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# Mechanism of the oxidation of aromatic sulfides catalysed by a water soluble iron porphyrin

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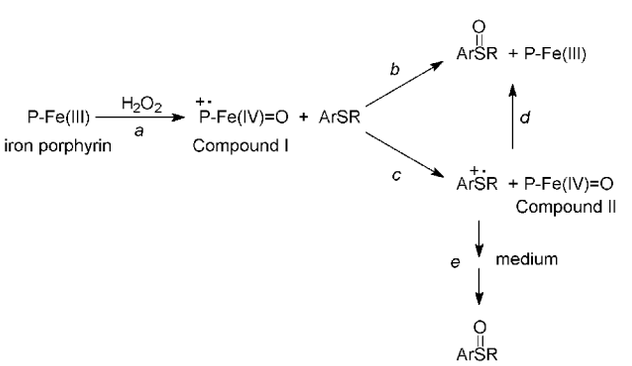
The oxygen atom transfer–electron transfer (ET) mechanistic dichotomy has been investigated in the oxidation of a number of aryl sulfides by $H_2O_2$ in acidic (pH 3) aqueous medium catalysed by the water soluble iron(III) porphyrin 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine-*p*,*p*′,*p*″,*p*‴-tetrasulfonic acid iron(III) chloride (FeTPPSCl). Under these reaction conditions, the iron–oxo complex porphyrin radical cation, $P^{+\bullet}$ Fe(IV)=O, should be the active oxidant. When the oxidation of a series of *para*-X substituted phenyl alkyl sulfides (X = $OCH_3$, $CH_3$, H, Br, CN) was studied the corresponding sulfoxides were the only observed product and the reaction yields as well as the reactivity were little influenced by the nature of X as well as by the bulkiness of the alkyl group. Labelling experiments using $H_2{}^{18}O$ or $H_2{}^{18}O_2$ clearly indicated that the oxygen atom in the sulfoxides comes exclusively from the oxidant. Moreover, no fragmentation products were observed in the oxidation of a benzyl phenyl sulfide whose radical cation is expected to undergo cleavage of the β C–H and C–S bonds. These results would seem to suggest a direct oxygen atom transfer from the iron–oxo complex to the sulfide. However, competitive experiments between thioanisole ($E°$ = 1.49 V *vs.* NHE in $H_2O$) and *N*,*N*-dimethylaniline ($E°$ = 0.97 V *vs.* NHE in $H_2O$) resulted in exclusive *N*-demethylation, whereas the oxidation of *N*-methylphenothiazine (**10**, $E°$ = 0.95 V *vs.* NHE in $CH_3CN$) and *N*,*N*-dimethyl-4-methylthioaniline (**11**, $E°$ = 0.65 V *vs.* NHE in $H_2O$) produced the corresponding sulfoxide with complete oxygen incorporation from the oxidant. Since an ET mechanism must certainly hold in the reactions of **10** and **11**, the oxygen incorporation experiments indicate that the intermediate radical cation, once formed, has to react with PFe(IV)=O (the reduced form of the iron–oxo complex which is formed by the ET step) in a fast oxygen rebound. Thus, an ET step followed by a fast oxygen rebound is also suggested for the other sulfides investigated in this work.

## Introduction

The enzymatic oxidation of sulfides to sulfoxides by heme peroxidases [such as horseradish peroxidase (HRP), chloroperoxidase (CPO), lactoperoxidase (LPO) and lignin peroxidase (LiP)] is an important process from both the synthetic and mechanistic point of view.[1] In particular, a number of studies have been mainly directed to get information about the enzyme active site structure and to distinguish between the two possible reaction mechanisms, direct oxygen atom transfer ("oxene process") or electron transfer (ET).[2]

Such a mechanistic dichotomy is illustrated in Scheme 1




**Scheme 1** Oxygen atom transfer mechanism *vs.* ET-oxygen rebound.

where $P^{+\bullet}$Fe(IV)=O is the iron(IV)-oxo porphyrin radical cation (also called compound I) which is the active species involved in these reactions and is formed by reaction of the native enzyme P–Fe(III) (P is a protoporphyrin IX) with hydrogen peroxide (Scheme 1, path *a*).[1]

