A New Easy Access to Quinones from Iron Porphyrin-catalysed Oxidation of Methoxyarenes by Magnesium Monoperoxyphthalate

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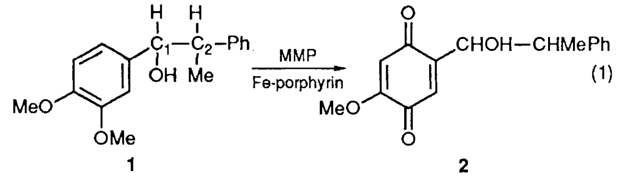
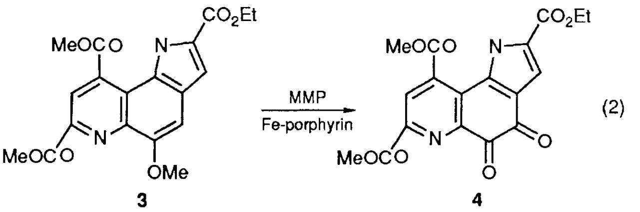
Electron-rich methoxyarenes were oxidized with high yields (55–100%) and under mild conditions to the corresponding paraquinones by magnesium monoperoxyphthalate in the presence of catalytic amounts of a water-soluble iron porphyrin; the reaction was used to prepare methoxatin.

Compound **1** has been used as a lignin model to study the mechanism of lignin degradation by lignin peroxidase,[1] because it undergoes oxidative cleavage of its C_1–C_2 bond in the presence of lignin peroxidase and H_2O_2.[2] In the course of a study of the oxidation of compound **1** by various chemical systems using an iron-porphyrin catalyst and an oxygen-atom donor, as potential models of lignin peroxidase, we observed that the oxidation of **1** by H_2O_2 in the presence of various iron-porphyrins gave products mainly from the cleavage of the C_1–C_2 bond whereas oxidation by Mg^{2+} monoperoxyphthalate (MMP) and water-soluble iron-porphyrins mainly gave the quinone **2** [eqn.(1)]. This Communication describes the latter reaction, and shows that, in a more general manner, quinones are formed in high yields upon oxidation of some methoxyarenes by MMP in the presence of catalytic amounts of a water-soluble iron-porphyrin. This method, which provides a new one-step route to quinones from methoxyarenes by using a readily available oxidant (MMP) under simple and mild conditions, was applied to prepare a triester of methoxatin, **4**, an orthoquinone of great biological interest, by oxidation of **3**, a methoxyarene precursor of methoxatin in the Corey synthesis[3] of **4** [eqn.(2)].

Progressive addition over 30 min at 20 °C of MMP (3 equiv.) to **1** dissolved in a mixture of MeCN and 0.1 mol dm^{-3} tartrate buffer pH 3 (1:4) containing a catalytic amount of a water-soluble tetraanionic iron(III)-porphyrin, led to quinone **2**, which was partly precipitated from the reaction mixture. Two catalysts containing sulphonato substituents at the *meso*-aryl groups of the porphyrin, the commercially available Fe^{III}(tspp) [iron-*meso*-tetrakis(4-sulphonatophenyl)porphyrin] and Fe^{III}(tdcspp) [iron-tetrakis(3-sulphonato-2,6-dichlorophenyl)porphyrin], a previously used lignin peroxidase





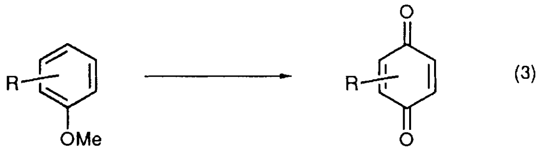
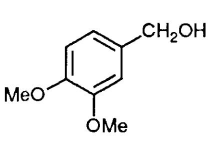
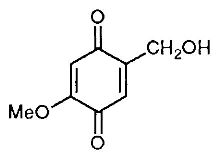
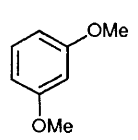
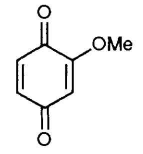
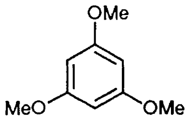
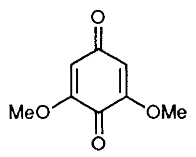


Table 1 Formation of quinones upon oxidation of methoxyarenes by MMP catalysed by Fe^{III}(TF$_4$PS$_4$P)

Starting compound	Quinone	Yield (%)[a]
1	**2**	55
3	**4**	55[b]
 **5**	 **6**	85
 **7**	 **8**	>95
 **9**	 **10**	>95

