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The Facile Oxidative Coupling of a Hindered Phenol, 2,6-Di-*t*-butylphenol, Driven by *N*,*N*′-Bis(ethoxycarbonyl)-1,4-benzoquinone Diimine; The Reaction Pattern Traced by ^{1}H NMR Spectroscopy

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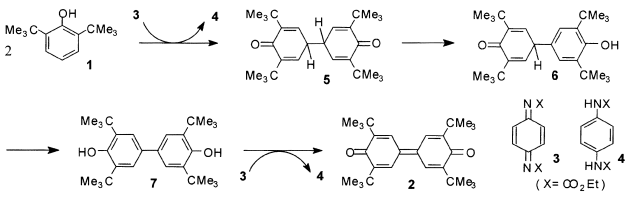
Good yields of 3,3′,5,5′-tetra-*t*-butyl-4,4′-diphenoquinone were obtained by the reaction of 2,6-di-*t*-butylphenol with *N*,*N*′-bis(ethoxycarbonyl)-1,4-benzoquinone diimine, which had been shown to undergo addition with aniline derivatives and phenols. The reaction was followed with ^{1}H NMR spectroscopy to deduce the reaction intermediates.

There have been reported for the oxidative coupling of a hindered phenol, 2,6-di-*t*-butylphenol (**1**) to 3,3′,5,5′-tetra-*t*-butyl-4,4′-diphenoquinone (**2**) by oxidation with nitric acid,[1a] base-catalyzed oxygenation,[1b] catalytic oxygenation with metallic compounds[1c] or 1,4-benzoquinone diimine derivatives,[1d] and reactions with 2,4,6-tri-*t*-butylphenoxyl,[1e] tellurium compounds,[1f] or a 1,2-benzoquinone monoimine derivative.[1g]

We reported that *N*,*N*′-bis(ethoxycarbonyl)-1,4-benzoquinone diimine (**3**) undergoes addition with unhindered aniline derivatives and phenols although their reaction site are different.[2] It has been discovered now that the mixing of **3** with **1** in equimolar amounts in solution under aerobic condition at the room temperature causes a reaction to give **2** in 65–94% depending on the solvents, diethyl 1,4-phenylenediamine-*N*,*N*′-dicarboxylate (**4**) being isolated in comparable amounts (Scheme 1). The reaction was faster in polar solvents than in nonpolar ones as shown in Table 1. ^{1}H NMR spectroscopy was used to trace the reaction pattern to deduce the reaction intermediates.

A 1:1 mixture of **1** and **3** in C_6D_6 was placed in the cavity of a 400 MHz NMR spectrometer and the spectra were recorded at intervals. The pertinent spectra are shown in Fig. 1A–1D.



Scheme 1.

Table 1. Yields of **2** and **4** in the Reaction of **1** with **3**[a)]

Solvent		C_6H_6	$CHCl_3$	MeCOMe	MeCN	AcOEt	THF
Reaction time[b)]		15d	15d	10h	10h	10h	10h
Yield/%	**2**	72	65	89	94	92	89
	4	60	56	85	75	86	76

a) $[\mathbf{1}]_0 = [\mathbf{3}]_0 = 0.1$ mol dm^{-3}. b) Required for consumption of **3**.

The peaks at 1.36 (peak a) and 4.93 ppm (the latter is not shown) due to the *t*-butyl and hydroxy protons of **1** gradually disappeared in 3 hours, and were substituted by a new singlet at 1.33 (peak b) and a multiplet at 2.74 (peak c) ppm. Peaks b and c had the same chemical shifts as those of *t*-butyl and methine protons of an authentic sample of 3,3′,5,5′-tetra-*t*-butyl-1,1′-bi(2,5-cyclohexadienyl)-4,4′-dione (**5**). At this stage, the signals due to quinone diimine **3** were still observable, while phenylenediamine **4** started to crystallize in the mixture. Also, at this stage the signal due to the *t*-butyl group of **2** began to appear at 1.43 (peak d) ppm (Fig. 1C), and then slowly but steadily grew within the next 40–100 hours at the cost of peak b of **5** (Fig. 1D). Peaks b and c eventually disappeared within several days. The overall picture showed that the reaction was slow in benzene, and that the formation of **5** was faster than its conversion to **2**. It was reported before[2b] that **5** is stable in nonpolar dry solvents.