In the oxygen atom transfer mechanism the sulfoxide is formed by direct oxygen transfer from the iron(IV)-oxo porphyrin radical cation to the sulfide, a process also called "oxene transfer" (Scheme 1, path *b*). In the ET mechanism, the transfer of one electron first occurs from the sulfide to $P^{+\bullet}$Fe(IV)=O (path *c*) to form a sulfide radical cation and P–Fe(IV)=O (compound II). The sulfoxide is then formed either by transfer of the oxygen atom from PFe(IV)=O to the radical cation, the so called "oxygen rebound" step (path *d*) or by reaction with the medium (path *e*). The available evidence quite clearly indicates that the sulfoxidations catalysed by peroxidases occur by an ET mechanism (paths *c* and *d* + *e*).[2a,2b,2f,3] An exception seems to be represented by CPO where an oxygen atom transfer mechanism has also been suggested.[2d] However, this enzyme differs from the other peroxidases for the fifth iron ligand, which is a cysteine thiolate instead of a histidine residue.

The studies on the enzymatic oxidation of sulfides have been complemented by several investigations carried out using synthetic peroxidase models, mainly iron tetraaryl porphyrins.[2c,2e,2f,4] These compounds represent good models for peroxidases since the active species, formed by reaction with a suitable oxygen donor, can again be described as an iron(IV)-oxo porphyrin radical cation and therefore closely resemble the enzyme active species compound I (Scheme 1, path *a*, where P is now a synthetic porphyrin).[5] Thus, also in the metalloporphyrin promoted sulfoxidations the attention has been focused on the mechanistic dichotomy described in Scheme 1.

In pioneering work Oae and coworkers suggested an ET mechanism (Scheme 1, path *c*) for the sulfoxidation of a series of aromatic sulfides promoted by an iron(III) porphyrin.[4a] However, Baciocchi and associates later presented results favouring a direct oxygen atom transfer mechanism[2c,2e] (Scheme 1, path *b*), a conclusion recently confirmed by Watanabe and coworkers on the basis of a correlation between the oxidation rate

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constants and the sulfide oxidation potentials.[2f] Only when a sulfide with a very low oxidation potential (0.96 V *vs*. NHE in $CH_3CN$) was used was the sulfoxidation suggested to proceed *via* an ET process. Thus, it would seem that, in contrast to peroxidases, the chemical models generally prefer to react by the oxygen atom transfer mechanism.

It should, however, be considered that the data with chemical models obtained so far refer to organic solvents and therefore do not allow a good comparison with peroxidase induced reactions which are run in water. Indeed, it is known that on passing from organic solvents to a much more polar aqueous medium the substrate oxidation potentials significantly decrease (by 0.2–0.4 V).[6] Thus, an ET mechanism might be more favoured in $H_2O$ than in an organic solvent and this might be the origin of the different behaviours of the enzymatic and biomimetic systems.

With this possibility in mind, we have thus studied the oxidation of a number of aromatic sulfides by $H_2O_2$ in aqueous acidic medium (pH 3) catalysed by the water soluble iron(III) porphyrin 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine-*p*,*p*′,*p*″,*p*‴-tetrasulfonic acid iron(III) chloride (FeTPPSCl) in the presence of imidazole. The low pH as well as the presence of imidazole should favour the heterolytic cleavage of the O–O bond in $H_2O_2$ and thus the formation of the iron(IV)-oxo porphyrin radical cation as it occurs in the peroxidase catalysed reactions (Scheme 1).[7] In particular, we have investigated the oxidation of the alkyl aryl sulfides **1**–**8**, benzyl aryl sulfide **9**, *N*-methylphenothiazine **10** and *N,N*-dimethyl-4-methylthioaniline **11** (Chart 1). These substrates span a significant range of oxidation potential values (from 0.88 V *vs*. NHE in $CH_3CN$ for **11**[8] to 1.85 V *vs*. NHE in $CH_3CN$ for **5**[2f]). Moreover it is known that in addition to producing sulfoxide, the radical cation of **9** also undergoes β C–H and C–S bond cleavage leading to benzylic derivatives (*vide infra*).[2d] Thus **9** may represent a mechanistic probe to detect the occurrence of an ET mechanism.

