crystalline residue was added cold MeOH (30 mL), and the mixture was stirred for 30 min at 0 °C. Filtration afforded 3,5,3',5'-tetra-*tert*-butyl-4,4'-diphenoquinone (**13**) (127 mg): reddish brown crystals from benzene, identical with an authentic sample[16] (^1H NMR, IR, and TLC), mp 240-241 °C (lit.[16] mp 240-241 °C). The filtrate was evaorated under reduced pressure below 30 °C. The crystalline residue was analyzed by ^1H NMR spectroscopy and TLC to be a mixture consisting of 2,4,6-tri-*tert*-butyl-6-(3,5-di-*tert*-butyl-4-hydroxyphenyl)cyclohexa-2,4-dien-1-one (**15**) (444 mg, 42%), 3,5,3',5'-tetra-*tert*-butyl-2,4'-dihydroxybiphenyl (**16**) (21 mg, 2%), and **13** (8 mg, 29% in total). The crude product (before chromatography) did not contain **16** as indicated by TLC. The residue was recrystallized from hexane below 30 °C, providing **15**. Pale yellow crystals: mp 127-130 °C dec; ^{13}C NMR (C_6D_6) δ 202.85, 153.03, 145.80, 140.47, 134.16, 132.63, 132.33, 128.21, 126.69, 62.44, 39.27, 34.85, 34.73, 34.64, 30.43, 29.79, 29.24, 28.11; UV 201 nm (log ε 4.6), 282 (3.5), 306 (3.6). For the ^1H NMR and IR spectra, see the text. Anal. Calcd for $C_{32}H_{50}O_2$: C, 82.35; H, 10.80. Found: C, 82.16; H, 10.75. The third fraction afforded 2,4,6-tri-*tert*-butyl-4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)cyclohexa-2,5-dien-1-one (**18**) (260 mg, 25%) as yellow crystals. Pale yellow crystals from hexane: mp 161.5-165 °C dec; ^{13}C NMR (C_6D_6) δ 184.65, 152.42, 146.41, 143.46, 134.92, 132.48, 125.53, 49.76, 38.94, 35.55, 34.61, 30.34, 29.79, 26.83; UV 204 nm (log ε 4.7), 240 (4.1), 278 (3.6, shoulder). For the ^1H NMR and IR spectra, see the text. Anal. Calcd for $C_{32}H_{50}O_2$: C, 82.35; H, 10.80. Found C, 82.23; H, 10.82.

De-*tert*-butylation of 15 and 18.

(A) With TFA. To **15** (50 mg) was added cold TFA (5 mL), and the mixture was stirred for 15 min at 0 °C. The mixture was poured into water, and extracted with petroleum ether. The extract was washed with water, dried, and evaporated under reduced pressure to leave **16** (45 mg, quantitative) as colorless crystals. Colorless crystals from MeOH: mp 189-190.5 °C (lit.[13b] mp 171-173 °C); ^1H NMR δ 7.32 (d, J = 2.4 Hz, 1 H), 7.23 (s, 2 H), 7.09 (d, J = 2.4 Hz, 1 H), 5.42 (s, 1 H), 5.30 (s, 1 H), 1.42 (s, 27 H), 1.34 (s, 9 H); ^{13}C NMR δ 153.36, 148.70, 141.50, 136.75, 134.74, 128.70, 128.33, 126.14, 124.64, 123.06, 35.09, 34.48, 34.30, 31.65, 30.28, 29.70; IR 3615, 3520 cm^{-1}. Anal. Calcd for $C_{28}H_{42}O_2$: C, 81.90; H, 10.31. Found: C, 81.63; H, 10.35. The reaction of **18** (70 mg) with TFA (5 mL) was conducted in the manner described above for that of **15**, yielding 3,5,3',5'-tetra-*tert*-butyl-4,4'-dihydroxybiphenyl (**12**) (63 mg, quantitative) as pale yellow crystals, identical with an authentic sample[4] (^{1}H NMR, IR, and TLC), mp 184-186 °C (lit.[4] mp 184.5-185.5 °C).

A reaction of **15** (25 mg) in benzene (10 mL) containing TFA (3 drops) at 30 °C for 20 min gave, after workup, a *ca.* 1:1 mixture of **15** (recovery) and **16**. The reaction for 2 h virtually completed the transformation into **16**. A similar reaction of **18** (25 mg) for 2 h gave a *ca.* 1:1 mixture of **18** (recovery) and **12**.

