Bis(trifluoroacetoxyiodo)benzene-Induced Activation of *tert*-Butyl Hydroperoxide for the Direct Oxyfunctionalization of Arenes to Quinones

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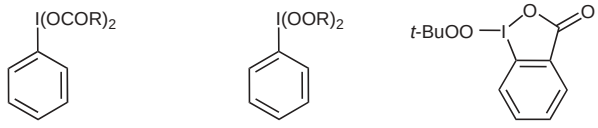
Abstract: Various aromatic hydrocarbons were oxidized with *bis*(trifluoroacetoxyiodo)benzene (PIFA)/*tert*-butyl hydroperoxide system to afford the corresponding quinones. The reaction conditions and scope have been discussed in detail.

Key words: hypervalent iodine, peroxyiodone, aromatic hydrocarbon, oxidation, quinone

In spite of extensive studies on the chemistry of hypervalent iodine reagents such as *bis*(acetoxyiodo)benzene (PIDA, **1a**) and *bis*(trifluoroacetoxyiodo)benzene (PIFA, **1b**), very little is known about peroxyiodanes, probably because of the fact that they show high tendency to decompose.[1] Milas and Plesnicar reported the reaction of *bis*(acetoxyiodo)benzene (**1a**) with *tert*-butyl hydroperoxide in dichloromethane and proposed the in situ generation of *bis*(*tert*-butylperoxyiodo) benzene (**2b**) to be an intermediate, which decomposes homolytically even at –80 °C to give *t*-butylperoxy radical and iodobenzene.[2] This ready decomposition of the (alkylperoxy)iodine can be attributed to the low dissociation energy of the apical hypervalent peroxy-iodine(III) bond and is facilitated by conjugative overlap of the breaking hypervalent bond with π-orbitals of the aromatic nucleus. Recently, Ochiai and co-workers have reported the synthesis and characterization of the first stable crystalline 1-(*tert*-butylperoxy)-1,2-benziodoxol-3(1*H*)-one (**3**), which oxidizes a number of organic substrates (Figure 1).[3]



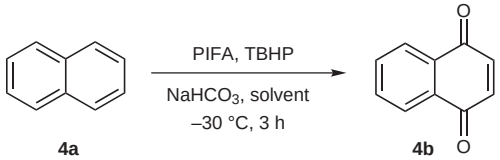
1a R = CH_3
1b R = CF_3
2a R = H
2b R = *t*-Bu
3

Figure 1

Preparative methods of quinones from phenols or phenyl alkyl ethers using hypervalent iodine reagents have been reported.[4] However, oxyfunctionalization of aromatic substrates that have no phenolic hydroxyl or amino substituents using hypervalent iodine reagents has so far not been reported. Very recently, we have described activation of hydrogen peroxide by the PIFA (**1b**) for the peroxidation of alkenes and aromatic hydrocarbons; the reactive intermediate has been postulated to be peroxyiodane **2a**.[5] To gain further insight into the chemistry of this peroxide-activation system, we have investigated the PIFA (**1b**)/*tert*-butyl hydroperoxide system. We report herein the first example of conversion of aromatic hydrocarbons to quinones using the PIFA/TBHP system.

Treatment of PIFA with anhydrous TBHP in methylene chloride at room temperature leads to the release of oxygen gas and produces iodobenzene. However, the reaction of PIFA with TBHP was found to be very slow at –30 °C. Thus, the peroxyiodane **2b** generated in situ may serve as active oxygen source for the oxyfunctionalization of organic substrates at low temperature. With this aim, the oxidation of naphthalene (**4a**), representing one of the most electron-deficient arenes, to 1,4-naphthoquinone (**4b**) was first studied at –30 °C to optimize the yield.[6] In view of the solvent effect, five different solvents were selected for a screening of the oxidation activity of the present system: EtOAc, THF, acetone, MeCN and methylene chloride. The oxidation in methylene chloride or acetonitrile resulted in the formation of a comparable yield of **4b** (Table 1, entries 4 and 5), while use of ethyl acetate, THF and acetone gave very poor results. In a control experiment, in which either PIFA or TBHP was excluded, no oxidation

