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A Mechanistic Approach to the Reaction of 2,6-Di-*tert*-butylphenol with an Iodinating Agent in Methanol: Electrophilically Assisted Solvolysis of Intermediary 4-Iodocyclohexa-2,5-dienones

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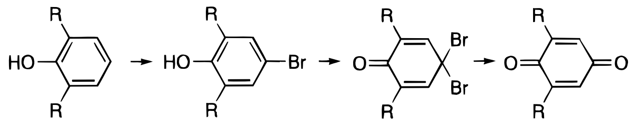
Reactions of the title phenol (**1**) and of 4-iodophenol **2** with an iodinating agent, I_2 and H_2O_2, are conducted in MeOH for varying times with varying amounts of I_2, and the results are compared. The reaction of **1** gives **2**, 4,4′-biphenol **3**, 4,4′-diphenoquinone **4**, 4-methoxyphenol **5**, and *p*-benzoquinone **6**, exclusively. The yields of the phenolic products (**2**, **3**, and **5**) vary with reaction time, but they disappear or almost disappear eventually, to make **4** and **6** the almost exclusive products. The reaction of **2** always gives **4** and **6** alone. In both of the reactions of **1** and of **2**, employment of a higher initial I_2 concentration not only completes the formation of **4** and **6** faster but also makes the final proportion of **6** higher. However, the ultimate yield of **6** from the reaction of **1** is significantly higher than that from the reaction of **2**, irrespective of the initial I_2 concentration. These results are interpreted as follows. 4-Iodocyclohexa-2,5-dienone **12**, the primary product of electrophilic iodination of **1**, undergoes solvolysis (methanolysis), which is electrophilically assisted by I_2. The solvolysis of **12** can be so fast as to overwhelm its prototropic rearrangement to give **2**. 4-Methoxycyclohexa-2,5-dienone **13**, which is the primary product of the methanolysis of **12** and is suggested to be detectable by ^{1}H NMR spectroscopy, is converted into **6** via **5**. Benzoquinone **6** can also arise from 4,4-diiodocyclohexa-2,5-dienone **7**, the product of iodination of **2**, by an analogous mechanism. The selectivity of the formation of **6** from **7** is low because the competing reaction, homolytic scission of the C−I bond in **7**, predominates. The mechanism of the formation of **3** and **4** is also discussed.

Molecular halogen (or hydrogen halide) and H_2O_2 in the presence or absence of an acid catalyst is one of the halogenating agents for phenols.[1,2] It also serves as a reagent for preparation from phenols of benzoquinones or halogenated benzoquinones such as chloranil or bromanil.[3−5] These benzoquinones have been shown to be formed by way of halogenated phenols. The active halogenating or oxidating species is molecular halogen, and H_2O_2 serves to generate or regenerate molecular halogen rapidly from hydrogen halide:

$$2HX + H_2O_2 \rightarrow X_2 + 2H_2O\ (X = Cl, Br, I)$$

2,6-Disubstituted benzoquinones can thus be prepared by exposing 2,6-disubstituted phenols to Br_2 (or HBr) and H_2O_2 in refluxing MeOH containing an acid catalyst.[5] The quinones have been suggested to arise via 4,4-dibromocyclohexa-2,5-dienones, the products of perbromination of the phenols:



The reaction of 2,6-disubstituted phenols with I_2 and H_2O_2 in MeOH may proceed similarly. The method employing I_2 and H_2O_2 did not seem attractive for synthesizing the quinones since the selectivity is quite poor. In an attempt to improve the method, we began studying the reaction of 2,6-di-*tert*-butylphenol (**1**) with this mildly iodinating agent under mild conditions. The reaction proved to be complex in spite of the limited number of the ultimate products. However, close study led to the finding of a new mechanism for the benzoquinone formation. The mechanism involves I_2-assisted solvolysis of intermediary 4-iodocyclohexa-2,5-dienones. This paper deals with the details of such a study.

Results and Discussion

The reaction of **1** was conducted for varying times with varying amounts of I_2 (0.5−2 molar equiv) in MeOH containing 36% H_2O_2[6] (excess; 18 molar equiv) (henceforth I_2/H_2O_2/MeOH) at 35 °C in the absence of an added acid catalyst. The product mixture obtained after the reaction was interrupted by quenching of the residual I_2 and H_2O_2 with aqueous $NaHSO_3$ was subjected to column chromatography for analysis. The product consisted exclusively of five compounds. They were 4-iodo-2,6-di-*tert*-butylphenol (**2**), 3,5,3′,5′-tetra-*tert*-butyl-4,4′-dihydroxybiphenyl (**3**), 3,5,3′,5′-tetra-*tert*-butyl-4,4′-diphenoquinone (**4**), 4-methoxy-2,6-di-*tert*-butylphenol (**5**), and 2,6-di-*tert*-butyl-*p*-benzoquinone (**6**), and their yields are summarized in Table 1 (runs 1−13). The product composition varied with varying reaction time and with varying the initial concentration of I_2. Quinoid products **4** and **6** increased with time until they were the almost exclusive products. In contrast, phenolic products **2**, **3**, and **5** disappeared or almost disappeared eventually. The higher initial concentration of I_2 not only completed the formation of **4** and **6** faster but also made the final proportion of **6** higher. The ultimate yield of **6** varied

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(1) Marsh, J. E. *J. Chem. Soc.* **1927**, 3164.

(2) Jurd, L. *J. Am. Chem. Soc.* **1955**, *77*, 5747.

(3) Cressman, H. W. J.; Thirtle, J. R. *J. Org. Chem.* **1966**, *31*, 1279.

(4) Lübbecke, H.; Boldt, P. *Tetrahedron* **1978**, *34*, 1557.

(5) Minisci, F.; Citterio, A.; Vismara, E.; Fontana, F.; De Bernardinis, S. *J. Org. Chem.* **1989**, *54*, 728.

