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Catalytic oxidative degradation of *s*-triazine and phenoxyalkanoic acid based herbicides with metalloporphyrins and hydrogen peroxide: Identification of two distinct reaction schemes

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ABSTRACT

Oxidative degradation of the herbicides atrazine (**1**), atraton (**2**), ametryn (**3**) and mecoprop (**4**), was carried out with hydrogen peroxide and metalloporphyrins as catalysts. Two different reaction conditions were studied, the first involving Mn(TDCPP)Cl in an aprotic solvent with buffer (**S-I**), and the second using Fe(TPFPP)Cl in a protic solvent (**S-II**). Reaction products were characterized, and based on these it is shown that there are two distinct reaction schemes.

In the case of the **S-I** conditions, it is suggested that the *s*-triazines were oxidized through hydroxylation of the alkyl side chains followed by dealkylation, while **S-II** was ineffective for these reactions. In contrast, mecoprop, was oxidized with high efficiency by **S-II**, leading to decarboxylation and further oxidation, while in the presence of **S-I**, low substrate conversion was observed, and reaction resulted mainly from oxidation at the benzyl position. Sulfoxidation of ametryn was observed with both systems.

The different reactivity shown by the two systems supports the involvement of different reactive species, which we assign to the oxo and hydroperoxy complexes. These routes show similarities with metabolic pathways, with the reactivity pattern of **S-I** analogous to the reported metabolism of these pollutants with cytochrome P450 enzymes, while **S-II** catalyses mecoprop decarboxylation *via* a similar pathway to that seen with peroxidase catalysed reactions.

1. Introduction

The oxygenation reactions of various substrates with metalloporphyrins have been reported to lead to new, more selective or "cleaner" procedures, with potential applications in areas including the fine chemicals industry and pollutant degradation [1–3]. Within such a Green Chemistry context, hydrogen peroxide is a very attractive oxidant [4,5]. However, different oxidation behaviour may be found for the same substrate, depending both on the metalloporphyrin and the reaction medium used [6–10]. To understand what causes such differences, and to be able to predict the appropriate reaction conditions for a specific reaction pathway, there is an urgent need for more detailed knowledge of the reaction mechanisms involved, in particular regarding the unambiguous assignment of the oxidizing species [11,12].

In previous studies on catalytic oxidation reactions with synthetic metalloporphyrins in the presence of either hydrogen peroxide [13] or hypochlorite [14], we have obtained experimental support for the formation of two distinct oxidizing species, with inherently different reactivity.

In many cases, a strong link is seen between the reactivity in these systems and those in biological ones, such as the reactivity of cytochrome P450. With certain enzymes, a high-valent oxo-species [porphyrin$^{\bullet+}$Fe(IV)═O] (formally equivalent to [Fe(V)═O]), has been suggested to be the main active oxidant and evidence for the existence of this intermediate has been presented [15]. In cytochrome P450, a hydroperoxy species [Fe(III)–O–O–H], has also been proposed as an intermediate in certain oxygenation reactions [16–18].

Mechanistic studies on model metalloporphyrin systems thus have the joint advantages of helping the design of reaction conditions for a particular oxidative degradation route, and elucidating the reactions of certain enzymes, such as cytochrome P450, in xenobiotic metabolism, thus complementing results from *in vivo* and *in vitro* studies using highly purified enzymes, but avoiding their ethical or economic drawbacks [19–22].

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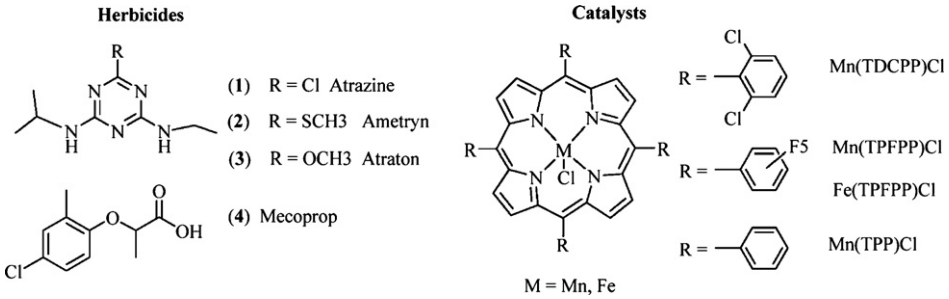


Fig. 1. Structure of herbicides and catalysts used in catalytic oxidations.

Oxidative pathways have proved particularly useful for the degradation of pesticides in both thermal [23] and photochemical reactions [24]. The *s*-triazines atrazine (**1**), atraton (**2**) and ametryn (**3**) are extensively used herbicides, with high persistence in the environment (Fig. 1) [25]. The high standard reduction potentials of these compounds make them difficult to oxidize [26]. Mecoprop is a chlorophenoxy propionic acid herbicide, also widely used to control broad-leaved weeds [27] (Fig. 1). All four herbicides are commonly found in surface and underground waters, from which there are indications that they may enter the food chain [28].

Although considerable insight has been obtained on the photooxidative degradation of triazines [24,30] and mecoprop [27], in particular in the presence of metalloporphyrins, much less is known about the thermal oxidation of these substrates with porphyrin catalysts [31].

We have, therefore, carried out a detailed study of the degradation of these herbicides (**1**–**4**) using different metalloporphyrin systems, in particular, system I, involving Mn(TDCPP)Cl in aprotic solvent with buffer (which we will term **S-I**), and system II, using Fe(TPFPP)Cl in protic solvent (**S-II**). Detailed isolation and characterization of the products were carried out, and, where possible, reaction intermediates identified to provide information on the oxidation mechanistic pathways. Reaction products will be compared with those reported for oxidation of these substrates by enzymes such as cytochrome P450 and peroxidases.

2. Experimental

2.1. General details

GC-FID analyses were performed with an Agilent 6890 GC system using hydrogen as the carrier gas (55 cm/s). The gas chromatographic conditions were: initial temperature (70 °C, 1 min); temperature rate (18 °C/min); final temperature (290 °C); injector temperature (290 °C); detector temperature (300 °C). Fused silica Supelco capillary columns SPB-5 (30 m × 0.25 mm i.d.; 0.25 μm film thickness) were used.

