Halogen Redox Assistance and Iron Controlled Selectivity in Oxidation of Organic Sulfides

Angela R. Suárez,*,† Ana M. Baruzzi,‡ and
Laura I. Rossi†

Departamento de Química Orgánica and Instituto de Investigaciones en Físicoquimica de Córdoba (INFIQC), Departamento de Fisicoquímica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Agencia Postal 4. CC 61. C.P. 5016, Argentina

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Introduction

Since alkyl sulfoxide derivatives can serve as nonfunctional as well as anionic synthons,[1] preparation of these compounds by efficient methods are of continuous interest in organic chemistry.[2]

In a previous paper,[3] we discussed the selective oxidation of organic sulfides into sulfoxides with nitric acid catalyzed by $[(FeBr_3)_2(DMSO)_3]$, **1**, and $FeBr_3$. Reactions were performed in a biphasic system with an aqueous phase made up of 1.6 M nitric acid as in oxidations reported by Gasparrini et al. with tetrahaloaurates as catalysts.[4] The organic layer was a dichloromethane solution of the substrates, whereas the catalysts were soluble in both phases. A substrate:catalyst ratio of 10:1 was used. In this paper we present a suitable mechanism for this reaction.

The main advantages of the method used in this work are mild reaction conditions and high selectivity in the sulfide into sulfoxide oxidation since overoxidation into sulfone is usually the main drawback in this process. Although there are numerous reports showing high selectivity for sulfoxides synthesis from their corresponding sulfides,[5] the use of easy handling media is much less frequent. Namely, the most current oxidants are hydrogen peroxide in high concentrations (85%)[6] and the very unstable *m*-chloroperbenzoic acid.[2,5] A similar problem occurs with the reaction conditions, since high pressure (40 atm) and high temperatures (>100 °C) have been reported.[7]

Results and Discussion

In this paper we present the results of catalyzed reactions, with benzyl phenyl sulfide, **2**, as substrate. In Table 1 are shown the yields of these reactions, entries **A** and **B**, as well as those of experiments carried out without nitric acid, **C** and **D**, and without catalyst, **E**.[8] No oxidation products were found in reactions **C**, **D**, or **E**.

In addition, an electrochemical study was carried out to analyze the role of the various components of the oxidative medium to propose a suitable mechanism for this reaction. Results were compared with those of conventional organic reactions previously mentioned.[3] A voltammetric analysis of benzyl phenyl sulfide and of the different catalysts used was performed, bearing in mind that the reported oxidation potential of sulfides is in the range 1.4−2.0 V (vs SCE on Pt).[9] Electrolysis at controlled potential was also carried out to ratify the development of the same product, the sulfoxide **3**, as in the nonelectrochemical oxidation.

Experimental conditions for electrochemical oxidations were similar to those used in the classical organic procedure with ultrapure water instead of the nitric acid solution. Figure 1 shows the voltammetric profile (dashed line) of $[(FeBr_3)_2(DMSO)_3]$. Two oxidative processes were observed at 0.7 and 1.2 V during the positive sweep. To identify the corresponding couples, the voltammograms of KBr and $FeBr_3$ were run and are also shown in Figure 1. As could be inferred from the reported *E* values,[10] Fe^{3+}/Fe^{2+} and Br_2/Br^- were the redox couples responsible for the observed processes:

$$Fe^{3+} + e^- \leftrightarrow Fe^{2+} \quad E_{ap} = 0.7\ \mathrm{V}$$

$$Br_2 + 2e^- \leftrightarrow Br^- \quad E_{ap} = 1.2\ \mathrm{V}\ (\text{vs SCE on } C_v)$$