(6) The concentration of H_2O_2 in a commercially available 30% H_2O_2 (from Wako Chemicals) was determined by iodometric titration to be in fact 36%.

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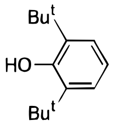
Table 1. Reaction of Phenol 1 with I_2 and H_2O_2 in MeOH[a]

run	I_2 (equiv)	time (min)	recovery of **1** (%)	product (%) **2**	**3**	**4**	**5**	**6**	(**5** + **6**)/2
1	0.5	15	76	6.6	2.4	2.9	5.7	3.6	1.4
2	0.5	50	43	20	2.4	11	5.2	16	1.1
3	0.5	120	12	31	3.4	20	2.3	30	1.0
4	0.5	240	0	22	1.5	39	0	35	
5	0.5	540	0	0	1.0	60	0	37	
6	1	6	73	5.3	1.7	2.9	9.1	5.7	2.8
7	1	15	53	9.0	1.5	8.1	8.1	18	2.9
8	1	50	5	20	1.0	20	2.0	49	2.6
9	1	150	0	1.0	0	42	0	54	
10	2	2	69	3.3	1.5	2.5	15	7.0	6.7
11	2	5	50	5.1	1.7	6.0	13	20	6.5
12	2	15	10	9.8	0.5	15	7.4	55	6.4
13	2	50	0	0	trace	27	0	71	
14[b]	2	7	66	6.9	2.0	4.7	8.9	9.3	2.6
15[b]	2	15	47	11	2.7	9.6	6.1	21	2.5
16[c]	2	5	41	5.9	1.5	4.2	12	32	7.5
17[c]	2	15	5	10	0.4	9.8	4.4	71	7.5
18[c]	2	50	0	1.0	trace	14	0	83	
19[d]	2	30	72	2.9	1.5	0.9	13	7.8	7.2
20[d]	2	90	49	4.8	1.2	6.1	10	25	7.3
21[d]	2	360	0	11	0.2	8.1	1.8	76	7.1

[a] Unless stated otherwise, the reactions were conducted using **1** (2 mmol) and 36% H_2O_2 (3 mL; 36 mmol) in MeOH (30 mL) at 35 °C. [b] Conducted in a solvent mixture of MeOH (60 mL) and H_2O (3 mL). [c] Conducted in the presence of H_2SO_4 (ca. 1.8 mmol). [d] Conducted at 0 °C.



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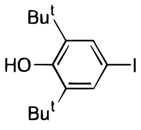

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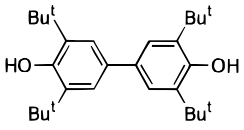

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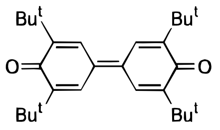

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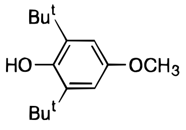

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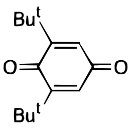

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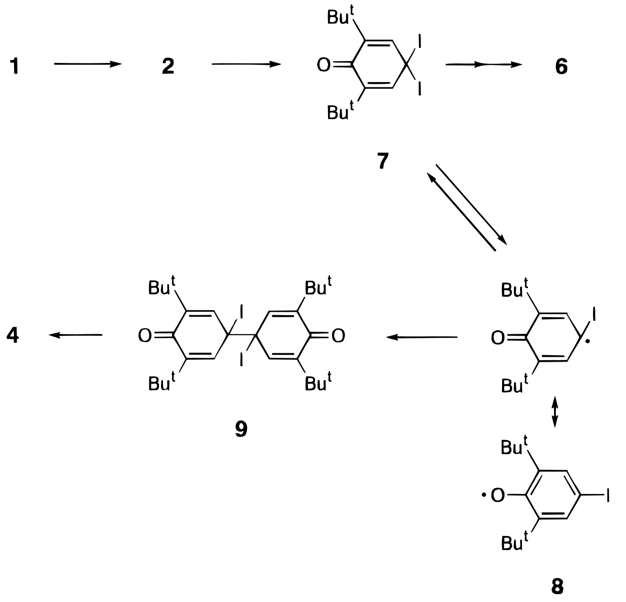
within a range of 37−71% while that of **4** ranged from 60% to 27%. Phenol **2** was similarly allowed to react with I_2/H_2O_2/MeOH (Table 2, runs 1−6). Regardless of the extent to which the reaction of **2** progressed, **4** and **6** were the sole products. The ultimate yield of **6** from the reaction of **2** also increased with an increase in the initial concentration of I_2, although it was always lower than that from the reaction of **1** and varied within a relatively narrow range (9−19%). In the absence of H_2O_2, the reaction of **1** or **2** with I_2 in MeOH containing H_2O[7] (henceforth I_2/H_2O/MeOH) also provided the same five or two products, respectively. The consumption of **1** or **2**, however, was reasonably fast only at the early stage and became significantly slow thereafter.

Table 2. Reaction of Phenol 2 or 10 with I_2 and H_2O_2 in MeOH[a]

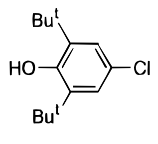
run	phenol	I_2 (equiv)	time (min)	recovery of **2** or **10** (%)	product (%) **4**	**6**	**11a**
1	**2**	0.5	50	68	30	1.6	
2	**2**	0.5	240	0	90	9.0	
3	**2**	1	50	36	57	6.4	
4	**2**	1	150	0	87	12	
5	**2**	2	15	48	42	10	
6	**2**	2	50	2	79	19	
7	**10**	2	15	51	trace	3.6	42
8	**10**	2	50	9	trace	8.0	80

[a] The reactions were conducted with **2** (2 mmol) or **10** (2 mmol) and 36% H_2O_2 (3 mL) in MeOH (30 mL) at 35 °C.

