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An efficient approach for aromatic epoxidation using hydrogen peroxide and Mn(III) porphyrins

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Efficient epoxidation, in very high conversions and selectivities, of aromatic hydrocarbons with hydrogen peroxide, in the presence of Mn^{III} porphyrins [Mn(TDCPP)Cl, Mn(βNO_2TDCPP)Cl, Mn(TPFPP)Cl] as catalysts is described; naphthalene and anthracene afford the *anti*-1,2:3,4-arene dioxides whereas with phenanthrene the 9,10-oxide is obtained.

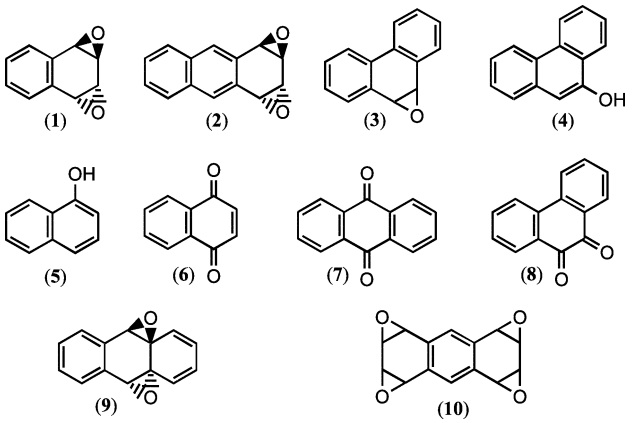
The formation and role of arene oxides during the metabolism of mono- and poly-cyclic aromatic hydrocarbons (PAHs) is an aspect with great significance for toxicological and carcinogenic studies.[1] These oxides are also important precursors in the synthesis of antibiotics,[2] tumour inhibitors[3] and in several asymmetric routes leading to potentially active biological molecules.[4]

Diepoxides are usually obtained in low yields from dibromoacetates and from the singlet oxygen reaction with conjugated dienes, followed by thermal or photochemical rearrangement of the endoperoxide affording the *syn*-isomers of the diepoxide. Those described procedures are expensive multi-step or time-consuming reactions and, in some cases, enzymatic or chemoenzymatic synthesis are also involved.[3,5]

The few reports on the direct epoxidation of aromatic hydrocarbons deal with inefficient systems, especially for weakly activated substrates. For instance, with an excess of *m*-chloroperbenzoic acid, naphthalene affords the *anti*-1,2:3,4-naphthalene dioxide (**1**) in 15–20% yield,[6,7] whereas phenanthrene can give rise to phenanthrene oxide (**3**), under the same conditions, at moderate yields (59%).[4] As far as we know, the diepoxide (**2**) and the tetraepoxide (**10**) of unsubstituted anthracene have not yet been reported in the literature.

The three aromatic hydrocarbons have different reactivities towards epoxidation. The 9,10-bond of phenanthrene is characterised by a very high π-bond order, which reacts more readily than the other bonds. On the other hand, the 9,10-positions of anthracene undergo oxidative reaction to give mainly the quinone (**7**), even in the presence of *m*-chloroperbenzoic acid.[3]

The cytochrome P450 enzymes are known to catalyse several *in vivo* oxygenations.[8] In recent years, several biomimetic approaches to cytochrome P450 activity have been achieved with several metalloporphyrins and various oxygen atom donors. The use of robust and easily obtainable metalloporphyrins as catalysts and of hydrogen peroxide as oxidant have led to efficient and ecologically clean procedures to perform many oxidative reactions.[9–13]



The *in vitro* aromatic epoxidation in the presence of biomimetic P450 models has been reported for phenanthrene[14] and the 9,10-phenanthrene oxide (**3**) was obtained. For naphthalene, the biomimetic oxidation reaction, catalysed by metalloporphyrins and in the presence of several oxidants, was reported to give rise only to aromatic hydroxylation, affording naphthols or 1,4-naphthoquinone (**6**).[15]

Here we report the results obtained on the oxidation of naphthalene, anthracene and phenanthrene with hydrogen peroxide (Table 1) catalysed by easily accessible manganese porphyrins (Scheme 1).[16–18] The reactions were carried out in the presence of ammonium acetate, as a required co-catalyst for the desired heterolytic cleavage of H_2O_2.[11]

