Selective Oxidative Cleavage of 1,2-Dimethoxyarenes to Muconic Diesters Catalysed by an Iron β-Sulfonated-tetrakis(pentafluorophenyl)porphyrin

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The water-soluble iron(III)[TF_5PS_4**P** = *meso*-tetrakis(pentafluorophenyl)-β-tetrasulfonatoporphyrin] catalyses the selective oxidation, by magnesium monoperoxyphthalate (or H_2O_2), of 1,2-dimethoxyarenes bearing an electron-withdrawing substituent (CN, CHO, COR) to muconic dimethyl esters which are formed in 30–40% yield and are the only reaction products obtained after CH_2Cl_2 extraction.

Iron-containing dioxygenases catalyse the oxidative cleavage of catechols to *cis,cis*-muconic acids.[1] However, very few enzymatic or model systems have been reported so far that catalyse the oxidative cleavage of non-hydroxy aromatic compounds to muconic acid derivatives. Benzene is oxidized by cytochrome P450 enzymes with the minor formation of muconaldehyde derivatives.[2] The oxidation of veratryl alcohol catalysed by lignin peroxidase mainly leads to veratraldehyde. However, under aerobic conditions, small amounts of lactones derived from the intermediate formation of muconic acid diesters were also detected.[3] Such ring cleavage products were also detected during the biomimetic oxidation of veratryl alcohol by Bu^{t}OOH in the presence of iron–protoporphyrin IX.[4]

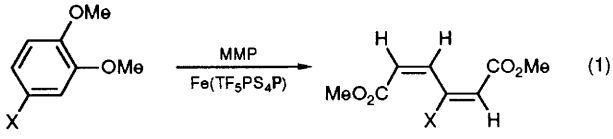
Recently, methoxyarenes were reported to be oxidized to quinones by biomimetic systems using a water-soluble iron-porphyrin catalyst and magnesium monoperoxyphthalate (MMP)[5] or $KHSO_5$[6] as oxidants. For instance, MMP in the presence of $Fe^{III}[TF_5PS_4P$ = *meso*-tetrakis(pentafluorophenyl)-β-tetrasulfonatoporphyrin] was reported to oxidize 1,2-dimethoxyarenes bearing an alkyl substituent to methoxyquinones in good yields.[5] Here, we show that $Fe^{III}(TF_5PS_4P)$ catalyses the selective oxidation by MMP (or H_2O_2) of 1,2-dimethoxyarenes substituted with an electron-withdrawing group to muconic dimethylesters according to eqn. (1). This novel reaction provides a new one-step access to muconic dimethylesters bearing various functions in β-position.

In a typical experiment, an aqueous solution of MMP (100 mg ml^{-1}) was added dropwise to a 2.5×10^{-2} mol dm^{-3} solution of the dimethoxyarene **1a** in a 1 : 4 mixture of MeCN and 0.1 mol dm^{-3} tartrate buffer pH 3 maintained at 0 °C and containing a catalytic amount of the water-soluble $Fe^{III}(TF_5PS_4P)$† (**1a**: catalyst molar ratio = 250). CH_2Cl_2 extracts of the reaction mixture only contained **2a** and **1a**, as shown by ^1H NMR spectroscopy. After the addition of *ca.* 3.5 equiv. of MMP (relative to **1a**), **1a** was completely consumed and **2a** was the only detected product extracted by CH_2Cl_2. Similar experiments performed on dimethoxyarenes bearing CN or COR substituents led to the corresponding muconic diesters **2** with yields between 30 and 40% (Table 1). Isolation of these products was very easy as they were the only compounds extracted by CH_2Cl_2. After purification by single column chromatography (SiO_2, hexane : AcOEt 70 : 30 for **2a** and **2d**, 50 : 50 for **2b** and $CHCl_3 : Et_2O$ 50 : 50 for **2c**), compounds **2** were completely characterized‡ by elemental analysis (C, H, N), mass spectrometry and ^1H NMR spectroscopy (Table 1). All of them exhibited the characteristic pattern of the three vinylic hydrogens of (2*E*, 4*Z*)-3-substituted-muconic diesters[7] (three doublets of doublets at *ca* 6.1, 7.1 and 6.5; $J \approx 12$, 1 and 2 Hz) (Table 1).

