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Mechanism of the Oxidation of Sulfides by Dioxiranes. 1. Intermediacy of a 10-S-4 Hypervalent Sulfur Adduct

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Abstract: Earlier studies established that dimethyldioxirane (**1a**) reacts with sulfides **2** in two consecutive concerted electrophilic oxygen-transfer steps to give first sulfoxides **3** and then sulfones **4**. The same sequential electrophilic oxidation model was assumed for the reaction of sulfides **2** with the strongly electrophilic methyl(trifluoromethyl)dioxirane (**1b**). In this paper we report on a systematic and general study on the mechanism of the reaction of simple sulfides **2** with DMDO (**1a**) and TFDO (**1b**) which provides clear evidence for the involvement of hypervalent sulfur species in the oxidation process. In the oxidation of sulfides **2a**−**c**, diphenyl sulfide (**2d**), *para*-substituted aryl methyl sulfides **2e**−**i**, and phenothiazine **2k** with **1b**, the major product was the corresponding sulfone **4**, even when a 10-fold excess of sulfide relative to **1b** was used. The sulfone:sulfoxide **4**:**3** ratio depends among other factors on the dioxirane **1a** or **1b** used, the sulfide substitution pattern, the polar, protic, or aprotic character of the solvent, and the temperature. The influence of these factors and also deuterium and ^{18}O tracer experiments performed allow a general mechanism to be depicted for these oxidations in which the key step is the reversible cyclization of a zwitterionic intermediate, **6**, to form a hypervalent sulfur species, **7**. The classical sequential mechanism which establishes that sulfides are oxidized first to sulfides and then to sulfones can be enclosed in our general picture of the process and represents just those particular cases in which the zwitterionic intermediate **6** decomposes prior to undergoing ring closure to afford the hypervalent sulfurane intermediate **7**.

Introduction

The oxidation with peroxides of sulfides and, in general, sulfur-containing organic molecules has attracted the interest of chemists due to the different types of reaction mechanisms involved as well as their importance in the metabolism of drugs and some amino acids.[1] Within the framework of our ongoing work on the oxidation of organic compounds with dioxiranes **1**, we have decided to explore the reactivity of these oxygen-transfer reagents toward sulfides **2**. These previously described reactions[2] have been found to have several applications in organic synthesis,[3] but to date their mechanism has not been clearly disclosed.

The earlier studies[2b−d] established that dimethyldioxirane (hereafter DMDO) (**1a**) reacts with sulfides **2** to give sulfoxides **3** and then with sulfoxides **3** to give the corresponding sulfones **4** (Scheme 1). The values for Hammett's ρ were determined[2] to be −0.77 and −0.76, respectively. These data are in good agreement with both the expected electrophilic character of peroxide **1a**[4] and the different nucleophilic strength of the sulfur in compounds **2** and **3**. It was then suggested[2] that two consecutive concerted electrophilic oxygen-transfer steps from

Scheme 1

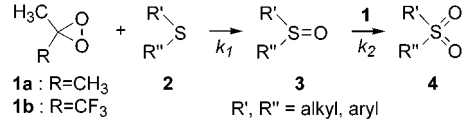

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Chart 1

2	R'	R''	2	R'	R''
2a	C_6H_5	CH_3	**2g**	*p*-ClC_6H_4	CH_3
2b	*n*-Bu	*n*-Bu	**2h**	*p*-CNC_6H_4	CH_3
2c	$C_6H_5CH_2$	$C_6H_5CH_2$	**2i**	*p*-$NO_2C_6H_4$	CH_3
2d	C_6H_5	C_6H_5	**2j**	C_6H_5	CF_3
2e	*p*-$CH_3C_6H_4$	CH_3	**2k**		
2f	*p*-$CH_3OC_6H_4$	CH_3			

1a gave first a sulfoxide, **3**, and then a sulfone, **4**, in a fashion similar to that described for the oxidation of sulfides **2** with peracids (Scheme 1). Accordingly, the transformation of sulfides **2** into sulfoxides **3** is feasible merely by adding the stoichiometric amount of **1a**. The same sequential electrophilic oxidation model was assumed[4] for the reaction of sulfides **2** with the strongly electrophilic methyl(trifluoromethyl)dioxirane (hereafter TFDO) (**1b**).

This mechanistic model was questioned[5b] in 1987, when the application of the thianthrene 5-oxide mechanistic probe,[5] designed to determine the electrophilic or nucleophilic character of oxidants, led Adam et al. to attribute an unexpected nucleophilic character to dioxiranes.[5a,b] The controversy[6] raised by this interpretation of the results was resolved later by the same authors[7] upon reexamination of the thianthrene 5-oxide oxidation products. The revision of the results firmly established the electrophilic character of **1a** and **1b** and allowed the return to the sequential electrophilic concerted oxygen atom transfer model for the dioxirane oxidation of sulfides **2** to sulfoxides **3** and sulfones **4**.

However, preliminary results of our study[8] on the reaction of simple sulfides **2** with **1b** revealed a rather different mechanistic picture. In fact, the main oxidation products were the corresponding sulfones **4**, which, rather than being derived from the oxidation of an initially formed sulfoxide **3**, seem to be formed by oxidation of a hypervalent sulfur intermediate. Our report found immediate synthetic application by Johnson et al.[9] in the preparation of episulfones, a class of compounds unavailable through regular sequential oxidation of the precursor sulfides due to the fast decomposition of the corresponding intermediate episulfoxide. In this paper we report on a systematic and general study on the mechanism of the reaction of simple sulfides **2** with **1a** and **1b**. Our findings provide clear evidence for the involvement of hypervalent sulfur species in the oxidation process.

Results and Discussion

Oxidation of Simple Sulfides 2 with Dioxiranes 1. Substituent, Temperature, and Solvent Effects. The oxidation of sulfides **2a**−**c,k** (Chart 1) with **1a** was performed in the dark under a nitrogen atmosphere by adding an aliquot of a thermostated acetone solution of the dioxirane[10a] (initial concentration ranging from 0.03 to 0.06 M) all at once to a methylene chloride solution of the sulfide at 0 °C. The oxidation of sulfides **2a**−**k** with **1b** was performed as described above, but with a ketone-free methylene chloride solution of **1b**[10b] (initial concentration from 0.03 to 0.06 M). After removal of the solvent under reduced pressure at 0 °C and redissolution in methylene chloride, the reaction mixtures were analyzed by means of GC, GC−MS, and ^{1}H NMR at 200 or 250 MHz. In the case of the oxidation of phenothiazine **2k** with **1b**, the reaction mixture showed a pink color. This was probably due to the presence of a phenothiazine radical cation which was reduced with an acetone solution of LiI prior to the NMR spectrum being recorded (see the Experimental Section). Results are collected in Table 1.