The reaction products were isolated by preparative thin layer chromatography (silica gel 60 DGF_{254}) using CH_2Cl_2 as eluent for naphthalene reactions and a mixture of CH_2Cl_2:petroleum ether (4:1) for the anthracene and phenanthrene reactions. The character-

Table 1 Oxidation of aromatic hydrocarbons with hydrogen peroxide catalyzed by Mn(III) porphyrins[a]

	Naphthalene (6 h reaction time)			Anthracene (2 h reaction time)			Phenanthrene (3 h reaction time)		
	3.5 mmol of H_2O_2 added			1.2 mmol of H_2O_2 added			1.8 mmol of H_2O_2 added		
Catalyst	Conv. (%)[b]	Products[c]	Sel. (%)[b]	Conv. (%)[b]	Products[c]	Sel. (%)[b]	Conv. (%)[b]	Products[c]	Sel. (%)[b]
Mn(TDCPP)Cl (**I**)	91	**1**	81	100	**2**	74	100	**3**	91
Mn(βNO_2TDCPP)Cl (**II**)	83	**1**	81	100[d]	**2**	64	100	**4** + **8**	58 + 42
Mn(TPFPP)Cl (**III**)	44	**5**	62	17	**7**	100	65	**4** + **8**	41 + 59
No catalyst	0	—	—	0	—	—	0	—	—

[a] Reaction conditions: substrate (0.3 mmol), catalyst (1 μmol) and ammonium acetate (0.2 mmol) were dissolved in 2 ml of CH_3CN [anthracene was dissolved in CH_2Cl_2–CH_3CN (1:1)] and stirred at room temperature. Aqueous H_2O_2 (30% w/w) was diluted in CH_3CN (2:5) and added to the reaction mixture in 37.5 μl aliquots every 15 min. [b] Conversion and selectivity are based on the ^1H NMR of the total reaction mixture. [c] Main products. [d] After 3 h of reaction and addition of 1.8 mmol of H_2O_2.

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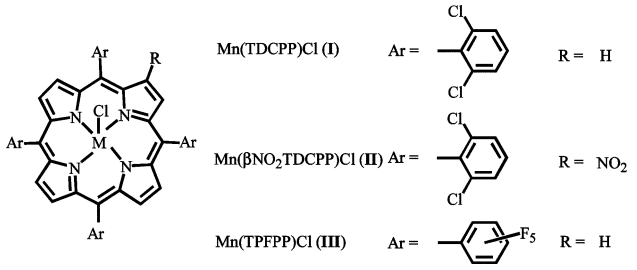

Scheme 1

isation of the products was made by NMR techniques, namely ^{1}H, ^{13}C, COSY, NOESY, HSQC and HMBC and mass spectrometry. The conversion percentages and products selectivity were determined directly from the ^{1}H NMR spectra of the reaction mixtures.

In the presence of Mn(TDCPP)Cl (**I**), naphthalene and anthracene were oxidised with high selectivity to the corresponding *anti*-1,2:3,4-arene oxides **1** (81%) and **2** (74%), at 91 and 100% of conversion, respectively. Keeping in mind that the formation of a diepoxide requires two cycles, the turnover numbers obtained with catalyst **I** were 442 for diepoxide **1** and 444 for diepoxide **2**. These results demonstrate that we are in the presence of a very useful procedure for the synthesis of **1** [19] and **2**.[20] Quinones **6** (12%) and **7** (7%) were detected only as minor products, as well as the *syn*-isomers of the dioxides **1** (7%) and **2** (9%).[21] In the case of anthracene oxidation reactions, small quantities of *anti*-9,9a:4a,10-anthracene dioxide **9** (3%)[22] and 1,2:3,4:5,6:7,8-anthracene tetraoxide **10** (5%)[22] were also observed. Compound **10** was observed in 26% yield after 3 h of reaction with catalyst **I**. Mn(βNO_2TDCPP)Cl (**II**) gave rise to similar results on the oxidation of naphthalene and anthracene. The tetraoxide **10** was observed as the main product in 42% yield after 6 h of reaction with catalyst **II**.

