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Iron Catalysed Insertion of Sulfur into the Non-Activated C-H Bond.

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Abstract: *The reaction of various sulfur reagents (S_8, H_2S, Na_2S, NaHS) with cyclohexane under Gif^{II}, GoAgg^{II} and GoAgg^{III} conditions affords the usual oxidation products in competition with cyclohexyl di- and poly-sulfide formation. Other cyclic hydrocarbons behave similarly. The sulfation reactions are considered to be biomimetic for the enzymes isopenicillin N synthase and biotin synthase.*

Introduction:

In the last decade interest in the selective functionalisation of saturated hydrocarbons has greatly increased. Most investigators, working at less than 100°C, are seeking to imitate mono-oxygenase enzymes.[1,2]

Since 1983 we have developed a series of biomimetic systems which oxidize saturated hydrocarbons under mild conditions to give selectively ketones with minor amounts of the secondary alcohols. For historic reasons these are called Gif systems, from the town of Gif-sur-Yvette in France where the first observations were made.[3]

With the exception of certain tertiary positions where radical chemistry (reaction with the solvent pyridine to give coupled products) is seen the Gif type reactions do not involve carbon radicals. Experiments with adamantane made clear this dichotomy.[3,5, see also ref.4]

Since the same iron species is formed from Fe^{II} + superoxide or from Fe^{III} + H_2O_2 we were led to postulate[3] that the active species for hydrocarbon substitution was an Fe^{V} oxenoid. This is considered to react in an insertion process with the hydrocarbon to furnish an Fe^{V}-carbon bonded species. The selectivity for the secondary position results from a compromise between bond strength and steric hindrance to insertion.

Two intermediates **A** and **B** have been detected between the initial hydrocabon and the ketone. Intermediate **A** is a σ-iron-carbon bond species that can be trapped by $(PhSe)_2$, $(PhS)_2$, $BrCCl_3$ and CCl_4[6,7] to give phenylseleno-, phenylthio-, bromo- and chloro-alkanes. The second intermediate **B** was recently shown to be a hydroperoxide by ^{13}C NMR and by chemical trapping (reduction to secondary alcohol).[8] The hydroperoxide is converted mainly to ketone under Gif conditions.

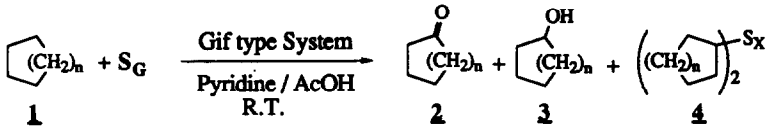
The ability of Gif type systems in presence of a sulfur reagent to change a carbon-hydrogen to a carbon sulfur bond might be a good model for enzymes like IPNS[9] (isopenicillin N synthase) or biotin synthase.[10] These enzymes convert unactivated C-H bonds into C-S bonds. The enzyme IPNS has at its active site a single non-heme iron species and has one of its coordination sites occupied by the thiol group of the tripeptide precursor of isopenicillin.[11] Less is known about biotin synthase, but there is good evidence that the last steps in the biosynthesis involve the formation of a C-S bond leading to the thiophane ring.[12]

Thus it was of interest to see if Gif systems could effect the insertion of sulfur into unactivated hydrocarbons. In preliminary work[13] we showed that indeed sulfur could be inserted into cyclohexane. We now give a full account of our experiments.

Results and Discussion:

Several sulfur reagents S_G have been introduced into the medium of Gif type reactions containing hydrocarbons (**1**, Scheme 1a).

Scheme 1a:



1 **2** **3** **4**

$S_G = S_8$, H_2S, Na_2S, NaHS

Gif type systems: Gif^{III}: $Fe^0 + O_2$

$GoAgg^{II}$: $Fe^{III} + H_2O_2$

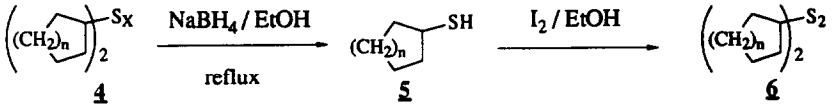
$GoAgg^{III}$: $L_3Fe^{III} + H_2O_2$ (L = Picolinic acid **7**)

Sawyer's: $L_2Fe^{II} + O_2 + H_2S$ (L = Dipicolinic acid **8** or Picolinic acid **7**)

The formation of the polysulfides **4** was detected as well as the usual oxygenated products **2** and **3**. We showed the presence in the reaction mixture of di, tri and tetrasulfides by GC-MS. However, in order to simplify the analysis, the yield of incorporation of sulfur into the C-H bond was determined by the following two methods.