GC–MS analyses were performed using an Agilent 5973 mass selective detector coupled to the Agilent 6890 GC System plus, operating in electron impact mode, equipped with an HP-5MS capillary column (12 m × 0.20 mm i.d.; 0.33 μm film thickness) using helium as the carrier gas (1 mL/min). The temperature program used was: initial temperature (120 °C, 2 min); temperature rate (20 °C/min); final temperature (270 °C); injector 240 °C; the transfer line was held at 280 °C.

HPLC analysis was performed with an Agilent 1100 series system equipped with a reverse phase C18, Zorbax ODS column (220 mm × 4.5 mm i.d., 5 μm) and an injector with a loop of 20 μL. For *s*-triazine analysis the mobile phase was (50:50, v/v) acetonitrile:aqueous ammonium acetate (0.15%); flow rate, 1.4 mL/min with the UV-detector set at 222 nm. For mecoprop analysis the mobile phase was (75:25, v/v) methanol:0.025 M KH_2PO_4, pH 3, the flow rate was 1.2 mL/min and the UV-detector was set at 230 nm.

Preparative thin layer chromatography of the oxidation reaction products was performed using silica gel plates with indicator 60 F_{254} (MN-Kieselgel).

UV/vis absorption spectra were recorded on a UV–vis. Hitachi U-2010 spectrophotometer.

^{1}H NMR spectra were recorded using a Bruker DRX 300 operating at 300.13 MHz. Chemical shifts are expressed in δ (ppm) values relative to tetramethylsilane as internal reference.

Hydrogen peroxide (35 wt% solution in water) was purchased from José Vaz Pereira and acetonitrile from Panreac. Atrazine, atraton, ametryn, mecoprop, deethylatrazine, deisopropylatrazine, deethyldeisopropylatrazine, hydroxyatrazine and deethylhydroxyatrazine standards were purchased from Riedel-de Haën. Methanol HPLC grade was purchased from Aldrich and ammonium acetate p.a. from Merck. All other chemicals and solvents were obtained from commercial sources and used as received or distilled and dried using standard procedures. Millipore (Milli-Q academic system) water was used in HPLC analysis.

2.2. Porphyrin synthesis

The free bases of the metalloporphyrins, were prepared according to the previously described nitrobenzene method [32,33]. Metallation of the free bases was carried out with $MnCl_2$ or $FeCl_2$, using Adler's dimethylformamide method [34].

2.3. Oxidation reactions

The oxidations of herbicides under study were carried out by progressive addition of hydrogen peroxide in the presence of the two different systems [metalloporphyrin/reaction medium]. The reactions were monitored by HPLC and GC-FID and the products were isolated and identified using various techniques. Metalloporphyrin stability was determined by comparison of the Soret band in the UV–vis absorption spectra of the reaction mixture at the beginning and at the end of the reaction. The reactions were considered to be complete when conversion of the substrate reached its maximum value and remained unchanged in successive analysis.

2.3.1. General procedure for oxidations in acetonitrile:ammonium acetate (*S-I*)

In a typical experiment, the substrate (0.1 mmol), metalloporphyrin (2 μmol) and ammonium acetate (0.2 mmol) were dissolved in acetonitrile (2 mL) and stirred at 22 °C. Aqueous hydrogen peroxide (35%, w/w), diluted with acetonitrile (1:10), was added to the reaction mixture in small aliquots every 15 min (43 μL; 0.05 mmol).

*2.3.2. General procedure for oxidations in methanol:dichloromethane (**S-II**)*

In a typical experiment, the substrate (0.1 mmol) and metalloporphyrin (2 μmol) were dissolved in 2 mL of methanol: dichloromethane (3:1) and stirred at 22 °C. Aqueous hydrogen peroxide (35%, w/w, diluted in the reaction solvent, 1:10) was added to the reaction mixture in small aliquots every 15 min (43 μL; 0.05 mmol).

2.3.3. Reactions in deuterated solvents

Reaction of atrazine with **S-I** in deuterated solvents followed the general oxidation procedure described in Section 2.3.1, the acetonitrile was replaced by a mixture of $CDCl_3$:CD_3OD (1:1), and imidazole (0.2 mmol) used as co-catalyst instead of ammonium acetate. The reaction of mecoprop with **S-II** followed the oxidation procedure described in Section 2.3.2, with the solvent replaced by CD_3OD:$CDCl_3$ (3:1).

2.4. Product isolation

The reaction mixtures were poured into water and extracted with dichloromethane. The organic phase was dried over anhydrous sodium sulfate and concentrated under vacuum.

The organic extracts were treated differently. For triazine reactions, isolation of the products was performed by preparative thin layer chromatography (TLC) on silica gel with indicator and the eluent was a mixture of toluene:ethyl acetate (3:2) for atrazine and ametryn and dichloromethane:methanol (5%) for atraton.

For mecoprop, the organic extract was treated with 1 mL of dried methanol and 0.5 mL of H_2SO_4, the flask was capped tightly, the mixture was swirled gently, and the reaction was allowed to occur at room temperature for 30 min. Buffer solution (ca. pH 10, 5 mL) and hexane (2 mL) were added to the methanol solution, the system mixed vigorously and allowed to partition. The organic phase was dried with anhydrous sodium sulfate and concentrated. The compounds were isolated by TLC using dichloromethane:*n*-hexane (10%) as eluent.

2.5. Characterization of compounds

A known feature of the NMR spectra of atrazine solutions, in aprotic solvents, is the splitting of its NMR signals for NH, CH_2 and CH groups [35]. In agreement with previously described NMR spectra of this compound, the split peak will be identified by the chemical shift (ppm) of the most intense signal.

Atrazine (**1**): δ_H (300 MHz, $CDCl_3$, 22 °C, Me_4Si) 1.21 [t, 3H, CH_3(Et), J = 7.1 Hz], 1.22 [d, 6H, CH_3(*i*Pr), J = 6.6 Hz]; 3.44 [q, 2H, CH_2(Et), J = 6.8 Hz], 4.15 [sp, 1H, CH(*i*Pr), J = 6.4 Hz]; 5.11 [m, 2H, NH]; MS (70 eV, EI): *m*/*z* (%): 215 (64) [M•+], 200 (100), 173 (28).