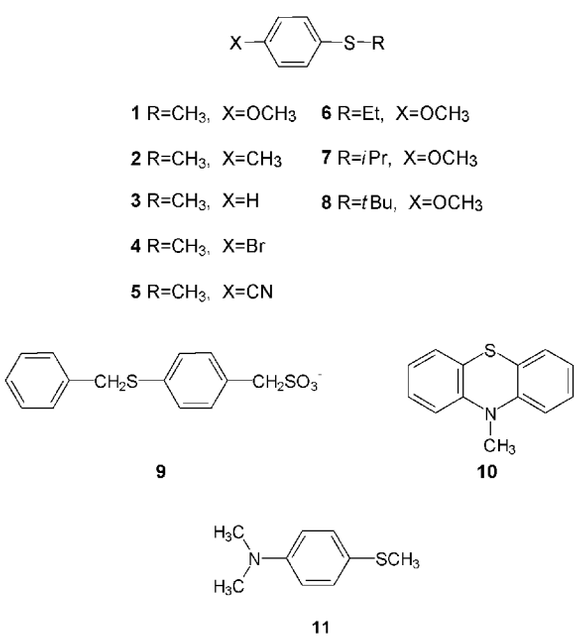



**Chart 1**

## Results and discussion

The sulfides were reacted for 1 h with an equimolar concentration of hydrogen peroxide in the presence of FeTPPSCl and imidazole[9] in 50 mM sodium tartrate buffered aqueous solution (pH 3) containing 5% acetonitrile as cosolvent, at 25 °C and under an argon atmosphere. The sulfide / FeTPPSCl / imidazole ratio used in these experiments was 1 / 0.03 / 3. In all cases, sulfoxides were the exclusive oxidation products. The only exception was **11** which also underwent *N*-demethylation (see Experimental). It was verified that either in the absence of FeTPPSCl or in the absence of $H_2O_2$ no products were formed. The sulfoxide yields [referring to the same time of reaction (1 h) and not optimised] are reported in Table 1. This table also shows the percent of $^{18}O$ incorporation in the sulfoxide when the oxidation of the sulfides was carried out in 50 mM sodium tartrate buffered aqueous solutions, pH 3, containing 10% $H_2{}^{18}O$ or when $H_2{}^{18}O_2$ was used as the oxidant.

**Table 1** FeTPPSCl catalysed oxidation of aryl sulfides **1**–**8** (4-$XC_6H_4SR$), **9**,**10** and **11** by $H_2O_2$ in the presence of imidazole.

| Substrate | Sulfoxide yield (%)[a] | $^{18}O$-incorporation | |
|---|---|---|---|
| | | $H_2{}^{18}O$ | $H_2{}^{18}O_2$ |
| **1** X = $CH_3O$, R = $CH_3$ | 79 | 0%[b] | 98% |
| **2** X = $CH_3$, R = $CH_3$ | 72 | 0% | 97% |
| **3** X = H, R = $CH_3$ | 57 | 0% | n.d. |
| **4** X = Br, R = $CH_3$ | 31 | 0% | n.d. |
| **5** X = CN, R = $CH_3$ | 32 | 0% | 97% |
| **6** X = $CH_3O$, R = Et | 90 | n.d. | n.d. |
| **7** X = $CH_3O$, R = *i*Pr | 78 | n.d. | n.d. |
| **8** X = $CH_3O$, R = *t*Bu | 31 | 0% | n.d. |
| **9** | 83 | n.d. | n.d. |
| **10** | 60 | 0% | 97% |
| **11** | 28[c] | 0% | >99% |

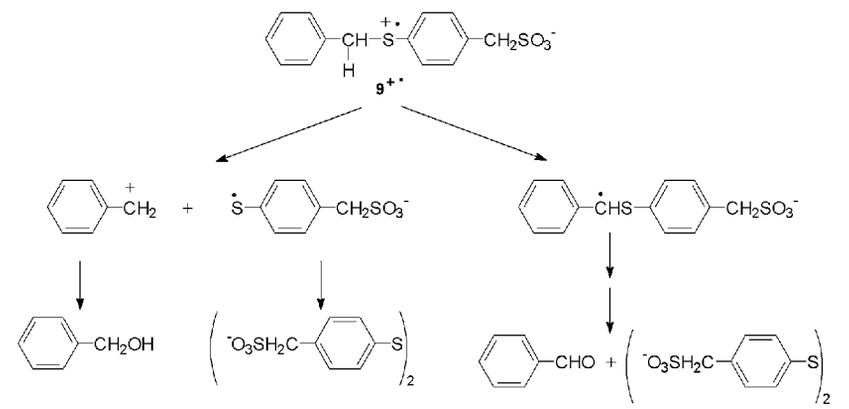
[a] Yields refer to the starting material, equimolar to $H_2O_2$. Average of at least two determinations, the error is in all cases < ± 1%. [b] The same area ratios for the $(m+2)/z$ and $m/z$ ions (±0.5%) were measured in the oxidations carried out under the same experimental conditions in $H_2{}^{16}O$. [c] Sulfoxidation was accompanied by the formation of a coupling product suggested as being derived from reaction of the *N*-demethylated product with **11** (for details, see Experimental).

