Pergamon

Tetrahedron, Vol. 52, No. 31, pp. 10287-10300, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00564-9

The Selective Functionalization of Saturated Hydrocarbons. Part 33.† Further Reactions which Take Place in the Fe^{II}-Fe^{IV} Manifold.

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Abstract: Utilization of the Fe^{II}-H_2O_2 system in the presence of diphenyl diselenide, phenylselenol, diphenyl disulfide and thiophenol converts saturated hydrocarbons into the corresponding alkyl phenyl selenide or alkyl phenyl sulfide. Starting with Fe^{III}-H_2O_2 no reaction occurs in presence of diphenyl diselenide but the Gif ^{IV} system (Fe^{II}/ $O_2^{\cdot -}$) is able to produce phenyl seleno derivatives along with the oxidation products. The presence of sodium sulfide with the Fe^{II} and Fe^{III}-H_2O_2 systems affords some dicyclohexyl disulfide. Mechanistic studies suggest than all these reaction are based on the Fe^{II}-Fe^{IV} manifold with a suitable carboxylic acid as ligand.

INTRODUCTION

The process of selective functionalization of saturated hydrocarbons which we call Gif chemistry takes place under mild conditions at room temperature near to neutrality.[1] Recently, we have shown that, in fact, two manifolds are involved.[2] The traditional Fe^{III}-Fe^{V} manifold, where carbon radicals are observed only under exceptional structural factors (such as the tertiary position in adamantane), and an Fe^{II}-Fe^{IV} manifold where carbon radicals are generated exclusively. It is important to note that the postulated Fe^{IV} and Fe^{V} species have an identical selectivity for saturated hydrocarbons with an adamantane selectivity of close to 1.0 and an identical Kinetic Isotope Effect for cyclohexane of 2.1. Fortunately, the chemical reactions of the two species are completely different.[2,3] The two manifolds can be differentiated by a simple titration[4] for Fe^{II}.

Another important factor is the recognition[3,5] that a special kind of carboxyl group is a necessary ligand for Fe^{II} and Fe^{III} in order that Gif chemistry can be observed. Such ligands are picolinic acid and isoquinoline-1-carboxylic acid and their congeners. In the earlier work a large excess of acetic acid afforded complexes of an undefined nature which served the same purpose.[1]

However, the earlier studies with acetic acid involved the liberation of a hydroperoxide as a precursor of the ketone. This is not seen with the complexes of picolinic acid and of isoquinoline-1-carboxylic acid, where quantitative C^{13} measurements[6] have defined that precisely two of the ligands are joined to each iron atom. There is also evidence that the active species in hydrocarbon functionalization involves at least one peroxyl ligand between two iron atoms when Fe^{III} is the iron valence state.[3,5]

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† Part 32: Barton, D. H. R.; Hu, B.; Taylor, D. K. and Rojas Wahl, R. *J. Chem. Soc. (Perkin Trans. II)* **1996**, in press.

Some years ago[7] we showed that diphenyl diselenide showed an extraordinary ability to phenylselenate saturated hydrocarbons with a selectivity that was the same as the oxidation process normally seen with oxygen. The reactions took place in the Fe^{II}-superoxide system using Fe^0 (Gif ^{III}) or Fe^{II}-Zn^0 (Gif ^{IV}). We showed also that diphenyldisulfide afforded comparable phenylthio-derivatives, but the reaction was less efficient. In an extension of this work,[8] sodium sulfide, H_2S and even sulfur were inserted into saturated hydrocarbons to furnish di- or poly-sulfides. The useful systems were as mentioned above as well as the Fe^{III}-H_2O_2 system, including activation using picolinic acid (PA) as a ligand.

In this prior work, no attempt was made to establish if Fe^{II} or Fe^{III} was involved in the chemistry observed. The present article will clarify the nature of the iron species and show that all these reactions take place in the Fe^{II}-Fe^{IV} manifold.

RESULTS AND DISCUSSION

Experiments using PhSeSePh and PhSeH

Diphenyl diselenide has been used as a source of phenylseleno radicals and as an effective radical trap. A rate constant of $2.6 \times 10^7\ M^{-1}\ s^{-1}$ at 25°C was obtained for the reaction of a primary alkyl radical with diphenyl diselenide.[9] It has also been used to trap radicals generated photochemically from thiohydroxamate esters.[10]

In a prior experiment[11] an Fe^{II} complex was oxidized with H_2O_2 in pyridine-acetic acid in the presence of PhSeSePh to give at first, cyclohexyl phenyl selenide and then, when the Fe^{II} had been oxidized to Fe^{III}, normal ketonisation replaced the phenylselenation reaction. Since the Fe^{II}-Fe^{IV} manifold produces carbon radicals[2] we suspected that the above mentioned selenide was formed by cyclohexyl radical addition to diphenyl diselenide.

