Oxidation of Dichloroanilines and Related Anilides Catalyzed by Iron(III) Tetrasulfonatophthalocyanine

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We investigated the degradation of polychlorinated pollutants, such as dichloroanilines and related anilides, catalyzed by iron(III) tetrasulfonatophthalocyanine (FePcS) with potassium monopersulfate or hydrogen peroxide as oxidant. The reaction is influenced by the positions of the two chloro-substituents and by the nature of the oxidant. The FePcS-catalyzed oxidation of 3,5-dichloroaniline with potassium monopersulfate leads to the formation of more biodegradable products (carboxylic acids) and to potentially toxic dimers (azo and azoxy compounds). The oxidation of 3,4-dichloroaniline by FePcS/H_2O_2 converts this pollutant into coupling products. The formation of dimers in the catalytic oxidation of dichloroanilines can be avoided by acylation of the amine function.

Introduction

Dichloroanilines (DCAs) are used as precursors on a large scale in the industrial synthesis of pesticides, plastics and dyes.[1] The contamination of aquatic environments by DCAs can occur directly through their accidental release during industrial processing or indirectly by microbial degradation of DCA-derived pesticides in soil. The herbicide Propanil (3,4-dichloropropionanilide, 3,4-DCPA) is used extensively around the world for control of weeds in rice cultures.[2] Although Propanil itself has a low toxicity, its conversion into 3,4-DCA by microorganisms in soil is a problem, since the acute exposure to this DCA isomer results in renal and hepatic toxicity in vivo.[3] In order to solve this problem several investigations have been carried out to find efficient systems for DCA degradation by reductive or oxidative dehalogenation. Using the latter method, Pieper et al. reported the degradation of 3,4-DCA by lignin peroxidase from *Phanerochaete chrysosporium*.[4] Whereas 60% of the pollutant was degraded to a quinoneimine, 10−15% of 3,4-DCA was transformed into the more toxic tetrachloroazobenzene.

We recently developed a new catalytic system for the oxidative degradation of recalcitrant pollutants, such as polychlorinated phenols[5] and polycyclic aromatic hydrocarbons,[6] using iron(III) tetrasulfonatophthalocyanine (FePcS) as a catalyst. We found that the FePcS-catalyzed oxidation of 2,4,6-trichlorophenol (TCP) with hydrogen peroxide leads to the formation of chloromaleic acid as the main product and also to carbon dioxide.[5a−5d] Because of its high catalytic activity in the degradation of TCP, we decided to investigate the FePcS-catalyzed oxidation of other poorly biodegradable compounds such as dichloroanilines.

In order to investigate the chemical degradation of dichloroanilines (DCA) we studied the catalytic oxidation of the following two isomers: 3,4-dichloroaniline (3,4-DCA) and 3,5-dichloroaniline (3,5-DCA). 3,4-DCA is formed during the biodegradation of the herbicide Propanil (3,4-dichloropropionanilide).[2] From 1970 to 1987, on average, 3−7 kg of Propanil/ha were applied each year to about 70 to 100% of rice culture in the United States.[7] 3,5-DCA, which is the most toxic DCA isomer, is a relevant precursor in the industrial synthesis of azo dyes.

Results

We first investigated the oxidative degradation of the two different dichloroanilines 3,5-DCA and 3,4-DCA using FePcS as the catalyst and potassium monopersulfate or hydrogen peroxide as the oxidant. The final concentrations of DCA and oxidant (H_2O_2 or $KHSO_5$) in the reaction mixture were 1 mM and 5 mM, respectively. The solution contained 0.03 mM of FePcS, which corresponds to a molar ratio of catalyst to substrate of 3%. The reactions were carried out at room temperature at pH 7 in an aqueous mixture of acetone/phosphate buffer (v/v = 1:9) with a final volume of 4 mL. The results are reported in Table 1.

Table 1. Oxidation of 3,4-DCA and 3,5-DCA

Run	Substrate	Oxidant	Conversion [%] after 10 min	30 min	Cl^-/DCA[a]
1	3,4-DCA	$KHSO_5$[b]	100	100	0.4
2	3,4-DCA	H_2O_2[b]	41	100	0.5
3	3,4-DCA	$KHSO_5$[c]	90	100	0
4	3,4-DCA	H_2O_2[c]	0	0	−
5	3,5-DCA	$KHSO_5$[b]	100	100	0.6
6	3,5-DCA	H_2O_2[b]	38	78	0.4
7	3,5-DCA	$KHSO_5$[c]	80	100	0.1
8	3,5-DCA	H_2O_2[c]	0	0	−

[a] Number of released chloride ions per converted DCA molecule (determined after 60 min). − [b] Reactions carried out with FePcS, molar ratio FePcS/DCA = 3%. − [c] Reactions carried out without FePcS.

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Under these conditions 3,4-DCA and 3,5-DCA were completely converted by the FePcS/$KHSO_5$ system within 10 min (runs 1 and 5). When hydrogen peroxide was used instead of potassium monopersulfate, the reaction rates decreased and the conversions of 3,4-DCA and 3,5-DCA were 41% and 38% after 10 min and increased to 100% and 78% within 30 min, respectively (runs 2 and 6). The average dechlorination values of these reactions corresponded to 0.5 released chloride ions per converted substrate molecule. In other words, one covalent chlorine atom of 50% of DCA molecules was transformed into a chloride ion.