1-Hydroxyethylatrazine (**1a**): ^{1}H NMR (300 MHz, CD_3OD/$CDCl_3$, 22 °C, Me_4Si): δ_H = 1.22 [d, 6H, CH_3(*i*Pr), J = 6.5 Hz]; 1.44 [d, 3H, CH_3(Et), J = 5.7 Hz], 4.14 [sp, 1H, CH(*i*Pr), J = 6.6 Hz]; 5.58 [q, 1H, CH(Et), J = 5.4 Hz].

Deethylatrazine (**1b**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.21 [d, 6H, CH_3(*i*Pr), J = 6.6 Hz]; 4.11 [sp, 1H, CH(*i*Pr), J = 6.6 Hz]; 5.23, 5.38, 5.96 [3s,3H, NH]; MS (70 eV, EI): *m*/*z* (%): 187 (35) [M•+], 172 (100), 154 (21).

Acetamidoatrazine (**1c**): ^{1}H NMR (300 MHz, CD_3OD/$CDCl_3$, 22 °C, Me_4Si): δ = 1.23 [d, 6H, CH_3(*i*Pr), J = 6.6 Hz]; 2.39 [s, 3H, CH_3(Et)]; 4.15 [m, 1H, CH(*i*Pr)]; MS (70 eV, EI): *m*/*z* (%): 229 (58) [M•+], 214 (33), 186 (15), 172 (100), 145 (14).

1-Methoxy-d_3-ethylatrazine (**1d′**): ^{1}H NMR (300 MHz, CD_3OD/$CDCl_3$, 22 °C, Me_4Si): δ = 1.22 [d, 6H, CH_3(*i*Pr), J = 6.4 Hz]; 1.41 [d, 3H, CH_3(Et), J = 5.8 Hz], 4.11 [sp, 1H, CH(*i*Pr), J = 6.7 Hz]; 5.48 [q, 1H, CH(Et), J = 5.8 Hz]; MS (70 eV, EI): *m*/*z* (%): 248 (3) [M•+], 230 (100), 214 (74), 188 (55), 172 (90).

Deethyldeisopropylatrazine (**1f**): MS (70 eV, EI): *m*/*z* (%): 145 (100) [M•+], 110 (42), 68 (39).

Atraton (**2**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.18 [t, 3H, CH_3(Et), J = 7.1 Hz], 1.20 [d, 6H, CH_3(*i*Pr), J = 6.6 Hz]; 3.42 [q, 2H, CH_2(Et)], 3.87 [s, 3H, –OCH_3]; 4.19 [m, 1H, CH(*i*Pr)]; 4.89 [m-broad, 2H, NH]; MS (70 eV, EI): *m*/*z* (%): 211 (100) [M•+], 169 (99), 169 (31), 154 (18).

Deethylatraton (**2a**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.20 [d, 6H, CH_3(*i*Pr), J = 6.5 Hz]; 3.89 [s, 3H, –OCH_3]; 4.17 [m, 1H, CH(*i*Pr)]; MS (70 eV, EI): *m*/*z* (%) = 183 (59) [M•+], 168 (100), 141 (47), 126 (10).

Acetamidoatraton (**2b**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.22 [d, 6H, CH_3(*i*Pr), J = 6.4 Hz]; 2.62 [s, 3H, CH_3(Et)], 3.95 [s, 3H, –OCH_3]; 4.20 [m, 1H, CH(*i*Pr)]; MS (70 eV, EI): *m*/*z* (%) = 225 (64) [M•+], 210 (44), 183 (18), 168 (100), 141 (15).

Deethyldeisopropylatraton (**2c**): MS (70 eV, EI): *m*/*z* (%): 141 (100) [M•+], 111 (79), 69 (79).

Ametryn (**3**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.18 [t, 3H, CH_3(Et), J = 7.1 Hz], 1.20 [d, 6H, CH_3(*i*Pr), J = 6.6 Hz]; 2.44 [s, 3H, –SCH_3]; 3.42 [q, 2H, CH_2(Et)], 4.18 [st, 1H, CH(i)]; 5.01 [s-broad, 2H, NH].

2-Ethyl-4-isopropyl-6-sulfomethyl-*s*-triazine (**3a**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.21 [t, 3H, CH_3(Et), J = 7.1 Hz], 1.24 [d, 6H, CH_3(*i*Pr), J = 6.8 Hz]; 3.20 [s, 3H, –SCH_3]; 3.47 [q, 2H, CH_2(Et), J = 7.0 Hz], 4.21 [sp, 1H, CH(*i*Pr), J = 6.8 Hz]; 5.60 [s-broad, 2H, NH]; MS (70 eV, EI): *m*/*z* (%): 259 (57) [M•+], 244 (72), 217 (11), 180 (100).

2-Amino-4-isopropyl-6-sulfomethyl-*s*-triazine (**3b**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.24 [d, 6H, CH_3(*i*Pr)]; 3.22 [s, 3H, –SCH_3]; 4.21 [m, 1H, CH(*i*Pr)]; 5.40 [m-broad, 3H, NH]; MS (70 eV, EI): *m*/*z* (%): 231 (27) [M•+], 216 (100), 189 (5), 151 (59).

2-Amino-4-ethyl-6-isopropyl-*s*-triazine (**3c**): MS (70 eV, EI): *m*/*z* (%): 196 (100) [M•+], 181 (86), 154 (21), 139 (14), 126 (11), 111 (8).

2,4-Diamino-6-isopropyl-*s*-triazine (**3d**): MS (70 eV, EI): *m*/*z* (%): 168 (56) [M•+], 153 (100), 126 (38), 111 (21).

Mecoprop methyl ester (**4-Me**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.67 (d, 3H, H-3, J = 6.8 Hz), 2.25 (s, 3H, H-7′), 3.77 (s, 3H, OMe), 4.74 (q, 1H, H-2, J = 6.8 Hz), 6.65 (d, 1H, H-6′ J = 6.7 Hz), 7.08 (dd, 1H, H-5′, J = 8.6 and 2.5 Hz), 7.14 (d, 1H, H-3′, J = 2.2 Hz). MS (70 eV, EI): *m*/*z* (%): 228 (87) [M•+], 169 (100) [−59], 142 (82) [−27], 107 (47) [–Cl]; 77 (32) [−30].