More systematic results are summarized in **Table 1**. Since the product of radical addition, cyclohexyl phenyl selenide, is readily oxidized by hydrogen peroxide as is diphenyl diselenide itself, it was necessary to reduce any oxidized Se^{IV} compounds formed to Se^{II} by sodium dithionite reduction. In **Table 1** the numbers for the products with and without dithionite reduction are given. The results, given in brackets are the correct values after reduction.[12]

In order to confirm this conclusion, we oxidized cyclohexyl phenyl selenide in pyridine with H_2O_2. The reaction was controlled by GC: the peak corresponding to the cyclohexyl phenyl selenide disappeared using a normal work-up (the cyclohexyl phenyl selenoxide which is soluble in water can not be quantified by GC after a work-up) and reappeared (75%) using a reducing work-up. The same experiment was made using diphenyl diselenide and we obtained the same result.

Table 1 (entries 1 to 3) showed that the yield of selenide depended on the amount of hydrogen peroxide (2 mmol) and not upon the amount of the diphenyl diselenide. The mass balances for PhSe and for H_2O_2, allowing for the overoxidation to Se^{IV} compounds were reasonable. Entry 4 showed that phenylselenol was, as expected, not present. Entry 5 was important because it showed no product was formed in the absence of a suitable ligand like picolinic acid. The formation of trapping products should be very fast because in presence of chloride, which usually gave alkyl chloride in less than 2 minutes,[2] no cyclohexyl chloride was observed (entry 6).

Further experiments using Fe^{III}-H_2O_2 with, or without, picolinic acid gave no formation of cyclohexyl phenyl selenide. This is in agreement with the earlier experiments by Sawyer and his colleagues.[11] Oxidation products were also not observed, no doubt due to the preferential oxidation of selenium.[13]

Table 1: Oxidation of cyclohexane in the presence of PhSeSePh or PhSeH.

Entry	Conditions	Products (mmol)			
		R-SePh	PhSeSePh	2-PhSe-Pyr	Other compouds
1	A+ PhSeSePh: 1 mmol	0.17 (0.36)	0.56 (0.88)	traces	n.d.
2	A+ PhSeSePh: 0.5 mmol	0.14 (0.33)	0.07 (0.16)	n.d.	n.d.
3	A+ PhSeSePh: 0.25 mmol	0.11 (0.30)	n.d.	traces	(-Pyr) o- 0.05 p- n.d.
4	A**+ PhSeSePh: 1 mmol	0.12 (0.34)	0.05 (0.94)	n.d. (0.02)	no $PhSeCH_3$ detected
5	A*+ PhSeSePh: 1 mmol	n.d.	0.53	n.d.	n.d.
6	A***+ PhSeSePh: 1 mmol	0.04 (0.19)	0.64 (0.78)	n.d. (n.d.)	(Cl) n.d.
7	A+ PhSeH: 2 mmol	0.76 (0.84)	0.40 (0.65)	0.06 (0.09)	n.d.
8	A+ PhSeH: 1 mmol	0.59 (0.60)	0.05 (0.21)	0.05 (0.05)	n.d.
9	A+ PhSeH: 0.5 mmol	0.23 (0.41)	0.03 (0.04)	0.03 (0.03)	(-Pyr) o- 0.11 (0.07) p- 0.11 (0.07)
10	A*+ PhSeH: 2 mmol	0.07 (0.09.)	0.23 (0.39)	n.d. (n.d.)	n.d.

Except as specified, these reactions were carried out with 20 mmol of cyclohexane, 2 mmol of H_2O_2 in 15 ml of pyridine at 0°C to RT, overnight, under argon. PA refers to picolinic acid, n.d. to not detected, ( ) mmol of products after a reducing work-up (thionite solution). (A) $Fe^{II}(ClO_4)_2 \cdot 6H_2O$: 0.5 mmol, PA: 1.5 mmol. * without PA. ** with 20 mmol of CH_3I. *** with 5 mmol of LiCl.

Adamantane selectivity has always played a key-role in the evaluation of the regioselectivity of hydrocarbon activation[14]. Using diphenyl diselenide with adamantane in the Fe^{II}-H_2O_2 system, the total ratio

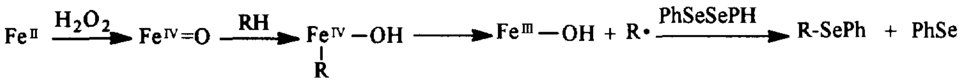
C_2/C_3 was 1.27 as it is shown in the **Table 2**; this value is similar to the one found in the LiCl[2] or Tempo experiments.[15] It is the same for the Kinetic Isotope Effect[16] with a value in the Fe^{II}-Fe^{IV} manifold of 1.95 for the diphenyl diselenide system, 2.1 for LiCl and 1.95 also for Tempo trapping.[15]