Scheme 1



The formation of **4** and **6** from the reaction of **2** may be accounted for by paths involving 4,4-diiodocyclohexa-2,5-dienone **7** as a common intermediate: homolytic scission of the C−I bond in **7** may lead to the formation of **4** via radical **8** and bis(iodocyclohexadienone) **9**.[8] The reaction of 4-chloro-2,6-di-*tert*-butylphenol (**10**) with I_2/H_2O_2/MeOH provided bis(chlorocyclohexadienone) **11a** in high yield along with a small amount of **6** (Table 2, run 8). It is reasonable that **4** and **6** were found among the products from the reaction of **1**, since **2** was also among them (Scheme 1). However, it is evident that the path involving **2** and **7** as the intermediates does not suffice to account for the formation of all of **6** from the reaction of **1**, since, as described above, the ultimate yield of **6** from this reaction always surpassed that from the reaction of **2**.



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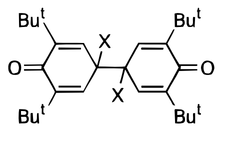

11a: X = Cl
11b: X = Br

The obtention of **5** from the earlier stages of the reaction of **1** provided a clue to finding an additional path for **6**. The lack of **5** in the products from the latter stages appeared to indicate that **5** was oxidized to **6** under the reaction conditions. Quantitative oxidation of **5** into **6** with I_2/H_2O_2/MeOH was verified experimentally. Phenol **5** may be formed by solvolysis (methanolysis) of 4-iodocyclohexa-2,5-dienone **12**, the precursor of **2**, and subse-

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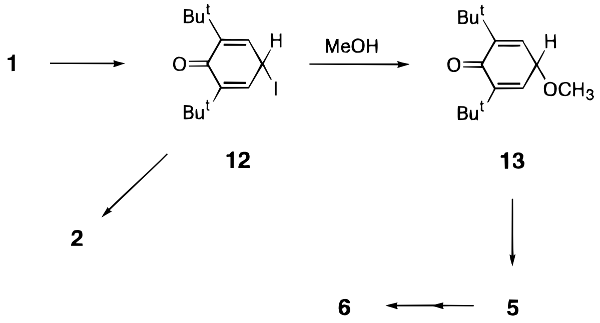
(7) The mixture was employed to simulate the solvent system in the reactions with I_2/H_2O_2/MeOH. The reaction of **1** or **2** with I_2 in MeOH not containing added H_2O proceeded similarly, but it was slower than that in H_2O/MeOH.

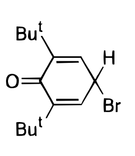
(8) Ley, K.; Müller, E.; Mayer, R.; Scheffler, K. *Chem. Ber.* **1958**, *91*, 2670.

Scheme 2



quent prototropic rearrangement (Scheme 2).[9] Indication of the formation of intermediary 4-methoxycyclohexa-2,5-dienone **13**, the primary product of methanolysis of **12**, was obtained from a ^1H NMR study. Thus, the spectrum (in $CDCl_3$) of the crude product obtained from the reaction of **1** with $I_2/H_2O_2/MeOH$, conducted at 0 °C and interrupted at the relatively early stage, included new, distinct signals. They appeared as a singlet at δ 3.40 and a triplet ($J = 3.1$ Hz) at δ 4.42 with relative intensities of ca. 3:1. Upon addition of pyridine-d_5, these signals disappeared from the spectrum, and a singlet at δ 3.76 attributable to the methoxy group in **5** was remarkably intensified. Column chromatography of the crude product on SiO_2 gave only the five products described above, and their yields suggested that most of the products were accounted for: no new substance was obtained (Table 1, run 19). It has been known that 4-hydro-4-substituted-cyclohexa-2,5-dienones, which are rarely isolable, are readily and irreversibly rearranged prototropically to give 4-substituted-phenols by catalysis with base or acid including SiO_2.[10,11] It is, therefore, reasonable to presume that the crude product contained **13**; the signals at δ 3.40 and 4.42 are attributable to the methoxy group and the hydrogen, bound to C-4, respectively. The crude product was estimated from the spectrum to contain **5** and **13** in approximate yields of 3% and 11% (or 35% based on reacted **1**), respectively. No indication was obtained from the spectrum of the crude product that it contained dienone **12**. Labile new dienone **13** was found to be producible in much higher yield from the Ag ion assisted displacement reaction of 4-bromo-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**14**) with MeOH. The ^1H NMR spectrum of **13** obtained from the reaction of **14** exhibited, in addition to the signals shown above, a doublet ($J = 3.1$ Hz) at δ 6.69 (vinylic hydrogens) and a singlet at δ 1.24 (*tert*-butyl groups).[12] These signals were also observable in the spectrum of the crude product from the reaction of **1** with $I_2/H_2O_2/MeOH$, described above. They also disappeared from the spectrum upon addition of pyridine-d_5. The conversion of **7** into **6** may similarly involve a solvolytic process.

Of particular interest to us was the dependence of the yield of **6** from the exhaustive reaction of **1** or **2** with $I_2/H_2O_2/MeOH$, on the initial concentration of I_2. This seemed to be best accounted for by assuming involvement of I_2 in the solvolytic process of iodocyclohexadienones **12** or **7** and assuming competition between the solvolysis and the prototropic rearrangement of **12** (to give **2**) or the homolytic scission of the C−I bond in **7** (to give **4** eventually) (cf. Scheme 1 and Scheme 2). To test the hypothesis, the reactions of the bromoanalogs of **12** and **7** with $I_2/H_2O/MeOH$ were investigated. They were **14** and 4,4-dibromo-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**15**), which can be prepared by brominating **1**[13,14] or 4-bromo-2,6-di-*tert*-butylphenol (**16**)[15] with Br_2. Dienone **14** has



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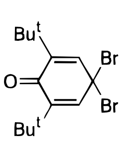

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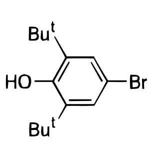