Figure 2 exhibited the voltammetric profiles corresponding to **1**, **2**, and a solution containing both species, in the biphasic reaction media reported above. When substrate **2** was the only species in solution, the current increase started at *E* values higher than 1.2 V, but when only catalyst **1** was present, the increase in current is evidenced at much lower *E* values. This current enhancement was noticeably higher when both catalyst and substrate were present. It became evident that at 1.25 V the direct oxidation of the sulfide was very poor. For this reason, we chose $E = 1.25$ V to perform bulk electrolysis of **2** on a graphite mesh. This potential corresponded to bromides into bromine oxidation on a C_v electrode. One of these electrolytic procedures was carried out with $[(FeBr_3)_2(DMSO)_3]$ as catalyst, **F**, and the other one without it, **G**. Data were processed keeping in mind that oxidation of sulfides into sulfoxides involved 2 mol of electrons per mol of substrate. Results are listed in Table 2. The amount of **3** obtained is considerably higher in the presence of **1**. It should be observed that in this case the amount of charge consumed is higher, although the current efficiency values are very close.

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* Corresponding author. Phone: 054-051-334170/73. Fax: 054-051-333030. e-mail: suarezar@dqo.fcq.unc.edu.ar; abaruzzi@fisquim.fcq.unc.edu.ar; lauraros@dqo.fcq.unc.edu.ar.

† Departamento de Química Orgánics.

‡ INFIQC.

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Table 1. Effect of the Components of the Reaction Medium on the Oxidation of 2 to Benzyl Phenyl Sulfoxide, 3[a]

entry	oxidative medium	*T*/h	% product **3**[b]
A	nitric acid 10% + **1**	2	93
B	nitric acid 10% + $FeBr_3$	2	91
C	ultrapure water + **1**	15	
D	ultrapure water + $FeBr_3$	15	
E	nitric acid 10%	15	

[a] Reactions were followed by both TLC and ^1H NMR of the organic layer. [b] Isolated from the organic layer, p.f. **A**, 122−123 °C; **B**, 120−122 °C.

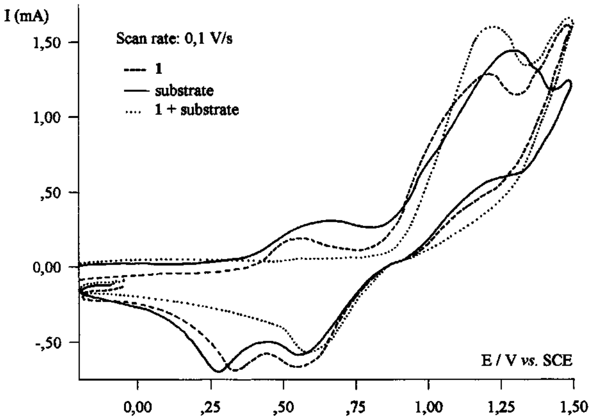


Figure 1. Voltammograms corresponding to $[(FeBr_3)_2(DMSO)_3]$, $FeBr_3$, and KBr over C_v.

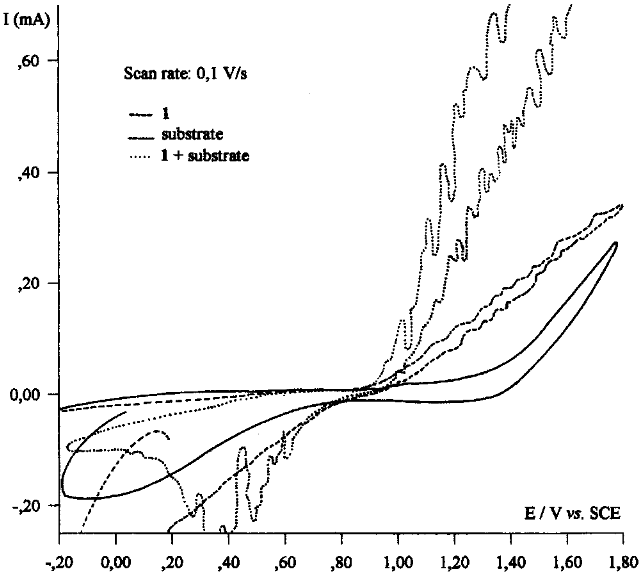


Figure 2. Voltammograms corresponding to $[(FeBr_3)_2(DMSO)_3]$, substrate, and both in the biphasic reaction media.

