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Oxygen atom transfer from a chiral N-alkyl oxaziridine promoted by acid. The asymmetric oxidation of sulfides to sulfoxides.

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Abstract: Chiral N-alkyl oxaziridines may be used as reagents for the asymmetric oxidation of sulfides in an acid-promoted reaction leading exclusively to the corresponding sulfoxides A planar transition state geometry seems consistent with the observed stereochemistry which should result from the steric interactions in the transition state. The influence of the solvent and the acid strength on the oxygen transfer reaction are discussed.

INTRODUCTION

The electrophilic amination of nucleophilic substrates by oxaziridines, introduced by Schmitz[1] (N-H oxaziridines) and later extended by Hata[2] to N-alkyl oxaziridines is now a well documented reaction.[3] The "nitrogen transfer" (actually amino group transfer) is thus the normal reaction of oxaziridines with nucleophiles. Nevertheless oxygen transfer may occasionally result with hindered oxaziridines and hindered nucleophiles.[4]

To achieve oxygen transfer, oxaziridines having electron-withdrawing substituents on the nitrogen atom or on both the nitrogen and the carbon atoms of the three membered ring have been developed. They proved to be especially useful in the oxidation of thioethers to sulfoxides which may be thus formed with Davis N-sulfonyl and N-sulfamyloxaziridines,[5] with Boyd's phosphinoyloxaziridines[6] and with DesMarteau's perfluorooxaziridines.[7] Chiral N-sulfonyl[8,9] and N-sulfamyloxaziridines[10] and chiral phosphinoyloxaziridines[11] have allowed the asymmetric oxidation of sulfides leading to chiral sulfoxides showing enantiomeric purities which may vary from low to high for a particular reagent as a function of the structure of the sulfide.

On the other hand, it has been shown that the oxidation of weakly basic nucleophilic substrates, as thioethers, by a normal (N-alkyl) oxaziridine may be performed if the oxygen transfer reaction is promoted by an acid.[12] The N-protonated oxaziridine is thought to be the active oxidizing species in this case.

The chiral oxaziridine **3**, which has been prepared from the corresponding dihydroisoquinoline **2** by metachloroperbenzoic acid oxidation (scheme 1) and fully characterized[13] was employed, as a model one, to assess if (classic) chiral N-alkyl oxaziridines may perform in the presence of acid, the asymmetric oxidation of prochiral thioethers. The results from the oxidation of a series of prochiral sulfides, which are here reported, confirm that chiral sulfoxides may be obtained with this new oxidizing system which takes advantage of the oxygen atom transfer ability of N-alkyl oxaziridines when their normal reactivity towards nucleophiles is

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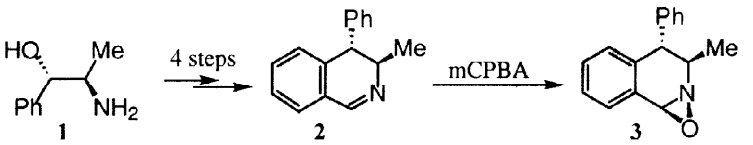
masked by the presence of acid. They allow in addition to get a better insight into the role of the acid and the factors controlling the oxygen transfer progress.

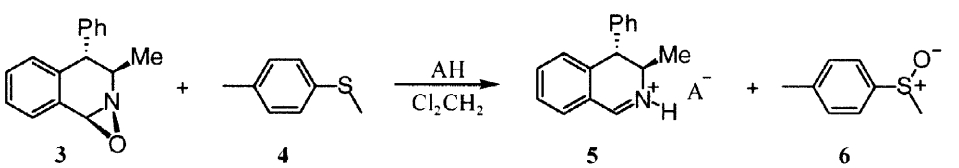


Scheme 1

RESULTS and DISCUSSION

In Table 1 are summarized the results of the oxidation of *para*-tolylmethylsulfide by the oxaziridine **3** using either trifluoroacetic acid (TFA) or methanesulfonic acid (MsOH) to promote the oxygen transfer. Both reactions were performed at room temperature on a 0.2 mmolar scale and with the acid in slight excess. The ee's of the sulfoxides were determined by HPLC. The absolute configuration of the major enantiomer was determined by comparison of the rotatory power of the isolated sulfoxide with that described in the literature for pure samples of *para*-tolylmethylsulfoxide of known absolute configuration.[14]

Table 1[a]