A similar ^{1}H NMR monitorimg of the reaction in acetone-d_6 showed drastically different dynamics (Fig. 2). The reaction was much faster and was completed within several hours wherein the *t*-butyl singlet of **2** at 1.37 ppm (peak c) increased at the expense of that of **1** at 1.43 ppm (peak a), as shown in Figs. 2A and 2D. In this region, the triplet methyl protons of the ethyl side chain of **3** and **4** also showed concurrent changes from 1.33 ppm (peak d for **3**) to 1.24 ppm (peak e for **4**). Figures 2B and 2C clearly show the "come and go" of these peaks. A singlet at 1.21 ppm (peak b) appeared immediately upon mixing and persisted at a low intensity, but eventually disappeared on completion of the reaction; this peak b was confirmed to be the *t*-butyl signal of **5** as follows. Upon the dissolution of an authentic sample of **5**, it showed a singlet at 1.24 ppm (peak a) for the *t*-butyl group, which rapidly disappeared within ca. 10 min (Fig. 3). For this recording, a C_6D_6-acetone-d_6 (3:7) mixture was used as solvent to dampen the fast trans-

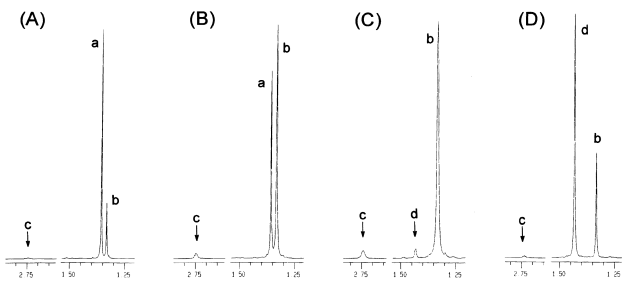


Fig. 1. ^{1}H NMR spectral changes of a solution of **1** (0.05 mol dm^{-3}) and **3** (0.05 mol dm^{-3}) in C_6D_6 at room temperature at 6 min (A), 1 h (B), 3 h (C), and 40 h (D) after mixing; see text for the assignment of peaks.

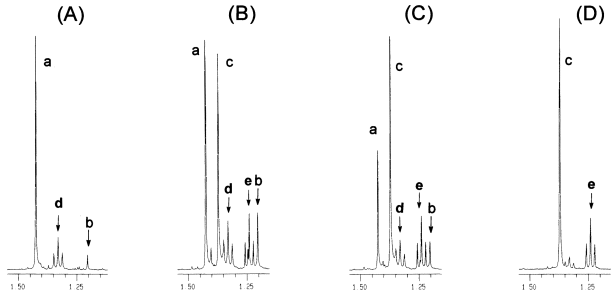


Fig. 2. ^{1}H NMR spectral changes of a solution of **1** (0.05 mol dm^{-3}) and **3** (0.05 mol dm^{-3}) in acetone-d_6 at room temperature at 6 min (A), 25min (B), 45 min (C), and 8 h (D) after mixing; see text for the assignment of peaks.