Methyl ester of (±)-2-(4-chloro-2-formylphenoxy)propanoic acid (**4a-Me**): ^{1}H NMR (300 MHz, $CDCl_3$, 22 °C, Me_4Si): δ = 1.71 (d, 3H, H-3, J = 6.8 Hz), 3.77 (s, 3H, OMe), 4.87 (q, 1H, H-2, J = 6.8 Hz), 6.79 (d, 1H, H-6′, J = 9.0 Hz), 7.45 (dd, 1H, H-5′, J = 8.8 and 2.7 Hz), 7.82 (d, 1H, H-3′, J = 2.7), 10.49 (s, 1H, H-7′); MS (70 eV, EI): *m*/*z* (%): 242 (15) [M•+], 183 (50), 155 (100).

Dimethyl ester of (±)-2-(4-chloro-2-carboxyphenoxy) propanoic acid (**4b-Me**): MS (70 eV, EI): *m*/*z* (%): 272 (28) [M•+], 213 (45), 154 (100), 126 (26).

4-Chloro-2-methylphenyl acetate (**4c**): MS (70 eV, EI): *m*/*z* (%): 184 (10) [M•+], 142 (100), 107 (51), 77 (20).

5-Chloro-2-methoxy-3-methyl-1,4-hidroquinone (**4d**): MS (70 eV, EI): *m*/*z* (%). 188 (20) [M•+], 173 (16), 145 (37), 129 (100), 113 (10), 79 (17).

3. Results and discussion

3.1. Atrazine oxidation

In the oxidation of atrazine, strong catalytic activity was obtained with the system **S-I** [Mn(TDCPP)Cl; CH_3CN; ammonium acetate (NH_4OAc)], resulting in 83% substrate conversion after

Table 1
Atrazine oxidation with H_2O_2 catalysed by metalloporphyrin systems[a].

Entry	Catalyst	Conditions	Conversion (%)[c]	t (h)	Selectivity (%)[c]				
					(**1b**) DEA	(**1c**)	(**1d**)	(**1e**) DIA	(**1f**) DEIA
1	No catalyst	**I**	0	15	–	–	–	–	–
2	Mn(TDCPP)Cl	**I**	83	15	94	4	0	0	2
3	Mn(TDCPP)Cl	*d*-solvents[b]	64	8	10	10	79	0	0
4	Mn(TPFPP)Cl	**I**	48	12	84	7	0	5	4
5	Mn(TPP)Cl	**I**	3	9	48	0	0	52	0
6	Fe(TPFPP)Cl	**II**	6	12	0	0	92	0	0

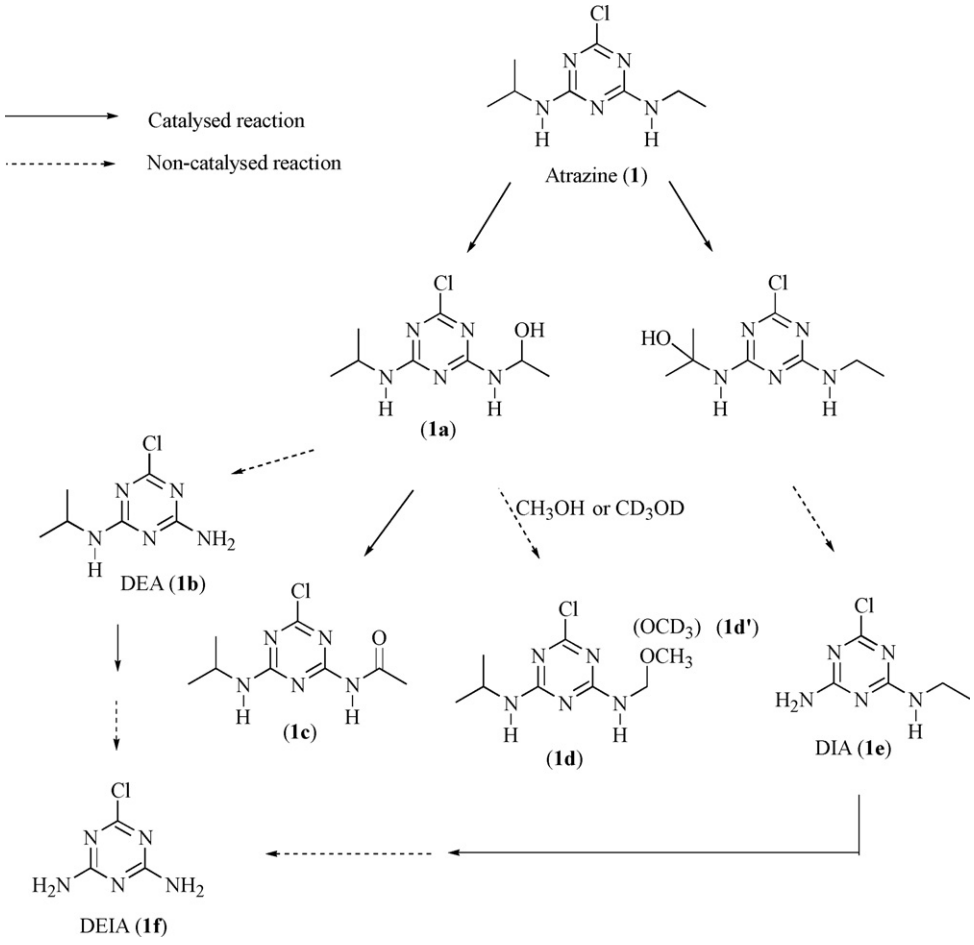
[a] Reactions performed at 22 °C, atrazine (50 μmol): metalloporphyrin (1 μmol). Conditions **I**: NH_4OAc (0.2 mmol); CH_3CN (2 mL). Conditions **II**: Fe(TPFPP)Cl:CH_3OH/CH_2Cl_2 (3:1) (2 mL).
[b] The reaction was performed as in footnote a but using in $CDCl_3/CD_3OD$ (1:1) as solvent and imidazole as co-catalyst.
[c] Determined by HPLC.

15 h (Table 1, entry 2). Products were isolated from the reaction mixture using preparative thin layer chromatography (TLC) and all compounds could be identified. The major product was deethylatrazine (DEA, **1b**), obtained with 94% selectivity (78% yield), and the other minor compounds identified were acetamidoatrazine (**1c**, 4% selectivity) and deethyldeisopropylatrazine (DEIA, **1f**, 2% selectivity).