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been shown to be easily isomerized to **16** in polar solvents such as EtOH[16] and a mixture of AcOH and H_2O[13b] as well as by catalysis with acid or base.[11,16] The dienone−phenol isomerization of **14** in MeOH containing H_2O (henceforth $H_2O/MeOH$) at 35 °C also was found to be remarkably rapid; it was complete within 5 min. Exposing **14** to I_2 (2 molar equiv) /$H_2O/MeOH$ for 5 min at 35 °C provided **5** (6%) and **6** (18%) together with **16** (62%). Compound **5** was convertible into **6** with $I_2/H_2O/MeOH$. Compounds **5** and **6** from the reaction of **14** were not formed via phenol **16**, because a similar treatment of **16** with $I_2/H_2O/MeOH$ provided no **5** and a trace of **6**; a large part (76%) of **16** was recovered unchanged, the major products being **4** (16%) and bis(bromocyclohexadienone) **11b** (8%). Therefore, **14** can undergo displacement with MeOH when assisted by I_2, and the displacement can compete with its prototropic rearrangement. Dienone **15** was poorly soluble in $H_2O/MeOH$. Treatment of **15** with $H_2O/MeOH$ at 35 °C for 10 min and subsequent filtration recovered most of **15**. The filtrate contained only 1% of **6** as well as an additional amount of **15** (91% recovery in total). In the presence of I_2 (2 molar equiv), in contrast, **15** completely dissolved in $H_2O/MeOH$ within 10 min. After workup, **6** was obtained in 49% yield while no **15** was recovered. The second major product was **16** (25%). The reaction of **15** with Br_2 (in place of I_2) /$H_2O/MeOH$ also provided **6** (66%) although some of **15** (23%) was recovered intact. Therefore, **15** is assumed to be solvolyzed similarly by the assistance of I_2 or Br_2. Spontaneous solvolysis of **15** has been proposed, since refluxing a solution of **15** in MeOH containing H_2O and H_2SO_4 (in the absence of added I_2 or Br_2) provides a significant

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(9) The substitution reaction of **12** with the other, minor nucleophiles, H_2O and H_2O_2, can also be considered (not shown in Scheme 2). 2,6-Di-*tert*-butylhydroquinone, the product expected from the hydrolysis of **12**, was found in none of the reactions of **1** with $I_2/H_2O_2/MeOH$ or $I_2/H_2O/MeOH$. The hydroquinone is presumed to have been readily oxidized to **6** under the reaction conditions. The product from the reaction between **12** and H_2O_2 is assumed to have also disintegrated into **6**.

(10) (a) Omura, K. *J. Org. Chem.* **1991**, *56*, 921. (b) Omura, K. *J. Org. Chem.* **1992**, *57*, 306.

(11) (a) de la Mare, P. B. D.; Singh, A.; Tillett, J. G.; Zeltner, M. *J. Chem Soc. B* **1971**, 1122. (b) de la Mare, P. B. D.; Singh, A. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1801. (c) de la Mare, P. B. D.; Singh, A. *J. Chem. Soc., Perkin Trans. 2* **1973**, 59. (d) de la Mare, P. B. D. *Acc. Chem. Res.* **1974**, *7*, 361.

(12) Attempted purification of the crude product of **13** obtained from the reaction of **14** has proved unsuccessful. The crude products of some other 4-hydro-4-alkoxy-2,6-di-*tert*-butylcyclohexa-2,5-dienones obtained by analogous means, however, have been successfully purified, and their structures have been unambiguously established. The results will be published elsewhere.

(13) (a) Volod'kin, A. A.; Ershov, V. V. *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1962**, 2022. (b) Fyfe, C. A.; Van Veen, L., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 3366.

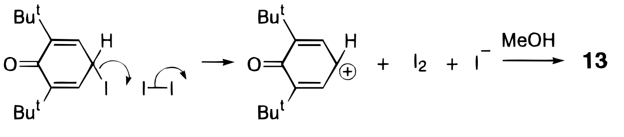
(14) Rieker, A.; Rundel, W.; Kessler, H. *Z. Naturforsch.* **1969**, *24b*, 547.

(15) Volod'kin, A. A.; Ershov, V. V. *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1963**, 152.

(16) Ershov, V. V.; Volod'kin, A. A. *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1962**, 730.

quantity of **6**.[5,17] It is, however, unlikely that all of **6** is produced through the unassisted solvolysis, because Br_2 is expected to be generated during the course of the reaction, from the reaction of **15** with HBr (see below), which should be generated when **15** is solvolyzed spontaneously but slowly.

It is proposed that I_2 (or Br_2) undergoes electrophilic attack on the halogen atom of 4-halocyclohexa-2,5-dienones **7**, **12**, **14**, or **15** generating the 4-oxocyclohexa-2,5-dienyl cations (or the phenoxy cations), which are readily attacked by MeOH. The reaction is formulated, for example, as follows.



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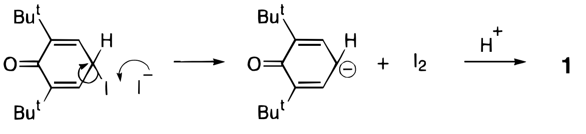
The electrophilic dehalogenation by I_2 of the halocyclohexadienones contrasts sharply with the nucleophilic dehalogenation by halide ion of 4-halocyclohexa-2,5-dienones. This reductive dehalogenation by halide ion has been established as the reverse of the primary reaction in the phenol halogenation reaction. Hydrodebromination of **14** with HI to give **1** was confirmed to be remarkably fast. The reaction of **12** or **7** with HI may be as facile. The reductive deiodination of **12** or **7** with HI rationalizes the aforementioned slowdown with time of the reaction of **1** or **2** with $I_2/H_2O/MeOH$, respectively.