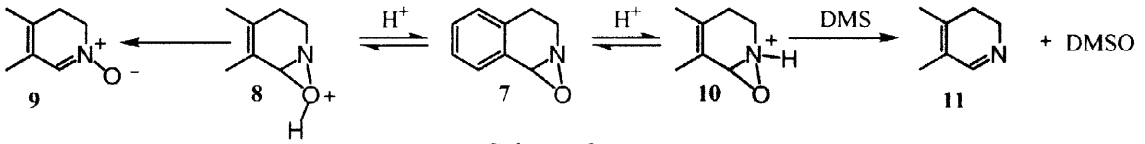
Entry	AH	3:AH	3:4	Time	Yield[b] %	ee[c] % (abs. conf.[d])
1	CF_3CO_2H	1:1.2	1:1.1	24 h[e]	50	42 (S)
2	$MeSO_3H$	1:1.05	1:1.1	1 min[f]	64	44 (S)

a)- reactions performed at r.t. using 0.2 mmol of **3** (0.2 M in CH_2Cl_2).
b)- sulfoxide isolated by preparative TLC. Yields are not optimized.
c)- determined by HPLC using a CHIRALCEL OD column.
d)- determined by polarimetry.
e)- unreacted sulfide and oxaziridine **3** still present as shown by TLC and potassium iodide test.
f)- oxaziridine **3** absent (potassium iodide test and TLC).

It follows from table 1 that a transfer of chirality from the optically pure oxaziridine **3** to the sulfoxide goes along with the oxygen transfer. Essentially the same ee's were observed in both reactions indicating that the asymmetric induction is insensitive to these acid strengths.

Stereochemically equivalent, both conditions are on the contrary chemically dissimilar. With TFA the reaction is slow and failed to go to completion even after a long reaction period (24 h) while it was "instantaneously" finished with the stronger acid.

The mechanistic approach depicted in scheme 2 had been proposed to rationalize the oxygen atom transfer from a racemic oxaziridine **7** to dimethylsulfide.[12]



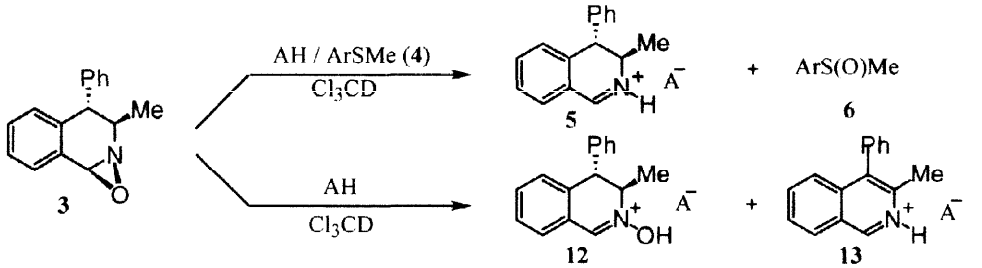
Scheme 2

Following this hypothesis, which should also apply to our case, an equilibrium is established between the oxaziridine **7** and the two protonated forms **8** and **10**. The later is theoretically the most populated (owing to the greater basicity of the nitrogen atom) and that able to transfer its oxygen to the highly nucleophilic sulfide (DMS) leading to the imine **11** and DMSO. In the absence of sulfide, the O-protonated form **8** leads to the corresponding nitrone **9**.

With respect to this preliminary report in which only the action of TFA had been examined, the disparity in reactivity shown in table 1 affords further information on the oxygen transfer reaction from an oxaziridine to a sulfide in the presence of acid. These different reactivities are likely in connection with the different acid strengths involved. Nevertheless, the factors actually playing a role are to be more precisely stated. With this purpose, a series of reactions were performed in deuterated chloroform and monitored by ^{1}H NMR. The results, which complete and enlarge those in table 1, are summarized in table 2. Thus, more detailed data on the reactivity differences reported in table 1 are given in entries 1 and 6 of table 2. In both cases the oxygen transfer on the sulfide was exclusively observed. In agreement with the previously accounted results[12] neither the isomerisation into the nitrone **12** nor the global dehydration (scheme 3) leading to the isoquinoline **13** which operate in the absence of sulfide (entries 2 and 7) were fast enough to compete with the oxygen transfer.