Table 2. Electrolysis of Benzyl Phenyl Sulfide, 2[a]

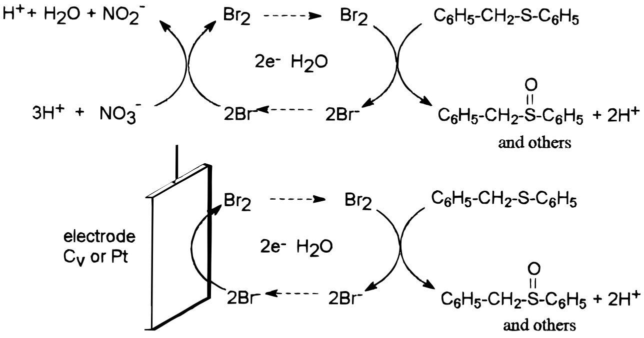
entry	catalyst	charge/C	mol e^-	**3** mol	% ce[b]
F	1	360	3.7×10^{-3}	1.3×10^{-3}	72.2
G		117	1.2×10^{-3}	0.4×10^{-3}	66.7

[a] Time, 5.00 h. [b] ce; current efficiency.

It is evident that, at this *E* value, the oxidation of **1** is the main electrochemical process. This step is followed by a chemical reaction between oxidized **1** and **2** to obtain the sulfoxide and to regenerate the catalyst.

In voltammetric experiments performed with $FeCl_3$ and KCl, we could observe that the current flow was lower than in the case of the bromides shown in Figure 1. The anodic peak was shifted toward more positive potential values than those of the brominated salts,[7,11] and it showed a more irreversible behavior.

Scheme 1. Role of the Nitric Acid Bromide Ions, and Water in Organic Sulfides to Sulfoxides Oxidations



These electrochemical results can be compared with those obtained when nitric acid was used as oxidant,[3] Scheme 1. The estimated potential of the 1.6 M nitric acid solution is 0.94 V, too low to generate bromonium ions, but high enough for bromide into bromine oxidation.[12] The typical band of bromine at 395.4 nm was found in electron absorption spectra of 1.6 M nitric acid solutions of both $FeBr_3$ and **1**, as well as in the spectra of the aqueous layer from sulfides oxidation. The absorbance/bromide molar ratio was higher in this last case, showing that the oxidation of bromides into bromine takes place mainly in the presence of the substrate.[13,14]

Data in Table 3 compare the results of the conventional organic procedure performed with **2** as substrate in dichloromethane solution, in the presence of **1**, $FeBr_3$, KBr, Br_2, $FeCl_3$, KCl, and Cl_2, respectively, and 1.6 M nitric acid as the oxidant.

From these results, it is noticeable that potassium halides as well as molecular halogens yielded nonselective oxidation and benzylic halogenation of **2**. These results matched reported oxidations of sulfides with bromine and chlorine,[15] indicating that they are poor oxidants.[4] On the other hand, it is evident that while

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Table 3. 1, $FeBr_3$, KBr, Br_2, $FeCl_3$, KCl, and Cl_2 Used as Catalysts in Oxidation of Benzyl Phenyl Sulfide, 2[a]

entry	catalyst	aqueous phase	T/h	products
H	$FeBr_3$	HNO_3 10%	2	**3**
I	1	HNO_3 10%	2	**3**
J	KBr	HNO_3 10%	4	**3** + others
K	$Br_{2\ (soln)}$	H_2O	7	**2** + **3** + others
L	Br_2	H_2O	25	**2** + **3** + others
M	$FeCl_3$	HNO_3 10%	24	**2** + **3**(traces) + others
N	KCl	HNO_3 10%	8	**2** + **3**(traces) + others
O	$Cl_{2\ (soln)}$	H_2O	5	**2** + **3**(traces) + others
P	$Cl_{2\ (bubbling)}$	H_2O	2	**2** + **3** + others

[a] Dichloromethane as organic solvent, at room temperature and continuous stirring. The substrate:catalyst ratio was that of conventional oxidations. [b] The reaction mixtures were evaluated by ^1H NMR: benzyl phenyl sulfoxide, 53%; benzyl phenyl sulfone, 10%; benzaldehyde, 7%; benzoic acid, 7%; halogenated products in the $-CH_2-$ benzylic, 23%.