Table 1 Oxidation of Naphthalene (**4a**) with PIFA/TBHP System[a]



4a **4b**

Entry	Solvent	Conversion (%)[b]	Yield (%)[c]
1	EtOAc	0	0
2	Acetone	0	0
3	THF	5	N.d.
4	MeCN	35	30
5	CH_2Cl_2	50	45

[a] Substrate (2 mmol), PIFA (3 mmol), TBHP (10 mmol), $NaHCO_3$ (10 mmol), solvent (10 mL), –30 °C, 3 h.
[b] Determined by GC-MS with internal standard.
[c] Isolated yield based on the converted starting material.

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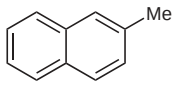
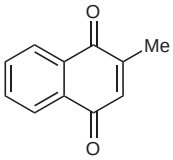
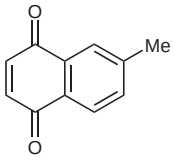
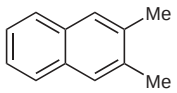
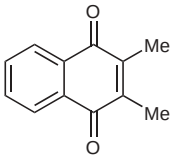
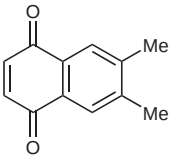
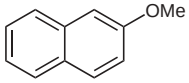
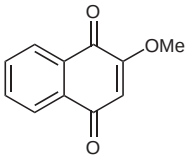
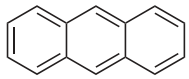
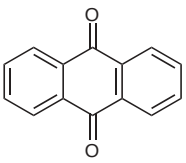
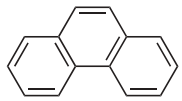
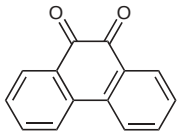
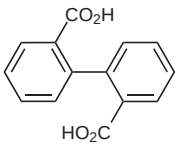
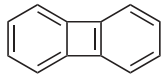
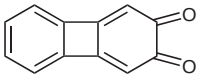
occurred or the starting material naphthalene (**4a**) was recovered completely; thus, both components are essential for the reaction.

Further oxidation of the quinones appears to be responsible as confirmed through an independent experiment in which suffered under the condition of run 5 (Table 1). When **4b** was treated with the PIFA/TBHP system under the identical condition 60% of **4b** was recovered after usual extraction and chromatography. The rest was mixture of other oxidation products, which were not identified. Working with an optimized condition, our attention was focused on oxidation activity and regioselectivity of the PIFA/TBHP system towards more electron rich-arenes as substrates. 2-Methyl-naphthalene (**5a**), 2,3-dimethyl-naphthalene (**6a**), and 2-methoxy-naphthalene (**7a**) were chosen as substrates for a comparative study (Table 2, entries 1, 2, and 3). Two tendencies can be seen from Table 2: (1) The conversion of arene rises with the number of electron-donating substituents at the aromatic ring while naphthalene (**4a**), the most electron-deficient one among the tested arenes **4a**–**10a**, shows the lowest reactivity [45% 1,4-naphthoquinone (**4b**) at 50% conversion; Table 1, entry 5]. Due to its higher reactivity 2-methyl-

Table 2 Oxidation of Arenes **5a**–**10a** with PIFA/TBHP System[a]

Entry	Substrate	Products		Conversion (%)[b]	Yield (%)[c]	Selectivity (%)
1	 **5a**	 **5b**	 **5c**	90	**5b** (55)[d] **5c** (5)[d]	91
2	 **6a**	 **6b**	 **6c**	>99	**6b** (60)[e] **6c** (7)[e]	95
3	 **7a**	 **7b**		>99	40[e]	100
4	 **8a**	 **8b**		>95	40[e]	
5	 **9a**	 **9b**	 **9c**	>95	**9b** (40)[e] **9c** (20)[d]	
6	 **10a**	 **10b**		>95	30[e]	