As shown in table 1 and in scheme 2, the oxygen transfer from the oxaziridine to a sulfide goes with the formation of bases (imine and sulfoxide). Both are stronger bases than the oxaziridine. The imine is undoubtedly the strongest one and the sulfoxide is also stronger than the oxaziridine as shown by entry 3 (see below). The effect of these bases upon the reaction progress may become crucial when only one equivalent of acid is used because they may favorably compete with the oxaziridine for the available protons. As the reaction proceeds, the concentration of the bases formed in situ (two equivalents by equivalent of reacted oxaziridine) increases and that of the unreacted oxaziridine decreases. In spite of these rate slowing factors the MsOH-promoted reaction (entry 6) is quantitative in less than one minute (actually too fast to be monitored by ^{1}H NMR at r.t.) which indicates that this reaction remains fast even by the end when the concentration of oxaziridine (and moreover of protonated oxaziridine) becomes necessarily low. It should thus be concluded that the oxygen transfer from the protonated oxaziridine is an efficient reaction, likely with a high rate constant. Nevertheless, the TFA-promoted reaction which is relatively fast at the beginning (though slower than the MsOH-promoted one) becomes extremely slow and thus practically blocked by the end (entry 1). It should thus be concluded that in this system the concentration of protonated oxaziridine decreases rapidly to fall beneath the threshold level (necessarily low as pointed out above) allowing an efficient oxygen transfer to take place. A so large difference in reactivity between both systems may hardly be attributed to a lower concentration of protonated oxaziridine through the reaction in the TFA case than in the MsOH case only resulting from the interaction oxaziridine-acid promoter (strong or weak) to the exclusion of other factors.

Table 2[a]



entry	AH	molar ratio[b]			time	conversions %[c,d]				
		3:AH	**3**:4	**3**:6		**3**[e]	**3→5**	**3→12**	**3→13**	**4→6**[f]
1	TFA	1:1.2	1:1.1	-	10 min.	33	67	-	-	67
					20 min.	24	76	-	-	76
					3 h	10	90	-	-	90
					12	5	95	-	-	95
					24 h	2	98	-	-	98
2	TFA	1:1.2	-	-	10 min.	54	-	46	(+)	-
					20 min.	41	-	58	1	-
					2 h	17	-	79	4	-
					7 h	7	-	83	9	-
					24 h	(+)	-	84	16	-
3	TFA	1:1.2	-	1	10 min.	94	-	6	-	-
					20 min.	91	-	9	-	-
					2 h	62	(+)	33	5	-
					24 h	7	(+)	59	34	-
					48 h	(+)	2	60	37	-
4	TFA	1:2.1	1:1.1	-	10 min.	12	87	(+)	-	87
					20 min.	7	93	-	-	93
					2 h	-	100	-	-	100
5	TFA	1:3	1:1.1	-	< 1 min.	-	100	-	-	100
6	MsOH	1:1.05	1:1.1	-	< 1 min.	-	100	-	-	100
7	MsOH	1:1.05	-	-	< 1 min.	-	-	100	-	-

a)- reactions performed at r.t. using 0.1 mmol of **3** (0.2M in Cl_3CD) ; Ar = p-tolyl.

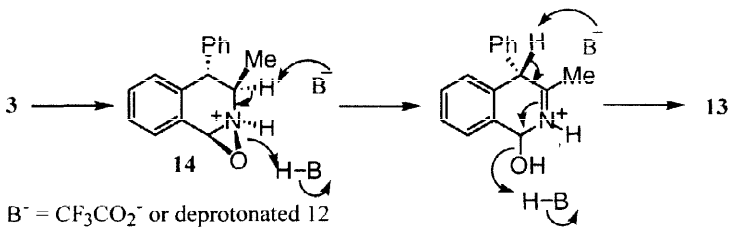
b)- at t = 0.

c)- determined by ^1H NMR.

d)- (+) means product observed, but the signals are too little to be conveniently integrated.

e)- unreacted oxaziridine **3.**

f)- conversion **4→6** corrected taking into account the molar ratio **3**:**4** at t = 0 (see experimental part).