Table 1 Characteristics of the *cis,cis*-muconic dimethylesters formed by oxidation of 1,2-dimethoxyarenes[a]

Substrate	MMP : **1** ratio used[b]	Yield of **2** (%)	M.p./°C (crystallization solvent)	^1H NMR data for X[c]
1a[d]	3.5	35	60 (CH_2Cl_2–hexane)	9.51 (1H, s)
1b	3.5	35	Oil	2.40 (3H, s)
1c	4	40	60 (Et_2O–pentane)	
1d	2.5	30	150 (CH_2Cl_2–hexane)	1.39 (3H, d, *J* 6.8) 4.16 (1H, q, *J* 6.8) 7.09–7.3 (5H, m)

[a] Conditions: dropwise addition of MMP in H_2O (100 mg ml^{-1}) to a 2.5×10^{-2} mol dm^{-3} solution of **1** (1.7×10^{-3} mol) in MeCN : 0.1 mol dm^{-3} tartrate buffer (1 : 4), pH 3, containing $Fe^{III}(TF_5PS_4P)$ 0.5×10^{-3} mol dm^{-3}, at 0 °C. [b] Amount of MMP added until complete consumption of starting **1** (MMP : **1** molar ratio). [c] ^1H NMR data for the X part of **2** ($CDCl_3$, δ relative to Me_4Si, *J*/Hz); the data concerning the 3 vinylic H are very similar for each compound and are given in footnote ‡. [d] Data for **1a** are in complete agreement with those reported previously.[7]



(1)

1

2

1a; X = CHO
1b; X = COMe
1c; X = CN
1d; X = COCH(Me)Ph

Using H_2O_2 (5 equiv. relative to **1**) instead of MMP also afforded the muconic derivatives **2** but in lower yields (15 for **2b** and 25% for **2c**). However, it is noteworthy that $Fe(TF_5PS_4P)$ seems unique in its ability to catalyse the oxidation of dimethoxyarenes **1** into muconic diesters **2**, as the two other water-soluble iron porphyrins used in this study, Fe^{III}[TPPS = *meso*-tetrakis(4-sulfonatophenyl)porphyrin] and Fe^{III}[TDCPPS = *meso*-tetrakis(2,6-dichloro-3-sulfonatophenyl)porphyrin],[8] were found unable to catalyse the formation of **2** under identical conditions. The former was completely bleached after addition of a few equivalents of MMP without significant transformation of **1** while the latter led to partial substrate consumption without formation of **2**. Dioxygen was not involved in muconic diester formation as identical results were obtained under anaerobic conditions.

The oxidative cleavage of dimethoxyarenes **1** by the MMP (or H_2O_2)–$Fe(TF_5PS_4P)$ system is a novel reaction which leads to a one-step synthesis and easy isolation of muconic dimethylesters bearing an electron-withdrawing group. The reaction is compatible with the presence of aldehyde, cyano and keto functions on the starting molecule. Moderate yields (30–40%) are obtained, presumably because of further oxidations of the very reactive muconic diesters, but only one product is obtained after CH_2Cl_2 extraction.

This cleavage reaction of dialkoxyarenes has very few chemical and biochemical precedents in the literature.[3,4] It should involve several steps (insertion of two oxygen atoms and cleavage of a C–C bond) and the particular ability of $Fe(TF_5PS_4P)$ to catalyse it in a selective manner, contrary to other water-soluble iron porphyrins not containing electron-withdrawing β-substituents on the pyrroles, should be due to the specific properties of the high-valent iron–oxo species formed by reaction of MMP with $Fe(TF_5PS_4P)$ (formally a Fe^{V}=O species).[9] In that respect, it is noteworthy that $Fe(TF_5PS_4P)$ is able to catalyse the multi-step oxidation of **1** to **2** with 100 turnovers without important degradation.

