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The oxidation of 2-alkoxy-3,6-di-*tert*-butylphenols. The reversible dimerization of 2-alkoxy-3,6-di-*tert*-butylphenoxy radicals

Gleb A. Abakumov, Vladimir K. Cherkasov, Vladimir I. Nevodchikov, Nikolai O. Druzhkov, Georgii K. Fukin, Yurii A. Kursky and Alexandr V. Piskunov*

G.A. Razuvaev Institute of Organometallic Chemistry, Tropinina str. 49, 603950 Nizhny Novgorod, Russia

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Abstract—The oxidation of 2-alkoxy-3,6-di-*tert*-butylphenols has been studied. It was found that 2-RO-3,6-di-*tert*-butylphenoxy radicals (R = Et, Pr, Ph) undergo dimerization by C–O coupling. The X-ray structure of 2-ethoxy-3,6-di-*tert*-butylphenoxy dimer has been determined. Radical dimers dissociate reversibly in solution to give two phenoxy radicals at 200–350 K. By using EPR spectroscopy the equilibrium concentration of the phenoxy radicals, equilibrium constants and ΔH and ΔS of dissociation have been determined.

Phenoxy radicals are often employed as reagents in organic, organometallic and biochemistry. The most commonly used methods for the preparation of phenoxy radicals are bimolecular oxidation or photolysis of the corresponding phenols. The formation of phenoxy radicals by oxidation of 2-alkoxy-3,6-di-*tert*-butylphenols has been reported.[1] Recently it was shown that 2-alkoxy-3,6-di-*tert*-butylphenolate complexes are the main products of the reaction between 3,6-di-*tert*-butylbenzoquinone and alkyl zinc or cadmium derivatives.[2] Herein we report the reversible dimerization of 2-alkoxy-3,6-di-*tert*-butylphenoxy radicals by C–O coupling to form the corresponding quinol ethers of alkoxyphenols.

The oxidation of 2-alkoxy-3,6-di-*tert*-butylphenols **1a**–**e** with PbO_2 (Scheme 1) in toluene solution gives phenoxy radicals as was evident by EPR-spectroscopy (Table 1). A drop in temperature leads to a decrease in the intensity of the EPR signal which disappears at 200 K. Increasing the temperature renews the initial spectra. Similar transformations of EPR spectra have been observed for 3,6-di-*tert*-butyl-2-methoxyphenoxy radicals.[3] These observations are evidence of reversible dimerization of phenoxy radicals in solutions. Williams and Kreilick[4] observed the formation a 2,6-di-*tert*-butyl-4-acetylphenol dimer and its dissociation to phenoxy radicals from the broadening of the ^1H NMR signal.

The phenoxy radicals can be prepared[5] by oxidation of diethyl ether solutions of **1a**, **b** and **e** using a basic solution of potassium ferrocyanide (Scheme 2). Compounds **3**–**5** are stable solids. The structures of **3**–**5** were confirmed by IR and NMR spectroscopy.[6–8] Unequivocal proof of the structure of **3** was obtained by X-ray crystallography (Fig. 1).[†]

The reversible dissociation of dimers **3**–**5** takes place in the temperature range 200–350 K. Investigation of the temperature dependence on the dissociation equilibrium

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Keywords: Phenol; Oxidation; Phenoxy radical; Reversible dissociation.

* Corresponding author. Tel.: +7 8312 127682; fax: +7 8312 127497; e-mail: pial@imoc.sinn.ru

[†] Crystal data for **3**: Light yellow crystals were grown from hexane, triclinic, $P2(1)/n$, $Z = 4$ in a cell of dimensions: $a = 11.7595(4)$ Å, $b = 16.2885(6)$ Å, $c = 15.9171(6)$ Å, $\alpha = 90°$, $\beta = 103.8860(10)°$, $\gamma = 90°$. $Z = 4$, $\rho = 1.119$ mg/m^3 $\mu = 0.072$ mm^{-1}, $F(000) = 1096$. A total of 23,174 reflections were measured, 5200 unique ($R_{int} = 0.0236$). F^2 refinement, $R_1 = 0.0350$, $wR_2 = 0.0909$.
CCDC 261258 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223 336033; E-mail address: deposit@ccdc.cam.ac.uk).