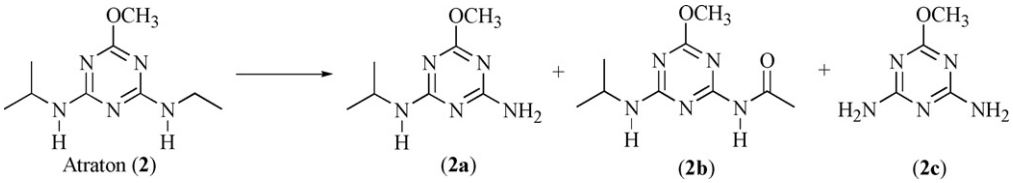
The oxidation of this pollutant was inefficient in the presence of the catalytic system **S-II** [Fe(TPFPP)Cl; CH_3OH], since the atrazine conversion was only 6% after 12 h (Table 1, entry 6). A minor amount of 1-methoxyethylatrazine (**1d**) was observed by GC–MS at the end of the reaction.

During atrazine degradation in the presence of **S-I**, an intense intermediate peak was observed by HPLC that was gradually converted to DEA. This transformation did not involve the metalloporphyrin, since it was also observed when the porphyrin Soret band was no longer present in the UV–vis spectrum. To identify this intermediate compound, the reaction has been carried out in deuterated solvents ($CDCl_3$:CD_3OD), using imidazole as co-catalyst [13] (entry 3). Again, the intermediate peak was observed, but was seen to be predominantly converted to 1-methoxy-d_3-ethylatrazine (**1d′**, m/z 248). The ^{1}H NMR spectrum of the reaction mixture allowed identification of the intermediate **1a** as 1-hydroxyethylatrazine.

These results allow us to elucidate the reaction profile for atrazine oxidation by **S-I**, as shown in Scheme 1. Compound **1a** is initially formed and its carbinolamine (hemiaminal) group can either undergo spontaneous dealkylation to form **1b** or can be



Scheme 1. Oxidative degradation of atrazine.



Scheme 2. Oxidative degradation of atraton.

Table 2
Atraton oxidation with H_2O_2 catalysed by metalloporphyrin systems[a].

Entry	Catalyst	Conditions	Conversion (%)[b]	t (h)	Selectivity (%)[b]		
					2a	**2b**	**2c**
1	No catalyst	**I**	4	9	100	0	0
2	Mn(TDCPP)Cl	**I**	98	9	86	4	9

[a] Reaction conditions: 22 °C, atraton (50 μmol); metalloporphyrin (1 μmol). Conditions **I**: NH_4OAc (0.2 mmol); CH_3CN (2 mL).
[b] Determined by HPLC.

Table 3
Ametryn oxidation with H_2O_2 catalysed by metalloporphyrin systems[a].

Entry	Catalyst	Conditions	Conversion (%)[b]	Time (h)	Selectivity (%)[b]	
					3a	**3b**
1	No catalyst	**I**	0	12	–	–
2	Mn(TDCPP)Cl	**I**	100	3	88	0
3	Mn(TDCPP)Cl	**I**	100	12	22	6
4	No catalyst	**II**	0	12	–	–
5	Fe(TPFPP)Cl	**II**	100	12	70	0

[a] Reactions performed at 22 °C, ametryn (50 μmol): metalloporphyrin (1 μmol). Conditions **I**: NH_4OAc (0.2 mmol); CH_3CN (2 mL). Conditions **II**: Fe(TPFPP)Cl:CH_3OH/CH_2Cl_2 (3:1, 2 mL).
[b] Determined by HPLC.

oxidized to **1c**. Further, the methoxy derivative (**1d)** is produced when the solvent is methanol.

During the oxidation of atrazine in the presence of **S-I**, the selectivity for isopropyl group oxidation was low, possibly as a consequence of considerable steric hindrance. To test this hypothesis [36], atrazine oxidation was also carried out in the presence of the less hindered metalloporphyrins Mn(TPFPP)Cl and Mn(TPP)Cl, using acetonitrile and ammonium acetate (Table 1, entries 4 and 5). Although lower degrees of conversion were observed, higher selectivity was found for formation of deisopropylatrazine [DIA, **1e**, 52% with Mn(TPP)Cl]. Compound **1e** (DIA) was identified using HPLC by comparison with an authentic commercial sample.

It has previously been shown that dealkylated derivatives of atrazine are less cytotoxic substances than the original herbicide [37], therefore the **S-I** can be considered as a useful catalytic system for atrazine degradation and detoxyfication.

3.2. Atraton oxidation

The oxidation of atraton (**2**) in the presence of **S-I** led to 98% substrate conversion after 9 h. After isolation and characterization of all the products, the reaction product profile was shown to be analogous to that of atrazine and deethylatraton (**2a**); acetamidoatraton (**2b**) and deethyldeisopropylatraton (**2c**) were isolated with relative yields of 86, 4 and 9%, respectively (Scheme 2 and Table 2).

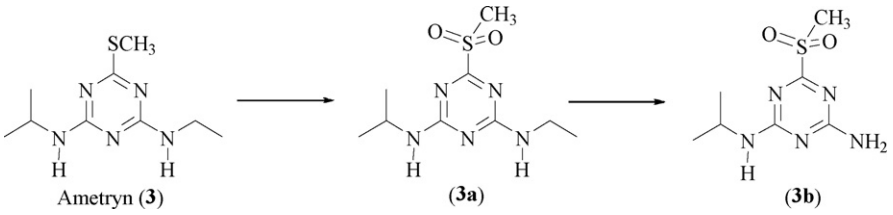
3.3. Ametryn oxidation

Using catalytic system **S-I**, the oxidation of ametryn was complete after 3 h (Table 3, entry 2). The main product, isolated by preparative TLC, was characterized as the sulfone derivative **3a**, obtained with 88% selectivity.