In control reactions we tested the behavior of these DCA molecules without FePcS catalyst. Surprisingly, we observed fast reactions of DCAs with $KHSO_5$ and the pollutants were completely converted within 30 min (runs 3 and 7). Despite full substrate conversions, the dechlorination values were negligible, suggesting the formation of oxidation products different to those obtained in the catalyzed reaction with FePcS/$KHSO_5$. A similar oxidation reaction was also observed on replacing acetone by ethanol, suggesting that a dioxirane was not entirely responsible for this noncatalyzed oxidation of DCAs (see ref.[8] for a review article on the formation of dioxiranes from ketones and monopersulfate). The absence of chloride release suggested that the amine function was the only oxidation site in these noncatalyzed oxidations with monopersulfate. The control reactions with hydrogen peroxide gave no substrate conversions without catalyst (runs 4 and 8).

These results indicate that the catalytic activity of FePcS is higher with potassium monopersulfate than with hydrogen peroxide. Nevertheless, full substrate conversion of 3,4-DCA could also be reached using the clean oxidant H_2O_2 (water being the only by-product after reaction). The dechlorination values in these catalyzed oxidations of DCA derivatives with $KHSO_5$ or H_2O_2 were similar and suggested the same level of pollutant degradation regardless of the nature of the oxidant.

In order to identify the reaction products we extracted the aqueous mixture after the oxidation of 3,5-DCA by FePcS/$KHSO_5$ and analyzed the organic phase by ^{1}H NMR spectroscopy and GC-MS. Three groups of oxidation products could be distinguished: (i) ring cleavage products, (ii) products resulting from oxidation of the amine function and (iii) oxidative coupling products (Figure 1). The formation of ring cleavage products probably occurred via the intermediates 2,6-dichloro-1,4-quinoneimine (**1**) and 2,6-dichloro-1,4-benzoquinone (**2**). Their respective reduced forms, 2,6-dichloro-4-aminophenol and 2,6-dichloro-1,4-hydroquinone, were identified by GC-MS. The ring cleavage of intermediates **1** and **2** can lead to the formation of chloromaleic acid (**3**) and formic acid (**4**) as occurs in the degradation of 2,4,6-trichlorophenol by FePcS/H_2O_2.[5] Carboxylic acids **3** and **4** were identified by ^{1}H NMR spectroscopy after extraction of the reaction mixture in the manner previously described for the TCP oxidation products.[5c] 3,5-Dichloronitrosobenzene (**5**) and 3,5-dichloronitrobenzene (**6**) resulted from the oxidation of the amine function. Both compounds are minor products of the catalytic oxidation reaction, since only traces of these compounds were detected by GC-MS and HPLC. Most of the 3,5-DCA was transformed into coupling products such as 3,5,3′,5′-tetrachloroazobenzene (**7**) and 3,5,3′,5′-tetrachloroazoxybenzene (**8**). A third dimer was also detected by GC-MS. The MS data for this compound ([M^+] = 316, isotopic peaks indicating four chlorine atoms) are in agreement with 1,3,6,8-tetrachlorophenazine (**9**).

In order to compare the distribution and the structure of the degradation products obtained with FePcS/$KHSO_5$ and the oxidation compounds of the noncatalyzed reaction, the oxidation of 3,5-DCA was carried out with $KHSO_5$ only. In this case, 38% of 3,5-DCA was transformed into 3,5-dichloronitrobenzene (**6**), which is the major reaction product quantified by HPLC. In accordance with the negligible dechlorination value (0.1 Cl^-/3,5-DCA), the other products

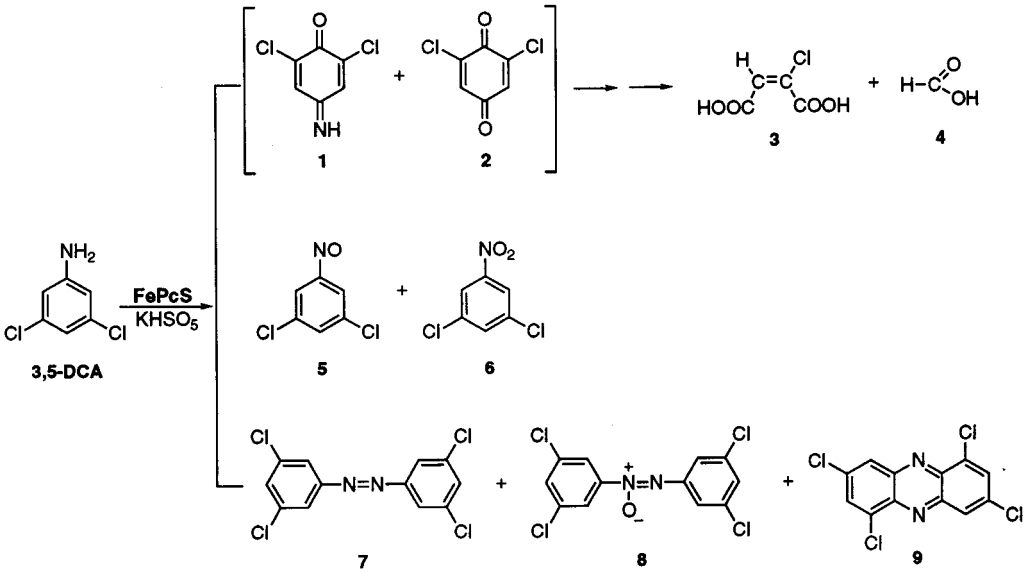

Figure 1. Products formed in the oxidation of 3,5-DCA by FePcS/$KHSO_5$

identified by GC-MS were 3,5-dichloronitrosobenzene (**5**) and small amounts of dimers **7** and **8**. It should be noted that no ring cleavage products could be identified by GC-MS in this noncatalyzed oxidation of 3,5-DCA.

We subsequently characterized the reaction products of the FePcS-catalyzed oxidation of 3,4-DCA with hydrogen peroxide as the oxidant (Figure 2). After a reaction time of 1 h, 69% of the pollutant was transformed into more hydrophobic products, which precipitated from the aqueous mixture. The separation of the precipitated components by column chromatography allowed the isolation and quantification of products **10**−**13**. As shown in Figure 2, this dichloroaniline was mainly transformed into tetrachloroazobenzene **10** (22%), whereas the tetrachloroazoxybenzene **11** (7%) and the two tetrachlorophenazine isomers **12** and **13** (3%) were isolated in lower yields. We also analyzed the aqueous phase after filtration, but no ring cleavage products could be identified.