(B) In MeOH. A solution of **15** (30 mg) in MeOH (3 mL) was heated at 60°C for 3 h. TLC suggested that the **15** disappeared from the solution in 2.5-3 h. Evaporation under reduced pressure left **16** quantitatively. The same treatment of **18** (30 mg) resulted in quantitative recovery of **18**.

(C) In Benzene. A solution of **15** (30 mg) in benzene (3 mL) was heated at 60 °C for 12.5 h. TLC suggested that the **15** disappeared from the solution in 11.5-12.5 h. Evaporation left a residue, which was analyzed by ^{1}H NMR spectroscopy and TLC to contain **16** in nearly quantitative yield and a small amount of an unidentified product. The same treatment of **18** (30 mg) for 9 h gave a mixture of **18** (78% recovery) and **13** (22%).

(D) On SiO_2 or Deactivated Neutral Al_2O_3 (Activity III). Quick column chromatography of **15** (30 mg) on SiO_2 (Merck, 10 g) with petroleum ether/benzene (10:1) gave a mixture cosisting of **15** (40% recovery) and **16** (60%). Quick column chromatography of **15** on the Al_2O_3 (15 g) with petroleum ether provided a mixture consisting of **15** (96% recovery) and **16** (4%). The same chromatography of **18** (30 mg) on SiO_2 or the Al_2O_3 resulted in quantitative recovery of **18**.

TFA-Interruption of Reaction between 1 and 2 (Table 2). The reaction was conducted in the manner described above for that with Et_3N, except that TFA (3 mL) was employed in place of Et_3N. Upon addition at one time of TFA, the blue color of the solution was replaced instantly by reddish brown. After the resulting solution was kept stirring for 15 min at 6-8 °C under N_2, it was washed with water, dried, and evaporated under reduced pressure below 30 °C. TLC suggested that the residue consisted almost exclusively of **5**, **12**, **13** and **16** and contained neither **15** nor **18**. Half of the residue was chromatographed on SiO_2 (100 g) with petroleum ether. The chromatographic procedure is described for run 1.The first fraction afforded **5** (656 mg, 56%). The second fraction gave **16** (519 mg, 56%). The third fraction yielded **12** (225 mg, 24%). The last fraction provided **13** (79 mg, 17%).

TFA-Interruption of Reaction between 1 and Phenoxy Radicals 24. The reaction was carried out in the manner described above for run 1, Table 2, except that 2-*tert*-butyl-6-methylphenol (**23a**) (738 mg, 4.5 mmol), 2,6-diisopropylphenol (**23b**) (801 mg, 4.5 mmol) or 2,6-dimethylphenol (**23c**) (549 mg, 4.5 mmol) was employed in place of **10**. Upon addition of these phenols to the solution of **1**, the deep blue color was rapidly reduced in intensity but was not discharged totally. The residual blue color was discharged instantly when TFA was added subsequently. The crude products were chromatographed on SiO_2 (80 g) with petroleum ether and/or a mixture of petroleum ether and benzene. The following products were eluted after **5** (58-64%).

3,5,3'-tri-*tert*-butyl-5-methyl-2,4'-dihydroxybiphenyl (**25a**) (1.163 g, 70%) from the reaction with **23a**: light yellow viscous oil (purification by thick layer chromatography on SiO_2); ^{1}H NMR δ 7.30 (d, J = 2.4 Hz, 1 H), 7.21 (d, J = 2.4 Hz, 1 H), 7.08 (d, J = 2.4 Hz, 1 H), 7.05 (d, J = 2.4 Hz, 1 H), 5.38 (s, 1 H), 4.86 (s, 1 H), 2.30 (s, 3 H), 1.44 (s, 18 H), 1.32 (s, 9 H); IR 3585, 3520 cm^{-1}. HRMS calcd for $C_{25}H_{36}O_2$ 360.2715; found 360.2717.