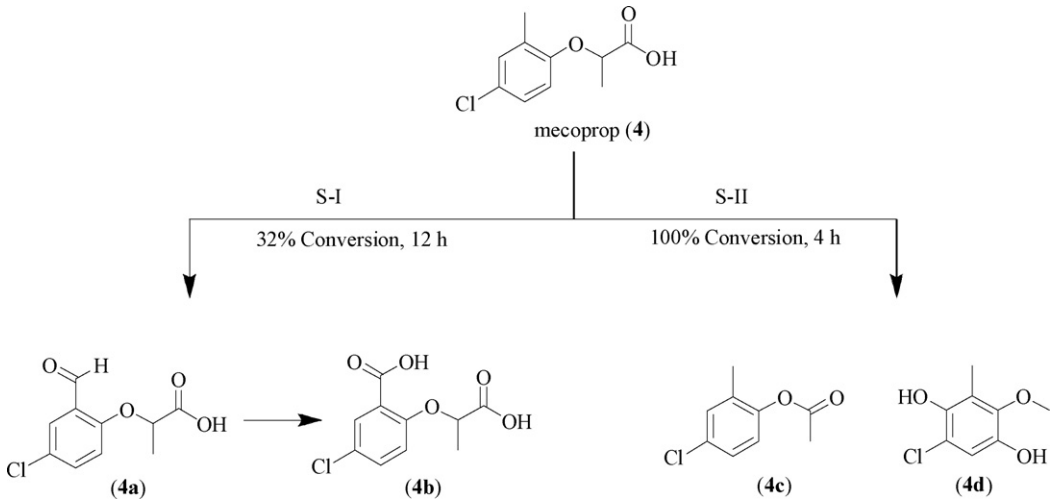
When reaction was continued for 12 h (entry 3), the selectivity for compound **3a** decreased to 22% with concomitant increase of other products. Compound **3b**, observed with 6% selectivity, was isolated by TLC and characterized as the dealkylation product of the sulfone derivative (2-amino-4-isopropyl-6-sulfomethyl-*s*-triazine, Scheme 3). Two other compounds were also observed in the reaction mixture, one minor product with 4% selectivity and m/z 196 (**3c**) and the major product having 62% selectivity with m/z 168 (**3d**). The mass spectra of both compounds is in agreement with the substitution of the methylsulfonyl group ($-SO_2CH_3$) of **3a** and **3b** by an $-NH_2$ group.

The nucleophilic substitution on the triazine ring has been previously described; for instance, it is known that the C–Cl bond of atrazine is rapidly hydrolysed to the hydroxyl derivative in the presence of acids, alkalis or at 70 °C in neutral aqueous media [38]. For compounds **3a** and **3b**, the presence of a good leaving group, such as the methylsulfonyl group [39], might improve the substitution reaction by nucleophiles, in particular by NH_3 present in excess in the reaction media, which results from the ammonium ion equilibrium.

In the presence of **S-II** (entry 5), the conversion of ametryn was also complete after 12 h and the major product was the sulfone **3a**, obtained in 70% yield. However, in this case, no dealkylation products were observed. The methoxy derivative (atraton, **2**) was identified in the reaction mixture in 29% yield by co-injection of a reference compound. Also, in this case, nucleophilic attack on methylsulfonyl group of **3a** can be performed by methanol, present in the solvent mixture. Analogously, during product isolation, the formation of hydroxyatrazine was also observed and confirmed by co-injection with the appropriate reference compound, indicating the hydrolysis of **3a** due to the presence of water in the reaction mixture.



Scheme 3. Oxidative degradation of ametryn.



Scheme 4. Oxidative degradation of mecoprop.

3.4. Oxidation of mecoprop

The oxidation of the chlorophenoxy propionic acid herbicide, mecoprop, followed two distinct patterns in the presence of the catalytic systems **S-I** or **S-II**, as depicted in Scheme 4.

In the presence of **S-I**, a relatively low substrate conversion of 32% was observed after 12 h by HPLC (Table 4, entry 2). Esterification of the carboxyl groups of the products was carried out by treatment of the reaction mixture with H_2SO_4/methanol to facilitate product isolation and GC analysis. Compound **4a-Me**, obtained with 29% selectivity, was characterized as the methyl ester of **4a** [(±)-2-(4-chloro-2-formylphenoxy)propanoic acid]. The dimethyl ester of **4b** [(±)-2-(4-chloro-2-carboxyphenoxy)propanoic acid], was the other product formed with 71% selectivity, *m*/*z* 272 together with the two successive losses of a CO_2Me group in the mass spectrum, confirmed the oxidation of the preceding aldehyde to a benzoic acid.

A third minor compound was also observed during the GC–MS analysis, with molecular ion at *m*/*z* 239 and main mass fragmentations corresponding to losses of HCN (*m*/*z* 27) and CO_2Me (*m*/*z* 59) units. This was probably due to the formation of a nitrile derivative inside the GC or MS apparatus through reaction between the carboxylic groups and ammonium ion present in the reaction medium.

In contrast with what was obtained with triazines, the catalytic system **S-II** is much more efficient for the oxidation of mecoprop than **S-I**. The oxidation reaction was followed by HPLC and after 4 h, 100% substrate conversion was observed (Table 4, entry 4). Compound **4c** showed *m*/*z* 184 for the molecular ion, together with mass fragmentations corresponding to losses of [$COCH_2$] and [Cl] groups, and corresponds to the structure of 4-chloro-2-methylphenyl acetate.

Compound **4d** was identified as 6-chloro-2-methoxy-3-methyl-1,4-hydroquinone (*m*/*z* 188). When the reaction was performed in deuterated solvents (CD_3OD:$CDCl_3$, 3:1), the methoxy group of **4d** was replaced by OCD_3 group, leading to formation of 6-chloro-2-methoxy-d_3-3-methyl-1,4-hydroquinone (*m*/*z* 191). This confirms that the methoxy group comes from attack by the methanol present as solvent. The formation of small quantities of mecoprop methyl ester (**4-Me**, *m*/*z* 228) was also observed.

When reaction with **S-II** was carried out in the absence of metalloporphyrin, only 4% conversion was obtained after 4 h, and the trace products observed are different from those obtained in the catalysed reaction (Table 4, entry 3).