Table 2: Adamantane selectivity

R-H	R-SePh secondary	R-SePh tertiary	R-Pyr tertiary	2-PhSe-Pyr	PhSeSePh	C_2/C_3	Mb (%)
8.20	0.67	0.47	o- 0.06 p- traces	0.13	0.15	1.27	94

This reaction was carried out with 10 mmol of adamantane, 3 mmol of $Fe^{II}(ClO_4)_2,6H_2O$, 9 mmol of PA, 3 mmol of PhSeSePh, 3 mmol of H_2O_2 in 30 ml of pyridine at 0°C to RT, overnight, under argon.
The C_2/C_3 ratio is defined as an the total secondary products divided by the total tertiary products. MB is mass balance.

A simple mechanism is proposed in the **Scheme 1** to explain all these experiments: an Fe^{IV} oxenoid species, coming from the reaction between Fe^{II} and H_2O_2, reacts with the hydrocarbon. The alkyl radical, produced by the fragmentation of the Fe carbon bond, reacts with a molecule of diphenyl diselenide giving the alkyl phenyl selenide and a phenyl selenium radical which will dimerise to diphenyl diselenide. We have written this scheme, as well as **Scheme 2** and **3**, with a single Fe^{II}. Since reactivity in these three schemes depends upon the presence of the right kind of carboxylic acid (picolinic acid or acetic acid in this article) it can be argued[3] that two Fe^{II} bridged by the carboxylic acid are needed. It is, of course, possible to insert this into **Schemes 1 to 3**. For simplicity we have not done this. All iron species are ligated to pyridine. This is also omitted.

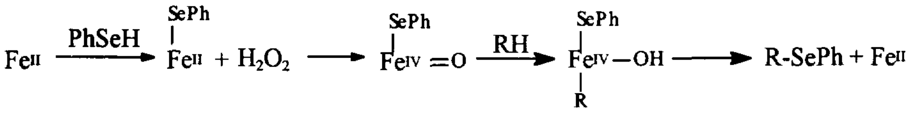


$$\mathrm{Fe^{II}} \xrightarrow{H_2O_2} \mathrm{Fe^{IV}{=}O} \xrightarrow{RH} \underset{\displaystyle \mathrm{R}}{\mathrm{Fe^{IV}{-}OH}} \longrightarrow \mathrm{Fe^{III}{-}OH} + \mathrm{R}\bullet \xrightarrow{\mathrm{PhSeSePH}} \text{R-SePh} + \text{PhSe}\bullet$$

Scheme 1

Phenylselenol is considered also as an excellent trap for carbon radicals by acting as a $H^{\cdot}$ transfer reagent with a very fast reaction rate: $k=2.0\times10^{9}\ M^{-1}\ s^{-1}$ at 25°C.[9] It was surprising then that using phenylselenol as selenium source in the Fe^{II}-H_2O_2 experiments (entries 7, 8 and 9 in **Table 1**), we observed an efficient reaction taking place producing cyclohexyl phenyl selenide. Without PA the reaction was almost inhibited (entry 10), only traces of trapping and oxidation products were detected. The carbon radical formed by the Fe^{II}-Fe^{IV} manifold should, in principle, be reduced back to the hydrocarbon. The formation of trapping products increased proportionally with the amount of benzeneselenol added in the reaction, which was not the case for the diphenyl diselenide experiments. We observed also, that there was not a big difference between the normal work-up and the (thionite reducing work-up). This can be explained by the fact than more oxidant was used to produce the trapping product, therefore less H_2O_2 was left to oxidize the seleno products. Mixing Fe^{III} and phenylselenol in pyridine gave 75% of Fe^{II} after only 10 minutes. As a consequence, we were not surprised to detect some cyclohexyl phenyl selenide when we carried out a reaction with Fe^{III}-H_2O_2 and phenylselenol.

A way to explain these phenomena is to have the phenylselenol bound to the Fe^{II} as is proposed in the **Scheme 2**. The Fe^{II} salt reacts with H_2O_2 to give an Fe^{IV} oxenoid species containing the phenylselenol group as ligand. The insertion of the hydrocarbon is followed by ligand coupling producing the cyclohexyl phenyl selenide and Fe^{II}, which is able to react with another molecule of H_2O_2. However, if a phenylseleno ligand were bonded to Fe^{III} then the reaction with a cyclohexyl radical would afford the observed selenide and Fe^{II}. Of course, the rate of a such reaction can not be predicted.



