Dienone Tautomers of 4-Alkoxy-2,6-di-*tert*-butylphenols

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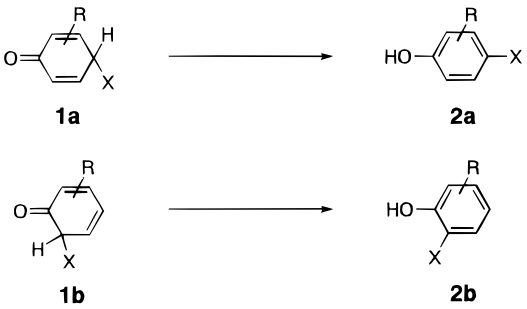
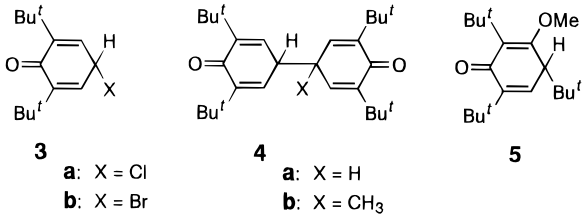
Generation and isolation of 4-alkoxycyclohexa-2,5-dienones **9**, the tautomeric forms of the title phenols (**10**), is described. They are generated efficiently by the Ag ion mediated reaction of 4-bromocyclohexa-2,5-dienone **3b** with simple alcohols, although they can be irreversibly isomerized into **10** under the reaction conditions. Crude materials with high amounts of **9** can be obtained by conducting the reaction with $AgClO_4$ in the presence of Na_2CO_3 or with $AgOCOCF_3$ and by interrupting the reaction shortly after the formation of **9** is complete. The $AgOCOCF_3$ reaction produces labile 4-(trifluoroacetoxy)cyclohexa-2,5-dienone **11** also, the formation of which becomes significant as the alcohol becomes bulky. All of **9** prove to be very much susceptible to the prototropic rearrangement into **10** by catalysis with base, acid, or SiO_2. Crude dienones **9** can be conveniently prepared directly from phenol **6** by treatment for a short time with Br_2 in alcohols containing $AgClO_4$ and Na_2CO_3. A one-pot synthesis from **6** of 4-oxyfunctionalized 2,6-di-*tert*-butylphenols, including **10**, is also described.

Cyclohexadienones **1a** or **1b** are the tautomeric forms of phenols **2a** or **2b**, respectively. In most cases, these species only exist transiently since they readily undergo prototropic rearrangement into more stable, phenol forms. Therefore, it is usual that they can not be isolated,



although they may be detectable by spectroscopic means under appropriate conditions.[1] 4-Halocyclohexa-2,5-dienones **3** and bis(cyclohexadienone)s **4** are among rare examples of dienones of type **1a** which can be isolated. Dienones **3** and **4** are obtained by electrophilic phenol halogenation[2] and phenoxy radical coupling,[3] respectively. Even these isolatable dienones are susceptible to irreversible isomerization into the corresponding phenols by catalysis with base, acid, or SiO_2. They also isomerize in polar media such as EtOH. 4-*tert*-Butyl-cyclohexa-2,5-dienone **5** has been isolated from irradiation of an isomeric cyclohexa-2,5-dienone.[4] It is noticeable that these isolatable dienones bear *tert*-butyl groups in the 2- and 6-positions. Simple dienones of type **1b** do not appear to have been isolated.[5]



Isolation of simple dienones of type **1a** where X is an oxyfunctional group appears to be hitherto unknown, although their intermediacy has been or may be reasonably postulated to account for the formation of the products from a number of reactions such as (i) reactions of phenols with oxygen electrophiles,[6] (ii) reactions of phenoxy radicals with oxygen radicals,[7] and (iii) reactions of chemically or electrochemically generated phenoxenium ions or related species with oxygen nucleophiles.[8] In this article, the generation and isolation of 4-alkoxy-2,6-di-*tert*-butylcyclohexa-2,5-dienones (**9**), the tautomeric forms of 4-alkoxy-2,6-di-*tert*-butylphenols (**10**), is described. Their generation was expected from 4-bromo-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**3b**) by a reaction analogous to the Ag ion induced nucleophilic displace-

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(4) Matsuura, T.; Ogura, K. *J. Am. Chem. Soc.* **1967**, *89*, 3846.

(5) For specifically substituted phenols including hydroxy derivatives of polycondensed aromatic hydrocarbons, the tautomeric cyclohexadienone forms of type **1a** or **1b** are known, which are isolable in the individual state or exist in an appropriate solvent. Some of these dienone forms are energetically favored over the phenol forms, and in limited cases only the dienone forms are known. The actual cyclohexadienone−phenol tautomerism, as a mobile equilibrium, has been rarely observed experimentally. See: (a) Ershov, V. V.; Nikiforov, G. A. *Russ. Chem. Rev.* **1966**, *35*, 817. (b) Forsén, S.; Nilsson, M. In *The Chemistry of the Carbonyl Group*; Patai, S., Ed.; Wiley: New York, 1970; Vol. 2, p 157. (c) Crozier, R. F.; Hewitt, D. G. *Aust. J. Chem.* **1972**, *25*, 183. (d) Highet, R. J.; Chou, F. E. *J. Am. Chem. Soc.* **1977**, *99*, 3538. (e) Teuber, H.-J.; Götz, N. *Chem. Ber.* **1956**, *89*, 2654. (f) Teuber, H.-J.; Thaler, G. *Chem. Ber.* **1959**, *92*, 667.