Table 1. Oxidation of Sulfides R′SR″ (**2**) with Dioxiranes **1a** and **1b**[a]

			molar ratio	convn	yield (%)		ratio
run	1	2	2:1	(%)	3	4	4:3
1	**a**	**a**	1:1	95	95	5	<0.1
2	**a**	**a**	2:1	55	100	0	0.0
3	**a**	**b**	1:1	90	94	6	<0.1
4	**a**	**c**	1:1	93	96	4	<0.1
5	**a**	**k**	2:1	49	100	0	0.0
6	**b**	**a**	1:1	58	21	79	3.8
7	**b**	**a**	2:1	31	27	73	2.7
8	**b**	**a**	3:1	20	35	65	1.9
9	**b**	**a**	3:1[b]	20	40	60	1.5
10	**b**	**a**	5:1	13	38	61	1.6
11	**b**	**a**	10:1	7	43	57	1.3
12	**b**	**b**	1:1	63	29	71	2.5
13	**b**	**b**	3:1	22	41	59	1.4
14	**b**	**b**	10:1	7	43	57	1.3
15	**b**	**c**	1:1	63	27	73	2.7
16	**b**	**c**	2:1	30	36	64	1.8
17	**b**	**c**	3:1	22	41	59	1.4
18	**b**	**c**	10:1	7	43	57	1.3
19	**b**	**d**	2:1	45	36	64	1.8
20	**b**	**e**	2:1	27	24	76	3.2
21	**b**	**f**	2:1	30	29	71	2.4
22	**b**	**g**	2:1	30	38	62	1.6
23	**b**	**h**	2:1	34	46	55	1.2
24	**b**	**i**	2:1	35	47	51	1.1
25	**b**	**j**	2:1	48	>99		
26	**b**	**k**	1:1	41	27	73	2.7
27	**b**	**k**	2:1	21	31	69	2.2
28	**b**	**k**	3:1	19	34	66	1.9

[a] Reactions were carried out at 0 °C in methylene chloride or methylene chloride/acetone; reaction mixtures were analyzed by GC except for entries 5 and 26−27, in which ^{1}H NMR was used. Substrate concentrations were 0.063 M for all runs except for entries 5 and 12−17, in which a 0.080 M substrate concentration was used. For all runs the oxygen transfer ranged from 95% to 100%. [b] A **1b** solution was added dropwise.

Sulfoxides **3a**−**c,k** were the main products in the **1a** oxidation of methyl phenyl sulfide (**2a**), dibutyl sulfide (**2b**), dibenzyl sulfide (**2c**), and phenothiazine **2k**, respectively (runs 1−5, Table 1). Only small amounts of the corresponding sulfones **4a**−**c,k** were detected when sulfide and dioxirane **1a** were mixed in equimolecular amounts (runs 1, 3, and 4, Table 1). However, when **2a** was reacted with **1a** in a 2:1 molar ratio (run 2, Table 1), only sulfoxide **3a** was obtained. These results are in good agreement with previous reports on the **1a** oxidation of sulfides.[2,3]

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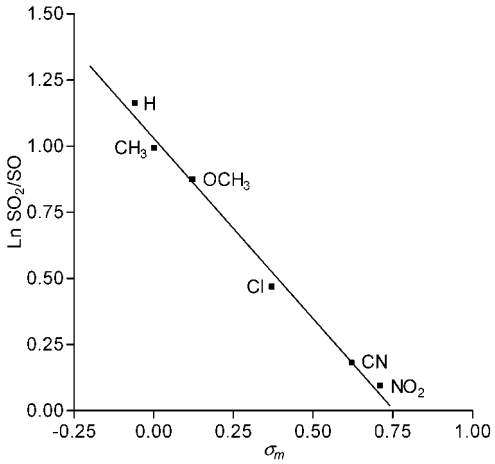

Figure 1. ln [**4**]/[**3**] against the σ_m values of the substituents.

Table 2. Influence of Temperature on the Reaction of Sulfides **2** with **1b**[a]

run	2	molar ratio 2:1	T (°C)	convn (%)	yield (%) 3	yield (%) 4	ratio 4:3
1	**a**	2:1	0	31	27	73	2.7
2	**a**	2:1	−40	31	32	68	2.1
3	**a**	2:1	−80	35	49	51	1.1
4	**a**	3:1	0	20	35	65	1.9
5	**a**	3:1	−40	22	41	59	1.4
6	**a**	3:1	−80	24	54	46	0.8
7	**c**	2:1	0	30	36	64	1.8
8	**c**	2:1	−40	34	41	59	1.4
9	**c**	2:1	−80	38	58	42	0.7

[a] Reactions were carried out at the desired temperature in methylene chloride with a substrate initial concentration of 0.063 M. The reactions were analyzed by means of GC.

The oxidation of sulfides with **1b**, on the other hand, follows a different trend. Thus, in the oxidation of sulfides **2a**−**c**, diphenyl sulfide (**2d**), *para*-substituted aryl methyl sulfides **2e**−**i**, and phenothiazine **2k** (runs 6−28, Table 1), the major product was the corresponding sulfone **4**, even when a 10-fold excess of sulfide relative to **1b** was used (runs 11, 14, and 18, Table 1) or when dioxirane **1b** was added dropwise (run 9, Table 1). Only in the case of phenyl trifluoromethyl sulfide (**2j**) was the product the expected sulfoxide **3j** (run 25, Table 1). In general, the sulfone:sulfoxide **4**:**3** ratio decreased as the initial molar ratio sulfide:dioxirane **2**:**1b** used was increased (runs 6−11, Table 1). As can be seen in Table 1, the results obtained in the oxidation of sulfides with **1a** and **1b** are divergent and only the less electrophilic **1a** allows the selective transformation of sulfides **2** into sulfoxides **3**.

On the other hand, the plot of the value of ln [**4**]/[**3**] against the σ_m values of the substituents in the oxidation of a series of *para*-substituted sulfides **2a** and **2e**−**i** (runs 7 and 20−24, Table 1) gave a straight line with an excellent correlation ($r^2 = 0.999$) and negative slope of −1.397 (Figure 1). Accordingly, the presence of inductive electron-withdrawing substituents at the sulfide **2** favors the formation of sulfoxide **3**. This trend reaches its limit for **2j**, which reacts with **1b** to give exclusively the sulfoxide **3j** (run 25, Table 1).

The oxidation of sulfides **2a** and **2c** with **1b** was also studied in the temperature range of 0 to −80 °C (see Table 2). The results show that the lowering of the temperature favors the formation of sulfoxide and consequently diminishes the sulfone: sulfoxide **4**:**3** ratio.

Table 3. Oxidation of Simple Sulfides (**2**) with TFDO (**1b**) in Different Solvents[a]

run	2	molar ratio 2:1b	solvent[b]	convn (%)	yield (%) 3	yield (%) 4	ratio 4:3
1	**a**	2:1	DC	31	27	73	2.7
2	**a**	2:1	CCl_4	25	20	80	4.0
3	**a**	2:1	DC/AC (1:19)	29	28	72	2.6
4	**a**	2:1	DC/AN (1:19)	32	28	72	2.6
5	**a**	2:1	DC/TFE (1:19)	34	53	47	0.9
6	**d**	2:1	DC	45	36	64	1.8
7	**d**	2:1	CCl_4	22	28	72	2.6
8	**d**	2:1	DC/TFE (1:19)	30	61	39	0.6
9	**h**	2:1[c]	DC	31	45	54	1.2
10	**h**	2:1[c]	DC/TFE (1:19)	44	77	23	0.3
11	**k**	2:1	DC	21	31	69	2.2
12	**k**	2:1	CCl_4	18	13	87	6.7
13	**k**	2:1	DC/TFE (1:19)	25	87	13	0.15
14	**k**	1:1	DC	41	27	73	2.7
15	**k**	1:1	DC/AA (15:1)	52	42	58	1.4
16	**k**	1:1	DC/AA (1.7:1)	75	69	31	0.45
17	**k**	1:1	DC/TB (1.7:1)	64	35	65	1.9
18	**a**	2:1	DC/TFA (2 equiv)	40	50	50	1.0
19	**a**	2:1	DC/TFA (10 equiv)	41	66	34	0.53
20	**a**	2:1	DC/TFA (20 equiv)	53	73	27	0.36
21	**a**	2:1	DC/TFA (1:19)	46	100	0	0.0
22	**a**	1:1	DC	58	21	79	3.8
23	**a**	1:1	DC/DMSO (1 equiv)	42[d]	28	72	2.6[e]
24	**a**	1:1	DC/DMSO (3 equiv)	27[d]	32	68	2.1[e]
25	**a**	1:1	DC/DMSO (5 equiv)	23[d]	40	60	1.5[e]

[a] Reactions were carried out at 0 °C, with substrate concentrations ranging between 0.063 and 0.080 M. The oxygen transfer ranged from 95% to 100% in all the cases. [b] Volume ratio except where noted. DC = methylene chloride, AC = acetone, AN = acetonitrile, TFE = 2,2,2-trifluoroethanol, TFA = 2,2,2-trifluoroacetic acid, AA = acetic acid, and TB = *tert*-butyl alcohol. [c] Reaction temperature −18 °C. [d] In the reaction mixture dimethyl sulfone was also produced (about 5%) from oxidation of the competing DMSO by TFDO (**1b**). [e] Only the **4a**:**3a** ratio is shown.