Scheme 2

We saw previously than the presence of Fe^{II} in the solution is one of the most important factors in order to obtain a good yield of the cyclohexyl phenyl selenide. **Table 3** shows the effect of different reducing agents known to transform Fe^{III} to Fe^{II}.[17]

The entry 1 is the normal reaction (without dithionite treatment) using diphenyl diselenide without any reducing agent. The addition of 1.5 mmol of ascorbic acid[18] or 2 mmol of diphenyl hydrazine doubled the amount of trapping product formed (entry 2 and 3). Adding more reducing agent did not increase the yield of the reaction (entry 4), except if more oxidant was added: the amount of trapping product was multiplied this time by 4 (entry 5). Using Zn/AcOH, the reaction became almost quantitative based on the amount of diphenyl diselenide introduced (entry 6). By titration, we saw than all the Fe^{II} was still present in the solution for the two last experiments.

Table 3: Experiments using a reductant to maintain Fe^{II} in the solution

Entry	Conditions	Products (mmol)				
		R=O	R-SePh	PhSeSePh	2-PhSe-Pyr	Fe^{II}
1	A	n.d.	0.78	1.44	0.10	---
2	A+ Ascorbic Acid: 1.5mmol	n.d.	1.60	0.76	0.21	---
3	A+ PhNHNHPh: 2 mmol	n.d.	1.60	0.72	0.18	---
4	A+ PhNHNHPh: 4 mmol	n.d.	1.53	0.52	0.24	---
5	B+ PhNHNHPh: 4 mmol	0.40	3.29	traces	0.40	0.91
6	C+ Zn: 20eq /AcOH: 3 ml	n.d.	3.76	n.d.	0.26	0.25

Except as specified, these reactions were carried out with 40 mmol cyclohexane,1 mmol of $Fe^{II}(ClO_4)_2,6H_2O$, 3 mmol of PA, 2 mmol of PhSeSePh in 30 ml of pyridine at 0°C to RT, overnight, under argon. (A) H_2O_2: 4 mmol. (B) H_2O_2: 9 mmol (3 x 3 mmol added every 10 minutes). (C) $Fe^{II}(ClO_4)_2,6H_2O$: 0.25 mmol, no PA, H_2O_2: 15 mmol (5 x 3 mmol added every 10 minutes). AcOH refers to acetic acid.

While studying the effects of various reducing agents on the reaction (**Table 3**), a new compound was detected by GC and GCMS. After verification with an authentic sample, this was identified as 2-phenylselenopyridine. Different blank experiments were made to try to understand how this product was made. The presence of the iron salt, H_2O_2 and a suitable carboxylic acid such as picolinic acid were required.

Table 4: Fe^{II} experiments using different amount of hydrocarbons

Entry	Conditions	Products (mmol)			
		R=O	R-SePh	PhSeSePh	2-PhSe-Pyr
1	A+ C_6H_{12}: 20 mmol	0.47	1.76	n.d.	0.33
2	A+ C_6H_{12}: 10 mmol	0.09	0.85	0.23	0.73
3	A+ C_6H_{12}: 0 mmol	---	---	0.67 (0.91)	1.11 (1.15)
4	B+ C_6H_{12}: 0 mmol	---	----	0.88 (2.00)	0.12 (0.22)
5	C+ C_6H_{12}: 0 mmol	---	---	1.24 (1.62)	0.40 (0.48)

These reactions were carried out with 1 mmol of $Fe^{II}(ClO_4)_2,6H_2O$, 3 mmol of PA in 30 ml of pyridine at 0°C to RT, overnight, under argon. (A) PhSeSePh: 2 mmol, PhNHNHPh: 2 mmol, 10 mmol of H_2O_2 (2 mmol added every 10 minutes). (B) PhSeSePh: 1 mmol, H_2O_2: 4 mmol. (C) PhSeH: 2 mmol, H_2O_2: 4 mmol

Experiments in **Table 4** show the relationship between the formation of the 2-phenylselenopyridine and the amount of hydrocarbon present in the solution. We can see in the entries 1 to 3 that the diminution of the concentration of hydrocarbon produced a decrease in the formation of cyclohexyl phenyl selenide and, at the same time, an augmentation of the 2-phenylselenopyridine. Also, the kinetics made with and without hydrocarbon showed that the two compounds have the same half time: $t_{1/2} < 5$min. It seems than these two products come from the same intermediate. The formation of this compound may be explained by the reaction between pyridine and diphenyl diselenide both attached to the Fe. Of course, we verified that 4-phenylselenopyridine was not formed in the reaction (only traces of this compound were detected). So the binding of the pyridine to the Fe^{II} to which the phenylseleno residue is attached is indeed important. Without a reducing agent, in presence of diphenyl diselenide or phenylselenol, 2-phenylselenopyridine is still formed, but in lesser amount.