[a] *Conditions*: substrate : MMP : Fe(porphyrin) = 1 : 3 : 0.01 (0.02 mol dm^{-3} substrate) in 2.5 ml MeCN : 0.1 mol dm^{-3} tartrate buffer pH 3 (1 : 4) 1 h at 20 °C. Yields are based on the starting compound and determined by ^{1}H NMR analysis of the crude extract by CH_2Cl_2 in the presence of an internal standard. Actually, all the quinones were obtained in an almost pure crystalline state after CH_2Cl_2 extraction. Their ^{1}H NMR spectra were identical to those previously described (ref. 9 for **6** and **8**, 10 for **10** and 3 for **4**). [b] Due to the low solubility of **3**, a 1 : 1 mixture of MeCN and 0.1 mol dm^{-3} tartrate buffer pH 3 was used in this case.

model,[4] and two catalysts containing four sulphonato substituents on the β positions of the pyrrole rings,† Fe^{III}(tF$_4$pS$_4$p) [iron-*meso*-tetrakis(2,3,5,6-tetrafluorophenyl)tetrasulphonatoporphyrin] and Fe^{III}(tF$_5$pS$_4$p) [iron-*meso*-tetrakis(pentafluorophenyl) tetrasulphonatoporphyrin], were used. The best yields and selectivities were obtained with the latter two catalysts, as the ^{1}H NMR analysis of the crystalline product obtained in this case after extraction by CH_2Cl_2 showed that the quinone **2**‡ was almost pure (only containing trace veratraldehyde) (55% yield based on starting **1**). With the two former catalysts, **2** was also produced in satisfactory yield but with larger amounts of veratraldehyde as a secondary product.

Almost identical results were obtained when the reaction was performed under anaerobic conditions, but **2** was not formed in reactions performed in the absence of the iron-porphyrin.

Oxidation of other methoxyarenes by the Fe(tF$_4$pS$_4$p)–MMP system also gave the corresponding quinones with high yields under identical conditions (Table 1). Oxidation of veratryl alcohol **5** gave quinone **6**[5] as the only product extractable in CH_2Cl_2 with no trace of veratraldehyde. 1,3-Dimethoxybenzene, **7**, and 1,3,5-trimethoxybenzene, **9**, were oxidized to the corresponding quinones, **8** and **10** respectively, quantitatively. The reaction was applied to a methoxyarene for which the formation of a paraquinone was impossible. Oxidation of compound **3**, which is an intermediate in the Corey synthesis of methoxatin,[3] by the MMP–Fe(tF$_4$pS$_4$p) system gave the expected quinone **4** as the only product extracted by CH_2Cl_2 in good yield (55%).

When Fe(tF$_4$pS$_4$p) was replaced by Fe(tdcspp) or Fe(tspp), oxidation of the aforementioned methoxyarenes to the corresponding quinones was also observed but with lower yields in most cases, much larger amounts of veratraldehyde for **1** and **5** and very low yields in the case of **3**.

Quinones are usually prepared by oxidation of the corresponding phenols[7] or by oxidation of methoxyarenes by an excess of cerium salts.[3] The new method described allows an easy access to quinones from methoxyarenes in one step [eqn.(3)] (with no need to prepare the corresponding phenols) by using the commercially available oxidant MMP and an iron

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† The water-soluble porphyrins tF$_4$pS$_4$pH$_2$ and tF$_5$pS$_4$pH$_2$ were prepared by sulphonation of *meso*-tetrakis-(2,3,5,6-tetrafluorophenyl)porphyrin, tF$_4$ppH$_2$ and of *meso*-tetrakis(pentafluorophenyl)-porphyrin, tF$_5$ppH$_5$, according to a previously described procedure,[6] using oleum (10 h at 110 °C for tF$_4$ppH$_2$ and 140 °C for tF$_5$ppH$_2$) instead of concentrated sulphuric acid. UV-VIS and ^{1}H NMR spectra showed that four pyrrole β-hydrogens were replaced by SO_3H groups during the sulphonation reactions: redshift of the Soret peak was as expected for the introduction of electron-withdrawing substituents on pyrrole β-positions,[4] and ^{1}H NMR signals corresponding to four pyrrolic protons as expected for the four possible isomers derived from substitution of four pyrrole protons of tF$_4$ppH$_2$ and tF$_5$ppH$_2$ by SO_3H groups. tF$_4$pS$_4$pH$_2$: UV–VIS in 0.1 mol dm^{-3} phosphate buffer pH 7; λ(ε, dm^3 mmol^{-1} cm^{-1}) 426(210), 526(10.7), 593(4.6) and 672(1.5) nm; ^{1}H NMR δ (CD$_3$ OD + NaOD), 7.64 and 7.88(m), 4H, *para* H; 8.4, 9.08, 9.19 and 9.21, 4H, broad singlets, pyrrole H. tF$_5$pS$_4$pH$_2$: λ(ε) = 428(157), 530(8.9), 594(4.4) 672(1.4) nm; ^{1}H NMR: 8.47, 9.07, 9.18 and 9.2, 4H, broad singlets, pyrrole H. The detailed preparation and characterization of tF$_4$pS$_4$pH$_2$ and tF$_5$pS$_4$pH$_2$ (mixture of four isomers, tetrasodium salts) will be described elsewhere. Fe^{III}(tF$_4$pS$_4$p) and Fe^{III}(tF$_5$pS$_4$p) were prepared by treatment of the free base porphyrins with 10 equiv. of $FeCl_2$ in refluxing water under argon and in the presence of $Na_2S_2O_4$ (24 h). Isolation of the iron complexes as tetrasodium salts was done according to a technique described previously.[6] UV-VIS in 0.1 mol dm^{-3} phosphate buffer pH 3: λ(ε) = 400(107), 412(106), 504(10.7), 584(6.8), 632(4.6) for Fe^{III}(tF$_4$pS$_4$p) and 396(88.3), 414(94.2), 501(8.9), 581(5.0) and 632(3.6) nm for Fe^{III}(tF$_5$pS$_4$p). The starting porphryins tF$_4$ppH$_2$ and tF$_5$ppH$_2$ were prepared by a classical technique: J. S. Lindsey and R. W. Wagner, *J. Org. Chem.*, 1989, **54**, 828.