[a] Substrate (2 mmol), PIFA (3 mmol), TBHP (10 mmol), $NaHCO_3$ (10 mmol), CH_2Cl_2 (10 mL), –30 °C, 3 h.
[b] Determined by GC-MS with internal standard.
[c] Yields based on the converted starting material.
[d] Yields determined GC-MS with internal standard.
[e] Isolated yields.

naphthalene (**5a**) yields 55% 2-methyl-[1,4]-naphthoquinone (vitamin K_3)[7] (**5b**) at 90% conversion. The best quinone yield is obtained for 2,3-dimethyl-naphthalene (**6a**). (2) The high regioselectivities found compare well with known results from the literature.[8] In the case of 2-methyl-[1,4]-naphthoquinone (**5b**) a 91:9 ratio for 2- and 6-methyl-[1,4]-naphthoquinone (**5c**) and 95:5 for 2,3-dimethyl-naphthoquinone regioisomers **6b** and **6c** are obtained. These results remarkably differ from regioselectivities obtained with metal-catalyzed systems. For instance, in metalloporphyrin-catalyzed oxidation of **5a** selectivity was found to be 53%. The electron-rich arene 2-methoxy-naphthalene (**7a**) was quite succeptible towards oxidation and led exclusively to 2-methoxy-[1,4]-naphthoquinone (**7b**).[9]

Anthracene (**8a**) gave anthraquinone as the sole product. In the oxidation of phenanthrene (**9a**), phenanthrene-9,10-dione (**9b**) was obtained as the major product besides biphenyl-2,2′-dicarboxylic acid (**9c**)[10] in a ratio of 65:35. Biphenylene (**10a**) readily undergoes fast conversion to 2,3-biphenylenequinone (**10b**)[11] and some unidentified compounds. A plausible reaction mechanism for the generation of *t*-butylperoxy radical and oxygen transfer to naphthalene **4a** is displayed in Scheme 1. PIFA (**1b**) is converted with TBHP to peroxyiodane **2b** by exchanging two trifluoromethyl acetate groups for two *tert*-butylperoxy groups. The initial step of the decomposition of peroxyiodane **2b** would involve the homolytic cleavage of the weak iodine(III)–peroxy bond, generating *tert*-butylperoxy radical and iodo-benzene. The *tert*-butylperoxy radical has been shown to be an efficient radical oxidant with the highly electrophilic nature for the conversion of sulfides to sulfoxides.[12] Addition of *tert*-butylperoxy radicals to **4a** leads to the intermediary formation of 1,4-*bis*-*t*-butylperoxy-1,4-dihydro-naphthalene, which might constitute one of the possible reaction pathways. To investigate the fate of the *tert*-butylperoxy groups of **2b**, ^{1}H NMR experiments were carried out in $CDCl_3$ at room temperature and products were analyzed: Acetone, *tert*-butyl alcohol and iodo-benzene were detected. It is a well known fact that *tert*-butylperoxy radical undergoes β-scission yielding acetone and methyl radical or *tert*-butyl alcohol by abstracting a hydrogen atom (Scheme 2).[13]

Thus, the present study provided the first example of direct oxyfunctionalization of aromatic hydrocarbons to quinones using PIFA/TBHP system. This method may be applied to other arenes. Depending on the reactivity of the arene, 10 mmol scale may be employed. Further work on peroxide-activation system is in progress, and the results of these studies will be reported in the future.