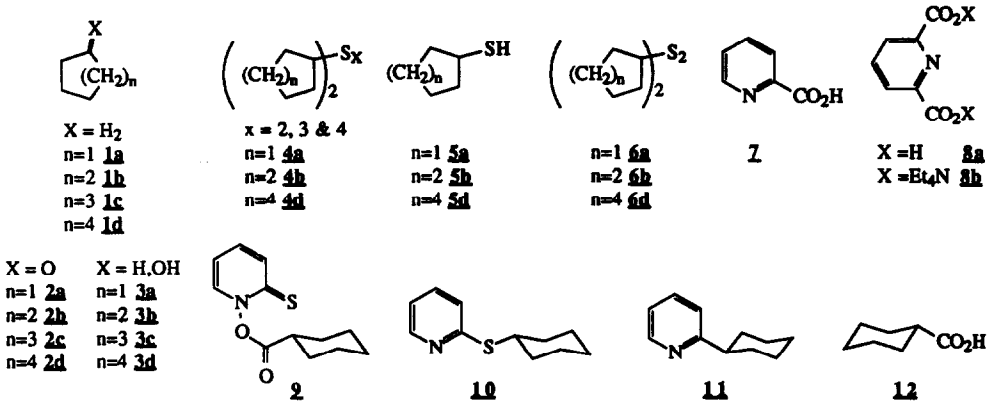
With method A (Scheme 1b), the polysulfide mixture **4** was reduced by sodium borohydride in refluxing ethanol and then reoxidized to the disulfide **6** with iodine. With method B, ^1H NMR measurements were recorded and showed the fact that all di, tri and tetra sulfides bear the same number of hydrogen α to the sulfur. The signals of these α hydrogens lie far apart from the aliphatic pack. Thus yields can be determined with the use of a suitable internal standard.

Scheme 1b:



4 **5** **6**

The yield of oxygenated products was determined as previously described,[3] by GC analysis using an internal standard.



When the various sulfur reagents S_G were introduced into the Gif^{III} system[3] using iron metal powder as a catalyst and reducing agent with dioxygen and cyclohexane **1b** (Table 1), the formation of the sulfide products **4b** was observed in competition with the oxygenated products **2b** and **3b**. The yield of the products **2b** and **3b** decreases when the amount of the sulfur reagent S_G is increased. The yield of the sulfide products **4b** increases when the amount of the sulfur reagent S_G is increased, up to a maximum of 10 mmol of S_G.

Table 1: Sulfur reagents S_G with Gif^{III} system and cyclohexane **1b** (50 mmol).[a]

Entry	Sulfur reagents : S_G mmol	Products mmol **2b**	**3b**	**6b**[d]	one/ol	η/e- [b] %	Y C-S/S_G [c] %
1	--	3.54	0.43	--	8.2	37	--
	H_2S						
2	0.7	3.02	0.19	traces	15.9	31	--
3	3.5	2.2	0.12	0.80	18.3	33	46
	S_8						
4	2 / 8	1.63	0.19	0.64	8.7	23.6	64
5	10 / 8[e]	1.38	0.08	1.10	17.2	25	22
6	20 / 8[e]	0.33	--	1.28	--	16	13
	$Na_2S,9H_2O$						
7	2	2.01	0.26	0.26	7.6	24	26
8	10	1.62	0.09	1.05	18	27	21
	H_2S + S_8						
9	0.7 2 / 8	2.11	0.14	0.47	15	26	35
10	0.7 4 / 8	2.4	0.12	0.82	20	33	35
11	0.7 10 / 8	0.82	0.06	1.19	14	20	22

*a) Typical procedure for a Gif^{III} reaction: cyclohexane **1b** (50 mmol), Fe° (20 mmol), acetic acid (40 mmol), the sulfur reagent S_G (as indicated) were added to pyridine (28 ml) and water (2 ml). The whole was stirred at room temperature for 20 hrs under O_2 at atmospheric pressure kept in a balloon to avoid the hydrogen sulfide smell. (b) Calculated from the redox equations: C-H + O_2 + 2H$^+$ + 2 e- → C-OH + H_2O, >CH_2 + 2O_2 + 4H$^+$ + 4 e- → >C=O + 3H_2O and 2 [C-H + O_2 + 2H$^+$ + 2 e- + S_G → C-SH + H_2O] → $(C\text{-}S)_2$ with respect to Fe°. (c) Yield of insertion of the sulfur S into the C-H bond calculated from [**6b** or **4b**] x 2 + [S_G]. (d) Method A was used. (e) Saturated solution of.*

No marked differences were observed between the three sulfur reagents used ($Na_2S,9H_2O$; H_2S; S_8). The use of a combination of the two latter has no marked effect upon the yield of the sulfide products **4b** (entries 9 to 11).