Reactions in different solvents and in the presence of additives were carried out under conditions similar to those described above by adding an aliquot of a methylene chloride solution of **1b** all at once to a solution of **2** in the selected solvent (methylene chloride, carbon tetrachloride, acetone, acetonitrile, 2,2,2,-trifluoroethanol, 2,2,2-trifluoroethanol/water) in the presence of the additive. Results are shown in Table 3.

When oxidations were carried out in a nonpolar solvent such as carbon tetrachloride (runs 2, 7, and 12, Table 3), the sulfone: sulfoxide **4**:**3** ratio increased as compared to the ratio obtained in each case in polar aprotic solvents such as methylene chloride, acetonitrile, or acetone (runs 1, 3, 4, 6, and 11, Table 3). In these latter solvents, no significant variations in the product distribution were detected. A dramatic change occurs, however, if a protic solvent is used. In 2,2,2-trifluoroethanol solution the amount of sulfoxide obtained increases greatly at the expense of the amount of sulfone (runs 5, 8, 10, and 13, Table 3). The same effect is observed when a protic additive is introduced into the reaction medium. For instance, in the oxidation of phenothiazine **2k** with **1b** in methylene chloride the sulfone: sulfoxide **4**:**3** ratio obtained was 2.7 (run 14, Table 3), while in the presence of *tert*-butyl alcohol the value of this ratio was only 1.9 (run 17, Table 3). The use of acid additives favors the formation of sulfoxides, and the effect is enhanced as the strength and/or concentration of acid increase (runs 15, 16, and 18−21, Table 3). For instance, the addition of only 2 equiv of trifluoroacetic acid in the reaction of **2a** with **1b** in methylene chloride reduces the sulfone:sulfoxide **4**:**3** ratio from 2.7 (run 1, Table 3) to 1.0 (run 18, Table 3). At the limit, the use of trifluoroacetic acid as a cosolvent allows the exclusive trans-

Table 4. Competitive Oxidations of $PhSCD_3$ (**2a-*d*$_3$**) and $PhSOCH_3$ (**3a**) with Dioxiranes **1**[a]

run	1	molar ratio 1:2a-d_3:3a	solvent[b]	reaction mixture composition (%)[c] 2a-d_3	3a-d_3 (3a)	4a-d_3 (4a)	O transfer[d] 2a-d_3:3a	ratio 4a-d_3:3a-d_3
1	**a**	1:1:1	DC/AC (1:1)	13	80 (93)	7 (7)	13.4	0.1
2	**b**	1:1:1	DC	58	11 (66)	31 (34)	2.1	2.8
3	**b**	1:1:3	DC	73	9 (80)	18 (20)	2.3	2.0
4	**b**	1:1:1	DC/TFE (1:9)	53	21 (70)	26 (30)	2.4	1.2

[a] Reactions were carried out at 0 °C with a concentration of the substrates ranging between 0.03 and 0.06 M. [b] DC = methylene chloride, AC = acetone, and TFE = trifluoroethanol. [c] Mixture compositions were calculated separately for CD_3- and CH_3-substituted compounds, and the values are the average of at least two identical runs within a standard error of ±2%. [d] Calculated as [[**3**-d_3] + 2[**4**-d_3]]/[**4**].

formation of **2a** into the corresponding sulfoxide **3a** (run 21, Table 3). A similar, although weaker, effect is observed upon addition of nucleophilic additives such as dimethyl sulfoxide (DMSO) to the medium. This effect also increases with the concentration of the additive (runs 23−25, Table 3). It should be noted that in this case, *sulfone **4a** is still the major oxidation product even in the presence of a 5:1 excess of dimethyl sulfoxide relative to sulfide* **2a** (run 25, Table 3).

Since sulfones **4** are predominantly formed even when a large excess of sulfide **2** relative to dioxirane **1b** is used, a sequential oxidation of sulfides **2** with **1b** similar to that depicted in Scheme 1 would only apply if the oxidation of sulfoxides **3** with **1b** happened much faster than the oxidation of their parent sulfides **2** ($k_2 \gg k_1$, in Scheme 1). On the other hand, the results on the influence of the substituents on the sulfone:sulfoxide **4**:**3** ratio (Figure 1) would indicate an electrophilic behavior of dioxirane **1b** and therefore a higher sensitivity to substituent effects in the second step of the sequential oxidation. This consequence would be in disagreement with reported[2] ρ values for the oxidation of sulfides and sulfoxides with **1a**. Another striking feature would be the lack of correlation between the sulfone:sulfoxide ratio **4**:**3** and the σ_p constant in the **1b** oxidation of aryl methyl sulfides **2a** and **2e**−**i**.

According to the sequential mechanism depicted in Scheme 1, the oxidations of sulfides **2** and sulfoxides **3** are bimolecular reactions which require a concerted transition state[6c,11] with some charge separation. Following this model, the temperature effect shown in Table 2 would reveal that the absolute value of the negative activation entropy for the oxidation of sulfides **2** is greater than for the oxidation of sulfoxides **3**. Since solvation of the transition state and activation energy are correlated, from our data the role of solvation in the stabilization of the transition state would be more important in the first than in the second step of the sequential oxidation. This observation would be in good agreement with theoretical calculations in the gas phase,[6c,11] which indicate a greater change in the polarity on going from the reagents to the transition state in the case of the oxidation of sulfides than in the case of the oxidation of sulfoxides. Values of $\mu_{TS} = 8.7$ and 6.0 D have been calculated,[11] respectively, for the transition states in the reaction of sulfides and sulfoxides with **1a**. Therefore, the classical sequential mechanism (Scheme 1) would hardly explain in terms of solvation phenomena the apparent nucleophilic character of the strong electrophile TFDO (**1b**).

However, the changes in the sulfone:sulfoxide **4**:**3** ratio associated with the presence or absence of protic additives or nucleophiles in the medium are not explained by differences in the polarity of the transition states corresponding to each step of the classical oxidation sequence (Scheme 1). Moreover, the sequential oxidation model cannot explain the efficient conversion of sulfides **2** into sulfones **4** even in the case that DMSO is added to the reaction medium (runs 23−25, Table 3). To justify this result, one would require unexpected additional factors that bias the oxidation toward the sulfoxide derived from the starting **2a**.