In earlier work,[7] the conversion of the unactivated carbon hydrogen bond into phenylseleno and phenylthio derivatives was described using the Gif^{III} (Fe^0) and Gif^{IV} (Fe^{II}-Zn^0) systems. In 1992, diphenyl diselenide and phenylselenol were again used in the Gif^{IV} system as reducing agents.[19] These compounds were very helpful to prove the presence of the intermediate alkyl hydroperoxide, but alkyl phenyl selenide was also detected towards the end of the reaction. It was shown than diphenyl diselenide was completely reduced by Zn / AcOH to phenylselenol which, as previously noted,is an excellent trap for carbon radicals. At this time, the very fast reaction rate for the hydrogen atom transfer of phenylselenol[9] suggested that no radicals were involved in this reaction. We tried in this work to identify which species are involved in the formation of cyclohexyl phenyl selenide using the Gif^{IV} (Fe^{II}-Zn^0) system. Of course, Gif^{III} (Fe^0) and Gif^{IV} contain excess of acetic acid and no ligand like picolinic acid.

The entry 1 (**Table 5**) is a typical Gif^{IV} experiment using PhSeSePh under oxygen: cyclohexanone was the major product with some cyclohexyl phenyl selenide, but in this case, no alcohol was formed. Phenylselenol is known to be oxidized rapidly by oxygen, and in this case, the oxidation of phenylselenol was faster than the reduction of the cyclohexyl hydroperoxide. When the reaction was carried out under air as in the previous work (entry 2), the reduction of the alkyl hydroperoxide gave more alcohol than ketone as well as the expected selenide. In the previous paragraphs, we showed that Fe^{III} was reduced by phenylselenol to Fe^{II} and, by addition of H_2O_2 in presence of hydrocarbon, the trapping product was formed in a good yield. The addition of MeI to the aliquots taken during these experiments showed than the phenylselenol was present in the solution during almost all the reaction (a quantification of methyl phenyl selenide was made and compared with an authentic sample). The presence of the phenylselenol ligated to the Fe is required to explain that carbon radicals are not reduced. This was highlighted by the results found in the entries 2 and 3. In the entry 2, an excess of diphenyl diselenide was used with respect to the iron salt: some of the phenylselenol formed was on the iron and the excess reduced the hydroperoxide (the ratio alcohol/ ketone was 2.3). When we added only the equivalent of diphenyl diselenide which, in principle, would be ligated to the Fe (entry 3), less phenylselenol was free to reduce the hydroperoxide (the ratio alcohol/ ketone was 0.7).

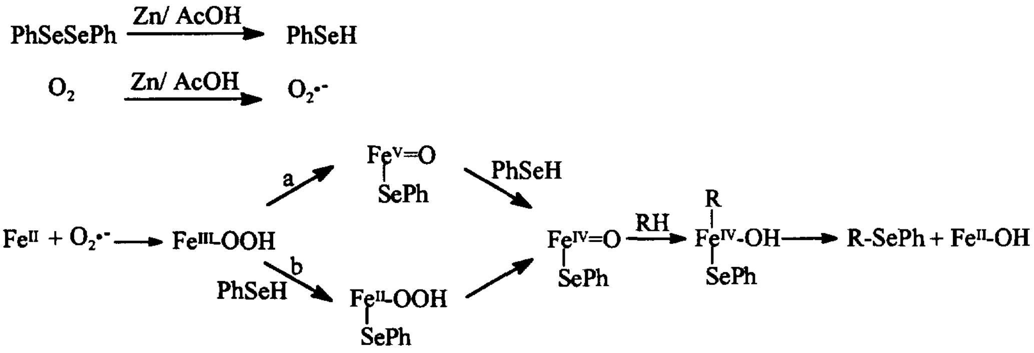
Table 5: Diphenyl diselenide in the Gif^{IV} system (Fe^{II}/ superoxide)

Entry	Conditions	Products (mmol)				
		R=O	R-OH	R-SePh	PhSeSePh	2-PhSe-Pyr
1	A+ PhSeSePh: 2 mmol, O_2	0.48	traces	0.18	1.78	n.d.
2	B+ PhSeSePh: 5 mmol, air	0.24	0.55	0.55	4.02	n.d.
3	C+ PhSeSePh: 1 mmol, air	0.46	0.34	0.09	1.01	n.d.
4	B*+ PhSeSePh: 2 mmol, air	---	---	---	1.98	0.25

Except as specified, these reactions were carried out with 40 mmol of cyclohexane, 20 mmol of Zn (powder), 3 ml of AcOH in 30 ml of pyridine at RT, overnight.
(A) $Fe^{II}(ClO_4)_2,6H_2O$: 0.25 mmol. (B) $Fe^{II}Cl_2,4H_2O$: 0.25 mmol. *without cyclohexane. (C) $Fe^{II}Cl_2,4H_2O$: 1 mmol.

