Oxidation of Arenes to *para*-Quinones with Hydrogen Peroxide Catalyzed by Hexafluoroacetone Hydrate

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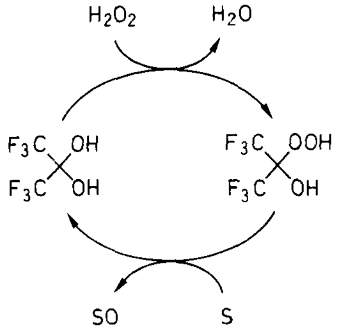
Received 24 August 1992; revised 2 October 1992

Various aromatic hydrocarbons were oxidized with aqueous hydrogen peroxide in the presence of hexafluoroacetone hydrate as catalyst to give *para*-quinones and/or the ring cleavage oxidation products. The regioselective oxidation of 2-methylnaphthalene to 2-methyl-1,4-naphthoquinone (vitamin K_3) was studied in detail.

Oxyfunctionalization of aromatic hydrocarbons with an inexpensive, easily available and convenient to handle oxidant such as aqueous hydrogen peroxide is an industrially important synthetic challenge. This reaction has a particular significance with regard to the preparation of 2-methyl-1,4-naphthoquinone (vitamin K_3) by the direct oxidation of 2-methylnaphthalene. The incentive to search for an alternative route of the above direct transformation derives from the fact that presently the hazardous chromium compounds are being used industrially as stoichiometric oxidants, which constitute a serious environmental problem. Alternative methods for oxidation of 2-methylnaphthalene to 2-methyl-1,4-naphthoquinone employ electrochemical oxidation[1], vapor-phase oxidation at elevated temperature over metal oxide catalysts,[2] cerium(IV) salts,[3] manganese(III) sulfate,[4] 3-chloroperoxybenzoic acid,[5] *tert*.-butyl hydroperoxide in the presence of molybdenyl acetylacetonate,[6] and hydrogen peroxide together with acid catalysts (cf. Table 1).



Scheme

2-Hydroperoxyhexafluoro-2-propanol, prepared from hexafluoroacetone or its hydrate and hydrogen peroxide, serves as a versatile oxygen transfer agent (Scheme) to oxidize alkenes to epoxides,[14] sulfides to sulfoxides or sulfones,[15] *tert*-amines to *N*-oxides,[15] aldehydes to carboxylic acids,[16] and ketones to esters (Baeyer–Villiger oxidation).[17] The literature also mentions use of this reagent for hydroxylation of aromatic compounds e.g. mesitylene to mesitol,[17] toluene to *p*-cresol,[18] anisole to *o*- and *p*-hydroxyanisole,[18] and phenol to polyhydroxybenzenes.[19] However, general application of this reagent for the oxyfunctionalization of arenes has so far not been reported. Herein we present our results on the oxidation of arenes with hydrogen peroxide catalyzed by hexafluoroacetone hydrate (Table 2).

The oxidation of 2-methylnaphthalene to 2-methyl-1,4-naphthoquinone (vitamin K_3) was examined in detail to optimize the yield of this commercially important food additive (entry 5, Table 2). The results on the variation of the amounts of catalyst and hydrogen peroxide and reaction temperature and time are given in Table 3. In a control experiment (run 1, Table 3), in which hexafluoroacetone hydrate was excluded, no oxidation occurred and the starting material 2-methylnaphthalene was recovered completely; thus, hexafluoroacetone hydrate is essential for the reaction. Increase in the catalyst amount resulted in an increase in the conversion of the arene but only a marginal increase in the yield of the quinone products (runs 2 and 3, Table 3) or even a decrease (run 4, Table 3). Further oxidation of the quinones appears to be responsible as confirmed through an independent experiment in which 2-methyl-1,4-naphthoquinone suffered under the condition of run 2 (Table 3) 16 % decomposition. Shorter reaction times resulted in moderate conversion and improved yields of the regioisomeric quinones (compare runs 3 and 5, Table 3). Increase in the reaction time (run 6, Table 3) led to higher conversion but lower yields, again due to further oxidation of quinones. The temperature has a more pronounced effect on the reaction; thus, at 45 °C the best yield of the quinones was obtained at moderate conversion (run 7, Table 3), while at 75 °C the conversion was complete but the yield of quinone was lower (run 8, Table 3). Lowering the amount of hydrogen peroxide led to an insignificant change in the conversions and yields (compare runs 3 and 9, Table 3). The optimal results with regard to quinone yield (51 % at 56 % conversion) constitutes run 7 (Table 3) which is specified in Table 2 as entry 5, and compares favorably with the ca. 60 % reported[12] in the palladium-catalyzed peracetic acid oxidation of 2-methylnaphthalene.