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Table 1. Alkoxy Dienones 9 from Bromo Dienone 3b[a]

				product (yield,[b] %)	
run	alcohol	Ag salt	additive	**9**	**10**
1	MeOH	$AgClO_4$		**9a** (35)	**10a** (54)
2	MeOH	$AgClO_4$	Na_2CO_3	**9a** (71)	**10a** (15)
3	MeOH	$AgClO_4$	H_2O[c]	**9a** (54)	**10a** (24)
4	MeOH	$AgOCOCF_3$		**9a** (82)	**10a** (6)
5	EtOH	$AgClO_4$	Na_2CO_3	**9b** (80)	**10b** (6)
6	*i*-PrOH	$AgClO_4$	Na_2CO_3	**9c** (81)	**10c** (7)
7	*t*-BuOH[d]	$AgClO_4$		**9d** (41)	**10d** (49)
8	*t*-BuOH[d]	$AgClO_4$	Na_2CO_3	**9d** (79)	**10d** (14)
9	*t*-BuOH[d]	$AgOCOCF_3$		**9d** (30)	**10d** (1)
10	*t*-AmOH[e]	$AgClO_4$		**9e** (74)	**10e** (16)
11	*t*-AmOH[e]	$AgClO_4$	Na_2CO_3	**9e** (88)	**10e** (3)

[a] Unless stated otherwise, the reaction was carried out for 2 min at 0 °C by using **3b** (2 mmol), $AgClO_4$ or $AgOCOCF_3$ (2 mmol), and an alcohol (30 mL). The amount of Na_2CO_3 employed as an optional additive was 8 mmol. [b] ^1H NMR spectroscopically determined yields of **9** and **10** contained in the crude product. Compound **9** was converted into **10** when chromatographed on SiO_2. See Experimental Section for products obtained by chromatography. [c] Conducted for 10 min with a solvent mixture of MeOH (28 mL) and H_2O (4 mL). [d] Conducted at 27 °C. [e] Conducted for 4 min.

ment of 4-bromo-4-alkyl-2,6-di-*tert*-butylcyclohexa-2,5-dienones with an alcohol.[9]

Results and Discussion

A solution of $AgClO_4$ (1 molar equiv) in MeOH was added in one portion to solid **3b**, and the mixture was vigorously stirred for a few minutes at 0 °C. As **3b** dissolved, yellow deposits of insoluble AgBr formed. The ^1H NMR spectrum (in $CDCl_3$) of the isolated organic product exhibited singlets ascribable to 4-methoxy-2,6-di-*tert*-butylphenol (**10a**) and weak singlets assignable to 4-bromo-2,6-di-*tert*-butylphenol (**7**), while the starting material (**3b**) was undetectable. In addition, the spectrum displayed new signals, which appeared at δ 6.69 (d, $J = 3.1$ Hz), 4.42 (t, $J = 3.1$ Hz), 3.40 (s), and 1.24 (s) with relative intensities of ca. 2:1:3:18. Upon addition of pyridine-d_5 to the $CDCl_3$ solution, these new signals disappeared rapidly from the spectrum, and the singlets due to **10a** were intensified. Column chromatography of the crude product on SiO_2 isolated **10a** and **7** in 89% and 5% yields, respectively, but did not afford the product responsible for the new NMR signals. The product, therefore, contained a labile new substance, and this appeared to be 4-methoxy-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**9a**), which underwent prototropic rearrangement into **10a** by catalysis with pyridine-d_5 or SiO_2. The NMR signals at δ 6.69, 4.42, 3.40, and 1.24 are assignable to vinyl, methine, methoxy, and *tert*-butyl protons, respectively. Combination of the analyses by ^1H NMR spectroscopy and chromatography suggested that the crude product contained **9a** and **10a** in 35% and 54% yields, respectively (Table 1, run 1).[10,11] The result suggests that Ag ion mediated removal of the bromide ion from **3b** to generate carbocationic intermediate **8** (a resonance form of the phenoxenium ion), which combines with solvent to give **9a**, is so efficient that it overwhelms the competing prototropic rearrangement of **3b** into **7** (Scheme 1). An ^1H NMR study confirmed that in the absence of $AgClO_4$ the prototropic rearrangement of **3b** in MeOH-d_4 was fast and was not accompanied by solvolysis of **3b**.[12] Solvolysis of 4-bromo-4-alkyl-2,6-di-*tert*-butylcyclohexa-2,5-dienones with alcohols can take place in the absence[13] or presence[14] of base.

Enrichment of **9a** in the crude product was tried by modifying the reaction conditions. It was presumed that the isomerization of **9a** was facilitated not only by MeOH but also by $HClO_4$, which is likely generated during the course of the $AgClO_4$-induced reaction of **3b** with MeOH (cf. Scheme 1). Neutralization of the $HClO_4$ as it was generated was expected to retard the isomerization and thus to increase the content of **9a**. The reaction of **3b** with $AgClO_4$ in MeOH was conducted in the presence of excess Na_2CO_3 (4 molar equiv). The crude product obtained was analyzed in a manner analogous to that described above for the reaction without Na_2CO_3. As expected, the amount of **9a** in the crude product was remarkably increased (71%) while that of **10a** was substantially decreased (15%) (Table 1, run 2).