Blank experiments showed that there is no formation of the products **2b**, **3b**, and **4b** in the absence of dioxygen. The oxygenated products are not intermediates of the sulfides. From these blank experiments, we see that the sulfur reagents S_G are not responsible for the activation of the C-H bond.

In this system the presence of acetic acid is essential as shown in Table 2. With an insufficient amount very little oxidation takes place (entry 1), and with an excess the oxygenated products **2b** and **3b** are favoured at the expense of the sulfide **4b** (entry 3). The addition of picolinic acid **7** (Table 2, entries 4, 5), which is used as a ligand in the $GoAgg^{III}$ system, has an effect on the selectivity of this reaction. With the use of an appropriate amount of **7** only the sulfides **4b** are formed (entry 5).

Table 2: Effect of the concentration and nature of the acid with Gif^{III} system, sodium sulfide (10 mmol) and cyclohexane **1b** (50 mmol).[a]

Entry	Acid (mmol)	Products mmol **2b**	**3b**	**6b**[d]	one/ol	η/e- [b] %	Y C-S/S_G [c] %
1	AcOH (20)	0.13	--	--	--	0.6	--
2	(40)	1.62	0.09	1.05	18	27	21
3	(60)	2.54	0.19	0.79	13.6	34	15.8
4	AcOH (40) + **7** (4)	0.42	--	1.15	--	16	23
5	**7** (6)	--	--	1.16	--	12	23

a) Same as in Table 1, except that the sodium sulfide (10 mmol) was used, the acetic acid was added as specified and when appropriate the picolinic acid 7 was added as indicated. (b) Same as in Table 1. (c) Same as in Table 1. (d) Method A was used

When these sulfur reagents S_G were introduced in the catalytic $GoAgg^{II\&III}$ systems[14] using hydrogen peroxide as an oxidant (Table 3), the sulfide products **4b** were also observed. However, a change in reactivity distinguishes them. The sulfide reagents bearing S-H bonds have a poor selectivity for sulfide products **4b** (entries 2 to 5 and 16 to 22). The sodium sulfide is highly selective (enties 9, 13, 14, 15), however the use of picolinic acid **7** enhance its selectivity (entries 10 to 14). Elemental sulfur is an inhibitor of oxidation in $GoAgg^{II}$ (without picolinic acid, entry 6), and a poor reagent in $GoAgg^{III}$ reactions (entry 7), affecting strongly the formation of oxygenated products **2b** and **3b**. No oxidation products were formed in the absence of catalyst or in the absence of hydrogen peroxide under argon. Like with Gif^{III}, the amount of sulfide products **4b** increases with the amount of sulfur reagents S_G up to a limit (here 8 mmol) after which the overall oxidation decreases (entries 14 ,15 and 20 to 22). This is due to the side reaction of oxidation of the sulfur reagent to elemental sulfur by hydrogen peroxide.

Table 3: Sulfur reagents S_G with $GoAgg^{II\&III}$ systems and cyclohexane **1b** (50 mmol).[a]