A mechanism is proposed in the **Scheme 3** to explain the formation of the adduct. Zn / AcOH is able to reduce diphenyl diselenide to phenylselenol, oxygen to superoxide and to keep the Fe^{II}. It was also already proved than Fe^{II}-superoxide is equivalent to Fe^{III}-OOH. We do not have any evidence to determine if Fe^{V} is reduced to Fe^{IV} (route a) or Fe^{III} to Fe^{II} (route b) by phenylselenol, but in both cases, it is the Fe^{II}-Fe^{IV} manifold which is involved in this reaction in the experiments described at the beginning of this work (Fe^{II}-H_2O_2 system) demonstrate.

The formation of the oxidation products is without ambiguity the result of the Fe^{III}-Fe^{V} manifold and does not result from the reaction between a carbon radical and oxygen. Indeed, if a carbon radical was free in the system, it should be reduced back to cyclohexane with phenylselenol by hydrogen atom transfer. We also showed that without hydrocarbon, the formation of the 2-phenylselenopyridine was detected as the only product in the reaction. However, the yield was less than before (entry 4, **Table 5**).



Scheme 3: Mechanisms proposed for the formation of alkyl phenyl selenide in the Gif^{IV} system.

Experiments using PhSSPh and PhSH

Diphenyl disulfide is also a trap for carbon radicals.[10] It is not so reactive as diphenyl diselenide. It has a rate constant of 1.7×10^5 M^{-1} s^{-1} at 25°c. As H atom transfer reagent, thiophenol has a rate constant of 1.4×10^8 M^{-1} s^{-1} at 25°c for a primary alkyl radical.[9] We have also studied the reactivity of these two sulfur reagents. In keeeping with our prior studies the reactions of thiophenol and of diphenyl disulfide were less efficient than the reactivity shown by the corresponding selenium analogues (*vide supra*). The low yields of cyclohexyl phenyl sulfide observed required picolinic acid as a ligand. The results obtained do not merit a detailed analysis.

Experiments using Na_2S

Some years ago,[8] the ability of different Gif systems to change a carbon hydrogen bond to a carbon sulfur bond in presence of sulfur reagents such as S_8, H_2S, NaHS and Na_2S was highlighted but, no clear mechanism was suggested. The results presented in **Table 6** permit us to clarify what really happened when we used sodium sulfide with Fe^{II}-H_2O_2 or Fe^{III}-H_2O_2.

Table 6: Oxidation of cyclohexane in the presence of sodium sulfide.

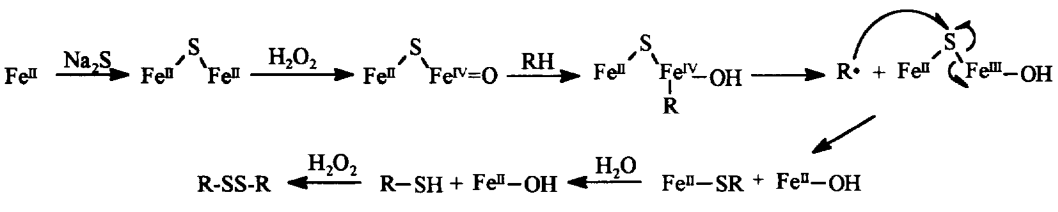
Entry	Conditions	Products (mmol)					
		R=O	R-OH	$(C_6H_{11}S)_2$	R-Pyr	$C_6H_{11}S$-Pyr	Fe^{II}
1	$Fe^{II}(ClO_4)_2 \cdot 6H_2O$: 1 mmol PA: 3 mmol	0.09	0.09	0.31	o- 0.13 p- 0.11	traces	0.84
2	$Fe^{II}(ClO_4)_2 \cdot 6H_2O$: 1 mmol	0.14	0.06	n.d.	n.d.	traces	n.d.
3	$Fe^{III}(PA)_2Cl_2HPyr_2$: 0.68 mmol	0.28	0.19	0.15	n.d.	traces	0.5

Except as specified, these reactions were carried out with 40 mmol of cyclohexane, 10 mmol of Na_2S, 4 mmol of H_2O_2 in 30 ml of pyridine at 0°C to RT, overnight, under argon.

Using cyclohexane and Fe^{II}-H_2O_2 in presence of picolinic acid, the major compounds detected were the dicyclohexyl disulfide and the pyridine coupling products (entry 1). Only trace amounts of oxidation products and 2-cyclohexyl thiopyridine were observed. By GC-MS and ^1H NMR, only the presence of the dimer was found. On the other hand, almost all the Fe^{II} remained at the end of the reaction. The disulfide formation is only seen in the presence of a reductant able to reduce Fe^{III} to Fe^{II}.[2] Sodium sulfide is a reductant and, in less than 10 minutes, it was able to reduce 1 mmol of Fe^{III} to Fe^{II} in pyridine. If the carboxylic acid was not present, almost no reaction occurred (entry 2).