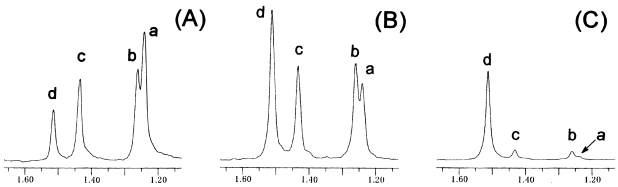
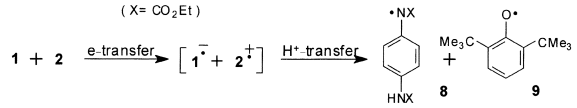


Fig. 3. ^{1}H NMR spectral changes of a solution of **5** (0.05 mol dm^{-3}) in C_6D_6–acetone-d_6 (3:7) at room temperature at 2.5 min (A), 7.5 min (B), and 18 min (C) after mixing; see text for the assignment of peaks.

formation in neat acetone. Also, a 90 MHz spectrometer was used for rapid tuning so that the recording could be started immediately after mixing. Figures 3A and 3B also show a singlet at 1.51 ppm (peak d) for *t*-butyl protons of **7**, which grow stronger quickly and dominate all at the end (Fig. 3C). They also show a pair of singlets with equal intensity at 1.26 and 1.43 ppm (peaks b and c); because they varied the intensity together and eventually disappeared to give peak d, they are assigned to the two *t*-butyl groups of intermediate **6**. This demonstrates that the proton migration in **5** occurs by a stepwise process, and very rapidly, to give **7**. Further, the mixing of a colorless solution of **7** and a faintly yellow solution of **3** in acetone-d_6 immediately developed a red solution which exhibited a singlet at 1.37 ppm due to *t*-butyl of **2** (peak c in Fig. 2). Thus, the dehydrogenation of **7** by **3** is also very rapid, and even faster than the formation of **7** in acetone, which explains the fact that in Fig. 2 the *t*-butyl signal of **5** appears (*albeit* with a low intensity) but the *t*-butyl signal of **7** does not. One can conclude that in acetone, acetonitrile, ethyl acetate and THF the proton migration of **5** to **7** and the subsequent oxidation to **2** are much faster than the formation of **5**. The fast conversion must arise from the fact that these solvents have hetero-atoms that assist a proton migration and oxidation. It follows that benzene and chloroform lack such a proton coordinating center, and do not facilitate the migration. This leads to the accumulation of **5** in benzene (Fig. 1).

Turning now to the formation of **5**, the most plausible route is coupling of the resonance-stabilized phenoxyl radical **9**, which has been widely assumed as the intermediate in such oxidation. The cyclic voltammogram in acetonitrile gave an irreversible wave with $E_{ox} = +0.8$ V vs SCE for **1** and a quasi-reversible wave with $E_{red} = -0.3$ V vs SCE for **3**. Electron transfer between them is not efficient, but is possible within a



Scheme 2.

complex as shown in Scheme 2. In a polar solvent, such as acetone, this rate should be much faster than in benzene. Quinone diimine **3** shows a broad tail hitching to the strong 282 nm peak stretching over to 470 nm in acetonitrile. Even in benzene, its solution developed a light red color upon the addition of **1**, which indicates the formation of a CT complex. At present it is not certain whether radicals **8** and **9** are directly formed by Scheme 2 or via the radical scission of a coupling product between **8** and **9**. Although there are many possible venues for **8** to reach **4**, we do not have any hint to suggest a preference.

Experimental

^{1}H NMR spectra were recorded with JEOL JNM-LA 400FT and JEOL JNM-FX90Q spectrometers. Compound **3** was prepared by a reported method.[2a] Authentic samples of **2**,[1b] **4**,[2a] **5**,[3] and **7**[1b] were prepared according to the literature.

Procedure of the Reaction of 3 with 2,6-Di-*t*-butylphenol (1). A reaction solution was made up by mixing 5 cm^3 of a 0.2 mol dm^{-3} solution of **1** with 5 cm^3 of a 0.2 mol dm^{-3} solution of **3**. The proceeding of the reaction was monitored by TLC analysis (eluent, hexane–ethyl acetate (4:1)). After confirming the consumption of **3**, the supernatant solution was separated from red crystals deposited and concentrated to a residue, from which **2** and **4** were isolated by flush column chromatography (eluent, hexane–ethyl acetate). Combined red crystals of **2** were recrystallized from $CHC1_3$–hexane. Colorless crystals of **4** were recrystallized from THF–hexane.

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