Entry	Sulfur reagents: S_G mmol	PicH 7 mmol	Products mmol 2b	3b	4b or 6b[d]	% of 6b in 4b [e]	η [b] %	Y C-S/S_G % [c]
1	--	1.29	2.66	0.24	--		58	--
	H_2S				4b			
2	2.2	1.29	2.5	0.28	0.19		57	17
3	3.9	1.29	1.63	0.28	0.43		44	22
4	6.1	1.29	1.07	0.28	0.54		35	18
5	8.4	1.29	0.56	0.22	0.99		33	23
	S_8				4b			
6	1	0	0.07	--	0.06		2.5	1.5
7	1	1.29	0.40	--	0.47		17.4	11.7
	$Na_2S,9H_2O$				6b			
8	2	1.29	0.82	--	0.35	74	23	35
9	4	1.29	--	--	0.70	60	14	35
10	8	0	0.02	--	0.77	22	16	19
11	8	0.2	0.04	--	1.07	45	22	27
12	8	0.43	0.06	--	0.85	40	18	21
13	8	0.64	--	--	0.82	30	16	20
14	8	1.29	--	--	1.13	46	22	28
15	12	1.29	--	--	0.52	25	10	8.6
	$NaHS,H_2O$				4b			
16	2	1.29	2.42	0.45	0.26	50	58	26
17	4	1.29	1.86	0.52	0.44	58	51	22
18	6	1.29	1.32	0.59	1.18	47	56	39
19	8	0	0.24	0.12	1.16	-	29	29
20	8	1.29	0.58	0.35	1.55	46	46	39
21	10	1.29	0.07	0.01	1.15	35	24.5	23
22	12	1.29	0.48	0.01	0.58	41	21	9.6

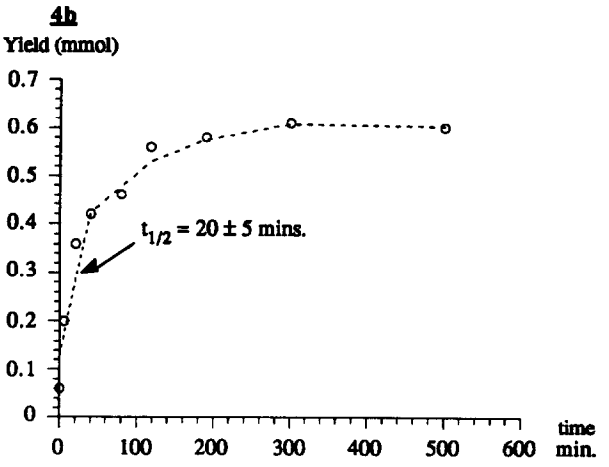
(a) Typical procedure for $GoAgg^{II\&III}$: Cyclohexane (50 mmol), sulfur reagent S_G (as specified), pyridine (15 ml), acetic acid (2.5 ml) and H_2O_2 30% (10 mmol) were stirred at room temperature with the appropriate catalyst for 30 mins. Catalyst for $GoAgg^{II}$: $Fe^{III}Cl_3,6H_2O$ (0.43 mmol), catalyst for $GoAgg^{III}$: $Fe^{III}Cl_3,6H_2O$ (0.43 mmol) with PicH 7 (as specified). (b) Same as in Table 1 with respect to H_2O_2 (10 mmol). (c) Same as in Table 1. (d) 4b method B was used, 6b method A was used. (e) Molar fraction x 100 of disulfide 6b contained in the polysulfide mixture 4b.

The rate of the reaction is enhanced by the presence of the sodium sulfide reagent. The half life drops from $t_{1/2}$ = 3 hr. for the usual oxygenation reaction with $GoAgg^{II}$,[14] to $t_{1/2} = 20 \pm 5$ min. when sodium sulfide is added (see Graph 1). A similar dramatic effect on the rate of the reaction was observed when electron rich ligands L, as picolinic acid or pyrazine-2-carboxylic acid, were added to the $GoAgg^{II}$ system, leading to the new $GoAgg^{III}$ system.[14] This effect can be explained by the coordination of these compounds on the iron species precursor of the intermediate A.

In a comparative study, using $GoAgg^{III}$ conditions on the oxygenation and the sulfation reactions, we show (Graph 2) that this system can be very efficient in product formation when enough hydrocarbon is introduced in the reaction mixture (up to 74% efficiency for over 80 mmol of cyclohexane **1b**).

Graph 1:
Kinetics of GoAgg^{II} with sodium sulfide and cyclohexane **1b**
T = 21°C

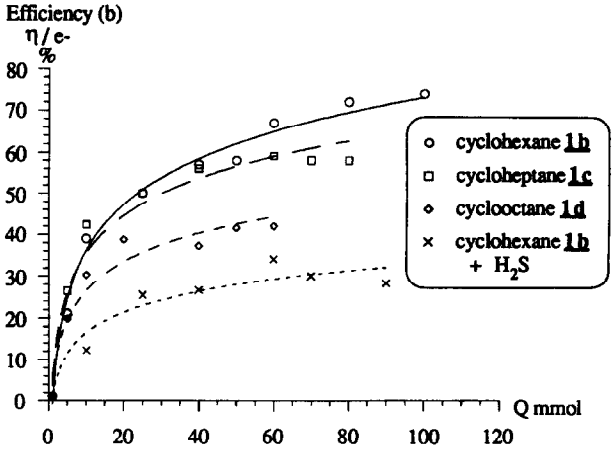
*Experimental procedure: cyclohexane **1b** (50 mmol), sodium sulfide (8 mmol), $FeCl_3,6H_2O$ (0.15 mmol), and H_2O_2 30% (10 mmol) were added to pyridine (15 ml) and acetic acid (2.5 ml) and stirred at room temperature. The aliquots are taken out and processed by method B.*