$B^- = CF_3CO_2^-$ or deprotonated 12

Scheme 3

The interaction between the bases arising from the oxygen transfer and the acid promoter should also be a determining factor leading to a different distribution of the protons in both systems. The bases arising from the oxygen transfer seem to play a minor role in the MsOH-promoted reaction but a more important one in the TFA-promoted reaction fixing preferentially the available protons. One would think that the weaker acid should more selectively protonate the stronger bases present in the system. Accordingly, as the initial molar ratio TFA: oxaziridine is increased (entries 4 and 5) and enough acid is available to efficiently protonate all the bases of the system including the weakest one, the unreacted oxaziridine, the concentration of protonated oxaziridine remains high enough throughout the reaction course and very fast oxygen transfers may result. For example with three equivalents of TFA (entry 5) the oxygen transfer was also quantitative in less than one minute as with a slight excess of MsOH (entry 6).

The interference of the sulfoxide is confirmed by entry 3. The isomerisation oxaziridine-nitrone (**3**→**12**), also involving a protonated form (O-protonated) as intermediate, in the presence of one equivalent of TFA is drastically slowed down by one equivalent of sulfoxide **6** (entry 3 *vs* entry 2). Results summarized in entry 3 also confirm that the sulfoxide is not oxidized into sulfone by the oxaziridine-acid system. The formation of **5** to a little extent (mainly after 24 hours) may be rationalized by the action of deprotonated **12** on N-protonated oxaziridine **14** (the related deoxygenation of nitrones by oxaziridinium salts has precedent[15]).

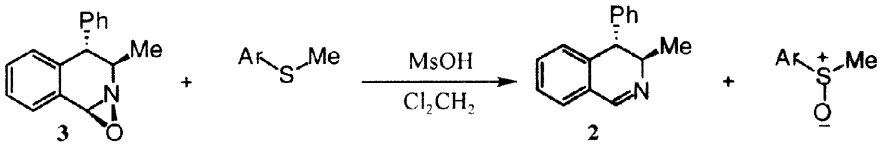
The above data show in one hand the role of the products formed as the reaction proceeds and in the other hand the role of the acid strength on the reaction rate. Stronger bases than oxaziridine **3** are formed. They slow down the acid-promoted oxygen transfer when the acid is not strong enough. With *p*-tolylmethylsulfide as substrate, a fast and quantitative oxygen transfer reaction was observed either with a slight excess of a strong acid (methanesulfonic acid) or with more than 100% excess of a weaker acid (trifluoroacetic acid).

Otherwise, the TFA-promoted oxygen transfer in the conditions of entry 1 (at the same temperature and with the same molar ratios) is greatly influenced by the nature of the solvent. Changing the solvent from dichloromethane or chloroform to acetonitrile, a more pronounced blockage was observed. The oxaziridine **3** does not vanished after 48h of stirring at room temperature in this polar aprotic and weakly basic solvent. On the contrary the blockage was avoided in methanol. The reaction was complete in 8h in this polar protic solvent. A ^{1}H NMR-monitored run (in methanol-d_4) revealed that at the first stages of the reaction the rate of the oxygen transfer is very close to that in chloroform-d (at t = 20 min., **4**→**6** = 75% in MeOH-d_4 *vs* **4**→**6** = 76% in Cl_3CD) to become progressively faster than that in chloroform-d (the conversion sulfide-sulfoxide **4**→**6** reached 90% at t = 2 h and 98% at t = 5 h in methanol while the same conversions were observed at t = 3 h and at t = 24 h in chloroform).

A series of arylmethylsulfides were oxidized into sulfoxides by oxaziridine **3** and methanesulfonic acid in CH_2Cl_2 (reaction conditions as in entry 2, table 1). The results are summarized in table 3.

These reactions are fast. They are all finished in less than one minute leading in general quantitatively to the corresponding sulfoxides. However, the less reactive sulfides, either by electronic reasons (entry 5) or by steric reasons (entries 10 and 12), are not quantitatively oxidized as a fraction (15-20%) of the oxaziridine **3** is isomerized into the nitrone **12**. In these entries, the oxygen transfer reaction is not fast enough to mask the acid-catalyzed isomerisation of the oxaziridine which, as shown in entry 7 of table 2, is also fast.