Enrichment in the content of **9a** could also be brought about by conducting the reaction of **3b** with $AgClO_4$ in a 7:1 (v/v) mixture of MeOH and H_2O (in the absence of Na_2CO_3). The reaction time was extended due to the limited solubility of **3b** in the medium, and **9a** constituted the major component (54% yield) (Table 1, run 3). The prototropic rearrangement of **3b** in a mixture of AcOH and H_2O (containing HBr) is slow as the proportion of H_2O becomes high.[2c]

The reaction between **3b** and MeOH was investigated also with $AgOCOCF_3$ (in the absence of Na_2CO_3), which was expected to generate CF_3CO_2H, a much weaker acid than $HClO_4$. The oily product was estimated to contain **9a** in as high as 82% yield (Table 1, run 4). Attempted purification of crude **9a** thus obtained by crystallization from nonpolar solvents such as hexane proved unsuccessful: chilling the solution slowly deposited only a crystalline mixture of **9a** and **10a**, and the proportion of **9a** to **10a** in it was always lower than that in the original oil. The isomerization of **9a** into **10a** progressed, though gradually, even in the nonpolar solvents.

We turned our attention to preparation of **9** other than **9a** by conducting similarly the reaction of **3b** in other alcohols with $AgClO_4$ and Na_2CO_3 or with $AgOCOCF_3$. The reaction with $AgClO_4$ and Na_2CO_3 was carried out in EtOH, *i*-PrOH, or *t*-AmOH (*tert*-amyl alcohol) at 0 °C or in *t*-BuOH at 27 °C. As shown in Table 1 (runs 5, 6, 8, and 11), all of the products from these reactions contained **9** (see below for their NMR data) in satisfactory amounts (79−88%). The **9**/**10** (including **9a**/**10a**) ratio obtained from the reaction at 0 °C tended to be high when the alcohol was bulky. Further examples of the decreased yield of **9** upon omission of Na_2CO_3 are also shown in the table (compare runs 7 and 10 with runs 8 and 11, respectively). The crude product of 4-ethoxy- (**9b**) or 4-isopropoxy-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**9c**) obtained from run 5 or 6, respectively, was oily. Their purification by crystallization from hexane or CCl_4 has

(9) Ronlán, A.; Parker, V. D. *J. Chem. Soc. C* **1971**, 3214.

(10) The isomerization of **9a** into **10a** upon chromatography on SiO_2 was assumed to be quantitative.

(11) Very recently, we have found that **9a** is contained, albeit in a small quantity, in the product obtained from the reaction of 2,6-di-*tert*-butylphenol (**6**) with I_2 and H_2O_2 in MeOH. See: Omura, K. *J. Org. Chem.* **1996**, *61*, 2006.

(12) Dienone **3b** (43 mg) was allowed to dissolve in MeOH-d_4 (0.6 mL) in ca. 80 s at 30 °C, and the progress of its decay at ca. 30 °C was followed by ^1H NMR spectroscopy. After 3 min about one-half of the **3b** was found to survive, and after 25 min only singlets due to **7** were observed.

(13) Coppinger, G. M.; Campbell, T. W. *J. Am. Chem. Soc.* **1953**, *75*, 734.