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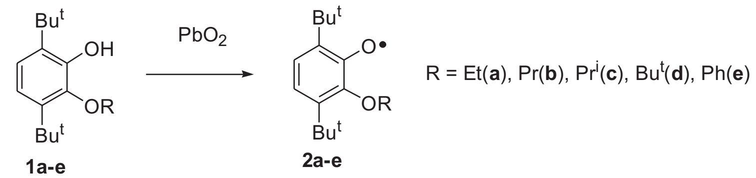


Scheme 1.

Table 1. The EPR spectral parameters of phenoxy radicals **2a**–**e** (toluene, 290 K)

Phenoxy radical	A_i (H_4), G	A_i (H_5), G	A_i (H_R), G	g_i
2a	8.0	0.8	1.7 (2H)	2.0050
2b	8.0	0.8	1.8 (2H)	2.0051
2c	7.8	0.7	1.2 (1H)	2.0050
2d	8.0	0.9	—	2.0050
2e	9.2	1.6	—	2.0049

for compounds **3** and **5** by EPR spectroscopy allowed determination of the phenoxy radical concentration (a solution of TEMPO radical was used as the standard). On the basis of these measurements the equilibrium constants could be calculated. They are approximately 10^{-6} mol/L for **3** and 10^{-9} mol/L for **5**, respectively ($T = 298$ K). From the dependence $-\ln K = f(1/T)$, the dissociation enthalpy and entropy have been calculated and are as follows: $\Delta H = 15.5 \pm 0.5$ kcal/mol; $\Delta S = 23.6 \pm 0.5$ cal/mol K for **3** and $\Delta H = 17.1 \pm 0.5$ kcal/mol; $\Delta S = 16.5 \pm 0.5$ cal/mol K for **5**.

Oxidation of **1c** under analogous conditions did not lead to a corresponding dimer. The presence of the labile hydrogen atom in the ^{i}Pr group of **2c** resulted in over-oxidation of the latter leading to the formation of the known[9] cyclic ether of 3,6-di-*tert*-butylcatechol **6** (Scheme 3). The phenoxy radical **2d** did not form a dimeric product either and underwent further transformations in solution; we were unable to isolate any of these reaction products.

In summary it should be noted that compounds **3**–**5** are very convenient sources of phenoxy radicals in solution. They are easy to handle and the radical concentration can be adjusted by simple dissolution in the most aprotic organic solvent.

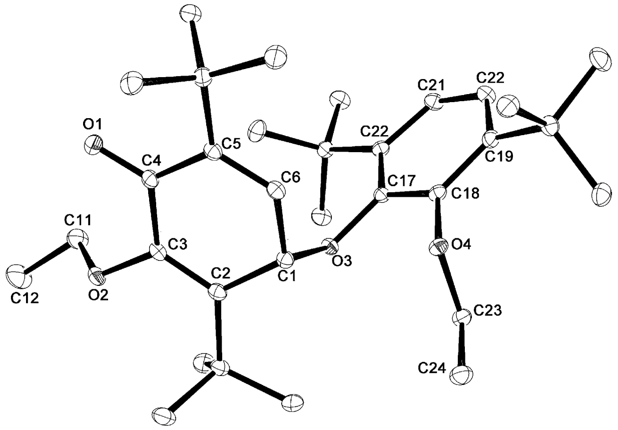
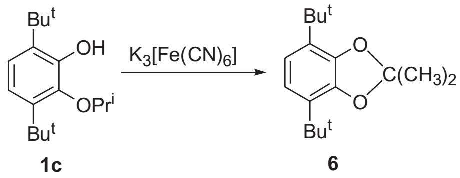


Figure 1. ORTEP diagram of **3** showing the X-ray molecular structure at the 30% probability level. All bond lengths and angles are in the same range as expected for comparable aromatic or cyclohexadienone systems, respectively.



Scheme 3.