The oxidation of phenanthrene by porphyrin **I** showed high selectivity for epoxidation of the 9,10-bond,[3,14] affording 91% of the epoxide **3**. With both catalysts **I** and **II** complete phenanthrene conversions were obtained. Catalyst **II** afforded compound **4** as the major product (58 %) and **8** as the minor one (42%).

With Mn(TPFPP)Cl (**III**) the aromatic hydroxylation of the substrates and the transformation of the phenols to the corresponding quinones were always the main transformations observed. These results are in agreement with our previous studies with catalyst **III**, which showed high chemoselectivity for aromatic hydroxylation.[12] With this catalyst, naphthalene was mainly transformed into 1-naphthol **5** (62%) and 1,4-naphthoquinone **6** (15%), whereas the dioxide **1** was obtained with 20% selectivity. Anthracene gave 100% selectivity for the anthraquinone **7**.

The oxidation of phenanthrene in the presence of catalyst **III** afforded only compounds **4** and **8** with 41 and 59% selectivity, respectively.

We also tried to oxidise benzene under the above oxidative conditions, but after 14 h of reaction only a very small product peak (< 5%, *m*/*z* $M^{+\cdot}$ 94) was detected by GC–MS. The total amount of this compound did not allow its identification.

Knowing that one of the main applications of the oxygenation reactions using biomimetic models of cytochrome P450 is the preparation of xenobiotic metabolites, it can be concluded that the reactions described in this work open a potential and fascinating way to the synthesis of polycyclic aromatic hydrocarbon metabolites or corresponding precursors. These catalytic reactions can also become new and efficient ways for a researcher to transform polycyclic aromatic hydrocarbons into other functionalised compounds.

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19 Spectroscopic data for **1**: ^{1}H NMR: δ 3.73–3.74 (m, 2H, H-1,4), 4.01–4.02 (m, 2H, H-2,3), 7.35–7.37 (m, 2H, H-6,7), 7.43–7.46 (m, 2H, H-5,8); ^{13}C NMR: δ 52.0 (C-1,4), 54.7 (C-2,3), 129.4 (C-6,7), 131.47 (C-4a,8a), 131.50 (C-5,8). MS (EI) *m*/*z* (rel. int. %): 160 ($M^{+\cdot}$, 23). The melting point (96–98 °C) compares favourably with that described (99–100 °C) in ref. 6.
20 Spectroscopic data for **2**: ^{1}H NMR: δ 3.94–3.95 (m, 2H, H-1,4), 4.07–4.09 (m, 2H, H-2,3), 7.51–7.54 (m, 2H, H-5,8), 7.81–7.84 (m, 2H, H-6,7), 7.91 (s, 2H, H-9,10); ^{13}C NMR: δ 52.6 (C-1,4), 54.8 (C-2,3), 127.2 (C-6,7), 127.7 (C-5,8), 128.4 (C-9a,9b), 131.7 (C-9,10), 133.3 (C-8a,10a). MS (EI) *m*/*z* (rel. int. %): 210 ($M^{+\cdot}$, 32).
21 Spectroscopic data for the *syn*-isomer of **1**: ^{1}H NMR: δ 3.93–3.95 (m, 2H, H-2,3), 4.01–4.02 (m, 2H, H-1,4), 7.41–7.44, 7.65–7.68 (m, 4H, H-5,6,7,8). Spectroscopic data for the *syn*-isomer of **2**: ^{1}H NMR: δ 3.98–4.00 (m, 2H, H-2,3), 4.16–4.18 (m, 2H, H-1,4), 7.55–7.57, 7.88–7.90 (m, 4H, H-5,6,7,8), 8.15 (s, 2H, H-9,10).
22 Spectroscopic data for **9**: ^{1}H NMR: δ 4.78 (s, 2H, H-9,10), 6.86–6.88 (m, 4H, H-1,2,3,4), 7.41–7.44 (m, 4H, H-5,6,7,8). Spectroscopic data for **10**: ^{1}H NMR: δ 3.70–3.72 (m, 4H, H-1,4,5,8), 4.00–4.02 (m, 4H, H-2,3,6,7), 7.50 (s, 2H, H-9,10).