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Scheme 1

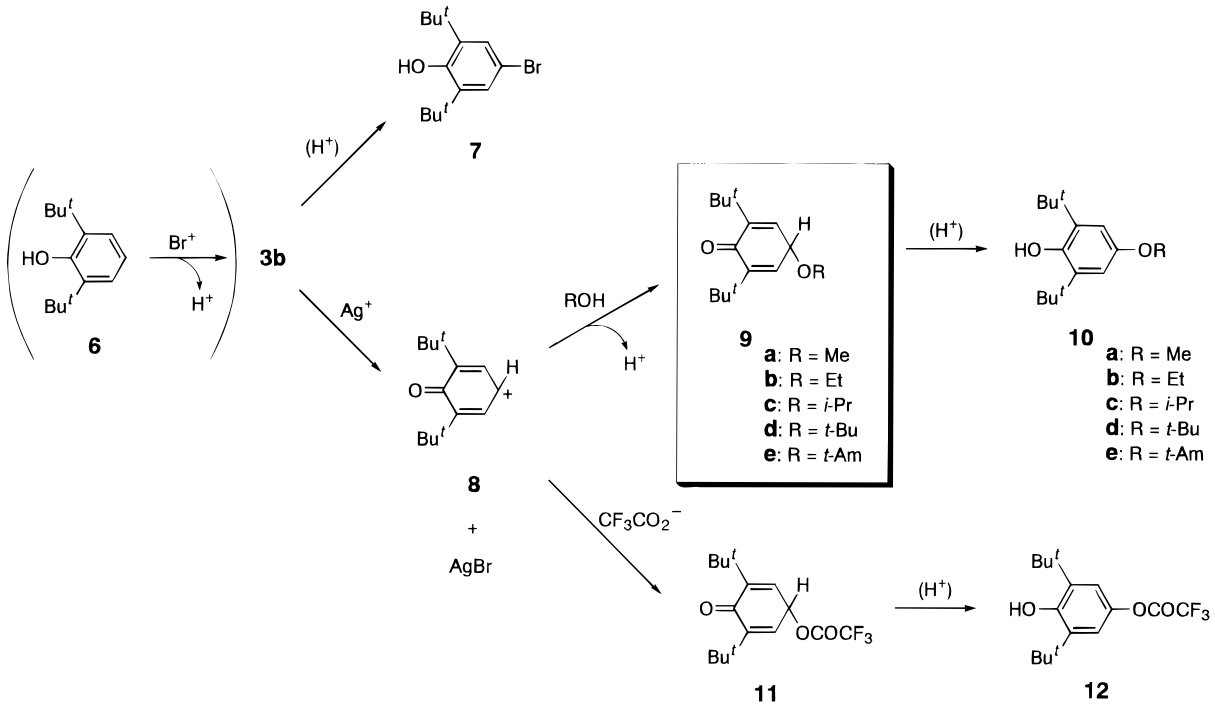


Table 2. ^{1}H NMR Data for Alkoxy Dienones 9 in $CDCl_3$

	δ (multiplicity, J in hertz)			
compd	H-3 and H-5	H-4	2- and 6-*t*-Bu	4-alkoxy
9a[a]	6.69 (d, 3.1)	4.42 (t, 3.1)	1.24 (s)	3.40 (s)
9b[a]	6.70 (d, 3.2)	4.46 (t, 3.2)	1.24 (s)	3.61 (q, 7.0), 1.26 (t, 6.9)
9c[a]	6.65 (d, 3.1)	4.47 (t, 3.1)	1.23 (s)	3.83 (hept, 6.1), 1.25 (d, 6.1)
9d[b]	6.52 (d, 3.1)	4.54 (t, 3.1)	1.22 (s)	1.34 (s)
9e[b]	6.53 (d, 3.2)	4.55 (t, 3.1)	1.22 (s)	1.62 (q, 7.5), 1.27 (s), 0.97 (t, 7.4)

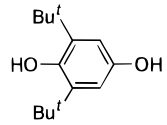
[a] Crude product obtained from run 4, 5, or 6, Table 1. [b] Analytically pure product obtained from run 8 or 11, Table 1.

been unsuccessful: at −20 °C, it progressed extremely reluctantly and slow isomerization of **9b** or **9c** into 4-ethoxy- (**10b**) or 4-isopropoxy-2,6-di-*tert*-butylphenol (**10c**), respectively, was observed. The crude product of 4-*tert*-butoxy-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**9d**) obtained from run 8 was crystalline. We were pleased to find that pure **9d** was readily isolated by simple recrystallization from hexane. Microanalysis of the compound, obtained as colorless crystals, suggested it to be isomeric with 4-*tert*-butoxy-2,6-di-*tert*-butylphenol (**10d**). Product identification by ^{1}H NMR spectroscopy was straightforward (Table 2). The ^{13}C NMR spectrum was also compatible with structure **9d**. The IR (1658 and 1639 cm^{-1}; Nujol mull) as well as UV [236 nm (log ϵ 3.92) in cyclohexane] spectra also supported the cyclohexa-2,5-dienone structure.[15] Purification by recrystallization of the crystalline crude product of 4-(*tert*-amyloxy)-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**9e**), obtained from run 11, was also facile. Structure **9e** for the compound was unambiguously demonstrated similarly from the ^{1}H (Table 2) and ^{13}C NMR, IR (1661 and 1639 cm^{-1}; Nujol mull), and UV [239 nm (log ϵ 3.95) in cyclohexane] spectra as well as microanalysis. Table 2 lists the ^{1}H NMR data of **9a**−**c** also. It is rational that the resonances of vinyl, methine (in the 4-position), and *tert*-butyl (in the 2- and 6-positions) protons in **9a**−**c** appear in the neighborhood of those in **9d** or **9e**. Stability was tested on the pure specimens of **9d** and **9e**. As proved by ^{1}H NMR spectroscopy, they were considerably stable in $CDCl_3$: **9d** or **9e** suffered little isomerization into **10d** or 4-(*tert*-amyloxy)-2,6-di-*tert*-butylphenol (**10e**), respectively, after allowing the solution to stand at ca. 35 °C for 15 h. In $CDCl_3$ containing pyridine-d_5, they were converted into the phenols very rapidly, as anticipated. In MeOH-d_4, they were unstable and their isomerization was completed within 15 min at ca. 35 °C. It was confirmed that **9d** and **9e** were quantitatively recovered as **10d** and **10e**, respectively, when chromatographed on SiO_2 with nonpolar eluents. In the solid states, both **9d** and **9e** remained unchanged for months when stored at −20 °C.

