Hydroxylation of substituted diatomic phenols and their derivatives

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Oxidation of 3,6-di-*tert*-butylpyrocatechol in protic media is accompanied by the formation of 3,6-di-*tert*-butyl-2-hydroxy-*para*-benzoquinone. Hydroxylation of the 3,5-isomer results in dealkylation and isomerization with the formation of 6-*tert*-butyl-2-hydroxy-*para*-benzoquinone and the quinone mentioned above, respectively. Their ratio depends on the nature of the solvent. Analogous processes accompany redox transformations of 2,6-di-*tert*-butylhydroquinone, 2,6-diphenyl-*para*-benzoquinone, and 2,4,6-tri-*tert*-butylphenol adsorbed on silica gel. Derivatives of 3,5-substituted pyrocatechols formed under conditions of heterophase oxidation in air are capable of transformations to form nitrogen-containing compounds.

Key words: diatomic phenols, quinones, redox transformations, hydroxylation, solid-phase autooxidation.

Hydroxylation is one of the most common types of transformations accompanying redox reactions of phenols under various conditions: in a wide pH range, in organic and aqueous solvents, and in the solid phase. This "versatility" is most likely due to the possibility of different mechanisms of insertion of the hydroxy group into the phenol molecule, which is related, to a great extent, to the participation of quinoid intermediates capable of both ionic and radical transformations. The validity of this assumption is confirmed by the present study of hydroxylation of *tert*-butyl-substituted diatomic phenols.

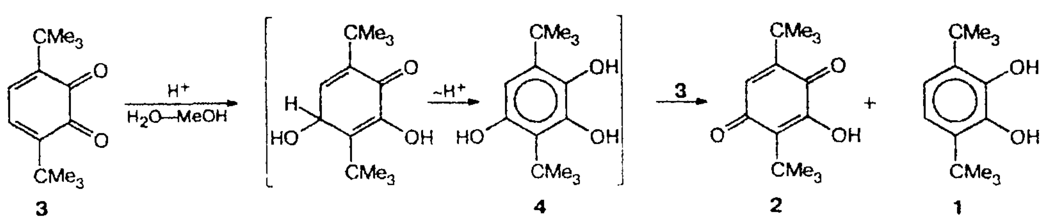
For example, the oxidation of 3,6-di-*tert*-butylpyrocatechol (**1**) in protic media is accompanied by the formation of 3,6-di-*tert*-butyl-2-hydroxy-*para*-benzoquinone (**2**), which is likely due to the 1,4-addition of H_2O to the primary oxidation product, *viz.*, 3,6-di-*tert*-butyl-*ortho*-benzoquinone (**3**). This mechanism is confirmed by the acid-catalyzed hydration of **3** in an H_2O—MeOH—H_2SO_4 medium.[1] In the absence of an oxidant, the yield of compound **2** in the hydration of quinone **3** is theoretically limited (50%) because of the redox reaction of the starting compound **3** with the intermediate 3,6-di-*tert*-butyl-1,2,4-trihydroxybenzene (**4**) (Scheme 1).

The use of $FeCl_3$ as an oxidant or $FeCl_2$ as an activator of oxidation by atmospheric oxygen makes it possible to perform complete conversion of pyrocatechol **1**. In the presence of $FeCl_2$, both the ionic and radical processes can occur in parallel (Scheme 2) where not only H_2O is the hydroxylating agent, but also the products of reduction of O_2 in its complex with compound **1** and $FeCl_2$ (hydrogen peroxide or $OH^{\cdot}$ radicals formed from it with the participation of $FeCl_2$).

This mechanism is consistent with the fast and almost quantitative formation of quinone **2** in a **1**—H_2O_2—$FeCl_2$ system.

Hydroxylation of 3,5-di-*tert*-butylpyrocatechol (**5**) is accompanied by a change in the carbon skeleton of the molecule due to dealkylation or isomerization. The ratio of these processes depends on the nature of the solvent: in an aprotic medium with a low nucleophilicity (CH_2Cl_2), both processes occur in parallel with a noticeable contribution of intramolecular isomerization to form compound **2**, whereas predominant dealkylation resulting in 6-*tert*-butyl-2-hydroxy-*para*-benzoquinone (**6**) occurs in MeOH. These transformations indicate that an intermediate with the structure of the