3,5-di*tert*-butyl-3',5'-diisopropyl-2,4'-dihydroxybiphenyl (**25b**) (1.138 g, 66%) from the reaction with **23b**: colorless crystals (from hexane); mp 120.5-121.5 °C; ^{1}H NMR δ 7.32 (d, J = 2.4 Hz, 1 H), 7.12 (s, 2 H), 7.07 (d, J = 2.4 Hz, 1 H), 5.39 (s, 1 H), 4.86 (s, 1 H), 3.20 (hept, J = 6.4 Hz, 2 H), 1.46 (s, 9 H), 1.33 (s, 9 H), 1.29 (d, J = 6.4 Hz, 12 H); IR 3585, 3520 cm^{-1}. Anal. Calcd for $C_{26}H_{38}O_2$: C, 81.62; H, 10.01. Found: C, 81.35; H, 10.23.

3,5-di-*tert*-butyl-3',5'-dimethyl-2,4'-dihydroxybiphenyl (**25c**) (579 mg, 39%) from the reaction with **23c**: colorless crystals (from hexane); mp 146-147 °C; ^{1}H NMR δ 7.28 (d, J = 2.4 Hz, 1 H), 7.06 (s, 2 H), 7.02 (d, J = 2.4 Hz, 1 H), 5.37 (s, 1 H), 4.70 (s, 1 H), 2.30 (s, 6 H), 1.44 (s, 9 H), 1.31 (s, 9 H); IR 3580, 3520 cm^{-1}. Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26. Found: C, 80.99; H, 9.34.

REFERENCES AND NOTES

1. Müller, E.; Rieker, A.; Mayer, R.; Scheffler, K. *Liebigs Ann. Chem.* **1961**, *645*, 36-52.
2. Becker, H.-D. *J. Org. Chem.* **1965**, *30*, 982-989.
3. Matsuura, T.; Nishinaga, A.; Cahnmann, H. J. *J. Org. Chem.* **1962**, *27*, 3620-3628.
4. Omura, K. *J. Org. Chem.* **1991**, *56*, 921-927.
5. Ley, K.; Müller, E.; Mayer, R.; Scheffler, K. *Chem. Ber.* **1958**, *91*, 2670-2681.
6. Isomeric o-quinol ethers or the products derived from them (e. g., o-hydroxydiphenyl ethers) are obtained much less frequently. See: Matsuura, T.; Nishinaga, A.; Ogura, K.; Omura, K. J. Org. Chem. **1969**, *34*, 550-555.
7. More precisely, their observation was that the deep blue color of **1** was once discharged upon completing addition of **10** but the color was (partly) recovered after a few minutes. To achieve the discharge, however, employment of a little more than the proposed amount of **10** was needed. Our run was conducted with an exactly 2:1 molar ratio of **1** and **10**.
8. Omura, K. *J. Org. Chem.* **1992**, *57*, 306-312.
9. de la Mare, P. B. D.; Singh, A. *J. Chem Soc., Perkin Trans. 2* **1973**, 59-62.
10. Radical **19** (and hence **20**) may be formed also by dehydrogenation of **14** with **1**. However, it may be as slow as the dehydrogenation of **11** with **1**. It is possible that the dehydrogenation of **14** (and **17**) makes a significant contribution to the formation of **13** in the absence of Et_3N.
11. DaRooge, M. A.; Mahoney, L. R. *J. Org. Chem.* **1967**, *32*, 1-6.
12. de la Mare, P. B. D.; Singh, A.; Tillet, J. G.; Zeltner, M. *J. Chem. Soc. B* **1971**, 1122-1129.
13. Compound **21** was not obtained from the reactions with Et_3N either. An authentic sample of **21** was prepared by dehydrogenating **16** with PbO_2 in benzene. Cf.: (a) Kessler, H.; Rieker A. *Tetrahedron Lett.* **1966**, 5257-5262; (b) Komissarov, V. N.; Ukhin, L. Yu.; Kharlanov, V. A.; Vetoshkina, L. V.; Konstantinovskii, L. E.; Aldoshin, S. M.; Fillipenko, O. S.; Novozhilova, M. A.; Atovmyan, L. O. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1991**, 1121-1129.
14. Rieker, A.; Zeller, N. *Tetrahedron Lett.* **1968**, 4969-4972.
15. Mahoney, L. R.; DaRooge, M. A. *J. Am. Chem. Soc.* **1970**, *92*, 890-899.
16. Omura, K. *J. Org. Chem.* **1984**, *49*, 3046-3050.

(*Received in Japan* 9 *March* 1995; *accepted* 24 *April* 1995)