The oxidation of chlorinated aromatic amines leads to the formation of chlorinated azo and azoxy compounds, which are cytotoxic and teratogenic molecules.[1] In order to avoid the formation of these dimers during the oxidation of DCA we decided to protect the amine function with an acetyl or a propionyl group and we synthesized the 3,4-dichloropropionanilide 3,4-DCPA (Propanil) and the 3,5-dichloroacetanilide 3,5-DCAA. To compare the reaction behavior of these anilides with that of the corresponding anilines, we checked the degradation of 3,4-DCPA and 3,5-DCAA with hydrogen peroxide or potassium monopersulfate using FePcS as a catalyst. The reaction conditions were identical to those of DCA oxidations and the results are shown in Table 2.

The FePcS-catalyzed oxidations of 3,4-DCPA and 3,5-DCAA with potassium monopersulfate led to conversions of 34% and 22% within 30 min, respectively (runs 1 and 5). The catalytic system using hydrogen peroxide as the oxidant was able to convert 34% of 3,4-DCPA, while only a small amount of 3,5-DCAA was oxidized (runs 2 and 6). We also checked the reaction behavior of the anilides in the absence of a catalyst: the control reactions with $KHSO_5$ led to negligible conversions (runs 3 and 7) and no reaction occurred with H_2O_2 (runs 4 and 8).

Table 2. Oxidation of 3,4-DCPA and 3,5-DCAA

Run	Substrate	Oxidant	Conversion [%] after 10 min	30 min	Cl^-/DCA[a]
1	3,4-DCPA	$KHSO_5$[b]	31	34	0.3
2	3,4-DCPA	H_2O_2[b]	15	34	1.0
3	3,4-DCPA	$KHSO_5$[c]	1	2	0
4	3,4-DCPA	H_2O_2[c]	0	0	0
5	3,5-DCAA	$KHSO_5$[b]	22	22	0
6	3,5-DCAA	H_2O_2[b]	1	3	0
7	3,5-DCAA	$KHSO_5$[c]	4	8	0
8	3,5-DCAA	H_2O_2[c]	0	0	0

[a] Number of released chloride ions per converted 3,4-DCPA or 3,5-DCAA molecule (determined after 60 min). − [b] Reactions carried out with FePcS, molar ratio FePcS/3,4-DCPA and FePcS/3,5-DCA**A** = 3%. − [c] Reactions carried out without FePcS.

The dechlorination value of the oxidation of 3,4-DCPA by $FePcS/H_2O_2$ corresponded to one released chloride ion per converted substrate molecule and indicated an advanced degradation of the anilide. In order to identify the degradation products, the reaction mixture was extracted after the oxidation of 3,4-DCPA by $FePcS/H_2O_2$ and the organic phase was analyzed by ^1H NMR spectroscopy and GC-MS. Four oxidation products were distinguishable and the proposed structures have to be considered as current working hypotheses (Figure 3).

3,4-DCPA was degraded to 2-chloro-hydroxy-*N*-propionyl-1,4-quinoneimine (**14**), which is the most oxidized product that was identified by GC-MS. The additional oxygen atom is probably introduced into the ring as the mass fragment of the propionyl group was unchanged after the oxidation. The GC-MS data of another product indicated the oxidation of the aromatic ring of 3,4-DCPA. In accordance with a molecular peak $[(M_{3,4\text{-DCPA}} + 16)^+]$ and a mass fragment suggesting an unchanged amide function we propose the formation of 3,4-dichlorohydroxypropionanilide (**15**). We detected a second product having a molecular peak

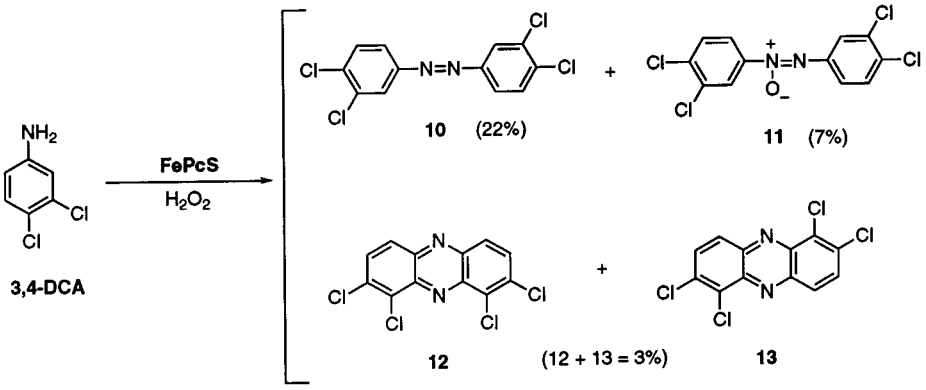

Figure 2. Products formed in the oxidation of 3,4-DCA by $FePcS/H_2O_2$; indicated percentages are isolated yields after a 69% conversion of the substrate