Beginning with Fe^{III}, we can see a competition between the formation of ketone coming from the Fe^{III}-Fe^{V} manifold and dicyclohexyl disulfide coming from the Fe^{II}-Fe^{IV} manifold (entry 3). We also observed than the Fe^{II} coming from the reduction of the Fe^{III} by Na_2S was still present at the end of the reaction. As usual, without a carboxylic acid no product was formed.

Although the carboxylate function is needed to see any carbon-sulfur bonding, the nature of the dianionic sulfide may permit a supplementary kind of bridging between two Fe^{II} species (**Scheme 4**). The usual Fe^{II}-Fe^{IV} would then produce a cyclohexyl radical which could attack the sulfur bonded to Fe^{III} to produce, after hydrolysis, cyclohexyl thiol, affording on mild oxidation the observed disulfide.



Scheme 4

CONCLUSION

The transformation of the carbon hydrogen bond of saturated hydrocarbons into a carbon-selenium or carbon sulfur bonds can be achieved by the use of the Fe^{II}-H_2O_2 system. In the case where the trap is a good hydrogen transfer agent like phenylselenol and thiophenol, there must be ligation to the iron. If not, the free radical would be reduced back to the hydrocarbon and there would be no product.

Starting with the Fe^{III}-H_2O_2 system, a reducing agent is required to reduce Fe^{III} to Fe^{II} before the product is formed.

In all these systems, a suitable carboxylic acid like picolinic acid or acetic acid, is required to afford a reaction product.

EXPERIMENTAL

Unless otherwise stated, all the chemicals were purchased from commercial sources and, after verification, used without further purification. ^1H and ^{13}C spectra were performed in deuterochloroform with tetrachloroethane as an internal standard on a Varian XL-200 spectrometer. Chemical shifts are reported relative to TMS ($\delta = 0.00$ ppm). UV-visible spectra were recorded on a Beckmann Du-7 spectrophotometer. Melting pts, were mesured using a Thomas-Hoover apparatus. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 series II gas chromatograph using a DB-Wax or a DB-1 capillary column (15 meters long, film thickness 0.25 μm, J&W scientific). GC-MS analysis were carried out on a Hewlett-Packard 5890 serie II gas chromatograph coupled to a Hewlett-Packard 5791 mass selective detector using a DB-5 column (30 meters long, film thickness 0.25 μm).

Authentic samples (when not commercially available):

1 Adamantyl phenyl selenide was previously prepared in the laboratory by photolysis of the Barton PTOC derivative of the corresponding *tert*-carboxylic acid in presence of diphenyl diselenide. The same procedure was used for the *ortho-* and *para- cyclohexylpyridines and for the ortho-* and para *tert-adamantylpyridines.*

Cyclohexyl phenyl selenide,[7b] phenylselenol[20] and methyl phenyl selenide[21] were prepared according to previously reported methods and their identities were confirmed by ^1H, ^{13}C NMR spectroscopy and MS.

2-Adamantyl phenyl selenide: 22.2 mmol of 2-adamantane carboxylic acid [22] dissolved in dry CH_2Cl_2 were added slowly, in the dark at 0°C, to a solution of DCC (22.2 mmol) and *N*-hydroxythiopyridone in

CH_2Cl_2 under argon. The reaction mixture was stirred at room temperature until the reaction was complete (the reaction was following by TLC). The solvent was removed by evaporation and the residue was purified by flash chromatography (silicagel, CH_2Cl_2) affording 4.5g (70%) of 2-adamantyl Barton PTOC ester (yellow crystals).

2-Adamantyl Barton PTOC ester (5 mmol) was added to a solution of diphenyl diselenide (10 mmol) at 0°C under argon. The solution was irradiated at room temperature until the total consumption of the Barton PTOC ester. The solvent was removed by evaporation and the residue was purified by column chromatography (silicagel, hexane, ethyl ether increasing the polarity) affording 0.73g (50%) of a colorless oil. The ^1H and ^{13}C NMR were in agreement with the data already reported.[7b]

2-Phenylselenopyridine: $NaBH_4$ was added to a solution of diphenyl diselenide (5 mmol) in DMF, previously deoxygenated, at RT under argon until the solution became colorless. Then a solution of 2-bromopyridine (10 mmol) in DMF was added and the reaction was monitored by TLC. The reaction mixture was poured into water and extracted 3 times with ether. The etheral extracts were washed with a NaOH solution 10%, with water and dried over $MgSO_4$. The solvent was evaporated affording a residue which was purified by column chromatography (silicagel, petroleum ether, ethyl ether increasing the polarity) affording 0.9g (60%) of slightly yellow oil. The ^1H and ^{13}C NMR were in agreement with the data already reported. [23] ^1H NMR ($CDCl_3$), δ (ppm): 8.3-8.4 (m, 1H), 7.5-7.7 (m, 2H), 7.3-7.4 (m, 2H), 6.9-7.0 (m, 2H); ^{13} C NMR ($CDCl_3$), δ (ppm): 158.5, 149.6, 136.4, 135.9, 129.4, 128.6, 127.5, 123.9, 120.16.