This effect is observed with other substrates, however with a less marked effect due to their lower reactivity and solubility,[7] and with the sulfation reaction using hydrogen sulfide, even so the efficiency goes up only to 30%. These results show that when there is enough substrate present in the reaction mixture to react with the proposed [Fe^{V}=O] species, the activation of the C-H bond becomes the predominant pathway to the detriment of side reactions such as decomposition of H_2O_2.

Graph 2:
Effect of increasing amount (Q) of hydrocarbon **1** with GoAgg^{III} systems (a)

*(a) Experimental procedure: The hydrocarbon **1** (Q mmol) was added to pyridine (15 ml), acetic acid (2.5 ml), $FeCl_3,6H_2O$ (0.43 mmol), PicH (1.29 mol) and H_2O_2 30% (10 mmol) and stirred at room temperature. x : to the same conditions with cyclohexane **1b** (Q mmol) was added hydrogen sulfide (8.1 mmol). (b) Same as defined in Table 1.*



The effect of the concentration of acetic acid in GoAgg^{III} also differs from the non catalytic system Gif^{III} (Table 4). The increase of its concentration improves the selectivity in the sulfide products **4b** up to a limit (ratio Py/AcOH = 2.83, entry 7) before it starts to inhibit the formation of sulfides (entries 4 to 8). The oxygenated products **2b** and **3b** are formed in a very good yield in the presence of small amount of acetic acid (entry 4 and 5). The strength of the carboxylic acid has also its importance, as seen with the trifluoroacetic acid, which gives

a less efficient system than acetic acid (entries 9 to 11), and the decreasing of its concentration leads to a better yield of oxygenated products **2b** and **3b**. These observations are opposite to those made on the oxygenation reactions carried out without sulfur reagents.[15] The total replacement of acetic acid by trifluoro-methanesulfonic acid leads to a very small amount of oxidation (entry 3 and 12).

In addition to these observations, the picolinic acid seems to be essential for a good activity of the system, regarding the low yield in product formation for the $GoAgg^{II}$ reactions (entry 1 to 3).

Table 4: Effect of concentration and nature of the acid with $GoAgg^{II\&III}$ systems, sodium sulfide (8 mmol) and cyclohexane **1b** (50 mmol).[a]

Entry	Acid	Ratio Py / Acid mmol / mmol	Products mmol **2b**	**3b**	**4b** [d]	% of **6b** in **4b** [e]	η [b] %	Y C-S/S_G % [c]
				$GoAgg^{II}$				
1	AcOH	4.24	0.02	--	0.77		16	19
2	CF_3CO_2H	5.72	0.37	0.19	0.30		15.3	7.5
3	CF_3SO_3H	4.24	0.19	0.04	0.25		9.2	6
				$GoAgg^{III}$				
4	AcOH	24.1	3.0	0.68	0.18	68	70.4	4.5
5		11.6	3.63	0.79	0.28	66	86	7
6		4.24	0.23	0.17	0.91	61	24.5	23
7		2.83	0.20	0.15	1.22	37	30	30
8		1.77	0.13	0.02	0.74	25	17.6	18.5
9	CF_3CO_2H	32.3	0.87	0.41	0.65	87	34.5	16
10		15.7	0.17	0.10	0.73	43	19.2	18
11		5.72	0.07	0.04	0.58	17	13.4	14.5
12	CF_3SO_3H	4.24	0.06	--	0.32	-	7.6	8

*(a) Same as in Table 3 except that the solvant (pyridine / acid) ratio is used as specified (17,5 ml), with sodium sulfide (8 mmol) N.B.: Ratio (Py/AcOH) = 4.24 ⇒ (Py 15 ml / AcOH 2.5 ml). (b) Same as in Table 1 with respect to H_2O_2 (10 mmol). (c) same as in Table 1. (d) **4b** method B was used. (e) Same as in Table 3*

Knowing the important results presented by Sawyer,[16] with his catalytic system of oxidation of cyclohexane using organic and inorganic compounds as source of electrons for reduction of dioxygen, it was of interest to look also for the formation of sulfide compounds with H_2S. Experiments were made to match Sawyer's system conditions and are shown in Table 5. Despite the low turn over observed, we have evidence that this system is catalytic by successive additions of reducing agent. The change of color allowed us to follow the course of the reaction. Increase of oxygenated and sulfide products was observed after the addition of a second amount of H_2S (entries 2, 3; Table 5).