Examination of the data for the oxidation of sulfides **1**–**8** indicates that substantial sulfoxidation occurs in all cases. The more reactive compound was 4-methoxythioanisole (79% yield) whereas 32% of sulfoxide was observed with 4-cyanothioanisole. Sulfoxide yields are not significantly influenced by the bulkiness of the R group. Considering the R groups, the sulfoxide yields were very high (80–90%) for R = Me, Et, *i*-Pr. A lower yield (31%) was found when R = *t*-Bu.

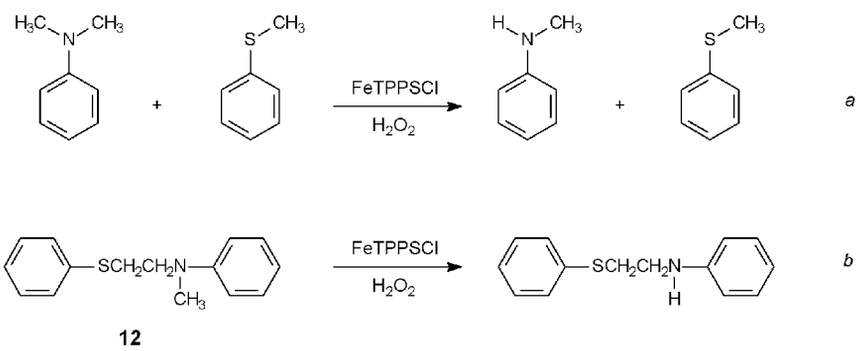
Several competitive experiments have clearly shown that the rate of sulfoxidation decreases by decreasing the substituent's electron donating power. Thus, 4-methoxythioanisole was 6.4 times more reactive than thioanisole whereas 4-cyanothioanisole appears to be 0.22 times less reactive than thioanisole. The reaction selectivity is however not very large as also observed by Watanabe and associates, albeit obtained in organic solvents.[2f]

When the oxidations were carried out in labelled water, no $^{18}O$ incorporation was observed in the product sulfoxides, which indicates that the oxygen in the product does not derive from the solvent but exclusively from the iron-oxo complex. This result was fully confirmed by using $^{18}O$ labelled $H_2O_2$: a complete incorporation of $^{18}O$ in the sulfoxide was always observed. Interestingly, complete $^{18}O$ incorporation from $H_2{}^{18}O_2$ was also found with **10** and **11**. Thus, in this respect, substrates with an oxidation potential as low as 0.65 V *vs*. NHE in $H_2O$[11] behave as thioanisole and the other less easily oxidisable sulfides.

Another important observation was that the oxidation of **9** by FeTPPSCl led exclusively to the formation of the corresponding sulfoxide without the formation of fragmentation products, disulfide, benzyl alcohol and benzaldehyde, that are instead expected when $\mathbf{9}^{+\bullet}$ is a reaction intermediate, as shown in Scheme 2 and as it was actually found in the oxidations catalysed by HRP[2d] and LiP[12] which indeed occur by an ET mechanism.



**Scheme 2** Fragmentation pathways for $\mathbf{9}^{+\bullet}$.



**Scheme 3**

There is no doubt that the lack of fragmentation products in the oxidation of **9** coupled with the complete incorporation of $^{18}O$ from $H_2{}^{18}O_2$ in the sulfoxide (or the absence of $^{18}O$ incorporation in the reaction carried out in $H_2{}^{18}O$) appear fully consistent with the previous hypotheses suggesting that sulf-oxidation catalysed by synthetic iron porphyrins generally takes place by an oxygen atom transfer mechanism. In addition, our data would seem to indicate that such a mechanism should also hold with substrates of very low oxidation potential like **10** and **11**.