^{2}H Isotopic Tracer Experiments. At this point, the rationalization of the data collected in Tables 1−3 in terms of the sequential mechanism described in Scheme 1 requires an accurate estimation of the relative rate constants for the steps involved in the sequence. With this in mind, we designed a series of competition experiments to measure the relative reaction rates of sulfides and sulfoxides with **1a** and **1b**. We selected phenyl trideuteriomethyl sulfide (**2a-*d*$_3$**) and methyl phenyl sulfoxide (**3a**) as model substrates because the minimum structural differences at the sulfur substituents allow obviation of electronic or steric effects derived from them. Competitive oxidation experiments were carried out by adding an aliquot of a solution of **1a** in acetone or **1b** in methylene chloride to a mixture of **2a-*d*$_3$** and **3a** in the selected solvent in the dark and under an inert atmosphere. The concentrations of the products were determined by means of GC−MS. The concentration of the products was determined by integration of the GC areas corresponding to the sum of sulfoxides **3a-*d*$_3$** and **3a** and sulfones **4a-*d*$_3$** and **4a** and integration of the MS monoisotopic molecular ion abundance profile (*m*/*z* 140 and 143 for **3a** and **3a-*d*$_3$**, respectively, and *m*/*z* 156 and 159 for **4a** and **4a-*d*$_3$**, respectively). Calibration curves had been previously recorded for these same sulfoxide and sulfone pairs. The results are summarized in Table 4.

The major oxidation product of an equimolecular mixture of **2a-*d*$_3$** and **3a** with **1a** was the sulfoxide **3a-*d*$_3$**, along with small amounts of sulfones **4a-*d*$_3$** and **4a** (run 1, Table 4). *Surprisingly, the same reaction with* **1b** *yielded sulfone* **4a-*d*$_3$** *as the major product even when a 3:1 excess of sulfoxide* **3a** *relative to sulfide* **2a-*d*$_3$** *was used* (runs 2 and 3, Table 4). It is to be noted that although sulfoxide **3a** was also oxidized with **1b** to the corresponding sulfone **4a** under these reaction conditions, the oxygen transfer occurs preferentially toward the sulfide **2a-*d*$_3$** to give mainly the sulfone **4a-*d*$_3$** (runs 2 and 3, Table 4). The **4a-*d*$_3$**:**3a-*d*$_3$** ratio decreased from 2.8 to 1.2 when dichloromethane was substituted for 2,2,2-trifluoroethanol as solvent in good agreement with the results reported in Table 3. In 2,2,2-trifluoroethanol solution the sulfone derived from **3a** appeared in a larger proportion (**4a**:**4a-*d*$_3$** = 1.2) (run 4, Table 4) but even in this case, the oxygen transfer occurs preferentially to the sulfide. It is worth noting that the greater the initial amount of **3a** used, the lower the value of the ratio **4a-*d*$_3$**:**3a-*d*$_3$** found, a fact which is in good agreement with the data reported in

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Table 3 regarding the effect of nucleophilic additives. An independent measurement of the relative oxidation rate for sulfoxides **3a** and **3a-*d*$_3$** gave a value of $k_H/k_D = 0.94 \pm 3\%$. This effectively rules out any relationship between the results in Table 4 and any kinetic isotopic effect.

Rather than bolstering the case for the classical sequence model, our data point to a mechanistic oxidation model for sulfides **2** with **1b** in which sulfide **2** would first give rise to a reactive intermediate that can either evolve into the sulfoxide **3** or undergo further oxidation by **1b** to give the sulfone **4**, this latter oxidation being much faster than the oxidation of either the sulfide or the sulfoxide.[12] The data in Tables 1−3 indicate that this intermediate is labile toward acids and nucleophiles as these reagents inhibit the formation of sulfones **4** to a certain extent while favoring the production of sulfoxides **3**. Moreover, if oxidations with dioxiranes **1** had to be explained with the same reaction model, then the formation rate and reactivity of the suspected intermediate would also depend on both the nature of the dioxirane **1a** or **1b** from which it derives and the reaction conditions.

^{18}O Isotopic Tracer Experiments: Evidence for a Sulfurane Intermediate. The results of our experiments led us to propose the existence of a hypervalent sulfur intermediate for dioxirane-mediated oxidations of sulfides **2**. This, in itself, is not new as hypervalent sulfur derivatives are often intermediates in the oxidation of sulfides.[13] For instance, the participation of species of this type in the oxidation of sulfides with dioxetanes[13l] is well-known, and many additional examples can be found in the oxidation of sulfides with singlet oxygen.[13c−j]

The fast reaction of sulfides **2** with **1b** does not permit the direct observation of the intermediate by means of the usual spectroscopic techniques; we therefore decided to investigate the reaction mechanism using chemical methods that could not only reveal the existence of an intermediate, but also give an indication as to its nature. The structural characteristics and types of bonds involved in hypervalent sulfur derivatives are well-known.[14] Martin et al. have investigated[15] in depth the reactivity of these compounds toward substrates carrying active hydrogen atoms such as alcohols, amines, or amides and have shown that these derivatives give rise to ligand exchange reactions on the hypervalent sulfur atom. These properties have, in turn, allowed other authors[13] to ascertain the intermediacy of hypervalent sulfur compounds in a number of oxidation reactions of sulfides. Taking this into consideration, we designed ^{18}O tracer isotope experiments that would promote ligand exchange reactions in the hope of obtaining evidence for the involvement of a hypervalent sulfur intermediate by incorporation of ^{18}O into the oxidation products. Three different ^{18}O carriers were assayed, namely, trifluoroacetone hydrate **5-*^{18}O***, $H_2{}^{18}O$ in neutral or acid medium, and trifluoroacetic acid-*^{18}O*. Trifluoroacetone hydrate **5-*^{18}O*** (49% atom labeled) was obtained in situ by mixing equimolar amounts of $H_2{}^{18}O$ (Aldrich, 98% atom labeled) and trifluoroacetone in a 4:1 acetonitrile/methylene chloride solution at 0 °C and under an inert atmosphere. Reactions with $H_2{}^{18}O$, $H_2{}^{18}O/CF_3COOH$ and trifluoroacetic acid-*^{18}O* were performed in 1:4 methylene chloride/trifluoroethanol to provide a homogeneous medium. Details of the method are described in full in the Experimental Section. **2a** was oxidized with an equimolar amount of **1b** in the presence of ^{18}O tracers under an inert atmosphere at 0 °C in the above specified solvent for each ^{18}O carrier. Control experiments revealed that compounds **3a** and **4a** do not undergo noticeable oxygen exchange under our experimental conditions. The reaction mixtures were analyzed by GC−MS, and the results are summarized in Table 5.

Table 5. Oxidation of **2a** with **1b** in the Presence of ^{18}O Isotopic Tracers[a]

run	additive (equiv)	solvent[b]	convn (%)	yield (%) (% labeled fraction)[c] **3a** (^{18}O)	**4a** (^{18}O)	ratio **4a**:**3a**
1	**5-*^{18}O***[d] (100)	DC/AN (1:4)	56	34 (23)	66 (12)	1.7
2	$H_2{}^{18}O$[d] (100)	DC/TFE (1:4)	41	33 (11)	67 (6)	2.0
3	$H_2{}^{18}O$[d] (100), TFA (2.5)	DC/TFE (1:4)	67	47 (21)	53 (5)	1.1
4	TFA-*^{18}O*[d] (200)	DC	54	94 (1.1)	6 (0.5)	<0.1

[a] Reactions were carried out at 0 °C with an initial **2a**:**1b** molar ratio of 1:1. Reaction mixtures were analyzed by GC−MS. [b] DC = methylene chloride, AN = acetonitrile, TFE = 2,2,2-trifluoroethanol, and TFA = trifluoroacetic acid. [c] The percent ^{18}O labeling was calculated by applying the equation $100[(I+2) - (I+2)_{nat}]/[I + (I+2)]$ to the normalized relative intensities corresponding to the peaks $m/z = 125$ $[M - CH_3]^+$ and $m/z = 140$ $[M]^+$ for the sulfoxide **3a**/**3a-*^{18}O*** and to the peaks $m/z = 141$ $[M - CH_3]^+$ and $m/z = 156$ $[M]^+$ for the sulfone **4a**/**4a-*^{18}O***, respectively, and obtaining the average value. Mass spectra were recorded at least three times. The estimated error was less than 1%. [d] **5-*^{18}O***: 49 atom % labeled; $H_2{}^{18}O$: 98 atom % labeled; TFA-*^{18}O*: 49 atom % labeled.