The iron dichloride is as good a catalyst for the activation of dioxygen as the iron perchlorate (entries 2, 1). Picolinic acid **7** and dipicolinic acid **8a** and **8b** are both good ligands. The used of compound **8b** does not improve the yields of oxygenated nor sulfide products.

Table 5: Effect of the nature of catalyst and ligand with Sawyer's system with cyclohexane **1b** (15mmol).[a]

Entry	Catalyst (0.28 mmol)	Ligand (ratio Fe:L)	H_2S mmol	Products mmol **2b**	**3b**	**4b** [d]	η [b] %	Y C-S/S_G [c] %
1	$Fe^{II}X_2L_4$ [e]	**8b** (1:2)	5.4	0.16	--	0.11	10	4
2	$Fe^{II}Cl_2,4H_2O$	**8a** (1:2)	5.4	0.18	--	0.07	9.2	2.6
3	"	**8a** (1:2)	8.1[f]	0.27	--	0.15	7.0	3.7
4	"	**8a** (1:2)	10.8	0.42	--	0.10	10	1.8
5	"	**7** (1:2)	5.4	0.20	0.05	0.10	12	3.7
6	"	**7** (1:4)	5.4	0.19	0.05	0.10	11.6	3.7

*(a) Typical procedure: cyclohexane (15 mmol), the catalyst (as specified), the ligand (as specified), the hydrogen sulfide (as specified) in pyridine (13 ml) and acetic acid (5 ml) were stirred at room temperature under O_2 atmospheric pressure held in a balloon until the reaction mixture turn brown. (b) Same as in Table 1 with respect to H_2S. (c) Same as Table 1. (d) **4b** method B was used. (e) X = ClO_4, L = CH_3CN. (f) Same pot reaction as previous one with addition of a second amount of H_2S (2.7 mmol).*

Other substrates were used with Gif^{III} and $GoAgg^{II\&III}$ systems with a sulfur reagent S_G (Table 6). Cyclic hydrocarbons undergo the sulfation reaction with good yields. The order of reactivity observed is as follow:

cyclohexane **1b**	>	cyclopentane **1a**	>	cyclooctane **1d**
1		0.80		0.40

This order of reactivity is similar to the one reported in our previous study of bromination using $GoAgg^{III}$ system and shown to be opposite to that of radical bromination.[7]

Table 6: Reactivity of other hydrocarbons **1** with Gif^{III} and $GoAgg^{II\&III}$ systems, and sulfur reagents S_G.[a]

Entry	Hydro-carbon (mmol)	Sulfur reagents : S_G (mmol)	Products mmol **2**	**3**	**4** or **6** [d]	one/ol	η [b] %	Y C-S/S_G % [c]
				Gif^{III}				
	1d	$Na_2S,9H_2O$	**2d**	**3d**	**6d**			
1	(50)	0	1.38	0.06	--	23	14	--
2	(50)	10	1.23	0.06	0.67	21	19.2	13.4
				$GoAgg^{III}$				
	1d	$NaHS,H_2O$	**2d**	**3d**	**4d**			
3	(50)	0	2.0	0.16	--	13	42	--
4	(50)	8	0.7	0.33	0.57	2	29	14.2
	1a		**2a**	**3a**	**4a**			
5	(50)	8	traces	traces	1.35	--	27	33.7

*(a) Same Gif^{III} conditions were used as in Table 1 with hydrocarbon (as specified), and sulfur reagent (as specified), same $GoAgg^{III}$ were used as in Table 3 with hydrocarbon (as specified), and sulfur reagent (as specified). (b) Same as in Table 1 with respect to Fe° (20 mmol) with Gif^{III} and H_2O_2 (10 mmol) with $GoAgg^{III}$. (c) Same as in Table 1. (d) **4** method B was used, **6** method A was used*