Scheme 1



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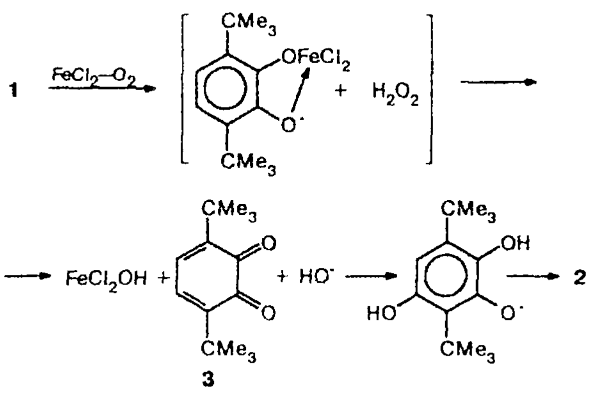
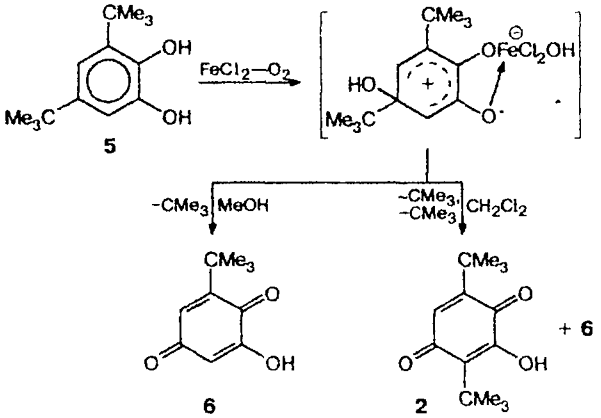
Scheme 2



arenonium ion probably participates in the process (Scheme 3).

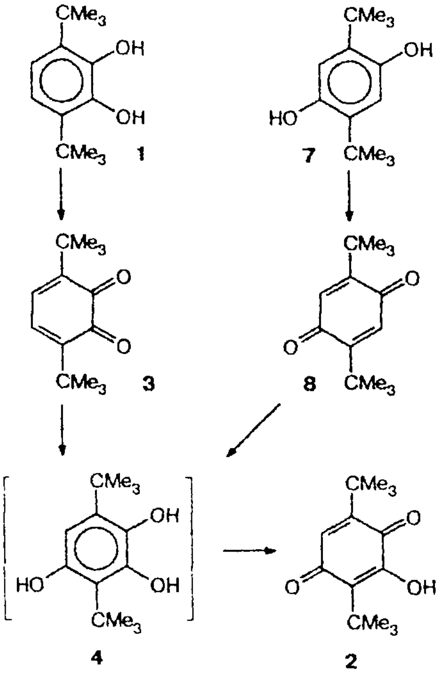
Scheme 3



The data on hydroxylation of compounds **1** and **5** in solutions are used for explanation of the specific features of heterophase autooxidation of substituted phenols and their derivatives adsorbed on silica gel (Silufol). It is established that hydroxylation is important in heterophase redox transformations and tightly related to processes that result in the formation of nitrogen-containing compounds and that have been observed for the first time[2] for pyrocatechol **5** (Scheme 4).

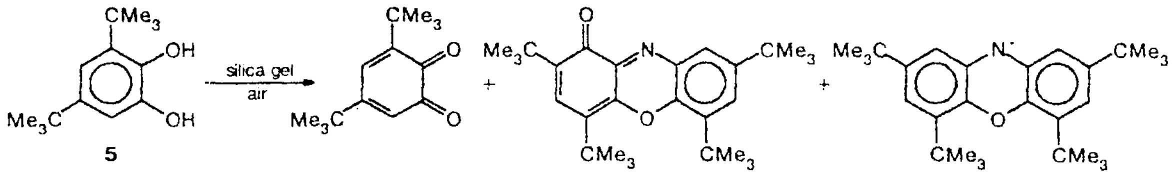
Results were obtained that indicate that 1,2-diols generated on SiO_2 *in situ* due to the hydroxylation of the corresponding precursors can participate in similar processes. Most likely, the symmetrically shielded compound **1** and its derivatives are the exceptions: the products of their transformations do not contain nitrogen-containing compounds. The oxidation of pyrocatechol **1** on silica gel gives quinones **2** and **3**. 2,5-Di-*tert*-butylhydroquinone (**7**) behaves similarly. Its oxidation results in the formation of 2,5-di-*tert*-butyl-*para*-benzoquinone (**8**) and quinone **2** probably *via* intermediate **4**, which is common with **1**, and the chain of transformations of compounds **1** and **7** is terminated by the oxidation of this intermediate (Scheme 5).