The effect of protic additives on the sulfone:sulfoxide **4**:**3** ratio (see data in Table 5) are fully consistent with those reported in Table 3. This ratio drops to a minimum value (<0.1) for the oxidation of **2a** in the presence of 200 equiv of TFA-*^{18}O* (run 4, Table 5). GC−MS analysis of the reaction products showed ^{18}O incorporation in products **3a** and **4a** in various amounts depending on the reaction conditions assayed (Table 5). Thus, in the oxidation of **2a** with an equimolar amount of **1b** in 4:1 acetonitrile/methylene chloride in the presence of a 100-fold excess of 1,1,1-trifluoroacetone-*^{18}O* hydrate (**5-*^{18}O***), 23% sulfoxide **3a-*^{18}O*** (34% yield, 23 atom % ^{18}O) and 12.2% sulfone

(12) Following the classical sequential model, the intermediate should be the excited sulfoxide **3**. Although the oxidation of sulfides with **1b** is highly exothermic, a vibrationally excited sulfoxide would not live long enough (10^{-12} s) to react with **1b** even in a diffusion-controlled oxidation ($k_{dif} = 10^{-10}$ s^{-1}). Furthermore, the products derived from the characteristic reactivity of these intermediates, such as, for example, α-fragmentation or hydrogen abstraction, have never been detected. Finally, the intermediacy of an electronically excited sulfoxide does not explain the solvent and additive effects described.

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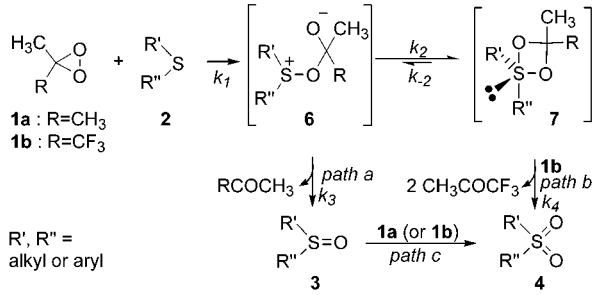
Scheme 2



4a-*[18]*O (66% yield, 6 atom % ^{18}O) were obtained (entry 1, Table 5). When the same oxidation reaction was carried out in the presence of 100 equiv of $H_2{}^{18}O$, the molar fractions of labeled sulfoxide **3a-*[18]*O** and sulfone **4a-*[18]*O** were 11% and 6%, respectively (run 2, Table 5). Low label incorporation was achieved only when the tracer was TFA-*[18]O* (200 equiv) (run 4, Table 5). In contrast, the presence of TFA (2.5 equiv) did not inhibit the incorporation of the label when $H_2{}^{18}O$ was the carrier (run 3, Table 5).

These results further disqualify the sequential concerted electrophilic oxygen-transfer mechanism for the oxidation of sulfides and sulfoxides with **1b** since it does not account for the incorporation of ^{18}O in the oxidation product.

The Proposed Mechanism. The above-described experimental results can be satisfactorily explained with the involvement of a hypervalent intermediate. A new reaction mechanism invoking this intermediate during the dioxirane oxidation of sulfides **2** is proposed in Scheme 2.

The first step in the new mechanism is the electrophilic attack of the peroxide **1** on the sulfur atom in **2** to form a covalent S−O bond. The interaction in the solvent cage of the resulting positively charged sulfur atom with the negatively charged oxygen atom in the zwitterionic species **6** would give rise to the reversible formation of the sulfurane intermediate **7**. Elimination from **6** (path a, Scheme 2) would result in the formation of the parent ketone along with sulfoxide **3**. Alternatively, the bimolecular oxidation of **7** by a second dioxirane molecule (path b, Scheme 2) would yield the corresponding sulfone **4**. In principle, we cannot exclude the formation of **4** in part by direct oxidation of the corresponding sulfoxide **3** (path c). The value of each rate constant will mainly depend on the nature of the dioxirane used, the structure of the sulfide, and the reaction conditions. In general, those factors preventing the ring closure of **6** or favoring the opening of the cyclic sulfurane should lead to lower **4**:**3** ratios. Thus, in the case of oxidations with **1b** the usual high value of the **4**:**3** ratio (Table 1) and the unexpected formation of **4a-*d*$_3$** in the competitive experiments depicted in Table 4 show that the oxidation of **7b** occurs faster than the oxidation of the starting sulfide **2** ($k_4 \gg k_1$) or the ketone elimination process ($k_4 \gg k_3$).

The proposed hypervalent intermediate **7** is a 10-S-4 sulfurane with four ligands and a lone electron pair on the sulfur atom. Its structure is that of a *pseudo* trigonal bypyramid (TBP) with two apical and two equatorial ligands and the lone electron pair at the third equatorial position. The molecular orbital model[14] for 10-S-4 sulfuranes implies a three-center, four-electron hypervalent bond joining the two apical ligands to sulfur. The four electrons of the hypervalent bond are placed into the two lower energy molecular orbitals made up of linear combinations

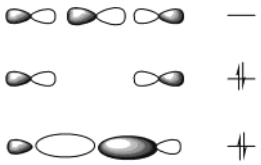


Figure 2. MO description of the four-electron hypervalent bond in 10-S-4 sulfuranes.

of collinear p-orbitals on the sulfur and the ligands (Figure 2) in such a way that the HOMO is a nonbonding (NBMO) orbital. The apical bonds thus contain only two electrons in a bonding MO and are consequently polarized and weaker than equatorial bonds; therefore, the minus charge is localized on the apical atoms. This model explains the preference for apical positions seen for the more electronegative substituents.[14]

The sulfur $3p_z$ orbital does not contribute to the NBMO of the hypervalent bond and results in relatively high positive charge localization at the sulfur. The two oxygen atoms in **7** are connected and enclosed in a four-membered ring. This structural requirement forces one of the oxygen atoms to occupy an equatorial position regardless of the higher electronegativity of oxygen as compared to carbon. The different electronegativities of the apical ligands impose a distorted trigonal bipyramid geometry[16] on **7**, much like that characteristic of sulfonium salts. In addition, the apical S−O bond will be longer and the oxygen negative charge density greater than in regular symmetric sulfuranes. In sulfuranes derived from asymmetric sulfides the second apical position would be most probably occupied by the most electronegative substituent in the parent sulfide.

According to this description, the most striking features affecting the reactivity of intermediate **7** will be that it contains a highly basic and reactive apical oxygen along with an electrophilic sulfur. Electrophiles will thus be expected to attack at the apical oxygen site, while nucleophiles will react with the hypervalent sulfur atom.