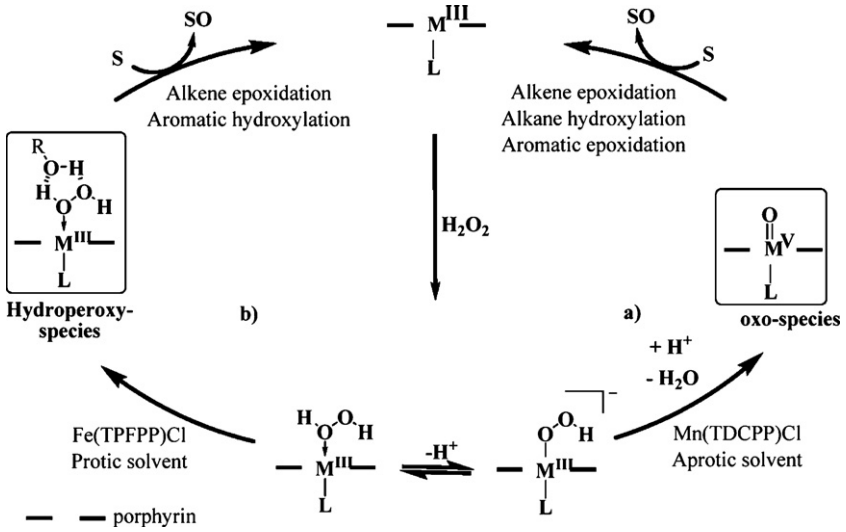
To obtain more detailed mechanistic insights about the reaction of mecoprop in the presence of **S-II**, various test assays were also performed. Previous studies have shown that benzoic acid is decarboxylated upon reaction with hydroxyl radicals (•OH) [40]. To obtain indications on the possible involvement of hydroxyl radical in the **S-II** mechanism, the oxidation of benzoic acid was also studied with this system. However, no conversion of benzoic acid was observed, showing that involvement of •OH radicals is of minor importance in this mechanism.

The methyl ester of mecoprop does not react with **S-II** after 4 h, indicating that a carboxyl group is necessary, probably due to the carboxylate group being coordinated by the metal complex [41].

Table 4
Mecoprop oxidation with H_2O_2 catalysed by metalloporphyrin systems[a].

Entry	Catalyst	Conditions	t (h)	Conversion (%)[b]	Selectivity (%)[c]				
					4a	**4b**	**4c**	**4d**	Others
1	No catalyst	**I**	12	0	–	–			
2	Mn(TDCPP)Cl	**I**	12	32	29	71			
3	No catalyst	**II**	4	4			0	0	100
4	Fe(TPFPP)Cl	**II**	2	70			24	35	39
			4	100			26	30	44
5	Fe(TPFPP)Cl	**II**, 50 °C	2	46			32	52	16
			4	100			32	40	32

[a] Reactions performed at 22 °C, ametryn (50 μmol): metalloporphyrin (1 μmol). Conditions **I**: NH_4OAc (0.2 mmol); CH_3CN (2 mL). Conditions **II**: CH_3OH/CH_2Cl_2 (3:1) (2 mL).
[b] Determined by HPLC.
[c] Determined by GC-FID.



Scheme 5. Formation and reactivity of different metalloporphyrin oxidizing species.

3.5. Mechanistic considerations

Two different porphyrin based systems have been compared for the catalytic degradation of four herbicides and different reactivity has been observed for the two types of substrates studied. Both systems **S-I** and **S-II** are very efficient in sulfoxidation of the thiomethyl group of ametryn, leading to the sulfone derivative. However, differences were observed with the other oxidative pathways, since while **S-I** promotes alkyl side chain hydroxylation of *s*-triazines, which are followed by spontaneous dealkylation in high conversion yields, these reactions are inefficient in the presence of **S-II**. Also, with **S-I**, mecoprop was only oxidized with low yields, and at the aromatic methyl group, while with **S-II**, a different, and more efficient, pathway of mecoprop degradation was found involving oxidative decarboxylation and subsequent reactions.

The above results confirm the involvement of two different active species in oxidation of substrates (**1**–**4**) by mixtures of metalloporphyrins and hydrogen peroxide. In system I [Mn(TDCPP)Cl; CH_3CN; NH_4OAc], the heterolytic cleavage of the peroxide bond (Scheme 5a) is facilitated by acid/base catalysis induced by ammonium acetate used as a buffer system and by the moderately electron withdrawing Mn-porphyrin. The formation of a high-valent metal-oxo-species is considered to be the responsible for hydroxylation reactions of normally inert C–H bonds. In addition to the present application in pesticide degradation, this reaction obviously has considerable synthetic potential.

In system II [Fe(TPFPP)Cl; CH_3OH], the metal-peroxide group can establish hydrogen bonding with the protic solvent (Scheme 5b). The strongly electron withdrawing characteristics of the porphyrin and the absence of a buffer solution lead to a decrease in the rate of the heterolytic cleavage of the peroxide bond and consequently to the inhibition of oxo-species formation. However, the peroxide bound oxygen becomes electrophilic enough to oxidize substrates in a similar fashion to that seen with peroxy acids activated by electron withdrawing groups, such as *m*-chloroperoxybenzoic acid (*m*-CPBA) [4]. These are known to be efficient epoxidation reagents but are unable to induce alkane hydroxylation reactions.

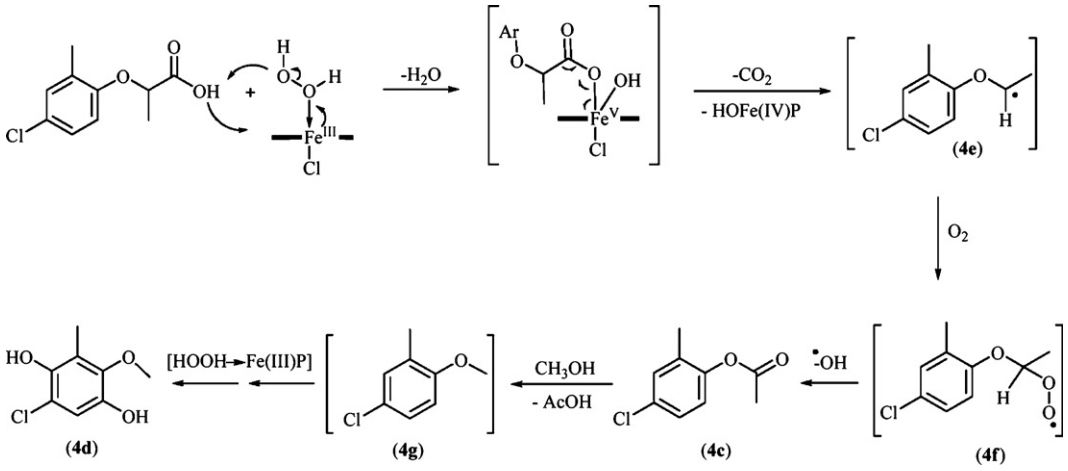
The present data are in line with our previous results [13], further corroborating our proposal that **S-I** activates an oxo-species as intermediate oxidant, while **S-II** induces the formation of an active hydroperoxy species.