Table 3. Oxygen transfer reactions from oxaziridine **3** to sulfides[a]



Entry	Ar-S-R		Yield %[b] (conversions)	ee %[c] (abs. conf.[d])
	Ar	R		
1	*para*-tolyl	Me	64 (100)	44 (S)
2	*para*-tolyl	iPr	48 (100)	25 (S)
3	*para*-tolyl	tBu	82 (100)	7[e] (R)
4	4-methoxy-phenyl	Me	57 (100)	26 (S)
5	4-cyano-phenyl	Me	61 (85)	35[e] (S)
6	4-terbutyl-phenyl	Me	68 (100)	40[e] (S)
7	phenyl	Me	50 (100)	32 (S)
8	2-methylphenyl	Me	76 (100)	5[f]
9	2,4-dimethylphenyl	Me	80 (100)	7[f]
10	2,6-dimethylphenyl	Me	57 (80)	22[f]
11	3,5-dimethylphenyl	Me	77 (100)	35[e,f]
12	2,4,6-trimethylphenyl	Me	68 (80)	21 (S)

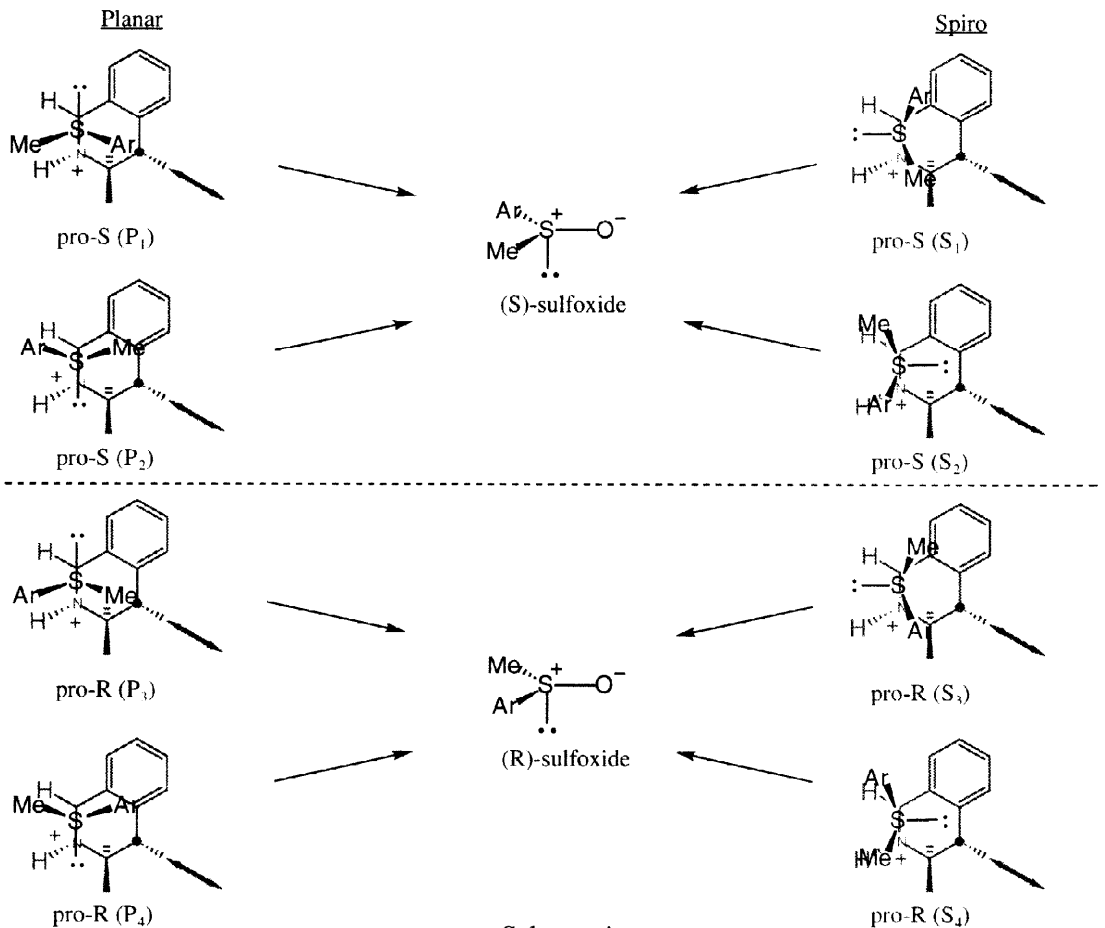
a)- 0.5 mmol of sulfide (0.25M), 1.05 equivalent of acid and 1 equivalent of oxaziridine **3**.
b)- sulfoxide isolated by preparative TLC. Yields not optimized.
c)- determined by HPLC using CHIRALCEL OD column.
d)- determined by polarimetry.
e)- determined by ^{1}H NMR using (R)-(-)-(3,5-dinitrobenzoyl)-α-phenylethylamide[16] as chiral shift reagent.
f)- absolute configuration of the major enantiomer not determined.