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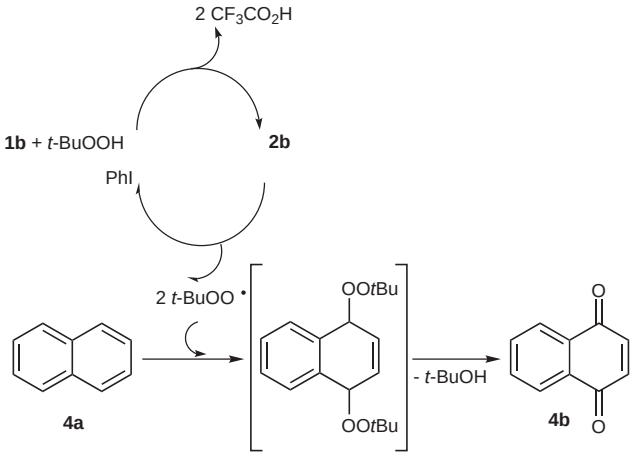
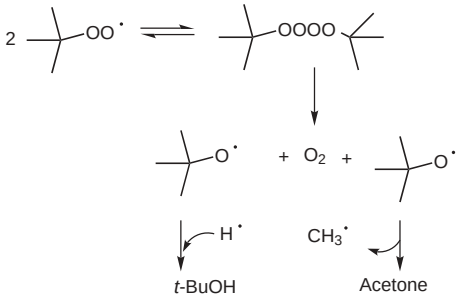


Scheme 1 Proposed mechanism for the generation of *t*-butylperoxy radical and oxidation of naphthalene to 1,4-naphthoquinone



Scheme 2 Decomposition mechanism of *t*-butylperoxy radical

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(6) **General Procedure for Oxidation of Arenes with PIFA/TBHP System:** (Caution! Although we have never experienced explosion, the oxidation of arenes with TBHP/PIFA system was carried out behind shields.) To a solution of arene (2 mmol) and anhyd TBHP (10 mmol) in 10 mL of CH_2Cl_2 at –30 °C was added $NaHCO_3$ (5 mmol). Then, a freshly prepared solution of PIFA (3 mmol) in 10 mL of CH_2Cl_2 was added within 2 h. The temperature was slowly increased to r.t. within 1 h. The suspension was filtered and the solution was washed with sat. $NaHCO_3$ solution and H_2O. The organic layer was dried over $MgSO_4$ and the solvent was removed at reduced pressure (5 °C/50 mbar). The products were purified on a silica gel column (40 g) by eluting with hexane–EtOAc (90:10). First fractions gave iodobenzene. Further elution afforded analytically pure quinones. In the case of **5a**, 2-methyl- and 6-methyl-1,4-naphthoquinone could not be separated. Compound **5b** was obtained from the mixture by crystallization from EtOH. The

mixture of both naphthoquinones **5b** and **5c** was also directly analyzed by ^{1}H NMR and GC-MS (equipped with a non-polar column using EI ionization at 70 eV). Compound **5b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.18 (d, 3 H, *J* = 1.5 Hz), 6.83 (q, 1 H, *J* = 1.5 Hz), 7.68–7.75 (m, 2 H), 8.01–8.12 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.5, 186.9, 150.1, 137.6, 135.6, 135.5, 134.2, 134.1, 128.5, 128.0, 18.4. Compound **6b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.11 (s, 6 H), 7.60–7.64 (AA part of AA′BB′ system, 2 H), 8.01–7.97 (BB′ part of AA′BB′ system, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 185.6, 144.2, 134.1, 133.0, 127.0, 13.7. Compound **6c**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.40 (s, 6 H), 6.90 (s, 2 H), 7.82 (s, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 186.2, 144.6, 139.4, 130.8, 128.5, 21.1. Compound **7b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.89 (s, 3 H), 6.15 (s, 1 H), 7.76–7.65 (m, 2 H), 8.12–8.03 (m, 2 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 185.6, 180.9, 161.3, 135.2, 134.2, 132.9, 132.0, 127.5, 127.0, 110.8, 57.3. Compound **10b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.62 (s, 2 H), 7.73 (s, 4 H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 180.4, 157.3, 148.6, 136.1, 124.9, 116.8.

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