Acknowledgements

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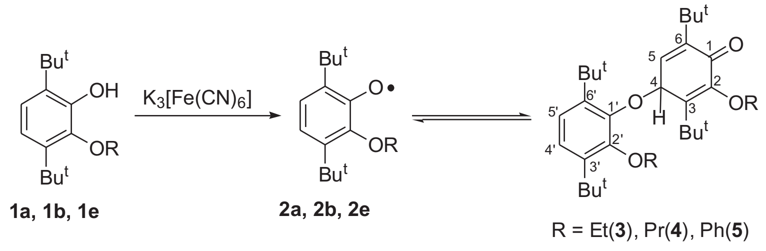

Scheme 2.

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5. Details of the experiment are as follows: To 100 mL of an aqueous solution of 20 g of $K_3[Fe(CN)_6]$ and 3 g of KOH under continuous stirring, 5 g of phenol **1a**, **b**, **e** in 50 mL of diethyl ether was added. After 30 min of stirring, the organic layer was separated and washed with water. The ether was evaporated and the residue was recrystallized from hexane.
6. *3,6-Di-tert-butyl-4-(3,6-di-tert-butyl-2-ethoxyphenoxy)-2-ethoxycyclohexa-2,5-dienone* (***3***): Yield 89%; mp = 116 °C; Found (%): C 77.24; H 10.13. Calculated for $C_{32}H_{50}O_4$ (%): C 77.11; H 10.04. IR (Nujol): 1655, 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ/ppm J/Hz: 0.91 (s, 9H, Bu^t (6′)); 1.22 (s, 9H, Bu^t (6)); 1.39 (t, 3H, CH_3, $J = 6.9$); 1.39 (s, 9H, Bu^t (3′)); 1.47 (t, 3H, CH_3, $J = 7.1$); 1.49 (s, 9H, Bu^t (3)); 3.66 and 4.49 (m, 1H each, $O(2')CH_AH_B$); 3.94 (m, 2H, $O(2)CH_AH_B$); 5.93 (d, 1H, H(4), $J = 4.5$); 6.47 (d, 1H, H(5), $J = 4.5$); 6.89 and 6.93 (d, 1H each, H(4′) and H(5′), $J = 8.5$).
7. *3,6-Di-tert-butyl-4-(3,6-di-tert-butyl-2-propoxyphenoxy)-2-propoxycyclohexa-2,5-dienone* (***4***): Yield 83%; light yellow oil; Found (%): C 77.72; H 10.20. Calculated for $C_{34}H_{54}O_4$ (%): C 77.57; H 10.27. IR (Nujol): 1655, 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ/ppm J /Hz: 0.91 (s, 9H, Bu^t (6′)); 1.01 (t, 6H, CH_3, $J = 7.5$); 1.22 (s, 9H, Bu^t (6)); 1.39 (s, 9H, Bu^t (3′)); 1.49 (s, 9H, Bu^t (3)); 1.61–2.10 (m, 4H, CH_2CH_3); 3.54 and 4.35 (m, 1H each, $O(2')CH_AH_B$); 3.82 (t, 2H, $O(2)CH_2$, $J = 7.0$); 5.91 (d, 1H, H(4), $J = 4.7$); 6.47 (d, 1H, H(5), $J = 4.7$); 6.91 (s, 2H, H(4′) and H(5′)).
8. *3,6-Di-tert-butyl-4-(3,6-di-tert-butyl-2-phenoxyphenoxy)-2-phenoxycyclohexa-2,5-dienone* (**5**): Yield 92%; mp = 151 °C; Found (%): C 80.70; H 8.45. Calculated for $C_{40}H_{50}O_4$ (%): C 80.81; H 8.41. IR (Nujol): 1650, 1670 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz) δ/ppm J/Hz: 0.94 (s, 18H, Bu^t (3′) and Bu^t (6′)); 1.30 and 1.32 (s, 9H each, Bu^t); 5.83 (d, 1H, H(4), $J = 4.7$); 6.75 (d, 1H, H(5), $J = 4.7$); 7.11 (s, 2H, H(4′) and H(5′)); 6.70–7.41 (m, 10H, OC_6H_5).
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