As cited above, a high amount of **9a** in the crude product was obtained from the reaction of **3b** with $AgOCOCF_3$ in MeOH. The reactions to give **9** with $AgOCOCF_3$ and other alcohols, however, proved not to be quite successful, owing to occurrence of a competing reaction generating a new, labile dienone, 4-(trifluoroacetoxy)-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**11**). Compound **11** was not isolable, but its formation was supported by the following representative observations. The ^{1}H NMR spectrum (in $CDCl_3$) of the crude product from the reaction in *t*-BuOH (at 27 °C) (run 9, Table 1) suggested that it contained, in addition to **9d** and **10d**, two new compounds. One of them (minor component) was found to be 4-(trifluoroacetoxy)-2,6-di-*tert*-butylphenol (**12**). The other (major component) showed signals at δ 6.53 (d, J

(15) The spectral properties of cyclohexadienones have been described in detail. See: (a) Rieker, A.; Rundel, W.; Kessler, H. *Z. Naturforsch* **1969**, *24b*, 547. (b) Rieker, A.; Berger, S. *Org. Magn. Reson.* **1972**, *4*, 857.

= 3.2 Hz) (overlapped with the doublet due to **9d**), 5.98 (t, J = 3.2 Hz), and 1.25 (s). In $CDCl_3$ containing pyridine-d_5, the ^1H NMR spectrum of the product consisted exclusively of singlets due to **10d** and **12**. Column chromatography of the product on SiO_2 provided four compounds almost excusively, **10d**, **12**, 2,6-di-*tert*-butylhydroquinone (**13**), and 2,6-di-*tert*-butyl-*p*-benzoquinone (**14**). Compounds **13** and **14** were artifacts formed from **12** during the chromatography.[16] It is thus reasonable



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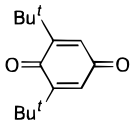

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to assume that the crude product contained **11**, to which the aforementioned new NMR signals are ascribable, and that **11** underwent prototropic rearrangement by base, acid, or SiO_2, providing **12**. Similarly, the crude products obtained from the reactions (at 0 °C) of **3b** with $AgOCOCF_3$ in other alcohols (including MeOH) contained **11** and **12** in addition to **9** and **10**. The (**9** + **10**)/(**11** + **12**) molar ratios were estimated to be 30, 8.0, 2.6, 0.5, and 0.5 for the reactions in MeOH, EtOH, *i*-PrOH, *t*-BuOH, and *t*-AmOH, respectively: the **9**/**10** ratios and the **11**/**12** ratios were in general high. The formation of **11** may be the result of the reaction of carbocation **8**, generated from the interaction between **3b** and $AgOCOCF_3$, with the freed CF_3CO_2 anion (Scheme 1).[17] Competition for **8** between CF_3CO_2 anion (giving **11**) and an alcohol (giving **9**) is shown to become in favor of the former as the alcohol becomes bulky.[18] Generation of **9** by displacement reaction of **11** with an alcohol is unlikely, since extending the time of the reaction in *t*-BuOH, described above, altered neither the total yield of **9d** and **10d** nor that of **11** and **12**, although the **9d**/**10d** and **11**/**12** ratios were both decreased.

It was found that **9** can be conveniently obtained directly from 2,6-di-*tert*-butylphenol (**6**), by brominating it to generate **3b** *in situ* in an alcohol containing $AgClO_4$ and Na_2CO_3 (cf. Scheme 1). Molecular bromine (1 molar equiv) in DME was added quickly to a vigorously stirred solution (0 °C) of **6** and $AgClO_4$ (2 molar equiv) in an alcohol[19] containing excess Na_2CO_3 (4 molar equiv), and the stirring was continued for a few minutes at 0 °C. As shown in Table 3, the crude product contained **9** in a yield comparable to that obtained from the corresponding reaction of **3b** with $AgClO_4$ and Na_2CO_3. Success of the process is indebted to the rapidity and selectivity of both the bromination and the subsequent debromination. Half of the $AgClO_4$ employed was consumed in the bromination step.

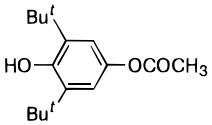
It is natural that a one-pot synthesis of **10** from **6** was also possible. Quick addition of methanolic Br_2 (1 molar equiv) to a stirred solution of **6** and $AgClO_4$ (2 molar equiv) in MeOH (not containing Na_2CO_3) readily afforded

Table 3. Alkoxy Dienones 9 from Phenol 6[a]

alcohol	product (yield,[b] %)	
	9	**10**
MeOH	**9a** (75)	**10a** (14)
EtOH	**9b** (86)	**10b** (7)
i-PrOH	**9c** (83)	**10c** (6)
t-BuOH[c]	**9d** (91)	**10d** (3)
t-AmOH	**9e** (82)	**10e** (3)

[a] Unless stated otherwise, the reaction was carried out for 2 min at 0 °C by using **6** (2 mmol), Br_2 (2 mmol), $AgClO_4$ (4 mmol), and Na_2CO_3 (8 mmol) in a mixture of an alcohol (30 mL) and DME (7 mL). [b] ^1H NMR spectroscopically determined yields of **9** and **10** contained in the crude product. [c] Conducted for 3 min in a mixture of *t*-BuOH (20 mL) and DME (17 mL in total: see Experimental Section).