In order to verify that the mechanism involved in the reaction process does not lead to a radical intermediary, we introduced the radical precursor **2**, an acyl derivative of N-hydroxy-2-thiopyridone, into the Gif type system medium in the presence of a sulfur reagent (Scheme 2, Table 7). This method has already been used to show that the formation of oxygenated products do not come from a radical intermediate.[3]

Scheme 2:

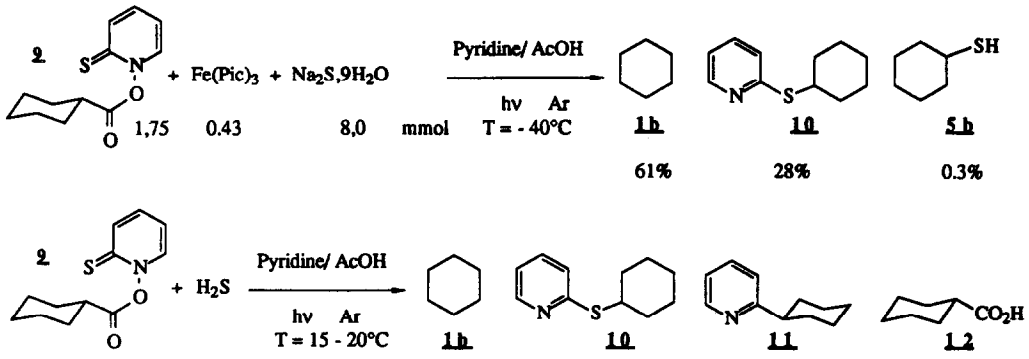


Table 7: Effect of hydrogen sulfide on free radical generated in Gif type system medium from precursor **2** (1.75 mmol)

entry	H_2S mmol	Products (yield %) **1b**	**10**	**11**	**12**	Σ %
1	7.2	85	0	0	0	85
2	4.1	78	0	0	0	78
3	2.0	43	3	22	13	81
4	1.0	18	15	18	21	72

*(a) Typical procedure: The radical precursor **2** is introduced progressively in 17.5 ml of solvant previously flushed under argon (pyridine 15 ml, acetic acid 2.5 ml) containing hydrogen sulfide (as specified). The temperature is kept between 15-20°C with a cooling bath when photolysing with two W lights (150W).*

When **2** is placed in the pyridine/acetic acid mixture with sodium sulfide at room temperature the side reaction of hydrolysis of the starting material is very fast. At - 40°C, this compound was successfully photolyzed by tungsten light, in a reasonable time (3hrs). The major amount of the cyclohexyl radical is quenched by the sulfide to give the cyclohexane **1b**. The replacement of sodium sulfide, a very good nucleophile, by hydrogen sulfide allowed us to carry out this reaction at room temperature, without substantial increase of the hydrolysis side reaction. It is seen that when the hydrogen sulfide is present in large exces, only the hydrocarbon **1b** is formed. When it is present in insufficient quantity, then side reactions take place. The propagation chain reaction leading to the rearranged product **10**, and the coupling with pyridine giving compound **11**. In none of these experiments were the di or polysulfides **6b** and **4b** detected, showing that in our systems their formation does not proceed *via* a radical pathway. However, if there were any radicals formed, they would be quenched back to the hydrocarbon by the sulfur reagent.

Albeit the mechanism of formation of the polysulfide **4** compounds is not yet clear, we believe that their formation is the result of the trapping of the intermediate A (σ-Fe-C bond) by the sulfur reagents S_G.

Experimental:

Unless otherwise stated, the experimental methods including work up procedures and GC analyses used throughout this work are as reported previously.[3]

Gif^{III}, $GoAgg^{II\&III}$ reactions were carried out as described in the Tables. The sulfur reagents were added as specified.

The modifications of acid concentration in $GoAgg^{III}$ were made so the volume of solvent is kept constant. This applies to the use of other acids as trifluoroacetic acid and trifluoro-methanesulfonic acid. The picolinic acid was added as specified. With the Gif^{III} system the acetic acid is added into the reaction mixture as specified in the Table 2.

The ^1H NMR were performed on a Varian XL-200 or Gemini 200 and Brucker 200 or 250 instruments. GC-MS were performed on a Delsi/Nermag 30 Mass spectometer (EI mode, 70 ev) equiped with a 25 meter capillary column Cpsil 5 with programmated temperature or with a Hewlett-Packard 5890 GC-MS system. GC analyses were carried out on a Girdel series 300 gas chromatograh equiped with a 2 meter Carbowax 20M 10% column for the oxygenated products and a 1,5 meter OV 17 5% column for the sulfide products, both using N_2 gas carrier.