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As shown in Table 2, the decay of **2** or **10** proceeds reasonably fast after treatment with $I_2/H_2O_2/MeOH$. As illustrated below, the decay of **2** or **10** was found to be markedly retarded if **1** is coexistent in an appropriate quantity. This fact proved to be related to the mechanism of the formation of 4,4′-biphenol **3**, from which **4** is also assumed to be derived, as the minor product from the reaction of **1** with $I_2/H_2O_2/MeOH$. An equimolar mixture of **1** and **2** was exposed to I_2 (2 equiv per equiv of **1** or **2**)/$H_2O_2/MeOH$, and the consumptions of **1** and **2** were compared. The exposure for 15 min at 35 °C consumed most of **1** (95%) but recovered most of **2** (98%), although a small amount of **2** produced from the reaction of **1** must have been included in the total recovery of **2**. If **1** was omitted in this experiment, only 48% of **2** was found to be recovered (Table 2, run 5). If **2** was omitted, on the other hand, 90% of **1** was found to be consumed (Table 1, run 12). The exposure for 30 min of the 1:1 mixture of **1** and **2** made the cosumption of **1** complete and that of **2** significant (37% consumption). When an equimolar mixture of **1** and **10** was treated similarly with $I_2/H_2O_2/MeOH$ for 15 min, most of **1** (97%) was consumed while most of **10** (94%) remained intact. If **1** was omitted, 49% of **10** was found to be consumed (Table 2, run 7). The treatment for 30 min of the 1:1 mixture of **1** and **10** made the cosumption of **1** complete and that of **10** significant (32% consumption). It can, therefore, be concluded not only that the decay of **2** or **10** is retarded by the presence of **1** but also that the decay of **1** is facilitated by the presence of **2** or **10**.

Scheme 3

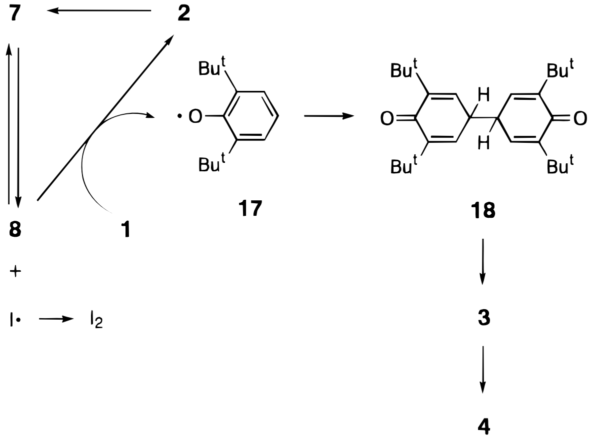

Table 1 shows that the yield of **2** from the reaction of **1** with $I_2/H_2O_2/MeOH$ increases steadily and begins to fall only after most or all of **1** is consumed. This perhaps reflects the suggested "stability" of **2** in the presence of **1**. The mechanism of the "stabilization" of **2** by **1** may be as follows (Scheme 3; cf. also Scheme 1). Phenol **2** is iodinated by $I_2/H_2O_2/MeOH$, but the product (**7**) can revert to **2** if **1** is coexistent. The reversion is the result of hydrogen donation by **1** to phenoxy radical **8**, which is generated by the dissociation of **7** and from which **4** can be derived via **9**. The dissociation of **7** may be reversible. The hydrogenation of **8** with **1** will help displace the equiliblium between **7** and the dissociation products (**8** and atomic iodine) in favor of the products and will thus make the selectivity of the formation of **6** from **7** even poorer. In the presence of a sufficient quantity of **1**, therefore, **7** mostly reverts to **2** via **8** whereas the formation of **4** (via **9**) and **6** from **7** is negligible. Phenoxy radical **17** generated from **1** after the dehydrogenation by **8** dimerizes affording bis(cyclohexadienone) **18**.[18] This rationalizes the obtention of **3**, the product of prototropic rearrangement of **18**, albeit in generally low yield from the reaction of **1** with $I_2/H_2O_2/MeOH$. The low yield may be inevitable since **3** is expected to be subjected to oxidation under the reaction conditions, and this is another path for the formation of **4**. The path accounts for the steady and significant increase in the yield of **4** even at the early stage of the reaction of **1** with $I_2/H_2O_2/MeOH$ (see Table 1) where product **2** is "stable" and the formation of **4** by the dimerization of **8** is negiligible. Quinones **4** and **6** can be concluded to be formed from the reaction of **1** mainly by the paths shown in Scheme 3 and Scheme 2, respectively, at the earlier stage where **1** amply resides and principally by the paths shown in Scheme 1 at the latter stage where **1** barely resides.

The mechanism suggested above for the solvolysis of **12** proposes that the reaction between **12** and I_2 (the rate-determining step in the solvolysis) is second order overall, first order in **12** and in I_2, whereas the competing prototropic rearrangement of **12** in the present system may be assumed to be first order or pseudo first order. Thus, the rate of the solvolysis of **12** relative to that of its prototropic rearrangement (*S*/*R* ratio) is expected to

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[17] See also: Karhu, M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1595.

[18] Other reactions of **17** may be couplings with **8** and with atomic iodine (to give **12**) (not shown in Scheme 3).