10a in 84% yield as well as AgBr (2 molar equiv).[20] The actual species for brominating **6** must be Br_2 itself. However, $BrClO_4$ (or BrOMe after its reaction with MeOH) generated from the reaction between Br_2 and $AgClO_4$ may as well be responsible for the bromination of **6**. Indeed, addition of Br_2 to methanolic $AgClO_4$ (1 molar equiv) immediately discharged the Br_2 color and precipitated AgBr (1 molar equiv, isolated by filtration), and the filtrate was capable of brominating **6** rapidly. Hence **10a** was obtained also by adding **6** to a mixture of Br_2 (1 molar equiv) and $AgClO_4$ (2 molar equiv) in MeOH. Electrophilic halogenation of aromatic substrates with a combination of molecular halogen and Ag ion has been documented.[21] The same methoxylation could be achieved by adding Br_2 to a solution of **6** and $AgClO_4$ in DME containing a limited amount (12 molar equiv) of MeOH, without much sacrifice to the yield of **10a** (79%). 4-Alkoxyphenols **10b**, **10c**, and **10d** were obtained in 76−79% yields from similar reactions with limited amounts (8−10 molar equiv) of EtOH, *i*-PrOH, and *t*-BuOH, respectively. The reaction with H_2O (28 molar equiv) provided **13** (79%). Acetoxylation of **6** to give 4-acetoxy-2,6-di-*tert*-butylphenol (**15**) was successful (78%) only when a large quantity of AcOH was employed. Examples of synthesis of oxyfunctionalized phenols directly from phenols are scarce because substantial overoxidation takes place usually.[8b,d,e,22]



15

In summary, 4-alkoxycyclohexa-2,5-dienones **9**, the tautomeric forms of 4-alkoxyphenols **10**, can be obtained as crude products from the fast reaction of 4-bromocyclohexa-2,5-dienone **3b** either with $AgClO_4$ and Na_2CO_3 in alcohols or with $AgOCOCF_3$ in the same solvents. They can also be obtained directly from phenol **6** by treatment with Br_2 in alcohols containing $AgClO_4$ and Na_2CO_3. Crude 4-*tert*-alkoxycyclohexa-2,5-dienones **9d** and **9e** can be purified facilely by recrystallization, and they are fully

(16) Compounds **13** and **14** were also obtained in small quantities from the reactions with $AgClO_4$ (see Experimental Section).

(17) An alternative mechanism may not be excluded in which **3b** is attacked by Ag ion and by an alcohol or CF_3CO_2 anion concertedly and free cation **8** accordingly is not generated.

(18) The reaction at 0 °C of **3b** with $AgClO_4$ in an equimolar mixture of MeOH and *t*-BuOH (not containing Na_2CO_3) gave rise to **10a** and **10d** in 76% and 14% yields, respectively, after chromatography of the crude product.

(19) In the reaction with *t*-BuOH, DME was employed as a cosolvent to avoid freezing (see Experimental Section).

(20) If Br_2 was added slowly, namely, over a period of 6 min, the yield of **10a** was reduced to 56% while recovery of **6** (21%) and formation of **14** (14%) became significant. Compound **10a** was oxidized rapidly by Br_2 in MeOH containing or not containing $AgClO_4$, giving **14** quantitatively.

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characterized. Dienones **9** are susceptible to (irreversible) tautomerization into phenols **10** by catalysis with base, acid, or SiO_2. A one-pot synthesis of 4-oxyfunctionalized 2,6-di-*tert*-butylphenols from **6** is achieved.

Experimental Section

^1H (90 MHz) and ^{13}C (22.6 MHz) NMR spectra were taken in $CDCl_3$. Column chromatography was conducted on Merck SiO_2 60 by using gradient elution (100% petroleum ether to 50%/50% petroleum ether/benzene). TLC was run on SiO_2. GC analyses were performed at 150 °C on a column packed with 10% FAP-S on Chromosorb W. Commercially available $AgClO_4$ (Wako) and $AgOCOCF_3$ (Aldrich) were used as received. Reactions with the Ag salts were carried out in a stoppered vial.

Silver Ion Induced Reaction of Bromo Dienone 3b with Alcohols (Table 1). With $AgClO_4$ in the Presence of Na_2CO_3 (Runs 2, 5, 6, 8, and 11). To a mixture of powdered **3b**[2c] (570 mg, 2 mmol) and finely powdered anhydrous Na_2CO_3 (0.85 g, 8 mmol) was added at once a cold (0 °C) solution of $AgClO_4$ (415 mg, 2 mmol) in an alcohol (30 mL), and the resulting mixture was stirred magnetically for 2 min at 0 °C. The reaction with *t*-BuOH (run 8) was run at 27 °C. The reaction with *t*-AmOH (run 11) was carried out for 4 min. The mixture was filtered into a flask containing stirred, cold water (200 mL). The contents of the flask were extracted with petroleum ether (200 mL × 2). The extract was washed with water, dried over anhydrous Na_2SO_4, and evaporated to dryness under reduced pressure below 30 °C. The residual product (containing alkoxy dienone **9** and 4-alkoxyphenol **10**) was readily subjected to analysis by ^1H NMR spectroscopy. Column chromatography of the product provided successively 4-bromophenol **7** (15−33 mg, 3−6%), **10** (see below for the yield), *p*-benzoquinone **14** (3−24 mg, 1−5%), and hydroquinone **13** (none or trace). Compound **10d** or **10e** was in part obtained as a mixture with **14**, and the amounts of **10d** or **10e** and of **14** in the mixture were estimated by ^1H NMR spectroscopy. Compounds **7**, **10a**−**e**, and **14** were purified by recrystallization from hexane or MeOH.