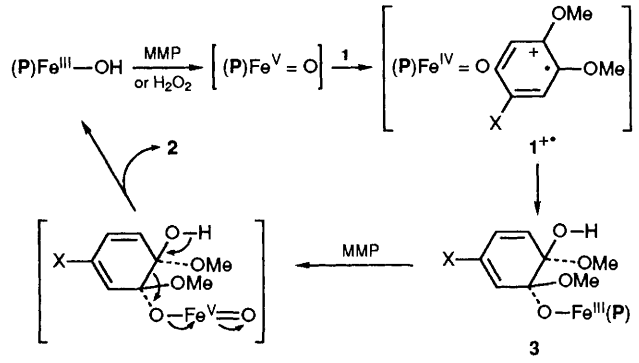
† The characterization of $TF_5PS_4PH_2$, which was obtained in 50% yield (it represents 70% of the reaction mixture) by sulfonation of TF_5PPH_2 [= *meso*-tetrakis(pentafluorophenyl)porphyrin] using oleum for 10 h at 140 °C, according to ref. 5, was further done after treatment by PCl_5–$POCl_3$, at the level of its sulfochloride derivative $TF_5P(SO_2Cl)_4PH_2$ which is neutral and very soluble in organic solvents (UV–VIS in CH_2Cl_2: 439, 536, 612 and 670 nm). Its mass spectrum (chemical ionization with NH_3): 1369, M^+, 7%; 1305, $[M - SO_2]^+$, 27%; 1271, $[M - SO_2Cl + 1]^+$, 100%; 1207, $[M - SO_2Cl - SO_2)^+$, 22%, confirmed that the pentafluorophenyl groups remained intact and that sulfonation occurred on the β-pyrrolic positions. Its ^1H NMR spectrum showing only two sets of signals for pyrrole H and NH with a 4H : 2H ratio was in agreement with a tetrasulfonation of the tetrapyrrole β-positions. The presence of only singlets for pyrrole H (δ 9.63, 9.51, 9.37 and 8.81) and the appearance of NH as a singlet at δ −2.2 is expected for a mixture of the four possible isomers obtained by introduction of only one sulfonato group on each pyrrole ring. *A priori*, a total of six pyrrolic protons singlets could be expected for these four isomers. However, some of these protons could have identical chemical shifts because of almost identical chemical environments, explaining why only four singlets are observed.

‡ *Selected spectroscopic data*: **2a**: mass spectrum (chemical ionization with NH_3): $[M + NH_4]^+$ 95%, $[M + 1]^+$ 100%; ^1H NMR (conditions in Table 1) (*J*/Hz): 6.17 (1H, dd, *J* 12 and 0.65), 6.55 (1H, dd, *J* 2.2 and 0.65) 7.04 (1H, dd, *J* 12 and 2.2), 3.78 (3H, s), 3.65 (3H, s).

2b: mass: $[M + NH_4]^+$ 50%, $[M + 1]^+$ 100%; ^1H NMR: 6.10 (1H, dd, *J* 11.7 and 1), 6.44 (1H, dd, *J* 2.2 and 1), 7.19 (1H, dd, *J* 11.7 and 2.2), 3.74 (3H, s), 3.64 (3H, s).

2c: mass: $[M + NH_4]^+$ 100%; ^1H NMR: 6.16 (1H, dd, *J* 12 and 1), 6.52 (1H, dd, *J* 2 and 1), 7.15 (1H, dd, *J* 12 and 2), 3.78 (3H, s), 3.76 (3H, s).

2d: mass: $[M + NH_4]^+$ 100%, $[M + 1]^+$ 80%; ^1H NMR: 6.07 (1H, dd, *J* 11.6 and 0.8), 6.43 (1H, dd, *J* 2.2 and 0.8), 7.03 (1H, dd, *J* 11.6 and 2.2), 3.63 (6H, s). The ^1H NMR signals of the X group of compounds **1** are described in Table 1.



Scheme 1

According to the known properties of such (porphyrin) Fe^{V}=O species,[9] a possible mechanism (Scheme 1) would involve (*i*) the formation of a radical cation of **1** and a Fe^{IV}=O species, (*ii*) the addition of H_2O at the cationic site and Fe^{IV}=O at the radical site of $\mathbf{1}^{+\cdot}$ leading to the intermediate formation of a Fe^{III}–cyclohexadienolate **3**, (*iii*) oxidation of the Fe^{III} of **3** by MMP, and (*iv*) cleavage of a C–C bond of **3**.[10] The particular ability of the MMP–Fe(TF_5PS_4**P**) system to perform this reaction should be due to a very good control of the intermediates $\mathbf{1}^{+\cdot}$ and **3** by the Fe^{IV}=O and Fe^{III} states of the catalyst. The mechanism of cytochrome P-450-dependent oxidation of benzene to muconaldehyde is not known;[2] at least some of its steps could be similar to those of Scheme 1.

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