Scheme 5

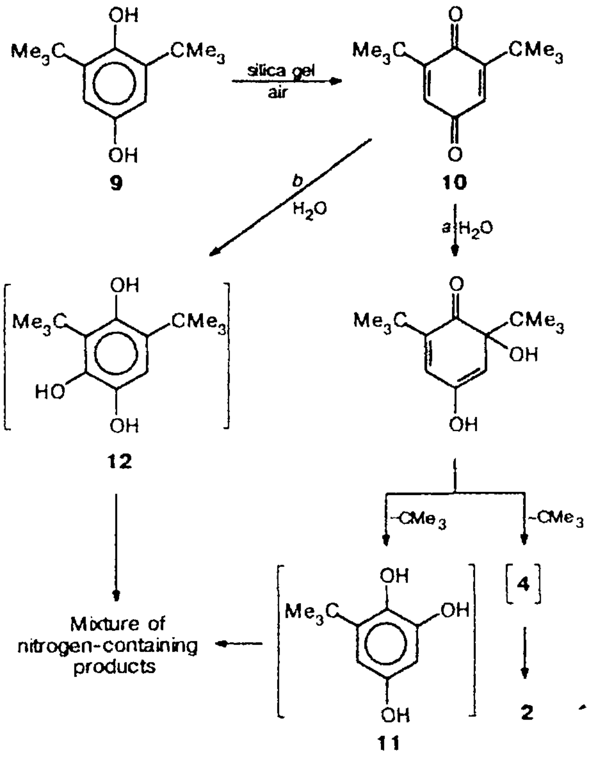


Nitrogen was detected in the products of transformation of 2,6-di-*tert*-butylhydroquinone (**9**), which can be explained in terms of Scheme 6 including the formation and possible hydroxylation of 2,6-di-*tert*-butyl-*para*-benzoquinone (**10**) through two alternative directions.

Scheme 4

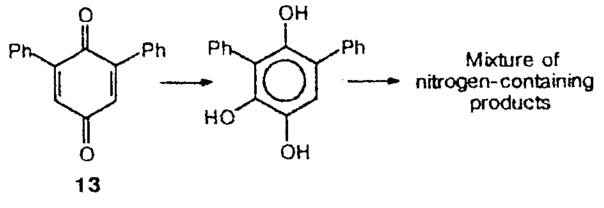


Scheme 6



Phenols **11** and **12**, similarly to pyrocatechol **5**, can probably participate in the formation of nitrogen-containing compounds. Quinones **2** and **10** were isolated and identified, which confirm the route "a." For the other products of transformations of hydroquinone **9**, due to their lability, only the nitrogen content was determined (1.5±0.5%). Most likely, we can interpret similarly the formation of nitrogen-containing compounds upon prolonged exposure in air of 2,6-diphenyl-*para*-benzoquinone (**13**) adsorbed on silica gel (Scheme 7).

Scheme 7



Monoatomic phenols that can form the corresponding substituted quinones and 1,2-diols in stepwise transformations including hydroxylation can participate as the starting compounds in heterophase synthesis of nitrogen-containing compounds. For example, nitrogen was detected in a mixture of products of transformation of 2,4,6-tri-*tert*-butylphenol (**14**) on silica gel. This result can be easily explained, because 3,5-di-*tert*-butyl-*ortho*-benzoquinone (**15**) and *para*-quinone **10** were observed in the products of transformation of phenol **14**.

Alternative nitrogen sources for the formation of nitrogen-containing compounds (admixtures of NH_3 and nitrogen oxides in air) are not considered in this work. This is the subject of a special study with the use of isotopically labeled compounds, which is currently in progress.

Experimental

^1H NMR spectra were recorded on a Bruker WM-400 spectrometer using $CDCl_3$ as the solvent. Silufol UV_{254} plates (Kavalier) were used for TLC and heterophase reactions. 3,6-Di-*tert*-butylpyrocatechol (**1**),[3] 3,6-di-*tert*-butyl-*ortho*-benzoquinone (**3**),[4] 3,5-di-*tert*-butylpyrocatechol (**5**),[5] 2,6-di-*tert*-butylhydroquinone (**9**),[6] 2,6-di-*tert*-butyl-*para*-benzoquinone (**10**),[7] and 2,4,6-tri-*tert*-butylphenol (**14**)[8] were synthesized by known procedures. 2,5-Di-*tert*-butylhydroquinone (**7**) was commercially available from Merck, and 2,6-diphenyl-*para*-benzoquinone (**13**) was presented from Akzo.

Hydration of 3,6-di-*tert*-butyl-*ortho*-benzoquinone (3). Quinone **3** (0.22 g, 1 mmol) was dissolved in an MeOH—H_2O (10 : 1) mixture (20 mL), conc. H_2SO_4 (0.1 mL) was added, and the mixture was stored for 2 h. The reaction mixture was diluted with water, and the products were extracted with ether and separated by preparative TLC in a hexane—ether (5 : 1) mixture. Compounds **1** (0.1 g; 45%), m.p. 96 °C (hexane) (*cf.* Ref. 2: m.p. 96 °C) and **2** (0.11 g; 44%), m.p. 85 °C (*cf.* Ref. 1: m.p. 85 °C) were isolated.