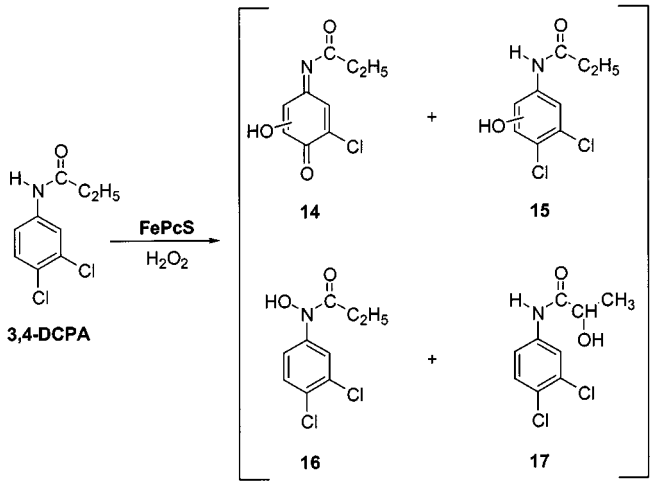

Figure 3. Proposed structures for the products of the oxidation of 3,4-DCPA by FePcS/H_2O_2

$[(M_{3,4\text{-DCPA}} + 16)^+]$. The corresponding mass spectrum indicated that oxidation on the aromatic ring or on the propionyl group had not taken place. These characteristics are in agreement with the proposed formula of 3,4-dichloro-*N*-hydroxypropionanilide (**16**). Furthermore, we detected a product with a mass spectrum suggesting the incorporation of an oxygen atom into the propionyl substituent. The following structural hypotheses have to be considered: (i) formation of an ester by insertion of an oxygen atom, (ii) oxidation of the methylene group or (iii) oxidation of the methyl group. A carbonyl group can be oxidized to the corresponding ester by an oxygen atom donor such as *m*-chloroperbenzoic acid or $KHSO_5$ through a Bayer−Villiger reaction.[9] This kind of reaction is rather unexpected in the presence of hydrogen peroxide even if a nucleophilic Fe^{III}-peroxo species is formed with FePcS.[5c] Therefore, we propose the oxidation of the acyl methylene group, since secondary C−H bonds of a methylene group in the α-position with respect to a carbonyl group should be weaker than tertiary C−H bonds of a methyl group. The proposed product is the 3,4-dichloro-2-hydroxy-propionanilide **17**. Coupling products, such as the azobenzene **10** and the azoxybenzene **11**, were not detected in the degradation of 3,4-DCPA by FePcS/H_2O_2.

Discussion

In the first part of this work we investigated the behavior of two dichloroanilines, 3,4-DCA and 3,5-DCA, in oxidations catalyzed by FePcS. In order to check the influence of the chloro-substituents on the reaction rate we compared the conversions obtained for these two dichloroaniline isomers. The reactions catalyzed by FePcS with potassium monopersulfate as oxidant were too fast to detect differences in the reaction rates by HPLC analyses. However, in the catalytic oxidations with hydrogen peroxide, 3,4-DCA is converted faster than 3,5-DCA, suggesting a lower oxidation potential for the isomer with chloro-substituents in positions 3 and 4.

The oxidation of both DCA derivatives catalyzed by FePcS is faster with potassium monopersulfate than with hydrogen peroxide. Sorokin et al. reported that the oxidation of 2,4,6-trichlorophenol (TCP) catalyzed by FePcS was also remarkably influenced by the oxidant and occurred much faster with $KHSO_5$.[5] This characteristic could be explained by the formation of different active species of the catalyst with potassium monopersulfate or hydrogen peroxide. The authors proposed that the activation of $KHSO_5$ by FePcS leads to the formation of an iron(IV)-oxo species ($Fe^{IV}=O$), which is able to abstract electrons from aromatic substrates such as DCA or TCP, but unable to transfer the oxygen atom of the iron(IV)-oxo species to an olefin, styrene or cyclohexene.[5c] Furthermore, recent data regarding the oxidation of polycyclic aromatic hydrocarbons by FePcS/H_2O_2 indicate that the activation of H_2O_2 by FePcS probably generates two different kinds of active species: an iron(IV)-oxo entity ($Fe^{IV}=O$) and an iron(III)-hydroperoxo species ($Fe^{III}-OOH$).[6] The oxidation potential of the iron(IV)-oxo species is expected to be higher than that of the lower valent iron(III)-hydroperoxo entity. When potassium monopersulfate is used as the oxidant, the concentration of iron(IV)-oxo species is higher than with hydrogen peroxide and, consequently, we obtained faster substrate conversions.

The formation of the oxidation products from 3,5-DCA can be explained in terms of the mechanism depicted in Figure 4. Two successive one-electron oxidations of 3,5-DCA and a deprotonation lead to the formation of the cation **A**, with a positive charge delocalized on the nitrogen atom and on the *ortho* or *para* positions of the ring. The nucleophilic addition of a water molecule to the nitrogen atom and further deprotonation gave the 3,5-dichloro-hydroxylaniline **B** (pathway a). As proposed by Pothuluri et al.,[2] compound **B** can react with another substrate molecule to form the 3,5,3′,5′-tetrachlorohydrazobenzene **C**, which is then oxidized to the 3,5,3′,5′-tetrachloroazobenzene (**7**) and to the 3,5,3′,5′-tetrachloroazoxybenzene (**8**). The addition of a water molecule at the *para* position of the cation **A** (pathway b in Figure 4) generates intermediate **D**, which is transformed into 2,6-dichloro-1,4-quinoneimine (**1**) by deprotonation and removal of two electrons. The proposed reaction mechanism suggests that the degradation of dichloroanilines and their transformation into dimers proceeds via the same intermediate **A**. In the case of 3,5-DCA, two successive one-electron oxidations are necessary to generate the 3,5-dichloro-hydroxylaniline **B**, whereas four electrons have to be abstracted from 3,5-DCA to produce the 2,6-dichloro-1,4-quinoneimine **1**. This electrophilic compound can then be further oxidized to ring-cleavage products by addition of peroxidic oxidants, either activated or not activated by FePcS, as shown in quinone intermediates observed in the oxidative degradation of 2,4,6-trichlorophenol.[5c]