Concerning the stereochemistry of these reactions, we observed that the asymmetric inductions are strongly influenced by the structure of the sulfides. Thus, increasing the size of the alkyl group R from Me to tBu (entries 1-3) the enantioselectivity strongly decreases meaning that, as already pointed out in connection with similar asymmetric oxidations,[8,10] the difference in size between the groups attached to the sulfur play a major role and that when this difference decreases the asymmetric induction decreases. This seems less straightforward when the aryl group Ar varies from phenyl to mesityl (c.f. entries 7-12 and 1). The better enantioselectivities are associated to the 4-substituted (entry 1), the *meta*-disubstituted (entry 11) and the unsubstituted (entry 7) phenyl rings and not to the "more bulky " *ortho*-disubstituted ones (entries 10 and 12). In addition, a monosubstitution *ortho* to the -SMe group gives rise to a considerable drop in the asymmetric induction (entries 8 and 9). Nevertheless a reasonable explanation for these facts may be proposed following an examination of the transition states involved in the oxygen transfer from the oxaziridine **3** to the sulfides.

Oxygen transfer from electrophilic reagents to sulfides are thought to be S_N2 displacements and they are rationalized in terms of two transition states, planar and spiro.[17] In a planar transition state, both electron pairs on the sulfur are in the plane of the electrophilic oxygen-containing functional group and in a spiro one, the

plane containing the two electron pairs on the sulfur is perpendicular to the plane of the electrophilic oxygen-containing functional group. Theoretical studies on the hypothetical oxidation of hydrogen sulfide by oxaziridine[17] (which modeled the oxidation of sulfides by chiral N-sulfonyloxaziridines) have shown that there are only very slight energy differences between both geometries, suggesting that the asymmetric inductions noted experimentally most likely arises from the steric interactions in the transition state.

The planar and spiro transition states for the oxidation of arylmethylsulfides by the oxaziridine **3** are depicted in scheme 4. The rotamers of each pro-(R) (planar and spiro) and pro-(S) (planar and spiro) geometries (as for example P_1 and P_2) are included as they lead to sulfoxides of the same absolute configuration.[14]



Scheme 4

On the basis of a qualitative evaluation of the steric interactions in each arrangement, the spiro geometries appear as not suited to account for the observed selectivities. The large and the small groups of the sulfide lie both on the same side of the oxaziridine ring. In the pro-(S)/pro-(R) pair of arrangements S_1 and S_3 both sulfur-attached groups lie on the hindered side of the oxaziridine (maximum of repulsion). The corresponding rotamers S_2 and S_4 have the S-attached groups on the unhindered side of the oxaziridine ring and should have the weaker steric repulsions. But if such transition states involving weak and very similar steric repulsions are considered it seems clear that no asymmetric induction should result.

On the contrary, in each pair P_1-P_3 and P_2-P_4 of the planar transition states the small and the large groups of the sulfide lie respectively on the opposite sides of the oxaziridine ring. In these pairs the pro-(S) and the

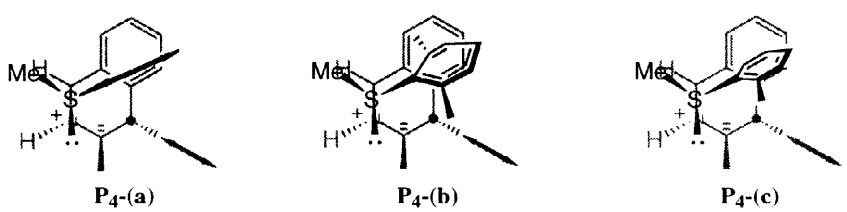
pro-(R) geometries involve dissimilar steric interactions. They are thus suitable to lead to an enantioselective oxygen transfer. The pair P_1-P_3 seems nevertheless not adequate to account for the observed ee's. The pro-(R) arrangement P_3 in which the aryl (large) group of the sulfide is on the unhindered side of the oxaziridine should be favored over P_1 thus leading to the (R)-sulfoxide as the major product which is contrary to the experimental results. Conversely, the pro-(S) arrangement P_2 should be, for the same reasons as above, the most favored one in the couple P_2-P_4. It is thus likely that the observed ee's arise from the steric interactions in the couple of planar arrangements P_2-P_4.