Compound **7**: identical with an authentic sample[3b] (^1H NMR and TLC); mp 82−84 °C (lit.[3b] mp 80−82 °C).

Compound **10a**: obtained from run 2 (407 mg, 86%); identical with a commercially available sample (from Aldrich) of **10a** (^1H NMR and TLC); mp 105−106 °C (lit.[23] mp 106−107 °C).

Compound **10b**: obtained from run 5 (432 mg, 86%); mp 84.5−85.5 °C (lit.[24] mp 83−84 °C).

Compound **10c**: obtained from run 6 (463 mg, 88%); mp 60−62.5 °C (lit.[25] mp 59−60 °C).

Compound **10d**: obtained from run 8 (515 mg, 93%); mp 99.5−100 °C (lit.[26] mp 99−100 °C).

Compound **10e** obtained from run 11 (532 mg, 91%); colorless crystals from hexane; mp 64.5−65 °C; ^1H NMR δ 6.76 (s, 2H), 4.85 (s, 1H), 1.63 (q, J = 7.2 Hz, 2H), 1.41 (s, 18H), 1.21 (s, 6H), 1.00 (t, J = 7.2 Hz, 3H); IR ($CHCl_3$) 3620 cm^{-1}; UV (cyclohexane) 283 nm (log ϵ 3.40), 203 (4.47). Anal. Calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 77.76; H, 11.19.

Compound **14**: identical with an authentic sample[27] (^1H NMR and TLC); mp 65−67 °C (lit.[23] mp 67−68 °C).

With $AgClO_4$ in the Absence of Na_2CO_3 (Runs 1, 3, 7, and 10). The procedure described above for the reaction with $AgClO_4$ in the presence of Na_2CO_3 was followed except that Na_2CO_3 was omitted. The reaction in a mixture of MeOH (28 mL) and H_2O (4 mL) (run 3) was carried out for 10 min. Column chromatography of the product gave **7** (3−5%), **10** [**10a** (89%, run 1), **10a** (78%, run 3), **10d** (90%, run 7), or **10e** (90%, run 10)], **13** [0−15 mg (3%)], and **14** (trace to 6%).

With $AgOCOCF_3$. The procedure described above for the reaction with $AgClO_4$ in the presence of Na_2CO_3 was followed except that $AgOCOCF_3$ (442 mg, 2 mmol) replaced $AgClO_4$ and Na_2CO_3 was omitted. MeOH (run 4), EtOH, *i*-PrOH, *t*-BuOH (run 9), or *t*-AmOH was employed as the alcohol. The reaction mixture obtained from run 9, containing fine particles of AgBr (passable through a filter paper) was poured into brine (200 mL) for the subsequent extractive workup. Column chromatography of the product obtained from run 4 afforded **7** (4%), **10a** (88%), **13** (1%), and **14** (2%). Column chromatography of the product obtained from run 9 provided successively **7** (2%), 4-(trifluoroacetoxy)phenol **12** (190 mg, 30%), a mixture of **10d** (31%) and **14** (5%) as analyzed by ^1H NMR spectroscopy, and **13** (141 mg, 32%). Compounds **12** and **13** were purified by recrystallization from hexane.

Compound **12**: colorless crystals; mp 46−47 °C; ^1H NMR δ 6.97 (s, 2H), 5.22 (s, 1H), 1.43 (s, 18H); IR ($CHCl_3$) 3620, 1790 cm^{-1}. Anal. Calcd for $C_{16}H_{21}O_3F_3$: C, 60.37; H, 6.65. Found: C, 60.55; H, 6.66. Ester **12** was also obtained in nearly quantitative yield by treating **13** with excess $(CF_3CO)_2O$ at rt. Ester **12** suffered significant degradation upon chromatography, giving **13** and **14**.

Compound **13**: identical with an authentic sample prepared by $NaBH_4$ reduction of **14** (^1H NMR and TLC); mp 105−106 °C (lit.[23] mp 110−111 °C). Hydroquinone **13** suffered partial degradation into **14** upon chromatography.

Isolation and Identification of *tert*-Alkoxy Dienones 9d and 9e. Analytically pure **9d** and **9e** were obtained by recrystallizing the crude products obtained from runs 8 and 11, Table 1, respectively.

Compound **9d**: colorless crystals from hexane (227 mg, 41%); mp 107−109 °C; ^{13}C NMR δ 185.9, 146.9, 139.7, 75.1, 64.6, 34.7, 29.3, 28.1. Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.40; H, 11.01.

Compound **9e**: colorless crystals from hexane (267 mg, 46%); mp 84−86.5 °C; ^{13}C NMR δ 186.0, 146.9, 139.8, 77.5, 64.3, 34.7, 33.6, 29.3, 25.4, 8.8. Anal. Calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 77.99; H, 10.99.

The ^1H NMR, IR, and UV spectra of **9d** and **9e** as well as their stability are described in the text.