In the second part of this work we investigated the catalytic oxidation of the dichloroanilides 3,4-DCPA and 3,5-

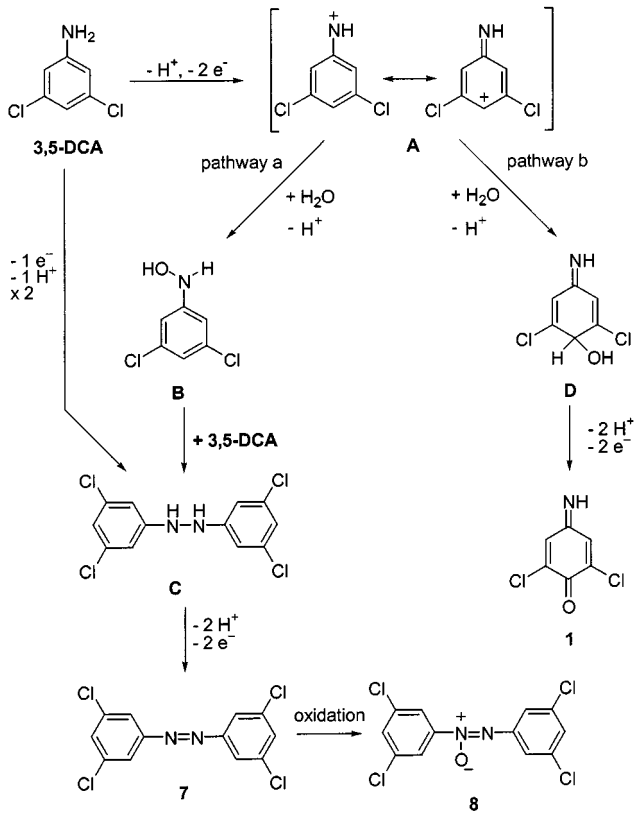

Figure 4. Proposed mechanism for the oxidation of 3,5-DCA by FePcS/$KHSO_5$; compounds indicated by numbers have been identified whereas derivatives assigned by capital letters are only putative intermediates

DCAA, prepared by reacting the respective DCA isomers with propionic or acetic anhydride. The results of the catalytic oxidations indicate that the introduction of an electron-withdrawing substituent such as a propionyl or an acetyl group reduced the conversion rates of these anilides compared with the corresponding amines. In addition, the anilide 3,5-DCAA, with two chloro-substituents on positions 3 and 5 of the aromatic ring, is more difficult to oxidize than the 3,4-isomer 3,4-DCPA. It should be noted that we observed the same tendency in the oxidations of 3,5-DCA and 3,4-DCA because only the latter was fully converted by FePcS/H_2O_2 (Table 1, runs 2 and 6).

The oxidation of 3,4-DCPA by FePcS/H_2O_2 gave the hydroxylated *N*-propionyl-quinoneimine **14**, which is formed after release of one chloride. The analytical data suggest that the formation of products **15**, **16** and **17** resulted from oxidations of the aromatic ring, the amide function or the acyl chain of 3,4-DCPA, respectively. The dechlorination value (1.0 Cl^-/converted 3,4-DCPA) indicates that other unidentified dechlorinated products should be formed, since **14** is the only mono-chlorinated compound observed.

Coupling products such as azo or azoxy compounds were not detected in the catalytic oxidation of 3,4-DCPA by FePcS/H_2O_2. The presence of the propionyl substituent on the aniline derivative blocked the formation of toxic dimers such as the azobenzene **10** and the azoxybenzene **11**, which were always produced in the catalytic oxidations of DCA derivatives under similar conditions.

Conclusion

The present study indicates that the catalytic systems FePcS/$KHSO_5$ and FePcS/H_2O_2 are able to oxidize recalcitrant pollutants such as dichloroanilines and related anilides. One part of the pollutant 3,5-DCA was partially transformed by FePcS/$KHSO_5$ into more biodegradable products such as chloromaleic acid (**3**) and formic acid (**4**), whereas the other part of 3,5-DCA was oxidized to toxic dimers such as the azobenzene **7** and the azoxybenzene **8**. The FePcS-catalyzed oxidation of 3,4-DCA with hydrogen peroxide gave mainly coupling products without ring cleavage products.

The noncatalyzed oxidations of DCA isomers with $KHSO_5$ led to fast conversions of the pollutants without chlorine release, indicating that the FePcS catalyst is necessary for the oxidative ring cleavage of the dichloroaniline derivatives.

The oxidation of DCA by these bio-inspired systems is, like the degradation of 3,4-DCA by lignin peroxidase from *Phanerochaete chrysosporium*,[4] a double-edged sword, since the formation of more biodegradable compounds and toxic dimers occurs simultaneously. The formation of oligomers could be avoided when these amines were converted into amides before the catalytic oxidation. Unfortunately, the electron-withdrawing acyl substituents are responsible for slower substrate conversions, but the optimization of the reaction conditions might be able to produce full substrate conversions without the formation of toxic coupling products in these catalytic degradation reactions of dichloroaniline derivatives.