During previous studies using metalloporphyrins as synthetic models of cytochrome P450 enzymes, a complex reactivity panorama has frequently been reported. Different metalloporphyrins and reaction media lead to differences in conversion and selectivity [4,3]. Other apparently inconsistent observations have frequently been left unexplained, such as the need of a co-catalyst for hydrogen peroxide activation by Mn-porphyrins [13,42] and the negative effect of the same co-catalyst when employing Fe-porphyrins [13,43]. The present study clarifies these observations and gives a key for understanding and exploring the potentialities of these systems based on the formation of specific active species, which are relevant both to synthesis and to the application of such catalytic routes as advanced oxidative processes (AOPs) [29] for pollutant degradation.

Further mechanistic considerations on the individual reactions described in the present work can also be noted. Hydroxylation reactions of C–H bonds [44,45] and the oxidations of alcohols to ketones [46,47] by an oxo-species, have been extensively implicated in mechanistic proposals. The oxidation of the thiomethyl group of ametryn is efficiently catalysed by both systems **S-I** and **S-II**. These reactions indicate that attack of the S lone pairs is possible at the electrophilic oxygen sites of both active species.

The present results also provide some mechanistic insight through the oxidation reaction of mecoprop by **S-II** (Scheme 6). The formation of $^{\bullet}OH$ radical was considered to be a minor process in this reaction, and evidence was obtained that the major pathway involves the intervention of a hydroperoxy species, as well as the free carboxylic group of mecoprop. Initially, coordination of the carboxylic group to the central metal of the hydroperoxy species can induce decarboxylation with formation of a carbon radical (**4e**). Dioxygen trapping by the radical species and loss of $^{\bullet}OH$ by the peroxy radical species (**4f**) can lead to compound **4c**.

Species **4c** can suffer nucleophilic substitution by methanol present as the solvent with loss of acetic acid, leading to **4g**. This step is confirmed by the formation of the $-OCD_3$ derivative, when the reaction was carried out in deuterated methanol [48]. The –OMe group significantly activates the aromatic ring in comparison with the acetoxy group and compound **4g** can undergo aromatic dihydroxylation to afford the product **4d**. The particular ability of the hydroperoxy species to perform aromatic hydroxylation reactions is in line with our previous results [13] and a mechanistic proposal was advanced in studies on mutants of cytochrome P450



Scheme 6. Mechanistic proposals for mecoprop oxidation reactions catalysed by **S-II**.

enzymes, where amino acids are sequenced to induce the formation of a hydroperoxy species [49].

Benzoic acid was inert towards **S-II**, which supports the proposed mechanism, since the formation of the phenyl radical is very unfavourable.

Although it has previously been reported that decarboxylation reactions of α-arylcarboxylic acids are catalysed by iron porphyrins [50], and are also typical reactions of horseradish peroxidise [51,52], it has also been suggested that iron porphyrins and horseradish peroxidase probably act by different mechanisms [50]. Some considerations on this will be given next.

The oxidative metabolism of pollutants (**1**–**4**) has previously been studied, both *in vivo* and *in vitro*. For atrazine and atraton, the *in vitro* metabolism involves 1-hydroxylation of the side chains, followed by dealkylation reactions. For ametryn, sulfoxidation and dealkylation reactions were reported. In addition to these reactions, the *in vivo* studies consider hydrolysis and conjugation reactions [38,53,54]. Mecoprop is not metabolised in animals and, in plants, is oxidized at the benzyl position [38].

These results are in excellent agreement with the oxidation studies obtained in the present work with **S-I** and strongly indicate that **S-I** is good a model for cytochrome P450 enzymes. In contrast, the results show that the oxidations in the presence of **S-II** are in poor agreement with the reported *in vitro* or *in vivo* metabolisms.

Probably, the successful modelling of cytochrome P450 action on metabolism of xenobiotics with the Mn(TDCPP)Cl system in an aprotic solvent with a co-catalyst, is a consequence of the electronic, spin, and/or other characteristics of this porphyrin system, mimicking closely electronic aspects of the activity of cytochrome P450 [55].

The oxidation of mecoprop in the presence of **S-II** is analogous to the degradation of this herbicide observed in soils, where mecoprop is transformed to 2-chloro-2-methylphenol, with hydroxylation of the aromatic ring occurring as a minor pathway.

Decarboxylations of carboxylic acids have been reported as typical reactions involving horseradish peroxidase. This enzyme promotes, for example, the decarboxylation of α-(*p*-isobutylphenyl)propionic acid (Ibuprofen) leading to alcohols and ketones [50]. Similar behaviour has been observed with iron porphyrins and is obtained in the present work for mecoprop oxidation by **S-II**, suggesting parallels with peroxidase activity.

4. Conclusion

Effective degradations of the persistent herbicides (**1**–**4**) have been obtained by oxidation with hydrogen peroxide in the presence of metalloporphyrins. Two distinct reaction conditions were studied. System I [Mn(TDCPP)Cl; NH_4OAc; CH_3CN] was the most efficient for *s*-triazine degradation, and the reaction conversions were dependent on herbicide structure. Reactivity increased in the order atrazine (83%) < atraton (98%) < ametryn (100%). The products obtained are predominantly dealkylated compounds for atrazine and atraton or sulfoxidation and dealkylation derivatives for ametryn. System II [Fe(TPFPP)Cl; CH_3OH] was only efficient in ametryn oxidation and led exclusively to sulfoxidation.

Mecoprop, in contrast, was degraded more efficiently with **S-II**, leading to 100% conversion, through decarboxylation and aromatic ring hydroxylation. In the presence of **S-I**, only 32% conversion was observed, resulting mainly from reaction at the aromatic methyl position.

The extensive product characterization allowed the determination of the reaction pathways and confirmed assignment of distinct mechanisms for the different [metalloporphyrin/reaction condition] systems, involving oxo or hydroperoxy oxidizing species. The results also allowed some mechanistic considerations and provided a correlation between cytochrome P450 reactivity and the **S-I** model system [Mn(TDCPP)Cl; aprotic solvent; buffer], but not with **S-II** [Fe(TPFPP)Cl; protic solvent]. The **S-II** degraded mecoprop in a similar process to the reaction pattern of carboxylic acids involving horseradish peroxidase.

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