be proportional to the I_2 concentration. It was desirable to prove this experimentally. This was originally thought to be a difficult task owing to the complexity of the overall reaction of **1** with $I_2/H_2O_2/MeOH$. After finding the "stabilization" of **2** by **1**, however, the task now seemed possible, to some extent. At the early stage of the reaction of **1**, the yield of **2** can represent the rate of the prototropic rearrangement of **12** because product **2** is "stable", while the total yield of **5** and **6** can represent the rate of the solvolysis of **12** because the formation of **6** by the other path is negligible. Then the (**5** + **6**)(yield)/**2**(yield) ratio should represent the *S*/*R* ratio. Table 1 also lists the calculated (**5** + **6**)/**2** ratios (runs 1−3, 6−8, and 10−12). At each initial I_2 concentration, the (**5** + **6**)/**2** ratio varies with reaction time but only within a relatively narrow range. The (**5** + **6**)/**2** ratio is expected to be kept constant provided that the I_2 concentration is maintained constant throughout the early stage of the reaction. The observed lack of strict constancy of the (**5** + **6**)/**2** ratio may be ascribable not only to experimental error but also to the lack of strict constancy of the I_2 concentration during the reaction: the I_2 concentration in the reacting mixture may be decreased, though not substantially, as the reaction progresses, that is, as the formation of **2** progresses.[19] Indeed, the (**5** + **6**)/**2** ratio appears to tend to decline accordingly within that narrow range, as the reaction progresses. It is noteworthy that the approximate constancy of the (**5** + **6**)/**2** ratio is maintained until the concentration of **1** in the reacting mixture becomes quite low, probably indicating that the retardation of the decay of **2** was brought about even by a small amount of **1**. As anticipated, the (**5** + **6**)/**2** ratios are higher when the initial I_2 concentration is higher. As anticipated, employment of a larger quantity of solvent resulted in the smaller (**5** + **6**)/**2** ratios (Table 1, runs 14 and 15; compare with runs 10−12 in the table). The data obtained here are not sufficient to prove rigorously the proportionality of the *S*/*R* ratio to the I_2 concentration, but they may suffice to show at least that the ratio does increase with an increase in the I_2 concentration and that the solvolysis of **12** in the presence of enough I_2 overwhelms its prototropic rearrangement. The reaction in the presence of a small amount of H_2SO_4 was found to increase the (**5** + **6**)/**2** ratio and thus to improve the ultimate yield of **6** up to over 80% (Table 1, runs 16−18). Lowering the reaction temperature also served to increase the ratio, although the reaction was slowed down (Table 1, runs 19−21). The acid and temperature effects were not investigated further.

The reaction of phenol **1** with I_2 and H_2O_2 in MeOH proves complex, although the ultimate products are quinoid products **4** and **6** alone. Through the detailed analyses of the products from the reaction conducted under various conditions, the paths leading to **4** and **6** are elucidated. Molecular iodine cannot electrophilically iodinate phenols **1** and **2** only but also electrophilically deiodinates the products, 4-iodocyclohexa-2,5-dienones **12** and **7**. The electrophilic deiodination by I_2 of the iodocyclohexadienones contrasts with the nucleophilic dehalogenation by halide ion of 4-halocyclohexa-2,5-dienones. The attack by I_2 on the iodocyclohexadienones results in their solvolysis (methanolysis), and the solvolysis products are converted into **6** eventually. Labile 4-methoxycyclohexa-2,5-dienone **13**, the primary product of the methanolysis of **12**, is suggested to be detectable by ^1H NMR spectroscopy. The I_2-induced solvolysis of **12** can be so fast as to compete well with or overwhelm its rapid prototropic rearrangement to give **2**. The present study may provide a new aspect to the chemistry of the phenol halogenation reaction. The generality of electrophilic dehalogenation of halocyclohexadienones by positive halogen reagents is being investigated. The results of preliminary experiments include that the reaction of 4-bromo-2,4,6-tri-*tert*-butylcyclohexa-2,5-dienone with MeOH at 0 °C in the presence of *N*-iodosuccinimide provides 4-methoxy-2,4,6-tri-*tert*-butylcyclohexa-2,5-dienone rapidly and quantitatively.

Experimental Section

^1H NMR (60 or 90 MHz) and IR spectra were taken in $CDCl_3$ and in $CHCl_3$, respectively. GC analyses were performed at 150 °C on a column packed with Silicone OV-17 on Chromosorb W. Column chromatography was conducted with Merck SiO_2 60 (25 g) by using gradient elution (100% petroleum ether to 50%/50% petroleum ether/benzene). TLC was run on SiO_2.

Preparation of 4-Iodophenol 2. To a stirred solution of phenol **1** (41.2 g, 0.2 mol) in a mixture of MeOH (400 mL) and ethylenediamine (75 mL) was added dropwise a solution of I_2 (41.0 g, 0.16 mol) and KI (62 g, 0.37 mol) in water (40 mL) over a 20-min period. The mixture was stirred for 20 min and filtered. The filtrate was poured into water and extracted with petroleum ether. The extract was washed with water, dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was passed through a column packed with SiO_2 (120 g) with petroleum ether. The first fraction provided a nearly colorless crystalline mixture, which was recrystallized from hexane yielding **2** (33.3 g, 50%) as colorless crystals, mp 88−90 °C (lit.[20] mp 88−90 °C). The **2** was free from **1** as suggested by GC.

Preparation of 4,4-Dibromocyclohexa-2,5-dienone 15. To a stirred solution of **1** (20.6 g, 0.1 mol) in MeOH (300 mL) was added a solution of Br_2 (32.0 g, 0.2 mol) in MeOH (50 mL) over a 10-min period. The mixture was stirred for 50 min at room temperature (ca. 20 °C). Water (50 mL) was added slowly to the mixture, and the resulting mixture was cooled with ice. Filtration provided a light brown crystalline mixture, which was recrystallized from petroleum ether yielding **15** (16.1 g, 44%) as light yellow crystals, mp 127.5−129.5 °C (lit.[14] mp 129−131 °C).