Experimental Section

Materials: Potassium monopersulfate (the triple salt $[KHSO_5]_2[KHSO_4][K_2SO_4]$, Curox®) was a gift from Peroxid Chemie GmbH. Hydrogen peroxide was obtained from Acros as a 35 wt.% solution. 3,4-DCA, 3,5-DCA, 3,5-dichloronitrobenzene and 2,6-dichloro-1,4-benzoquinone were purchased from Aldrich. Iron tetrasulfonatophthalocyanine (FePcS) was prepared according to the modified method of Weber and Busch.[11][12]

Analytical procedures: The conversions of substrates were monitored by HPLC (Waters 510 pump, Waters 486 detector) using a μ-Bondapak C18 column. The eluent was a mixture of acetonitrile/phosphate buffer 0.05 M (pH 7.0) in proportions 55:45 (v/v) for oxidations of 3,5-DCA and 3,4-DCPA and 40:60 (v/v) for oxidations of 3,4-DCA and 3,5-DCAA. The flow rate was 1 mL/min and the detection was performed at 220 nm. Gas chromatography-mass spectrometry data (GC-MS), except for compounds **1** and **2**, were recorded on a Hewlett-Packard 5890 instrument by electron-impact ionization at 70 eV. The carrier gas for GC-MS was helium and a non polar capillary column (12 m × 0.2 mm HL-1, crosslinked methylsilicone) was used. The injector temperature was 250°C, and analyses were performed at 80°C for 2 min, then up to 250°C (10°C/min) for a further 15 min. The GC-MS data for

compounds **1** and **2** were obtained using a Hewlett-Packard 5890 spectrometer with a nonpolar capillary column (50 m × 0.22 mm BPX5). The injector temperature was 250°C, and analyses were performed at 100°C for 0.5 min, then up to 325°C (6°C/min) for a further 30 min. ^{1}H NMR spectra were recorded with a Bruker WM 250 spectrometer. The concentration of chloride ions was determined by the mercuric thiocyanate method.[10]

General Procedure for Catalytic Oxidations: The reaction mixture, with a final volume of 4 mL, contained 4 μmol of substrate, 0.12 μmol of FePcS and 5 μmol of $KHSO_5$ or 6 μmol of H_2O_2. The reaction mixtures were prepared as follows: 80 μL of a substrate solution (50 mM) in acetone was mixed with 80 μL of an internal standard (4-fluoronitrobenzene, 50 mM) in acetone. 1.5 mL of an aqueous FePcS solution (80 μM) was added and the reaction mixture was adjusted to a final volume of 4 mL with 400 μL of phosphate buffer (500 mM, pH 7), 240 μL of acetone and 1.7 mL of water for 3,5-DCA, 3,4-DCA and 3,4-DCPA (acetone/water = 1:9, v/v) or with 400 μL of phosphate buffer (500 mM, pH 7), 640 μL of acetone and 1.3 mL of water for 3,5-DCAA (acetone/water = 2:8, v/v). Finally, 175 μL of H_2O_2 (0.12 M) or 50 μL of $KHSO_5$ (0.4 M) was added and the reaction mixture was stirred at room temperature.

Characterization of the Oxidation Products of 3,5-DCA: The reaction was carried out under the conditions described for run 5 in Table 1 with a larger (25 times) reaction volume (100 mL). The reaction mixture was stirred for 1 h at room temperature. The acetone and water were then evaporated under vacuum at 50°C and the residue was dried for 1 h under vacuum at room temperature. The residue was dissolved in 10 mL of 1 M HCl saturated with NaCl (resulting pH = 2). The products were extracted with diethyl ether (4 × 60 mL). After evaporation of the ether, the dark brown residue was dried under vacuum for 2 h at room temperature and dissolved in 1 mL of diethyl ether. The resulting solution was analyzed by GC-MS. In order to analyze the product mixture by ^{1}H NMR spectroscopy the diethyl ether was evaporated and the residue was dissolved in 1 mL of deuterated dimethyl sulfoxide ([D_6] DMSO).

In order to identify the intermediate products, we modified the work-up described above and acidified the reaction mixture after 5 min of reaction time without prior evaporation of water and acetone. After extraction with 2 × 60 mL of diethyl ether and evaporation of the ether, the residue was contaminated with buffer salts because of their solubility in acetone. The residue was dissolved in 20 mL of diethyl ether and filtered to separate the salts from oxidation products.

2,6-Dichloro-1,4-quinoneimine (1): The mass spectrum corresponded to the 2,6-dichloro-4-aminophenol, which is the reduced form of compound **1**. GC-MS: m/z = 180 [$(M + 2)^+$], 178 [M^+], 144 [$(M + 2 - HCl)^+$], 142 [$(M - HCl)^+$], 116 [$(M + 2 - HCOCl)^+$], 114 [$(M - HCOCl)^+$].

2,6-Dichloro-1,4-benzoquinone (2): The mass spectrum corresponded to the 2,6-dichloro-1,4-hydroquinone, which is the reduced form of compound **2**. GC-MS: m/z = 179 [$(M + 2)^+$], 177 [M^+], 143 [$(M + 2 - HCl)^+$], 141 [$(M - HCl)^+$], 115 [$(M + 2 - HCOCl)^+$], 113 [$(M - HCOCl)^+$].

Chloromaleic acid (3): ^{1}H NMR ([D_6] DMSO): δ = 6.67 (s, CH). Chloromaleic acid formed an adduct with traces of unchanged 3,5-DCA under the conditions of GC-MS analysis. GC-MS data of the adduct: m/z = 277 [$(M + 2)^+$], 275 [M^+], 242 [$(M + 2 - Cl)^+$], 240 [$(M - Cl)^+$], 198 [$(M + 2 - CO_2Cl)^+$], 196 [$(M - CO_2Cl)^+$], 161 [$(M + 2 - CHCCl(CO)_2)^+$], 159 [$(M - CHCCl(CO)_2)^+$]. We verified the GC-MS data by co-injection of a solution containing 3,5-DCA and chloromaleic acid, and the same adduct (retention time and mass spectrum) was formed during the analysis. Chloromaleic acid was prepared according to the method of Gruzdev and Gruzdev.[13]

Formic acid (4): ^{1}H NMR ([D_6] DMSO): δ = 8.24 (s, CH). Formic acid formed an adduct with traces of unchanged 3,5-DCA under the conditions of GC-MS analysis. GC-MS data of the adduct: m/z = 191 [$(M + 2)^+$], 189 [M^+], 163 [$(M + 2 - CO)^+$], 161 [$(M - CO)^+$]. We verified the data by co-injection of a solution containing 3,5-DCA and formic acid, and the same adduct (retention time and mass spectrum) was formed during the analysis.