The columns were used as described below for the respective susbstrates:

1b: T = 110°C, P = 0.65 kg/cm^2, R_t (**2b**) = 352 sec., R_t (**3b**) = 514 sec., R_t (int.stand. $C_{15}H_{32}$) = 717 sec.;
1d: T = 140°C, P = idem, R_t (**1d**) = 82 sec., R_t (**2d**) = 373 sec., R_t (**3d**) = 643 sec., R_t (int.stand. $C_{15}H_{32}$) = 255 sec.;
6a: T = 190°C, P = 0.85 kg/cm^2, R_t (**4a**) = 228 and 606 sec., R_t (**6a**) = 228 sec.; **6b:** T = 140 to 180°C (2°/min.) then constant , P = 0.85 kg/cm^2, R_t (**4b**) = 1267 and 2611 sec., R_t (**6b**) = 1267 sec..

GC-MS column conditions for polysulfide mixtures:

4a: T = 60°C +10°C/min.; [Rt (min.: sec.); M^+ (i); M (i = 100)] = [10:28; 202 (18,9); 69 (100)]; [13:10; 234 (26); 69 (100)]; [15:49; 266 (5); 69 (100)]
4b: T = 100°C + 10°C/min.; [Rt (min.: sec.); M^+ (i); M (i = 100)] = [8:35; 230 (18); 83 (100)]; [11:02; 262 (16); 83 (100)]; [13:29; 294 (5); 83 (100)]
4d: T = 80°C + 10°C/min.; [Rt (min.: sec.); M^+ (i); M (i = 100)] = [16:12; 286 (5); 69 (100)]; [18:48; 318 (5); 69 (100)]

Analysis of sulfide products

Method A: To the entire or an aliquot of the reaction mixture was added at 0°C an equal amount of sulfuric acid 50%, and the neutral products were extracted with ether three times. The organic layer was washed with sodium hydroxide solution 5% and then with brine, dried with $MgSO_4$, filtered and concentrated under vacuum. The resulting oil was dissolved in 30 ml of ethanol in a two necked flask equipped with a condenser. An excess

of sodium borohydride is added in two or three portions into the refluxing mixture. *(care should be taken at this stage, poisonous hydrogen sulfide is released).* After an hour, the mixture is chilled before adding hydrochloric acid solution 10% until all the white solid dissolves, extracted with ether and decanted. Into the ether fraction is added an ethanolic solution of iodine until the reddish color persists. The solution is stirred for 10 minutes, then washed with a sodium thiosulfate solution to remove the excess of iodine, dried over $MgSO_4$, filtered and evaporated under vacuum. The collected oil is then dissolved in pentane, eluted through silica gel and concentrated under vacuum. The lightly yellow disulfide oil is then weighed until constant mass is attained.

Method B: An aliquot of the reaction is taken out and extracted as above. Traces of ether are cautiously removed from the oil under vacuum by evaporating three to four times with carbon tetrachloride. The resulting oil is then dissolved in an accurate volumetric flask to 1 ml with a deuterated chloroform solution containing an internal standard. The ratio of ^1H NMR intensities of the internal standard signal ($Ph_2C\underline{H}_2$, δ(ppm) = 3.90 (2H. s); ($C\underline{H}Cl_2)_2$, δ(ppm) = 5,95 (2H, s)) and of the α H to the sulfur of the sulfide mixture ((c$(CH_2)_5C\underline{H})_2S_2$, δ(ppm) = 2.50 - 2.75 (2H, m), (c$(CH_2)_5C\underline{H})_2S_3$, δ(ppm) = 2.80 - 3.15 (2H, m)) is measured and read through a standard curve prepared with accurate concentrations of an authentic sample of the dicyclohexyl-disulfide. This method was applied to dicyclooctyl and dicyclopentyl polysulfide mixtures ((c$(CH_2)_7C\underline{H})_2S_2$, δ(ppm)= 2.850 - 3.05 (2H, m), c$(CH_2)_7C\underline{H})_2S_3$, δ(ppm)= 3.10 - 3.40 (2H, m); c$(CH_2)_4C\underline{H})_2S_2$, δ(ppm)= 3.20 - 3.40 (2H, m), c$(CH_2)_4C\underline{H})_2S_3$, δ(ppm)= 3.45 - 3.70 (2H, m)).

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