In spite of the reasonableness of the above conclusion, it must, however, be recognised that the data at hand might be consistent as well with an ET mechanism where the oxygen rebound step of the radical cation is so fast as to completely overcome the other possible reactions of this species, *i.e.* fragmentation and/or reaction with the medium. In this respect, it has also to be noted that an ET mechanism should be still more likely with iron porphyrins than with peroxidases given the much higher oxidising power of the iron-oxo complex formed in the former case with respect to that of the active oxidant formed by peroxidases.[13] Therefore, we deemed it worthwhile to investigate further this possibility and to this purpose some competitive experiments were carried out where a sulfide was made to react with $H_2O_2$/FeTPPSCl in the presence of a compound of lower oxidation potential which was expected to react with FeTPPSCl under the same oxidising conditions by an ET mechanism. We felt that in case a preferential oxidation of the sulfide were observed, this would have been a quite decisive result in favour of a sulfoxidation occurring by the oxygen atom transfer mechanism.

Since previous studies had clearly demonstrated that the *N*-demethylation of *N,N*-dimethylanilines induced by FeTPPSCl is an ET reaction,[14] thioanisole ($E^\circ$ = 1.49 V *vs.* NHE in $H_2O$)[15] was reacted with $H_2O_2$/FeTPPSCl in the presence of *N,N*-dimethylaniline ($E^\circ$ = 0.97 V *vs.* NHE in $H_2O$).[16] The result was that only the *N*-demethylation product was formed (Scheme 3, reaction *a*), thus indicating that only the compound with the lower oxidation potential was oxidised. Interestingly, exclusive *N*-demethylation was also observed in the oxidation of **12**, where the arylsulfide and *N*-methylaniline moieties are in the same molecule, but isolated from one another (Scheme 3, reaction *b*).

These results clearly indicate that either *N,N*-dimethylaniline and thioanisole both react by the ET mechanism or that the ET reaction of *N,N*-dimethylaniline is much faster than the oxygen atom transfer reaction of thioanisole. A clearcut distinction between these two possibilities is certainly difficult, however, we feel that a quite reasonable choice in favour of the former possibility may be made on the basis of the results obtained in the oxidation of sulfides **10** and **11**which have both the *N*-methylamino and sulfur moieties directly bonded to the aromatic ring (Table 1).

Both **10** and **11** are aromatic *N*-methylamines with an oxidation potential lower than that of *N,N*-dimethylaniline. It is therefore very likely that, as observed with *N,N*-dimethylanilines,[14] and also in the light of the competitive experiment, they undergo an ET process when reacted with FeTPPSCl/$H_2O_2$. However, in this case, owing to the presence of the ring bonded sulfur functionality, the oxidation of these compounds led to sulfoxides, which clearly shows that the radical cation is an intermediate *en route* to the sulfoxide formation.[17] Still more important is that complete$^{18}O$ incorporation was observed in the sulfoxide formed from **10** and **11**. Hence, not only a radical cation is formed in these reactions, but this species must form the sulfoxide in an oxygen rebound step (Scheme 1, path *d*), which has to be a very fast process in order to overcome the tendency of the very stable $\mathbf{10}^{+\bullet}$ and $\mathbf{11}^{+\bullet}$ to diffuse in and to react with the medium.

The above results are very important as they indicate that complete $^{18}O$ incorporation from $H_2O_2$ can actually be consistent with an ET mechanism and that the occurrence of a fast oxygen rebound step is a very plausible hypothesis. Thus, in view of the higher oxidation power of the active oxidant of the iron porphyrins compared to that of peroxidases, there is no reason not to think that the ET mechanism is also valid with the other sulfides examined in this work, the absence of fragmen-

tation products found with **9** being probably ascribable too to an oxygen rebound step faster than fragmentation of the radical cation, a relatively slow reaction.[20] In fact, the oxygen rebound step for sulfides **1**–**8** is expected to be much faster than with **10** and **11**, given the much lower stability of $\mathbf{1}^{+\bullet}$–$\mathbf{8}^{+\bullet}$ with respect to $\mathbf{10}^{+\bullet}$ and $\mathbf{11}^{+\bullet}$.

## Conclusion

In conclusion, the data presented here make it possible to suggest that in water the sulfoxidation of aromatic sulfides catalysed by HRP and LiP as well as by biomimetic systems probably occurs by the same ET mechanism. The different behaviours of the two systems may simply be due to differences in the efficiency of the oxygen rebound step which appears to be much higher in the biomimetic than in the enzymatic reaction. Thus, in the former case it is much more difficult to get evidence for the presence of a radical cation intermediate by looking at the formation of fragmentation products or *via* $^{18}O$ incorporation studies. Such a difference in the oxygen rebound efficiency is probably due to the fact that in the enzymatic systems (compared to the biomimetic ones) it may be much more difficult for the radical cation, once formed, to approach the oxygen of PFe(IV)=O, due to the steric requirements of the enzyme active site, which are particularly stringent with HRP and LiP.[21] Such significant steric requirements should be absent in synthetic iron porphyrins.