3,5-Dichloronitrosobenzene (5): GC-MS: m/z = 177 [$(M + 2)^+$], 175 [M^+], 147 [$(M + 2 - NO)^+$], 145 [$(M - NO)^+$], 111 [$(M + 2 - HNOCl)^+$], 109 [$(M - HNOCl)^+$].

3,5-Dichloronitrobenzene (6): GC-MS: m/z = 193 [$(M + 2)^+$], 191 [M^+], 163 [$(M + 2 - NO)^+$], 161 [$M - NO)^+$], 147 [$(M + 2 - NO_2)^+$], 145 [$(M - NO_2)^+$]. – HPLC: product **6** was also characterized by co-injection of an authentic commercial sample which had the same retention time. The quantification of compound **6** in the oxidation of 3,5-DCA with $KHSO_5$, corresponding to run 7 in Table 1, was recorded by HPLC with 4-fluoronitrobenzene as an internal standard.

3,5,3′,5′-Tetrachloroazobenzene (7): GC-MS: m/z = 322 [$(M + 4)^+$, 12], 320 [$(M + 2)^+$, 20], 318 [M^+, 14], 175 [$(M + 2 - C_6H_3Cl_2)^+$, 18], 173 [$(M - C_6H_3Cl_2)^+$, 30], 147 [$(M + 2 - C_6H_3N_2Cl_2)^+$, 55], 145 [$(M - C_6H_3N_2Cl_2)^+$, 82].

3,5,3′,5′-Tetrachloroazoxybenzene (8): GC-MS: m/z = 338 [$(M + 4)^+$, 3], 336 [$(M + 2)^+$, 7], 334 [M^+, 6], 322 [$(M + 4 - O)^+$, 13], 320 [$(M + 2 - O)^+$, 24], 318 [$(M - O)^+$, 20], 175 [$(M + 2 - C_6H_3Cl_2O)^+$, 20], 173 [$(M - C_6H_3Cl_2O)^+$, 33], 147 [$(M + 2 - C_6H_3Cl_2N_2O)^+$, 64], 145 [$(M - C_6H_3Cl_2N_2O)^+$, 100].

1,3,6,8-tetrachlorophenazine (9): GC-MS: m/z = 320 [$(M + 4)^+$, 48], 318 [$(M + 2)^+$, 100], 316 [M^+, 76], 283 [$(M + 2 - Cl)^+$, 17], 281 [$(M - Cl)^+$, 20], 248 [$(M + 2 - Cl_2)^+$, 6], 246 [$(M - Cl_2)^+$, 9].

Characterization of the Oxidation Products of 3,4-DCA. – Procedure for the catalytic oxidation: The reaction mixture, with a final volume of 200 mL, contained 2 mmol of 3,4-DCA, 80 μmol of FePcS (catalyst/substrate ratio: 4%) and 10 mmol of H_2O_2. The reaction mixture was prepared as follows: 324 mg of 3,4-DCA and 82 mg of FePcS (M = 1022) were dissolved in a previously prepared solvent mixture containing 40 mL of acetone and 110 mL of water. Phosphate buffer (50 mL, pH 7, 500 mM) was added. Finally, 1 mL of H_2O_2 (12 M, 35 wt.%) was added in five aliquots (5 × 200 μL every 5 min) and the reaction mixture was stirred at room temperature.

Isolation of the Oxidation Products: After a reaction time of 60 min, the mixture was filtered and the remaining precipitate was dried for 3 h under vacuum. Yield: 223 mg (69%). In order to separate the hydrophobic products from paramagnetic iron salts, the precipitate was dissolved in diethyl ether and filtered. The filtrate was evaporated under vacuum and 155 mg (48%) of organic products were isolated. Afterwards, the products were separated by liquid chromatography (column on silica, eluent: dichloromethane/hexane = 65:35) and analyzed by GC-MS and ^{1}H NMR spectroscopy.

3,4,3′,4′-Tetrachloroazobenzene (10): Yield: 71 mg (22%). – GC-MS: m/z = 322 [$(M + 4)^+$, 10], 320 [$(M + 2)^+$, 19], 318 [M^+, 14], 175 [$(M + 2 - C_6H_3Cl_2)^+$, 18], 173 [$(M - C_6H_3Cl_2)^+$, 28], 147 [$(M + 2 - C_6H_3N_2Cl_2)^+$, 53], 145 [$(M - C_6H_3N_2Cl_2)^+$, 82]. – ^{1}H NMR ($CDCl_3$): δ = 7.61 (d, 1 H, J = 7.5 Hz, C_5-H, $C_{5'}$-H), 7.79

(dd, 1 H, J = 7.5 Hz, J = 2.5 Hz, C_6-H, $C_{6'}$-H), 8.00 (d, 1 H, J = 2.5 Hz, C_2-H, $C_{2'}$-H).

3,4,3′,4′-Tetrachloroazoxybenzene (11): Yield: 22 mg (7%). − GC-MS: m/z = 338 [(M + 4)$^+$, 3], 336 [(M + 2)$^+$, 7], 334 [M$^+$, 6], 322 [(M + 4 − O)$^+$, 13], 320 [(M + 2 − O)$^+$, 25], 318 [(M − O)$^+$, 20], 175 [(M + 2 − $C_6H_3Cl_2O$)$^+$, 21], 173 [(M − $C_6H_3Cl_2O$)$^+$, 32], 147 [(M + 2 − $C_6H_3Cl_2N_2O$)$^+$, 64], 145 [(M − $C_6H_3Cl_2N_2O$)$^+$, 100]. − ^{1}H NMR ($CDCl_3$): δ = 7.52 (d, 1 H, J = 7.5 Hz, $C_{2'}$-H), 7.57 (d, 1 H, J = 7.5 Hz, C_2-H), 7.98 (dd, 1 H, J = 10 Hz, J = 2.5 Hz, $C_{6'}$-H), 8.12 (dd, 1 H, J = 10 Hz, J = 2.5 Hz, C_6-H), 8.38 (d, 1 H, J = 2.5 Hz, $C_{2'}$-H), 8.39 (d, 1 H, J = 2.5 Hz, C_2-H).