Regarding the formation of sulfones **4**, the experimental data obtained in the oxidation of *para*-substituted aryl methyl sulfides **2a** and **2e**−**i** with **1b** correlate well with the substituent σ_m constant. This suggests that the second oxidation step (path b, Scheme 2) is not affected by resonance interactions between the aromatic ring and the oxidation site. This correlation rules out the oxidation of sulfoxides **3** as a significant route to sulfones **4** (path c, Scheme 3) in the oxidation of **2** with **1b** since this process is known to be sensitive to the substituent σ_p constant.[6a] Furthermore, the oxidation of the zwitterionic intermediate **6b** would occur most probably at the negatively charged oxygen site, and consequently the **4**:**3** ratio would be insensitive to the substituent effect. Concerning the oxidation of the hypervalent intermediate **7**, two different oxidation sites can be envisaged, namely, the highly nucleophilic apical oxygen and the lone electron pair at the sulfur. Apical aryl groups bearing inductive electron-withdrawing substituents will diminish the electron density at the apical hypervalent oxygen to **7** and hence are expected to slow the oxidation rate of the intermediate at this position, leading to lower values for the **4**:**3** ratio (Table 1 and

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Scheme 3

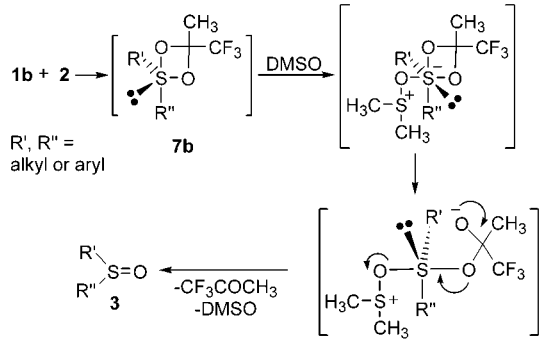


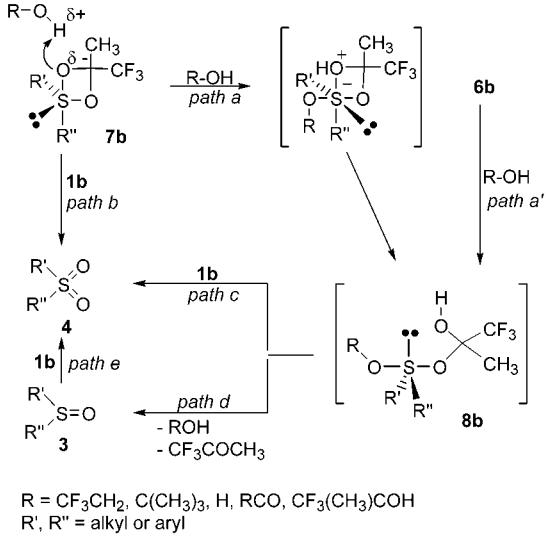
Figure 1) as found. On the other hand, the hypothetical oxidation of the lone electron pair in **7** would require, according to our data, a geometric restriction of resonance with the π-electron system of the aromatic ring. Consequently, at this moment it is not possible to envisage a detailed mechanism for the oxidation of sulfurane **7** to give sulfone **4**.

The different behaviors of **1a** and **1b** in their reactions with sulfides **2** can be rationalized according to our mechanistic proposal shown in Scheme 2. Thus, considering the relative stabilities of the corresponding acetone and 1,1,1-trifluoroacetone hydrates[17] and also the higher basicity at the negatively charged oxygen atom in the intermediate **6a** relative to **6b**, we must conclude that in the oxidations with **1a** $k_3 \gg k_2$ while in the case of **1b** $k_2 \gg k_3$. In fact, the different courses of the oxidations with **1a** and **1b** suggest that probably in the case of **1a** sulfurane **7a** is not even formed under the reaction conditions assayed. It should also be noted that oxidations with **1a** are always carried out in acetone solution, a polar solvent that favors charge separation.

Effects of Solvent, Temperature, and Additives. We have shown that the course of the oxidations of sulfides **2** with **1b** strongly depends on the solvent used and on the presence of protic (alcohols, acids) or aprotic (DMSO) additives. Since charge separation in the zwiterionic intermediate **6** is greater than in sulfurane **7** (Scheme 2), the relative value of the rate constants k_2 and k_{-2} will be solvent dependent.[18] Thus, polar solvents such as acetone, acetonitrile, or methylene chloride (runs 1, 3, and 4, Table 3) will slow the rate of formation of sulfurane **7**, favor the sulfurane ring opening once this is formed, and consequently increase the formation of sulfoxides **3** (path a, Scheme 2). On the other hand, nonpolar solvents, unable to solvate the zwiterionic intermediate **6** such as carbon tetrachloride (run 2, Table 3), will favor the ring closure and consequently the formation of sulfone **4**.

The differences in solvation of intermediates **6** and **7** are also reflected in the temperature effects observed. Formation of sulfurane **7** from the zwitterionic intermediate **6** implies a lowering of charge separation and consequently desolvation. Conversely, the solvent-assisted unimolecular ionization of **7** takes place with an increase in order due to the organization of the solvation sphere. Therefore, due to these entropic requirements the equilibrium is displaced to the left-hand side at low temperatures and to the right-hand side at higher temperatures.

Scheme 4



Accordingly, the data in Table 2 show that the amount of sulfoxide **3** increases at lower temperatures. Moreover, from our data sulfone **4** is derived to the greatest extent from the cyclic sulfurane **7b** and not from the zwitterionic intermediate **6b**; otherwise the effect of the temperature on the **4**:**3** ratio would not be observed.

The addition of DMSO to the reaction media also decreases the sulfone:sulfoxide **4**:**3** ratio (entries 23−25, Table 3). DMSO can either interact with the positive sulfur in **6** or promote the ring-opening process in sulfurane **7**. Evidence of nucleophilic substitution through associative mechanisms on hypervalent 10-S-4 species[19] shows that it proceeds in the equatorial plane along an *anti* trajectory with respect to the better acceptor equatorial bond to give a new pentacoordinate hypervalent intermediate bearing the new ligand in the equatorial position. The apical leaving group in this hypervalent intermediate is subsequently lost with simultaneous rearrangement of ligands. In the case of **7**, the nucleophilic attack should proceed *anti* to the equatorial oxygen. Subsequent scission of the apical hypervalent S−O bond with opening of the four-membered ring and rearrangement of ligands to place two oxygen atoms at the apical positions would allow for the elimination of 1,1,1-trifluoroacetone and DMSO to yield the corresponding sulfoxide **3** (Scheme 3).

The presence of acids and alcohols in the medium efficiently promotes the formation of sulfoxides **3** in the oxidation of sulfides (see Table 3). Martin et al.[15] have found that sulfuranes react with protic reagents such as alcohols, amines, or amides, through an initial apical ligand exchange reaction to give a new sulfurane from which the products are formed. This model of reactivity has been used in synthesis and provides a good explanation of our results (Scheme 4). Thus, the reaction of **6b** and/or **7b** with the protic reagent would give rise to the formation of a new open chain sulfurane, **8b**, with two apical alkoxide ligands, one of them derived from 1,1,1-trifluoroacetone with hemiacetal character (Chart 2, structures **8bI**−**8bV**). Sulfurane **8b** should decompose readily by β-scission of