Reaction of Phenol 1 with I_2 and H_2O_2 in MeOH (Table 1). General Procedure (Runs 1−13). To a magenetically stirred solution of **1** (412 mg, 2 mmol) and 36% H_2O_2[6] (3 mL, 1.24 g, 36 mmol) in MeOH (20 mL) was added at 35 °C a solution of I_2 [254 mg (1 mmol), 508 mg (2 mmol), or 1.016 g (4 mmol)] in MeOH (10 mL) in ca. 30 s. The mixture in a stoppered bottle was stirred at 35 °C for the time indicated in the table. The mixture was filtered into a flask containing a stirred, cold solution of $NaHSO_3$ (4.5 g) in water (200 mL). The filtration afforded 4,4′-diphenoquinone **4**: reddish brown crystals from benzene, identical with an authentic sample[20] (^1H NMR and TLC); mp 240−242 °C (lit.[20] mp 240−241 °C). 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 under reduced pressure. The residue was chromatographed. The first fraction gave a mixture of **1** and **2** (^1H NMR and GC), and their contents were determined by GC. The second fraction provided a mixture of 4,4′-biphenol **3**, a small amount of an additional crop of **4**, and 4-methoxyphenol **5** (^1H NMR and TLC), and the contents of the mixture was determined by ^1H NMR spectroscopy. The third fraction afforded *p*-benzoquinone **6**: orange crystals from

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[19] The formation of the other iodine-containing products (**7**, **9**, **12**, HI, etc.) may also contribute to the decrease in the I_2 concentration, but they are assumed to be only of transient existence and their concentrations in the reacting mixture are assumed to be extremely low. The content of I_2 (in mol) in the reacting mixture, therefore, is tentatively assumed to be the difference between the initial content of I_2 (in mol) and half the content of product **2** (in mol) in that mixture.

[20] Omura, K. *J. Org. Chem.* **1984**, *49*, 3046.

petroleum ether, identical with an authentic sample[21] (^{1}H NMR and TLC); mp 67−69 °C (lit.[21] mp 65−68 °C). For isolation and further identification of **3** and **5**, the mixture obtained from the second fraction was chromatographed on SiO_2 (15 g) with petroleum ether/benzene (10:1). The first fraction gave **3**: light yellow crystals from petroleum ether, identical with an authentic sample[10a] (^{1}H NMR and TLC); mp 186−187 °C (lit.[10a] mp 184.5−185.5 °C). The second fraction gave **4**. The third fraction yielded **5**: colorless crystals from MeOH, identical with a commercially available sample of **5** (^{1}H NMR, IR, and TLC); mp 105−107 °C (lit.[22] mp 106−107 °C).

In runs 14 and 15, the reaction was initiated by addition of a solution of I_2 (4 mmol) in MeOH (10 mL) to a solution of **1** (2 mmol) and 36% H_2O_2 (3 mL) in a mixture of MeOH (50 mL) and H_2O (3 mL).

In runs 16−18, the reaction was initiated by addition of a solution of I_2 (4 mmol) in MeOH (10 mL) to a solution of **1** (2 mmol), 36% H_2O_2 (3 mL), and concd H_2SO_4 (5 drops, ca. 1.8 mmol) in MeOH (20 mL).

In runs 19−21, the reaction was conducted at 0 °C.

Reaction of Phenol 2 with I_2 and H_2O_2 in MeOH (Table 2, runs 1−6). These reactions were conducted and worked up according to the general procedure described for the reaction of **1** with I_2 and H_2O_2 in MeOH (runs 1−13) except that **2** (664 mg, 2 mmol) replaced **1**.

Reaction of Phenols 1 or 2 with I_2 in H_2O/MeOH. The reaction of **1** was conducted by using I_2 (4 mmol), and the reaction mixture was worked up, according to the general procedure described for the reaction of **1** with I_2 and H_2O_2 in MeOH (runs 1−13) except that H_2O (3 mL) replaced 36% H_2O_2.[23] The reaction conducted for 5 min gave **1** (306 mg, 74% recovery), **2** (20 mg, 3%), **3** (6 mg, 1%), **4** (24 mg, 6%), **5** (23 mg, 5%), and **6** (40 mg, 9%). The reaction for 50 min gave **1** (68% recovery), **2** (5%), **3** (1%), **4** (10%), **5** (trace), and **6** (15%).

The reaction carried out similarly for 5 min by using **2** (2 mmol) in place of **1** gave **2** (505 mg, 76% recovery), **4** (92 mg, 23%), and **6** (7 mg, 2%). The reacion for 50 min gave **2** (50% recovery), **4** (48%), and **6** (3%).

Reaction of Phenol 10 with I_2 and H_2O_2 in MeOH (Table 2, runs 7 and 8). The reaction was undertaken and the reaction mixture was worked up, according to the general procedure described for the reaction of **1** with I_2 and H_2O_2 in MeOH (runs 1−13) except that **10**[24] (481 mg, 2 mmol) replaced **1**. Filtration of the reaction mixture afforded bis(chlorocyclohexadienone) **11a** as yellow crystals, identical with an authentic sample[8] (^{1}H NMR, IR, and TLC); mp 155−157 °C (lit.[8] mp 150−151 °C). The product mixture recovered from the filtrate was chromatographed. The first fraction provided **10**. The second fraction gave a mixture of **4** (trace) and a small amount of an additional crop of **11**. The third fraction gave **6**.

Reaction of an Equimolar Mixture of Phenol 1 and Phenols 2 or 10 with I_2 and H_2O_2 in MeOH. The reaction was conducted by using I_2 (4 mmol), and the reaction mixture was worked up, according to the general procedure described for the reaction of **1** with I_2 and H_2O_2 in MeOH (runs 1−13) except that a mixture of **1** (2 mmol) and **2** (2 mmol) or **10** (2 mmol) replaced **1** alone.

Reaction of the mixture of **1** and **2** conducted for 15 min provided **1** (21 mg, 5% recovery) and **2** [649 mg, 98% recovery (see the text)]. The reaction for 30 min provided **2** (63% recovery): phenol **1** was not recovered.

The product obtained from the reaction of the mixture of **1** and **10** was filtered into aqueous $NaHSO_3$. The product mixture recovered from the filtrate was chromatographed. The first fraction provided a mixture of **1**, **2**, and **10**. The contents of the mixture was determined by GC. Thus, the reaction conducted for 15 min gave **1** (14 mg, 3% recovery) and **10** (454 mg, 94% recovery). The products were **2** (51 mg, 8%), **3**, **4**, **5**, and **6**. Compond **11a** was not obtained. Reaction for 30 min gave **10** (68% recovery) while **1** was not recovered. The products were **2** (1%), **4**, **5**, **6**, and **11a**.