In one hand the drop in the enantioselectivity of the oxygen transfer observed as the alkyl group is of growing size (table 3, entries 1-3) may be rationalized considering a pair of arrangements analogous to P_2-P_4 but where the S-methyl becomes S-alkyl. In the pro-(S) arrangement (analogous to P_2), the alkyl group lies on the hindered side of the oxaziridine ring. Thus, more bulky the R group is, stronger are the non-bonded interactions in the pro-(S) arrangement which becomes less favored as the R group grows in size. The lowest ee is thus observed when R = tBu (entry 3). As the absolute configuration of the major isomer has changed, this result seems to indicate that in this case, the t-butyl group behaves as bulkier than the *para*-tolyl group.

On the other hand a reasonable hypothesis may be proposed for the apparently random enantioselectivities observed following the substitution pattern of the S-aryl group assuming that P_2 and P_4 are product-like transition states. The preferred conformation of arylmethylsulfoxides changes as a function of the substitution of the aryl group. Concerning for example the series of arylmethylsulfoxides where the aryl (Ar) groups are phenyl and mono- or poly- methyl-substituted phenyl rings, it has been shown that in the predominant conformers of phenylmethylsulfoxide[18,19] and *p*-tolylmethylsulfoxide[20] the S-O bond is almost coplanar with the aromatic ring. On the contrary an increasing degree of distortion from coplanarity was found on going from *ortho*-substituted[21] to *ortho*-disubstituted[19,21] phenyl rings. The trend for *ortho*-disubstituted phenyl rings is to be almost coplanar with the orbital containing the lone electron pair on the sulfur in the predominant conformer of the sulfoxide.[19,21]

The conformation of the pro-(R) arrangement P_4 in which the aryl ring of the developing sulfoxide lies on the hindered side of the oxaziridine should thus vary as a function of the substitution present on the S-aryl ring. The more this conformation is disfavored (and thus the arrangement P_4 relatively to P_2), the best the enantioselectivity associated to the oxygen transfer will be.

More detailed schematic representations of the preferred conformations of the pro-(R) transition state P_4 according to the substitution of the S-aryl group are depicted in scheme 5.



P_4-(a) **P_4-(b)** **P_4-(c)**

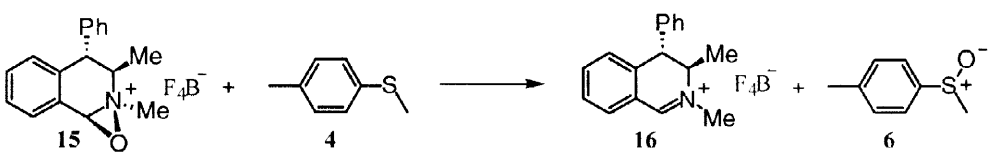
Scheme 5

The predominant conformation involving *ortho*-unsubstituted phenyl groups should be P_4-(a) where the S-aryl group is almost coplanar with the developing S-O bond and thus lies in a plane almost perpendicular to

the tetrahydroisoquinoline skeleton. This results in a relatively strong steric repulsion which disfavors the pro-(R) arrangement and leads to the better enantioselectivities (table 3, entries 1, 6, 7 and 11). The preferred conformation of the pro-(R) transition states involving (di)*ortho*-substituted phenyl rings should be P_4-(b) in which the S-aryl ring is almost coplanar with the orbital containing the free electron pair on the sulfur atom (as in the predominant conformers of the corresponding sulfoxides).[19,21] The interaction with the tetrahydroisoquinoline skeleton drops, not completely however as one of the *ortho*-methyl groups is directed toward the tetrahydroisoquinoline skeleton. P_4-(b) is relatively more favored than P_4-(a) and thus the enantioselectivity decreases (table 3, entries 10 and 12). The preferred conformation of the pro-(R) transition states involving (mono)*ortho*-substituted phenyl rings should be P_4-(c) in which the aryl ring may be less twisted from coplanarity with the S-O bond[19] than in P_4-(b) but the methyl group directed towards the tetrahydroisoquinoline skeleton is absent. This transition state P_4-(c) involves enhanced conformational mobility (the role of this factor has been already pointed out by F. Davis in connection with sulfamyloxaziridines in the oxidation of sulfides[10]) when compared with P_4-(a) and P_4-(b). Rotation about the S-aryl bond is less restricted than in P_4-(a) and P_4-(b) as the C_2-symmetry of the aryl groups in P_4-(a) and P_4-(b) is lost in P_4-(c). The steric repulsion between the aryl ring and the tetrahydroisoquinoline skeleton is thus released and the relative energies of the pro-(R) transition state P_4-(c) and the pro-(S) transition state P_2 become similar which accounts for the almost complete canceling of the enantioselectivity in the oxidation of the (mono)*ortho*-substituted phenylmethylsulfides by oxaziridine **3** (table 3, entries 8 and 9).