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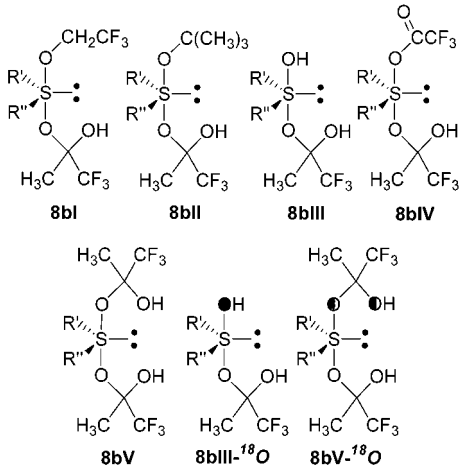
Chart 2



the C−O bond with loss of 1,1,1-trifluoroacetone to give the corresponding sulfoxide (path d, Scheme 4), or alternatively, **8b** could be oxidized further by a second equivalent of **1b** (path c, Scheme 4) to give sulfone **4**. In principle, the partial formation of **4** either by direct oxidation of sulfurane **7b** or by oxidation of a previously formed sulfoxide **3** (paths b and e, Scheme 4) cannot be ruled out. It has to be noted that the hemiacetal ligand derived from dioxirane is particularly well suited to perform the oxygen-transfer step to the sulfur atom. Alternative routes from **8b** involving the protic additive as the oxygen atom source for the generation of sulfoxide **3**, such as, for example, the olefin elimination in the case of *tert*-butyl alcohol (structure **8bII**), a nucleophilic substitution for 2,2,2-trifluoroethanol (structure **8bI**), or a nucleophilic addition/elimination in the case of trifluoroacetic acid (structure **8bIV**), would be much less energetically favorable than the simple elimination of 1,1,1-trifluoroacetone. The only feasible alternative would be in the case of water (structure **8bIII**) where proton transfer would compete effectively with the elimination of 1,1,1-trifluoroacetone hydrate. The observed decrease in the sulfone:sulfoxide ratio (Table 3) is consistent with the competition of path a (Scheme 4), which gives predominantly sulfoxide, with direct oxidation of **7b** (path b) to give sulfone.

In protic media the protonation of either apical oxygen in **8b** will promote the ionization of the hypervalent S−O bond, thereby facilitating the β-elimination at the opposite apical position by increasing the positive charge density on the sulfur atom (Scheme 4). On the other hand, because of its symmetric character at the apical positions, the hypervalent bond in **8b** with the negative charge shared by two oxygen atoms should be less polar than that of the parent sulfurane **7b**. Consequently, **8b** should be less reactive than the parent sulfurane **7b** toward oxidation by **1b**. Therefore, the formation of sulfoxide **3** from sulfurane **8b** efficiently competes with oxidation of the intermediate to give sulfone **4**.

Finally, the effect of the additive on the **4**:**3** ratio will depend greatly on the acid-catalyzed ligand exchange rate. Our data are in agreement with this hypothesis and show that the more acidic the protic additive, the more efficient the reaction which forms sulfoxide **3** (runs 5 and 16−18, Table 3).

^{18}O Isotopic Tracer Experiments. ^{18}O Incorporation into the products **3a**-*^{18}O* and **4a**-*^{18}O* when the oxidation of **2a** with TFDO **1b** is carried out in the presence of labeled protic additives (Table 5) is also readily explained by the ligand exchange mechanism proposed in Scheme 4. It is worth mentioning that the label can be incorporated only when the ^{18}O atom carrier introduces a ligand suited to perform the O atom transfer to the sulfur atom, that is, when it is carried by $H_2{}^{18}O$ (structure **8bIII**-*^{18}O*) or 1,1,1-trifluoroacetone-*^{18}O* hydrate (structure **8bV**-*^{18}O*). In fact, the symmetric substitution at the apical sites by the hemiacetal moiety in **8bV**-*^{18}O* ensures incorporation of the label. By contrast, reactions in the presence of trifluoroacetic acid-*^{18}O* do not produce labeled **3a** or **4a** to any significant extent.

From a statistical perspective, 25% is the maximum label incorporation attainable from 1,1,1-trifluoroacetone-*^{18}O* hydrate (49 atom % ^{18}O); the 23% observed (run 1, Table 5) is very close to this value. This fact not only indicates that under these conditions the sulfoxides **3a**-*^{18}O* and **3a** derive almost exclusively from the secondary sulfurane **8bV**-*^{18}O*, but it also implies that **3a** does not proceed directly from the zwitterionic intermediate **6** since this route would render a lower rate of label incorporation.

On the other hand, reactions in the presence of $H_2{}^{18}O$ and 2,2,2-trifluoroethanol as cosolvent (runs 2 and 3, Table 5) do not lead to as greate an ^{18}O incorporation. The 2,2,2-trifluoroethanol participates in ligand exchange processes and would give rise to a variety of secondary sulfurane intermediates of type **8b** from which a lower label incorporation is expected (run 2, Table 5). Interestingly, the extent of label incorporation increases in the presence of 2.5 equiv of trifluoroacetic acid (run 3, Table 5), which indicates that the hydronium ion may be responsible for the trapping of intermediates **6b** and **7b** as $H_2{}^{18}O$ rather than 2,2,2-trifluoroethanol is the main protonated species in the medium due to its higher basicity.

Although sulfone **4a** is the main reaction product in the ^{18}O isotopic tracer experiments, the label incorporation is not as great as in the case of **3a**. Experimental data (Table 5) show that the label incorporation into sulfone **4** and the **4**:**3** ratio decrease simultaneously. From this observation the formation of labeled sulfone by direct oxidation of a labeled sulfoxide (path e, Scheme 4) is unlikely. Moreover, formation of sulfone **4** by oxidation of **3** would be in conflict with the results of the competitive oxidation of deuterated sulfides and sulfoxides shown in Table 4. The label incorporation into **4a** is indicative of the existence of a route for the **1b** oxidation of the secondary sulfurane **8b**. Formation of **4**-*^{18}O* encloses the contribution of ligand exchange reactions and β-fragmentations in sulfuranes **7** and **8**. Therefore, cyclization of the zwitterionic intermediate **6b** to the primary sulfurane **7b** occurs readily even in the presence of protic additives or solvents. On the other hand, the low label incorporation observed in **4** relative to **3** is attributable to the following three reasons: (i) the oxidation of the primary sulfurane **7** preceding the ligand exchange with the ^{18}O-label carrier, (ii) the expected lower reactivity of **8** relative to **7** toward **1b**, and (iii) the efficient β-fragmentation of sulfurane **8** in protic media to give sulfoxide **3**.

Conclusions

Sulfones are the main oxidation products of sulfides with **1b** under different reaction conditions. The study of the substituent, temperature, and solvent effects associated with ^{2}H and ^{18}O isotopic tracer experiments allows the demonstration for the first time in these reactions that the main means of formation of

sulfones is the fast oxidation of an intermediate 10-S-4 hypervalent sulfur adduct **7** without participation of the corresponding sulfoxides. The mechanism involves an initial electrophilic attack of the dioxirane to the sulfur atom to give the zwitterionic species **6**, which in a reversible cyclization step gives rise to the hypervalent intermediate **7**. The β-elimination of 1,1,1-trifluoroacetone from **6b** leads to the formation of sulfoxides, while further oxidation of the hypervalent intermediates **7b** by **1b** gives the corresponding sulfones. Sulfones are the main product in these reactions since the hypervalent sulfur adducts **7b** undergo oxidation by **1b** faster than their parent sulfides. In general, all those factors preventing the cyclization of **6** or favoring the opening in the cyclic sulfurane **7** reduce the value of the sulfone:sulfoxide ratio. All the experimental results reported are fully consistent with the expected chemistry of the hypervalent intermediate **7** involved in the proposed mechanism.

The differences found in the behaviors of **1a** and **1b** in the oxidation of sulfides are easily rationalized by the different stabilities of the corresponding hemiacetalic zwitterionic intermediate **6** in each case. In fact, the classical sequential mechanism which establishes that sulfides are oxidized first to sulfoxides and then to sulfones is just a particular case of the mechanism proposed herein, and it is applicable to the specific instance in which the β-elimination of ketone on the zwitterionic intermediate **6** occurs faster than the cyclization to give the 10-S-4 hypervalent sulfur adduct.