Additional examples, to probe the scope of this new oxidation, are given in Table 2. Benzene did not undergo reaction under these conditions; however, the alkylbenzenes *o*-xylene and 1,2,4,5-tetramethylbenzene gave the respective benzoquinones in modest yield. Oxidation of naphthalene afforded 1,4-naphthoquinone and *E*-3-(2-carboxyphenyl)propenoic acid, the latter presumably by ring-opening of the intermediary 1-naphthol. The electron-rich arene 2-methoxynaphthalene was quite succeptible towards oxidation (high conversion even at 40 °C) and led under these conditions exclusively to *E*-3-(2-carboxyphenyl)propenoic acid. Anthracene gave [10,10′-bianthryl]-9,9′-dione as the major product besides 9,10-anthraquinone and a small amount of *E*-3-(2-carboxynaphth-3-yl)propenoic acid. In the oxidation of phenanthrene, biphenyl-2,2′-dicarboxylic acid was isolated as the only product. Phenol readily undergoes fast conversion to 1,4-benzoquinone. Although the product yields are modest to moderate (Tables 2 and 3), the hexafluoro-

Table 1. Methods for the Oxidation of 2-Methylnaphthalene to 2-Methyl-1,4-naphthoquinone by Hydrogen Peroxide and Appropriate Catalysts

Reagent (%)/Catalyst (%)	Solvent	Temp. (°C)	Time (h)	Yield (%)	Ref.
H_2O_2 (60)/CF_3CO_2H	AcOH	80	7	36	7
H_2O_2 (30)	AcOH	80	10	23.5	8
H_2O_2 (31)	HCO_2H/ AcOH	40	4	22	9
H_2O_2 (60)/Pd-PSx8[a,b] (0.24)	AcOH	60	8	58.7	10
H_2O_2 (60)/PdPSx12[a,c] (0.24)	AcOH	50	8	59.4	11
H_2O_2 (60)/Pd-PSx8[b] (0.24)	AcOH	60	8	59.9	12
H_2O_2 (60)/Pd-PSx8[b] (0.24)	–	60	8	57.1	13

[a] The run with the best results was chosen.

[b] Polystyrene sulfonic acid resin, DOWEX 50W-x8, 200–400 mesh with 0.24 wt % Pd(II).

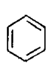
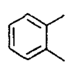
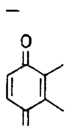
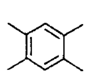
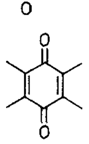
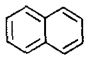
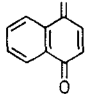
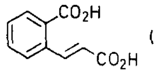
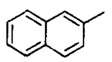
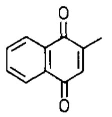
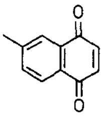
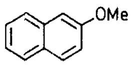
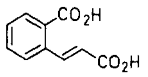
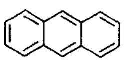
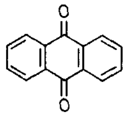
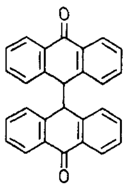
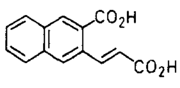
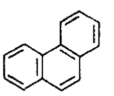
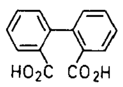
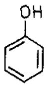
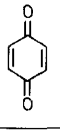
[c] Polystyrene sulfonic acid resin, DOWEX 50W-x12, 100–200 mesh with 0.24 wt % Pd(II).

acetone hydrate catalyzed oxidation of arenes constitutes a convenient method of general scope.

The catalytic cycle for the activation of the hydrogen peroxide and oxygen transfer to the substrate is displayed in the Scheme. Hexafluoroacetone hydrate is converted with hydrogen peroxide to 2-hydroperoxyhexafluoro-2-propanol by exchanging a hydroxy for a hydroperoxy group. The hydroperoxy alcohol possesses sufficient oxidation power to serve directly as oxygen transfer agent to the arene substrates. After the oxygen atom transfer, the hydroperoxyhexafluoro-2-propanol is converted back to the hexafluoroacetone hydrate and thereby the catalytic cycle is completed.

In conclusion, hexafluoroacetone hydrate, now made on commercial scale, acts as a convenient catalyst for the direct oxyfunctionalization of aromatic hydrocarbons to quinones by aqueous hydrogen peroxide. Preliminary results show that also the much cheaper hexachloroace-

Table 2. Oxidation of Arenes with H_2O_2 Catalyzed by Hexafluoroacetone Hydrate[a]

Entry	Substrate	Conv. (%)	Products (Yield (%))[b]
1		0	–
2		10	 (24)
3		58	 (19)
4		26	 (16)  (10)
5[c]		56	 (45)  (6)
6[d]		76	 (31)
7		90	 (22)  (47)  (4)
8		55	 (69)
9[e]		83	 (29)

[a] Substrate (20 mmol)/H_2O_2 (70%, 100 mmol)/Hexafluoroacetone hydrate (4 mmol)/1,2-dichloroethane (5 mL), 70 °C, 4 h.