Tetrachlorophenazines 12 and 13: Yield: 9.5 mg (3%). − GC-MS: m/z = 320 [(M + 4)$^+$, 48], 318 [(M + 2)$^+$, 100], 316 [M$^+$, 76], 283 [(M + 2 − Cl)$^+$, 17], 281 [(M − Cl)$^+$, 20], 248 [(M + 2 − Cl_2)$^+$, 6], 246 [(M − Cl_2)$^+$, 9]. − **3,4,6,7-tetrachlorophenazine 12:** ^{1}H NMR ($CDCl_3$): δ = 7.87 (d, 1 H, J = 9 Hz, C_2-H, C_8-H), 8.09 (d, 1 H, J = 9 Hz, C_1-H, C_9-H). − **1,2,6,7-tetrachlorophenazine 13:** ^{1}H NMR ($CDCl_3$): δ = 7.93 (d, 1 H, J = 9 Hz, C_3-H, C_8-H), 8.25 (d, 1 H, J = 9 Hz, C_4-H, C_9-H).

Preparation of 3,4-Dichloropropionanilide (3,4-DCPA): Propionic anhydride (20 mL, 156 mmol) was added to 3,4-dichloroaniline (600 mg, 3.7 mmol). The mixture was stirred at 60 °C for 4 h and then at 100 °C for 2 h. The propionic acid and unreacted propionic anhydride were removed by distillation (bath temperature: 70 °C) under vaccum. The remaining orange oil was dissolved in 5 mL of dichloromethane and the product was precipitated by addition of 100 mL of hexane. The white powder was filtered off and dried under vacuum for 4 h at 25 °C. − Yield: 550 mg (68%). − ^{1}H NMR ([D_6] DMSO): δ = 1.19 (t, 3 H, CH_3), 2.44 (q, 2 H, CH_2), 7.59 (dd, 1 H, C_6-H), 7.67 (d, 1 H, C_5-H), 8.12 (d, 1 H, C_2-H), 10.29 (s, 1 H, NH). − GC-MS: m/z = 219 [(M + 2)$^+$], 217 [M$^+$], 163 [(M + 2 − $COCH_2CH_2$)$^+$], 161 [(M − $COCH_2CH_2$)$^+$]. − $C_9H_9Cl_2NO$ (218): calcd. C 49.54, H 4.13, N 6.42; found C 49.62, H 3.79, N 6.38.

Preparation of 3,5-Dichloroacetanilide (3,5-DCAA): Acetic anhydride (10 mL, 102 mmol) was added to a solution of 3,5-dichloroaniline (300 mg, 1.85 mmol) in 10 mL of acetonitrile. The reaction mixture was stirred for 2 h at 100 °C. The acetic acid and unreacted acetic anhydride were removed by distillation (bath temperature: 100 °C) under vaccum. The remaining beige oil was dissolved in 5 mL of dichloromethane and the product was precipitated by the addition of 100 mL of hexane. The white powder was filtered off and dried under vacuum for 3 h at 25 °C. − Yield: 310 mg (82%). − ^{1}H NMR ([D_6] DMSO): δ = 2.18 (s, 3 H, CH_3), 7.36 (s, 1 H, C_4-H), 7.76 (s, 2 H, C_2-H, C_6-H), 10.41 (s, 1 H, NH). − GC-MS: m/z = 205 [(M + 2)$^+$], 203 [M$^+$], 163 [(M + 2 − $COCH_2$)$^+$], 161 [(M − $COCH_2$)$^+$]. − $C_8H_7Cl_2NO$ (204): calcd. C 47.06, H 3.43, N 6.86; found C 47.17, H 3.15, N 6.91.

Characterization of the Oxidation Products of 3,4-DCPA: The reaction was carried out under the conditions as described for run 2 in Table 2 with a larger (25 times) reaction volume (100 mL). The workup was identical to that used for the characterization of the oxidation products of 3,5-DCA.

2-Chloro-hydroxy-*N*-propionyl-1,4-quinoneimine (14): GC-MS: m/z = 215 [(M + 2)$^+$], 213 [M$^+$], 185 [(M − C_2H_4)$^+$], 161 [(M + 2 − CNC_2H_4)$^+$], 159 [(M − CNC_2H_4)$^+$].

3,4-Dichlorohydroxypropionanilide (15): GC-MS: m/z = 235 [(M + 2)$^+$], 233[M$^+$], 179 [(M + 2 − COC_2H_4)$^+$], 177 [(M − COC_2H_4)$^+$].

3,4-Dichloro-*N*-hydroxypropionanilide (16): GC-MS: m/z = 235 [(M + 2)$^+$], 233[M$^+$], 217 [(M + 2 − H_2O)$^+$], 215 [(M − H_2O)$^+$], 179 [(M + 2 − COC_2H_4)$^+$], 177 [(M − COC_2H_4)$^+$].

3,4-Dichloro-2-hydroxypropionanilide (17): GC-MS: m/z = 235 [(M + 2)$^+$], 233 [M$^+$], 191 [(M + 2 − CO_2)$^+$], 189 [(M − CO_2)$^+$], 163 [(M + 2 − $CO_2C_2H_4$)$^+$], 161 [(M − $CO_2C_2H_4$)$^+$].

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