One-Pot Synthesis of Crude Alkoxy Dienones 9 from Phenol 6 (Table 3). A cold (0 °C) solution of Br_2 (320 mg, 2 mmol) in DME (7 mL) was added in one portion to a vigorously stirred, cold, heterogeneous mixture of **6** (412 mg, 2 mmol), $AgClO_4$ (830 mg, 4 mmol), finely powdered anhydrous Na_2CO_3 (0.85 g, 8 mmol), and an alcohol (30 mL). The Br_2 color was discharged immediately. The stirring was continued for 2 min at 0 °C. The mixture was filtered into a flask containing stirred, cold water (200 mL). The reaction with *t*-BuOH was performed at 0 °C for 3 min by using the Br_2 solution in DME and a mixture of **6**, $AgClO_4$, Na_2CO_3, *t*-BuOH (20 mL), and DME (10 mL), and the reaction mixture was filtered into a flask containing a stirred, cold solution of NaCl (25 g) in water (200 mL). The contents of the flask were extracted with petroleum ether (200 mL × 2). The extract was washed with water, dried (Na_2SO_4), and evaporated to dryness under reduced pressure below 30 °C. The amount of **9** (as well as that of **10**) in the residual product was estimated readily by ^1H NMR spectroscopy.

Recrystallization from hexane of the products obtained from the reactions with *t*-BuOH and *t*-AmOH afforded spectroscopically (^1H NMR) homogeneous **9d** (220 mg, 40%) and **9e** (295 mg, 51%), respectively.

One-Pot Synthesis of 4-Oxyfunctionalized 2,6-Di-*tert*-butylphenols from Phenol 6. 4-Methoxyphenol 10a. Run A. To a stirred, cold (0°C) solution of **6** (412 mg, 2 mmol) and $AgClO_4$ (830 mg, 4 mmol) in MeOH (30 mL) was added quickly a cold solution of Br_2 (320 mg, 2 mmol) in MeOH (7 mL). The Br_2 color was discharged immediately, and yellow precipitates began to form soon. The stirring was continued for 3 min at 0 °C. The mixture was filtered to give AgBr (0.73 g, 97%). The filtrate was poured into water (200 mL) and extracted with petroleum ether (200 mL × 2). The extract was washed with water, dried (Na_2SO_4), and evaporated under

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reduced pressure, leaving a crystalline residue. Recrystallization from MeOH provided **10a** (340 mg, 72%). The filtrate from the recrystallization was evaporated, and the residue was chromatographed to give successively a mixture of **6** (22 mg, 5% recovery) and **7** (5 mg, 1%) as analyzed by GC, an additional crop of **10a** (58 mg, 84% in total), and **14** (10 mg, 2%).[20]

Run B. The reaction was conducted with a solution of **6** (2 mmol), $AgClO_4$ (4 mmol), and MeOH (1 mL, 25 mmol) in DME (15 mL) and a solution of Br_2 (2 mmol) in DME (7 mL), and the reaction mixture was worked up, in the manner described above for run A, giving **6** (5% recovery), **7** (5%), **10a** (79% in total), and **14** (8%).

Run C. To a stirred, cold solution of $AgClO_4$ (4 mmol) in MeOH (20 mL) was added a cold solution of Br_2 (2 mmol) in MeOH (7 mL). The Br_2 color was discharged immediately, and yellow precipitates began to form soon. After 1 min, a cold solution of **6** (2 mmol) in MeOH (10 mL) was added quickly to the stirred mixture. The stirring was continued for 5 min at 0 °C. The reaction mixture was worked up in the manner described above for run A, giving **6** (3% recovery), **7** (5%), **10a** (80% in total), and **14** (5%).

Run D. To a stirred, cold solution of $AgClO_4$ (2 mmol) in MeOH (25 mL) was added a cold solution of Br_2 (2 mmol) in MeOH (7 mL). After the stirring was continued for 30 s, the mixture was filtered into a flask containing a solution of **6** (2 mmol) in MeOH (5 mL). The filtration collected AgBr (98%). The contents of the flask were allowed to stand for 3 min at rt and poured into water. Extractive workup with petroleum ether provided a yellow oil (0.57 g), which was a 2.3:1 mixture of **3b** and **7** as estimated by ^{1}H NMR spectroscopy. A small amount of **6** (2% recovery) was also found. Phenol **10a** was not found.

Other 4-Oxyfunctionalized 2,6-Di-*tert*-butylphenols. The procedure described above for the synthesis of **10a**, run B, was followed except that EtOH (1 mL, 17 mmol), *i*-PrOH (1.5 mL, 20 mmol), *t*-BuOH (1.5 mL, 16 mmol), or H_2O (1 mL, 56 mmol) replaced MeOH. Acetoxylation was conducted with a solution of **6** and $AgClO_4$ in a 3:1 (v/v) mixture of AcOH and DME (30 mL) and a solution of Br_2 in the same solvent mixture (7 mL). Recrystallization of the product from hexane provided **9b** (318 mg, 64%), **9c** (290 mg, 55%), **9d** (380 mg, 68%), **13** (302 mg, 68%), or 4-acetoxyphenol **15** (322 mg, 61%). Additional crops of the 4-oxyfunctionalized phenols were obtained by chromatography of the filtrates from the recrystallization, and their total yields amounted to 76−79%.

Compound **15**: mp 91−92 °C (lit.[28] mp 87−88 °C).

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Supporting Information Available: ^{1}H NMR spectra of compounds **9d**,**e**, **10a**−**e**, **12**, and products containing compounds **9a**−**c** and **11**; ^{13}C NMR spectra of compounds **9d** and **9e** (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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