## Experimental section

### Methods

$^1$H-NMR spectra were recorded on a Bruker AC300P spectrometer in $CDCl_3$. GC-MS analyses were performed on a HP5890 GC (OV1 capillary column, 12 m × 0.2 mm) coupled with a HP5970 MSD. LC-MS analyses were performed on a Fisons Instruments VG-Platform Benchtop LC-MS (positive ion electrospray mass spectra, $ESP^+$) spectrometer and GC analyses on a Varian 3400 GC (OV1 capillary column, 25 m × 0.2 mm). HPLC analyses were carried out on a Hewlett Packard 1050 liquid chromatograph fitted with a UV–Vis detector and a reversed phase (C18) column.

### Materials

High purity commercial samples of thioanisole (Fluka), *N*-methylphenothiazine (Aldrich), *N,N*-dimethylaniline (Aldrich), 4-methoxyacetophenone (Fluka), imidazole (Fluka) and tartaric acid (Aldrich) were used as received. Tartrate buffer solution was prepared using Milli Q grade water. Acetonitrile (HPLC grade) was purchased from Carlo Erba. $H_2{}^{18}O$ (10%) and $H_2{}^{18}O_2$ (2.3 M, 90% $^{18}O$) were purchased from Isotec Inc. The $^{18}O$ content of $H_2{}^{18}O_2$ was determined according to the literature.[22] 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine-*p*,*p*′,*p*″,*p*‴-tetrasulfonic acid tetrasodium salt dodecahydrate (Aldrich) was metallated according to the literature procedure.[23]

*4-Substituted thioanisoles* were prepared by reaction of the corresponding thiophenols (Aldrich) with $CH_3I$ in basic methanol solution.[24] *4-Methoxyphenyl ethyl sulfide* (**6**) and *4-methoxyphenyl isopropyl sulfide* (**7**) were prepared by treating 4-methoxythiophenol with respectively EtBr[25] and *i*PrI[26] in $EtO^-$/EtOH.

*4-Methoxyphenyl tertbutyl sulfide* (**8**) was prepared by acid catalysed reaction of 4-methoxythiophenol with *t*BuOH.[27]

*Potassium 4-(benzylthio)benzyl sulfonate* (**9**) was synthesised according to the literature procedure.[2d]

*N,N-dimethyl-4-methylthioaniline* (**11**) was prepared by reacting 4-methylthioaniline with $CH_3I$ following the literature procedure.[28]

*N-methyl-N-(2-phenylthioethyl)aniline*(**12**) was synthesised by adding, over a period of 10 min, a solution of *N*-methylaniline (1.4 g, 13 mmol) in 5 mL of toluene to a stirred solution of (2-chloroethyl) phenyl sulfide[29] (0.92 g, 5.3 mmol) in 5 mL of toluene in a two-neck round bottom flask. The mixture was stirred under reflux for four days, it was then cooled to room temperature and 6 mL of 0.1 M NaOH were added in order to dissolve the hydrochloride. The mixture was extracted with ethyl acetate and the organic fractions were collected, dried over anhydrous $Na_2SO_4$ and evaporated under reduced pressure. Chromatography on silica gel using hexane/ethyl acetate (50:1) as an eluant gave 1.0 g of a white solid (75% yield). $^1$H-NMR ($CDCl_3$), $\delta$: 2.92 (s, 3H), $\delta$: 3.05 (t, 2H), $\delta$: 3.53 (t, 2H), $\delta$: 6.59–6.73 (m, 4H), $\delta$: 7.15–7.39 (m, 6H). EI-MS: *m/e* = 120 (100%), 77 (15%), 104 (8%), 243 ($M^+$, 7%), 51 (6%), 91 (4%).

### Reaction products

The sulfoxides of all substrates were prepared by reaction of the corresponding sulfides with sodium metaperiodate in aqueous ethanol solution.[30]

*N-(2-phenylthioethyl)-aniline* was prepared by reacting aniline and (2-chloroethyl)-phenyl sulfide[29] using the procedure reported for **12**. Yield: 85%. $^1$H-NMR ($CDCl_3$), $\delta$: 1.6 (broad s, 1H), $\delta$: 3.15 (t, 2H), $\delta$: 3.36 (t, 2H), $\delta$: 6.57–6.75 (m, 3H), $\delta$: 7.14–7.32 (m, 5H), $\delta$: 7.37–7.41 (m, 2H). EI-MS: *m/e* = 106 (100%), 124 (23%), 77 (21%), 229 ($M^+$, 14%), 65 (10%), 51 (9%).