‡ Structure of **2**, obtained after recrystallization in EtOH, was completely established by ^{1}H NMR and elemental analysis. m.p. = 70 °C; ^{1}H NMR δ (CDCl$_3$): 1.31(3H,d,*J* 6.5Hz), 3.07(1H,q), 3.38(3H,s), 4.81(1H,dd,*J* 6, *J* 1.3 Hz), 5.89(1H,s), 6.4(1H,d,*J* 1.3 Hz), 7.14–7.31(5H).

catalyst,[8] under simple and mild conditions (1 h at 20 °C). It is noteworthy that good yields were obtained even for compounds having other easily oxidised functions such as **1**, **3** and **5**, indicating an interesting chemoselectivity of the MMP–Fe(tF$_4$pS$_4$p) system for electron-rich methoxyarenes.

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References

1 M. Tien, *CRC Crit. Rev. Microbiol.*, 1987, **15**, 141.

2 K. E. Hammel, B. Kalyanaraman and K. T. Kirk, *Biochemistry*, 1986, **83**, 3708.

3 E. J. Corey and A. Tramontano, *J. Am. Chem. Soc.*, 1981, **103**, 5599.

4 (*a*) F. Cui and D. H. Dolphin, *ACS Symp. Ser.*, 1989, **399**(2), 519; (*b*) D. H. Dolphin, T. Nakano, T. K. Kirk, T. E. Maione, R. L. Farrell and T. P. Wijesekera, *Patent PCT Int. Appl.* WO 88/07988, 1988.

5 The formation of quinone **6** was also reported to occur upon oxidation of **5** by KHSO$_5$ in the presence of soluble or supported iron-porphyrins: G. Labat and B. Meunier, *New J. Chem.*, 1989, **13**, 801 and G. Labat and B. Meunier, *J. Org. Chem.*, 1989, **54**, 5008.

6 M. F. Zipplies, W. A. Lee and T. C. Bruice, *J. Am. Chem. Soc.*, 1986, **108**, 4433.

7 (*a*) R. D. Jones, D. A. Summerville and F. Basolo, *Chem. Rev.*, 1979, **79**, 139; (*b*) H. Zimmer, D. C. Lankin and S. W. Horgan, *Chem. Rev.*, 1971, **71**, 229.

8 MMP was previously used for Mn-porphyrin-catalysed oxidations of alkenes and alkanes: C. Querci and M. Ricci, *J. Chem. Soc. Chem. Commun.*, 1989, 889; C. Querci and M. Ricci, *Tetrahedron Lett.*, 1990, **31**, 1779, and, in a more general manner, water-soluble Fe- or Mn-porphyrins have been used as catalysts for hydrocarbon oxidations: J. R. Lindsay Smith and D. N. Mortimer, *J. Chem. Soc., Chem. Commun.*, 1985, 410 (see also ref. 6).

9 S. D. Haemmerli, H. E. Schoemaker, H. W. H. Schmidt and M. S. A. Leisola, *FEBS Lett.*, 1987, **220**, 149.

10 St. Berger and A. Rieker, *The Chemistry of the Quinonoid Compounds Part 1*, ed. S. Patai, John Wiley, 1974, ch. 4, p. 163.