[b] Based on the starting material converted.

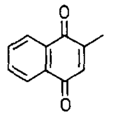
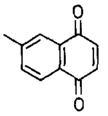
[c] Reaction conditions as in entry 7, Table 3.

[d] Reaction temperature 40 °C.

[e] Reaction time 1 h.

tone serves in this catalytic capacity, but the conversion and yields are usually lower and removal of the high-boiling and water-insoluble hexachloroacetone is tedious.

Table 3. Oxidation of 2-Methylnaphthalene[a] with H_2O_2 Catalyzed by Hexafluoroacetone Hydrate

Run	H_2O_2 (70%) (mmol)	$(CF_3)_2C(OH)_2$ (mmol)	Temp. (°C)	Time (h)	Conv. (%)	Yield (%)[b]	
							
1	100	–	60	3	–	–	–
2	100	1	60	3	29	21	4
3	100	4	60	3	74	25	4
4	100	8	60	3	96	18	2
5	100	4	60	1	55	39	6
6	100	4	60	6	95	23	4
7	100	4	45	3	56	45	6
8	100	4	75	3	100	27	4
9	40	4	60	3	72	27	4

[a] In all the runs 1.42 g (20 mmol) were used.

[b] Yields based on 2-methylnaphthalene converted. The rest was mixture of other oxidation products which were not identified.

All reagents were of commercial quality. Hexafluoroacetone hydrate was a generous gift from Hoechst and 2-methylnaphthalene from Degussa. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer and ^1H and ^{13}C NMR spectra were measured on Bruker AC 250 or Bruker AC 200 spectrometers. The mps were determined on a Büchi SMP 20 melting point apparatus. HPLC analysis was performed on a Kontron HPLC by using a silica gel column (4 mm x 25 cm) and the UV detector Anacomp 220.

General Oxidation Procedure:

For the oxidation of 2-methylnaphthalene the reactant quantities and reaction conditions are specified in Table 3. The product mixtures were analyzed by HPLC or by column chromatography on silica gel. The regioisomeric quinones were isolated as a mixture, their relative proportions were determined by ^1H NMR, and the quantitative results are given in Table 3.

Oxidation of Anthracene; Typical Procedure:

For the other substrates (Table 2), in a typical experiment a mixture of anthracene (20 mmol), aq H_2O_2 (70%, 100 mmol), hexafluoroacetone hydrate (4 mmol), and 1,2-dichloroethane (5 mL) were magnetically stirred at 40 or 70 °C for 1–4 h in a 25-mL roundbottom flask, which was fitted with a dry ice condensor and a N_2 balloon. The mixture was cooled to r.t., diluted with H_2O (20 mL), and extracted with Et_2O (2 x 30 mL). Insoluble material was removed by filtration and the organic layer was washed with H_2O, dried ($MgSO_4$), and the solvent evaporated. The oxidation products were separated by column chromatography on silica gel, further purified by crystallization, and identified by IR and ^1H NMR spectra, in some cases by comparison with the authentic sample.

(E)-3-(2-carboxynaphth-3-yl)propenoic Acid: yield 170 mg (4%); colorless plates ($EtOH/H_2O$), mp 189–190 °C.

IR (KBr): ν = 1690, 1630, 1615, 1410, 1400, 1280, 1210, 1130, 975, 910, 870, 785, 745 cm^{-1}.

^1H NMR ($CD_3OD/CDCl_3$): δ = 5.25 (d, J = 15.8 Hz, 1 H, =CH), 6.31 (s, 1 H, H_{arom}), 6.45 (m, 2 H, H_{arom}), 6.77 (m, 2 H, H_{arom}), 6.94 (s, 1 H, H_{arom}), 7.45 (d, J = 15.8 Hz, 1 H, HC=).

^{13}C NMR ($CD_3OD/CDCl_3$): δ = 120.9, 128.4, 128.6, 128.63, 128.9, 129.5, 133.1, 133.5, 133.7, 135.6, 137.6, 146.2, 169.9, 170.0.

Generous financial support by the Deutsche Forschungsgemeinschaft (SFB 347 "Selektive Reaktionen Metall-aktivierter Moleküle) and the Fonds der Chemischen Industrie are gratefully appreciated. We thank Dr. G. Goor and Dr. M. Bewersdorf (Degussa, A.G., Hanau) for calling attention to this oxidation problem and for stimulating discussions. We acknowledge J.P. Bialas for technical assistance and the Alexander von Humboldt Foundation for a fellowship to PAG.

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