Experimental Section

General Information. Sulfides **2a**−**j** were commercially available (Aldrich). *N*-methylphenothiazine (**2k**) was prepared according to known procedures.[20] Phenyl trideuteriomethyl sulfide (**2a-*d*$_3$**) was prepared by reaction of sodium thiophenoxide with methyl-d_3 iodide (Aldrich) in ethanol and purified by distillation. Authentic samples of sulfoxides **3a**−**k** and sulfones **4a**−**k** were prepared by oxidation with *m*-chloroperbenzoic acid. Solvents and reagents were purified by standard procedures.[21] Methyl(trifluoromethyl)dioxirane (**1b**)[10b] in dichloromethane solution, free of 1,1,1-trifluoropropanone, and dimethyldioxirane (**1a**)[10a] in acetone solution were prepared by previously reported methods.[10] Dioxirane solutions were carefully dried over anhydrous magnesium sulfate prior to use. 1,1,1-Trifluoropropanone for the synthesis of methyl(trifluoromethyl)dioxirane was purchased from Fluorochem and was distilled from concentrated H_2SO_4 before use. Caroate triple salt $2KHSO_5$–$KHSO_4$–K_2SO_4 was purchased from Fluka. Methyl *p*-chlorobenzoate (Aldrich), used as internal standard for GC analyses, was recrystallized from *n*-hexane−dichloromethane before use. $H_2{}^{18}O$ (98 atom %) was purchased from Aldrich and used as received.

GC and GC−MS (EI+, 70 eV) analyses were performed on a Thermo CE 9000 and a Thermo CE 8000 chromatograph coupled with a benchtop Trio 1000 quadrupolar mass spectrometer, both equipped with a BPX-5 capillary column (30 m, film thickness 0.25 μm, i.d. 0.22 mm). Sulfide conversions and product yields were corrected by corresponding response factors. ^{1}H NMR spectra were performed on a Bruker AC 250 spectrometer.

Reaction of Simple Sulfides with 1b. General Procedure. An aliquot of a solution of the sulfide, methyl *p*-chlorobenzoate as internal standard, and the corresponding additive (acetic acid, trifluoroacetic acid, or dimethyl sulfoxide), in the selected solvent (dichloromethane, carbon tetrachloride, acetone, acetonitrile, 2,2,2-trifluoroethanol, 2,2,2-trifluoroethanol/water, or dichloromethane/*tert*-butyl alcohol), at the selected temperature (0, −40, or −80 °C), was treated with an aliquot of a thermostated methylene chloride solution of dioxirane **1b** (ca. 0.20 M) free of 1,1,1-trifluoroacetone. The reactions were carried out under an inert atmosphere and in the dark. The initial concentration of the sulfide ranged between 0.063 and 0.080 M. After 10 min, the reaction mixtures were analyzed by GC. Conversions were determined by comparison with the t_0 chromatograms; yields were corrected by the product response factors. Data are reported in Tables 1−3.

In the case of **2k** the reaction mixture was treated with a 1.1 M lithium iodide solution in acetone. The solution was dried over anhydrous $MgSO_4$, and the solvents were removed under vacuum at 0 °C. The residue was redissolved in $DCCl_3$ and analyzed by ^{1}H NMR and GC.

Competitive Experiments between PhSCD$_3$ (2a-*d*$_3$) and PhSOCH$_3$ (3a) and Dioxiranes 1. To a solution of **2a-*d*$_3$** and phenyl methyl sulfoxide (**3a**) in the selected ratio and methyl *p*-chlorobenzoate as internal standard, in the selected solvent (sulfide initial concentration ranged between 0.03 and 0.06 M), at 0 °C and in the dark, an aliquot of dioxirane solution was added at once. After 10 min the reaction mixture was analyzed by GC−MS.

The concentrations of the products were determined by GC integration of the areas corresponding to the sum of sulfoxides **3a** and **3a-*d*$_3$** and sulfones **4a** and **4a-*d*$_3$** and integration of the MS monoisotopic molecular ions abundance profile (m/z = 140 and 143 for **3a** and **3a-*d*$_3$**, respectively, and m/z = 156 and 159 for **4a** and **4a-*d*$_3$**, respectively). Values were corrected by the response factors corresponding to the GC and MS measurements. The results are shown in Table 4.

1,1,1-Trifluoro-2-propanone-^{18}O Hydrate (5-^{18}O). 1,1,1-Trifluoro-2-propanone-^{18}O hydrate (**5-^{18}O**) was generated in situ by adding at 0 °C and under an inert atmosphere 0.14 mL (7.5 mmol) of water-^{18}O (98 atom %) to a solution of 0.71 mL of 1,1,1-trifluoropopanone (7.5 mmol) in acetonitrile (1 mL) and dichloromethane (0.25 mL). The reaction was vigorously stirred at 0 °C for 30 min and was then analyzed by mass spectrometry (EI+, 70 eV). The incorporation of the isotopic label was determined from the ion m/z = 95 $[CF_2COOH]^+$ by applying the equation

$$^{18}\text{O atom \%} = 100\{[(I+2) - (I+2)_{nat}] + [(I+4) - (I+4)_{nat}]/[I + (I+2) + (I+4)]\}$$

The values $(I+2)_{nat}$ and $(I+4)_{nat}$ were the average of at least three independent analyses of 1,1,1-trifluoropropanone hydrate.

Reaction of Phenyl Methyl Sulfide (2a) with 1b in the Presence of ^{18}O Isotopic Tracers. Phenyl methyl sulfide (8.8 μL, 0.075 mmol) was dissolved in a solution of **5-^{18}O**, prepared as described above, at 0 °C and in the dark. The mixture was treated with an aliquot of a 0.3 M solution of **1b** in dichloromethane (0.25 mL, 0.075 mmol). The reaction mixture was analyzed by GC−MS at least three times (standard error ±1%). The isotopic labelings of the sulfoxide and the sulfone were averaged, respectively, from the ions m/z = 140 $[M]^+$, 125 $[M - CH_3]^+$ and m/z = 156 $[M]^+$, 141 $[M - CH_3]^+$, by applying the equation

$$^{18}\text{O atom \%} = 100\{[(I+2) - (I+2)_{nat}]/[I + (I+2)]\}$$

The values $(I+2)_{nat}$ were the average of three independent analyses of **3a** and phenyl methyl sulfone (**4a**).

Trifluoroacetic acid-^{18}O was generated in situ by adding water-^{18}O (0.14 mL, 7.5 mmol) to a solution of trifluoroacetic anhydride (1.14 mL, 7.2 mmol) in dichloromethane. After **2a** (8.8 μL, 0.075 mmol) was dissolved in this solution, an aliquot of a 0.3 M solution of **1b** in dichloromethane was added at once.

The reactions in the presence of water-^{18}O and water-^{18}O/trifluoroacetic acid were carried out at 0 °C, by adding an aliquot of a 0.3 M TFDO solution in dichloromethane (0.25 mL, 0.075 mmol) to a solution of the sulfide **2a** (8.8 μL, 0.075 mmol) and the isotopic tracers (0.14

(20) Schumaker, R. R. Fr. Patent 1527778, 1968; *Chem. Abstr.* **1969**, *71*, 81175b.
(21) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1998.

mL of water-^{18}O, 6 μL of CF_3COOH) in dichloromethane/2,2,2-trifluoroethanol (1:4) as the solvent.

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