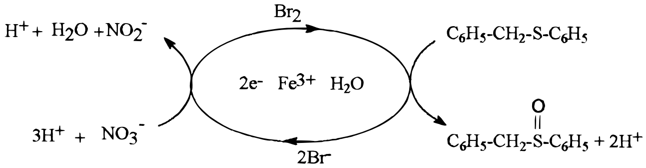
the substrate oxidation is not produced by the Fe(III) reduction, selectivity fails whenever this metal is absent. The importance of nitric acid in the reaction media became obvious from entries **K** and **L**. When pure bromine was added, the substrate was not completely oxidized.

In short, the role of the nitric acid was to oxidize bromides into bromine, and this couple was the redox-mediator in oxidation of sulfides, as outlined in Scheme 1. From the results reported here, it is evident that the high selectivity exhibited by reactions catalyzed by **1** and $FeBr_3$ was controlled by the transition metal. On the other hand, the potential for nitric acid under these conditions is about 1.0 V, too low for an efficient oxidation of chloride into chlorine.[5,6] Furthermore, the low current flow also suggested that oxidation of chlorides into molecular chlorine was poor and the voltammograms exhibited irreversible reaction profiles. All these facts account for the lack of selectivity and low yields obtained in conventional oxidations involving chlorine and chlorides.

Conclusions

Based on the above findings we suggest that the selectivity of this reaction was due to the activation of sulfide molecules in the coordination sphere of the metal to be oxidized and oxygenated,[16] as it has also been proposed for ruthenium catalysts.[17] Coordination of a sulfide as well as a water molecule should go with the departure of two halide ions from the metal, at this point the sulfide oxidation occurs. The following steps should correspond to the sulfide oxygenation by the water molecule and reduction of the molecular halogen on the transition metal coordination sphere. Displacement of the sulfoxide molecule reverted the oxidating system to the starting point. Concomitant protons turnover should take place as in biological oxidations catalyzed by Fe(III) complexes. The partial and overall reactions are depicted in Scheme 2.

Scheme 2. Selective Oxidation of Sulfide to Sulfoxide with Fe(III) as Ruler of Selectivity and the Bromide Ions as Redox Mediators



Experimental Procedure

All chemicals used were of the highest commercial purity and were used without further purification. The classical organic reactions were carried out in a biphasic system consisting of an aqueous layer formed by 16 mL of 1.6 M nitric acid, a solution of the substrate (5 mmol) in 16 mL of dichloromethane, and the metal halides or metal complex. The substrate:catalyst ratio was 10:1. The reactions were performed at room temperature under continuous stirring and followed by TLC on silica gel with ethyl acetate/benzene (60:40) as developing solvents.

Electron absorption spectra were recorded in a Shimadzu 260 PC spectrophotometer. For the electrochemicals experiments, a potentiostat DT 2101 (HITEK Instrument) potentiostat/galvanostat and waveform generator P.PRI (HITEK Instrument) were used. Cyclic voltammograms were recorded on either X−Y BAS or X−Y Linseis series LY 1800. A conventional three-electrode configuration was used with a glassy-carbon as the working electrode, a wire platinum counter electrode, and a saturated calomel electrode (SCE) as reference electrode.

Stationary cyclic voltammetry experiments shown in Figure 1 were performed using water as solvent and $(C_2H_5)_4NClO_4$ as supporting electrolyte.

Cyclic voltammetry experiments shown in Figure 2 were performed under stirring conditions in a biphasic media, except when the substrate was the only species present; in this case dichloromethane was used as solvent. The only purpose of this experiment under nonstationary conditions was to compare the current density in the presence and in absence of catalyst to choose an appropiate E value for the bulk electrolytic experiments.

Controlled potential electrolysis of **2** (5 mmol) as carried out under stirring in an undivided cell equipped with a graphite mesh as anode, for 5.00 h. The solvent was 40 mL of either Cl_2CH_2 or water or both; containing $(C_2H_5)_4NClO_4$ as supporting electrolyte. The applied positive potential was 1.25 V.

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