4-Phenylselenopyridine: NaH (15 mmol) was added to a solution of diphenyl diselenide (4 mmol) in dry DMF at 60°C under argon, until the solution became colorless. 4-Chloropyridine hydrochloride salt (6.7 mmol) was added slowly and the mixture was stirred at 80°C for 3h. The reaction was monitored by TLC. Then 2 mmol of methyl iodide was added to neutralize the excess of PhSeNa. The reaction mixture was worked up the same as before. The residue obtained was purified by column chromatography (silicagel, petroleum ether, ethyl ether 70/30) affording 45% of yellow oil. The ^1H NMR was in agreement with the data already reported.[23] ^1H NMR ($CDCl_3$), δ (ppm): 8.2-8.3 (m,2H), 8.5-8.6 (m,2H), 7.3-7.4 (3H), 7.0-7.1 (m,2H); ^{13} C NMR ($CDCl_3$), δ (ppm): 140.3, 145.5, 136.1, 129.7, 129.1, 126.0, 123.7.

Cyclohexyl phenyl sulfide:[7] PhSH (21.3 mmol) was added to a solution of cyclohexyl bromide.(12.3 mmol) and NaH 60% (40 mmol, previously washed with pentane and dried under an argon stream) in DMF at room temperature and the reaction was monitored by GC. The reaction mixture was treated as above using pentane as eluant for the purification affording 1.01 g of colorless liquid. ^1H NMR ($CDCl_3$), δ (ppm): 1.1-2.1

(m, 11H), 3.1 (m, 1H), 7.1-7.4 (m, 5H). ^{13}C NMR ($CDCl_3$), δ (ppm): 131.9, 130.3, 128.8, 126.6, 46.6, 33.4, 26.1 and 25.9.

General work-up procedure:

Normal work-up: an aliquot of the reaction mixture (1.0 ml) with a naphthalene solution in ether (1.0 ml) was washed with water, extracted with 10 ml of ether and dried over $MgSO_4$. The products were quantified by gas chromatography.

Reducing work-up: another aliquot of the reaction mixture (1.0 ml) with a naphthalene solution in ether (1.0 ml) was washed with a saturated solution of sodium dithionite and extracted with 5 ml of ether. The aqueous phase was then oxidized by a stream of air for 30 min to destroy the excess of hydrosulfide and, extracted again with 5 ml of ether. The organic phases were dried over $MgSO_4$.and the products were quantified by gas chromatography.

General procedure for Gif^{IV} (Fe^{II}-Zn^{o}):

$Fe^{II}Cl_2,4H_2O$ (0.25 mmol), Zn powder (20 mmol), diphenyl diselenide (2 mmol) and cyclohexane (40mmol) were dissolved in 30 ml of pyridine. The reaction was initiated by the addition of 3 ml of acetic acid at room temperature under air or oxygen. The reaction mixture was stirred overnight. General work-up procedure was followed to quantify the products by gas chromatography.

General procedure for Gif-type reactions with Fe^{II}-H_2O_2:

$Fe^{II}(ClO_4)_2 \cdot 6H_2O$ (0.5 mmol), picolinic acid (1.5 mmol), diphenyl diselenide (1 mmol) and cyclohexane (40 mmol) were dissolved in 30 ml of pyridine. The reaction was initiated by the addition of 2 mmol of 30 % H_2O_2 at 0°C under argon. The reaction mixture was stirred at room temperature overnight. General work-up procedure was followed to quantify the products by gas chromatography.

General procedure for Gif-type reactions with Fe^{III}- H_2O_2:

$Fe^{III}(PA)_2Cl_2HPyr_2$ (0.5 mmol) was dissolved in 30 ml of pyridine and cyclohexane (40 mmol) with diphenyl diselenide (1 mmol) was added under argon. The argon line was removed and the reaction was initiated by the addition of 4 mmol of 30% H_2O_2. The reaction mixture was stirred at room temperature overnight. General work-up procedure was followed to quantify the products by gas chromatography.

ACKNOWLEDGMENTS

We thank the Welch Foundation, the N.S.F. and the Schering-Plough Corporation for the support of this work.

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(*Received in USA* 17 *May* 1996; *accepted* 12 *June* 1996)