Hydroxylation of 3,6-di-*tert*-butylpyrocatechol (1) and 3,6-di-*tert*-butyl-*ortho*-benzoquinone (3) in the presence of $FeCl_3$ and $FeCl_2$. A saturated aqueous solution of $FeCl_3$ or $FeCl_2$ (0.5 mL) was added to a solution of **1** or **3** (0.22 g, 1 mmol) in MeOH (20 mL). The mixture was stored for 6—7 h, diluted with water acidified with HCl, extracted with ether, and dried. The ether was removed, and the product was crystallized from hexane to obtain quinone **2** (1.75 g, 75%).

Hydroxylation of 3,6-di-*tert*-butylpyrocatechol (1) in the H_2O_2—$FeCl_2$ system. A saturated aqueous solution of $FeCl_2$ (0.5 mL) and 33% H_2O_2 (1 mL) were added to a solution of **1** (0.22 g, 1 mmol) in MeOH (20 mL). The evolution of gas bubbles and appearance of a yellow color were observed. The reaction mixture was stored for 20 min, diluted with water acidified with HCl, and extracted with ether to isolate quinone **2** (0.2 g, 84%).

Hydroxylation of 3,5-di-*tert*-butylpyrocatechol (5) in the MeOH—$FeCl_3$—H_2O system. Pyrocatechol **5** (0.22 g, 1 mmol) was dissolved in MeOH (20 mL), and a saturated aqueous solution of $FeCl_3$ (0.5 mL) was added. The mixture was stirred for 6 h and diluted with water acidified with HCl. The products were extracted with CH_2Cl_2, the solvent was removed, and the residue was crystallized from a hexane—CH_2Cl_2 (20 : 1) mixture. Quinone **6** (0.14 g, 77%) was isolated, m.p. 115 °C. Found (%): C, 66.66; H, 6.71. $C_{10}H_{12}O_3$. Calculated (%): C, 66.65; H, 6.71. ^1H NMR (δ): 1.29 (s, 9 H, $C(Me)_3$); 6.06 (d, 1 H, J = 2.7 Hz); 6.52 (d, 1 H, J = 2.7 Hz); 7.24 (s, 1 H, OH).

Hydroxylation of 3,5-di-*tert*-butylpyrocatechol (5) in the CH_2Cl_2—$FeCl_3$—H_2O system. Pyrocatechol **5** (0.22 g, 1 mmol) was dissolved in CH_2Cl_2 (20 mL), and a saturated aqueous solution of $FeCl_3$ (10 mL) was added. The mixture was vigorously stirred for 6 h, water acidified with HCl was added (20 mL), the organic layer was separated, and the aqueous layer was additionally extracted with CH_2Cl_2 (5 mL). The combined extracts were dried. Quinones **2** and **6** were identified by TLC. Quinones **2** (0.07 g, 30%) and **6** (0.08 g, 45%) were isolated by preparative TLC under the conditions described above.

Reactions on silica gel. Solutions of compounds in ether or CH_2Cl_2 were applied on Silufol UV_{254} plates (the concentration of the applied substance was 0.05—0.10 mg cm^{-2}) and left in air for 1—7 days, the course of transformations being monitored by TLC. Then the products were extracted with ether or $CHCl_3$ and analyzed. In the case of transformations of compounds **13** and **14**, the whole reaction mixture was analyzed for nitrogen. The content of nitrogen was 1.2% and 1.4%, respectively.

Transformation of 3,6-di-*tert*-butylpyrocatechol (1) on silica gel. Plates with adsorbed pyrocatechol **1** (0.11 g, 0.5 mmol) were stored in air for 3 days. The starting compound **1** (traces) and quinones **2** and **3** were identified by TLC. The mixture of products was extracted with $CHCl_3$ and separated into individual components by TLC in a hexane—ether (5 : 1) mixture to obtain quinones **2** (0.02 g, 20%) with m.p. 84 °C (*cf.* Ref. 1: m.p. 85 °C), and **3** (0.08 g, 70%) with m.p. 199 °C (*cf.* Ref. 3: m.p. 199 °C).

Transformation of 2,5-di-*tert*-butylhydroquinone (7) on silica gel was performed similar to that described for compound **1**. Benzoquinone **8** (0.086 g, 78%) with m.p. 156—157 °C (hexane) (an authentic sample of quinone **8** was obtained by oxidation of **7** with Ag_2O in benzene) and quinone **2** (0.012 g, 10%) were obtained.

Transformation of 2,6-di-*tert*-butylhydroquinone 9 on silica gel. Plates with adsorbed compound **9** (0. 22 g, 1 mmol) were kept in air for 7 days. The products were extracted with $CHCl_3$ to isolate quinones **2** (0.011 g, ~5%) and **10** (0.15 g, 68%) with m.p. 67 °C (*cf.* Ref. 7: m.p. 67 °C) by TLC; according to the data of elemental analysis, the residue (~0.05 g) contains ~1.5% nitrogen.

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