The purity of all the synthesised compounds (> 99%) was checked by GC, GC-MS and $^1$H-NMR.

### General oxidation procedure

The sulfide (10 μmol), FeTPPSCl (0.3 μmol) and imidazole (30 μmol) were magnetically stirred in 5 mL of 50 mM sodium tartrate buffer solution, pH 3, containing 5% of acetonitrile as cosolvent, at 25 °C, under an argon atmosphere. $H_2O_2$ or $H_2{}^{18}O_2$ (10 μmol) in 0.5 mL of buffer solution was gradually added over 1 h using a syringe pump. After the addition of the internal standard (4-methoxyacetophenone) the products of the reaction were extracted with $CH_2Cl_2$ and dried over $Na_2SO_4$. The same experimental conditions were used when the oxidations were carried out in $H_2{}^{18}O$.

### Product analysis

Reaction products were characterised by GC, GC-MS, HPLC and $^1$H-NMR by comparison with authentic specimens. Yields were determined by GC, $^1$H-NMR and HPLC and referred to the starting material. A good recovery of materials (> 95%) was observed in all the experiments.

### Oxidation of *N,N*-dimethyl-4-methylthioaniline (11)

The same experimental procedure described above was followed. In addition to the corresponding sulfoxide a second reaction product was observed (yield referred to the starting substrate 12%), which showed the following properties: $^1$H-NMR ($CDCl_3$) $\delta$: 2.37 (s, 3H), $\delta$: 2.39 (s, 3H), $\delta$: 3.00 (s, 6H), $\delta$: 3.15 (s, 3H), $\delta$: 6.47–6.54 (m, 2H), $\delta$: 6.94–6.99 (m, 2H), $\delta$: 7.17–7.25 (m, 3H) and GC-MS *m/e* = 318 ($M^+$, 100%), 303 (30%), 256 (11%), 224 (9%), 137 (9%). This product should derive from the coupling between $\mathbf{11}^{+\bullet}$ and its *N*-demethylated product, *N*-methyl-4-methylthioaniline. To get a further support on the nature of this coupling product a mixture of **11** and *N*-methyl-4-methylthioaniline was reacted with the genuine one-electron oxidant potassium 12-tungstocobalt(III)ate[31] and the same kind of coupling product was observed.[32]

### Competitive oxidation of thioanisole and *N,N*-dimethylaniline

An equimolar amount of thioanisole and *N,N*-dimethylaniline (10 μmol each) were reacted with 0.6 μmol of FeTPPSCl and

1.0 μmol of $H_2O_2$ following the general procedure described above. After the work up, the reaction mixture was analysed by GC, GC-MS and $^1$H-NMR. The only product observed was *N*-methylaniline (comparison with an authentic specimen), in addition to the unreacted starting materials. There was no evidence for the formation of methyl phenyl sulfoxide.

### Competitive oxidation of thioanisole and 4-methoxythioanisole or 4-cyanothioanisole

An equimolecular amount of thioanisole and 4-methoxythioanisole or 4-cyanothioanisole (10 μmol each) were reacted with 0.6 μmol of FeTPPSCl and 1.0 μmol of $H_2O_2$ following the general procedure described above. After the work up, the relative yields of the two sulfoxides were determined by GC and $^1$H-NMR.

### $^{18}$O incorporation experiments

In the oxidations carried out using $H_2{}^{18}O$ as the solvent or $H_2{}^{18}O_2$ as the oxidant, $^{18}$O incorporation in the formed sulfoxide was calculated from the areas of the molecular ion peaks of 4-X–$C_6H_4$–S($^{18}$O)–R ($m$+2)/$z$ and 4-X–$C_6H_4$–S($^{16}$O)–R ($m$/$z$) determined *via* LC-MS for 4-$CH_3O$–$C_6H_4$–S(O)–$CH(CH_3)_2$ and GC-MS for the other sulfoxides. A correction was made to take into account the presence of $^{34}$S by subtracting its contribution to the ($m$+2)/$z$ ion of the sulfoxide produced.

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