Reaction of Phenol 5 with I_2 and H_2O_2 in MeOH. The reaction was conducted for 50 min by using I_2 (4 mmol), according to the general procedure described for the reaction of **1** with I_2 and H_2O_2 in MeOH (runs 1−13) except that **5** (472 mg, 2 mmol) replaced **1**. The reaction mixture was poured into a stirred, cold solution of $NaHSO_3$ (4.5 g) in water (200 mL). Extractive workup of the resulting mixture with petroleum ether yielded **6** (439 mg, quantitative).

The reaction carried out similarly by using H_2O (3 mL) in place of 36% H_2O_2 gave a mixture of **5** (26% recovery) and **6** (74%).[23]

Reaction of Dienone 14 with I_2 or HI in H_2O/MeOH. To pulverized crystals of **14**[13b] (570 mg, 2 mmol) was added at 35 °C a solution of I_2 (4 mmol) in a mixture of MeOH (30 mL) and H_2O (3 mL) in one portion. The mixture in a stoppered bottle was stirred magnetically for 5 min at 35 °C, poured into a stirred, cold solution of $NaHSO_3$ (0.55 g) in water (200 mL), and extracted with petroleum ether (200 mL × 2). The extract was washed with water, dried and evaporated to dryness under reduced pressure. The residual product mixture, which was suggested by ^{1}H NMR spectroscopy not to contain **14**, was chromatographed. The first fraction provided a mixture of **1** (21 mg, 5%), 4-bromophenol **16** (354 mg, 62%), and **2** (8 mg, 1%), as suggested by GC. The second fraction gave a mixture of **3** (3 mg, 1%), **4** (27 mg, 7%), and **5** (29 mg, 6%), as analyzed by ^{1}H NMR spectroscopy. The third fraction yielded **6** (77 mg, 18%). Reaction for 60 min gave **1** (2%), **2** (2%), **3** (trace), **4** (13%), **6** (24%), and **16** (59%).

The reaction of **14** was carried out similarly for 5 min in the absence of added I_2. The ^{1}H NMR spectrum of the residual product (565 mg) obtained after a similar workup of the reaction mixture suggested that it consisted exclusively of **16**.

The reaction of **14** was carried out similarly for 5 min by using 57% HI (0.90 g, 4 mmol) and H_2O (2 mL) in place of I_2 and H_2O (3 mL), respectively. Column chromatography of the residual product mixture obtained after a similar workup of the reaction mixture gave a mixture of **1** (82%) and **16** (14%). Other products were **3** (0.5%), **4** (0.2%), and **5** (0.2%).

Reaction of Phenol 16 with I_2 in H_2O/MeOH. The reaction was conducted for 5 min by using I_2 (4 mmol) in the manner described for the reaction of **1** or **2** with I_2 in H_2O/MeOH except that **16**[8] (570 mg, 2 mmol) replaced **1** or **2**. The reaction mixture was worked up in the manner described for the reaction of **14** with I_2 in H_2O/MeOH. The residual product mixture was chromatographed. The first fraction gave **16** (436 mg, 76% recovery). The second fraction provided a mixture of **4** (67 mg, 16%) and bis(bromocyclohexadienone) **11b** (43 mg, 8%) as suggested by ^{1}H NMR spectroscopy. Comparison with an authentic sample of **11b**[25] by TLC also suggested that the mixture contained **11b**. The third fraction yielded a trace amount of **6**.

Reaction of Dienone 15 with I_2 or Br_2 in H_2O/MeOH. The reaction with I_2 was conducted for 10 min in the manner described for the reaction of **14** with I_2 in H_2O/MeOH except that **15** (728 mg, 2 mmol) replaced **14**. The reaction mixture was filtered into a flask containing a stirred, cold solution of $NaHSO_3$ (0.55 g) in water (200 mL). The filtration provided a crystalline mixture of **4** (32 mg) and **11b** (15 mg, 3%). Extractive workup of the contents of the flask with petroleum ether afforded a residual product mixture, which was suggested by ^{1}H NMR spectroscopy not to contain **15.** The residue was chromatographed to provide successively **16** (144 mg, 25%), **4** (5 mg, 9% in total), and **6** (216 mg, 49%).

The reaction of **15** was carried out similarly by using Br_2 (640 mg, 4 mmol) in place of I_2, and the reaction mixture was worked up analogously. Filtration provided **15** (81 mg) (^{1}H NMR). The crystalline residue (450 mg) recovered from the filtrate was estimated by ^{1}H NMR spectroscopy to contain **15** (84 mg, 23% recovery in total), **6** (0.29 g, 66%), and **16** (14 mg,

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[21] Omura, K. *J. Org. Chem.* **1989**, *54*, 1987.

[22] Müller, E.; Ley, K. *Chem. Ber.* **1955**, *88*, 601.

[23] In the workup of the reaction mixture, $NaHSO_3$ (0.55 g) was employed.

[24] Starnes, W. H., Jr. *J. Org. Chem.* **1966**, *31*, 3164.

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

2%). Dienone **15** suffered decomposition when chromatographed on SiO_2.

The reaction of **15** was carried out similarly in the absence of added I_2 or Br_2, and the reaction mixture was worked up analogously. Filtration provided **15** (549 mg). The crystalline mixture (170 mg) recovered from the filtrate was estimated by ^{1}H NMR spectroscopy to contain **15** (0.11 g, 91% recovery in total), **6** (5 mg, 1%), and **16** (9 mg, 2%).

Acknowledgment. The author is thankful to Hideyuki Matsubara and Sayoko Kamatani (students) for experimental contributions.

Supporting Information Available: ^{1}H NMR spectra of the crude products containing compound **13**, obtained from run 19, Table 1, and from the Ag ion induced reaction, as well as the spectrum of compound **5** for comparison (6 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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