Finally, as the oxidation of sulfides by a racemic oxaziridinium salt has been described[22] and the chiral oxaziridinium salt **15** (derived from 3, by methylation[15]) was available, the oxaziridine **3**-acid oxidizing system was compared to **15** in the asymmetric oxidation of arylmethylsulfides using *p*-tolylmethylsulfide **4** as model compound. The results of the oxidation of **4** with the oxaziridinium **15** leading exclusively to *p*-tolylmethylsulfoxide **6** and the iminium salt **16**[15] are summarized in table 4.

Table 4. Oxygen transfer reactions with oxaziridinium **15** to *p*-tolylmethylsulfide[a]



Entry	solvent	Yield %[b] (conversion)	ee %[c] (abs. conf.)[d]
1	CH_2Cl_2	60 (100)	35 (S)
2	C_6H_6	76 (100)	37 (S)
3	n-C_5H_{12}	93 (100)	37 (S)

a)- reactions performed with 0.1M solution of **15** and 1 equivalent of sulfide.
b)- sulfoxide isolated by preparative TLC. Yields not optimized.
c)- determined by HPLC using CHIRALCEL OD column.
d)- determined by polarimetry.

These reactions are also very fast, a potassium iodide test indicating no active oxygen immediately after the addition of the sulfide. The corresponding ee's are essentially of the same order than those obtained with the

oxaziridine **3** acid-promoted system and no solvent effect on the asymmetric induction was observed to the difference from the oxygen transfer from the oxaziridinium **15** to unfunctionalized olefins.[15]

CONCLUSION

These results establish that chiral N-alkyl oxaziridines may be used as reagents for the asymmetric oxidation of sulfides in an acid-promoted reaction which leads exclusively to the corresponding sulfoxides without over-oxidation into sulfones.

The study of the solvent effect and of the influence of the acid strength on this process revealed that the reactivity of this three-component system (oxaziridine-sulfide-acid) is governed by subtle acid-base equilibria which favor the oxygen transfer from the oxaziridine to the sulfide, masking at the same time the known oxaziridine-acid (isomerisation) and oxaziridine-sulfide (electrophilic amination) reactions, which suggest that other weakly basic but highly nucleophilic substrates should also be oxidized with the oxaziridine-acid system. A planar transition state geometry seems consistent with the observed stereochemistry which should result from the steric interactions in the transition state.

EXPERIMENTAL

General. ^{1}H NMR were determined in $CDCl_3$ using a Bruker A-250 (250 MHz), AC-300 (300 MHz) and AC-400 (400 MHz). Chemical shifts (δ) are given in ppm relative to TMS (tetramethylsilane) and coupling constants (J) are given in Hertz (Hz). TLC were performed with silicagel coated foils Schleicher & Schuell ($F1500/LS_{254}$), staining with Dragendorff reagent and preparative thin layer chromatographies were performed on glass plates precoated silicagel Merck $60F_{254}$. The presence of oxidizing species in the reaction mixtures was determined by potassium iodide test. *Para*-tolylmethylsulfide, thioanisole and 4-(methylthio)benzonitrile are commercially available. The other sulfides were prepared following known methods.[23] Optical rotations were measured on a Perkin-Elmer 241 MC instrument. The enantiomeric excesses were determined by HPLC using a CHIRALCEL OD column, and by ^{1}H NMR using (R)-(-)-(3,5-dinitrobenzoyl)-α-phenylethylamide[16] as chiral shift reagent. These methods were validated with each racemic sulfoxide. The racemic sulfoxides were prepared by peracidic (mCPBA) oxidation of the sulfides and purified by preparative TLC. The oxaziridine **3**, mp 89°C(pentane), $[\alpha]_D$ -13.8 (c 4.9; $CHCl_3$), was synthesized following a procedure already described.[13]

Table 1. Entry 1: A solution of the oxaziridine **3** (47mg, 0.2mmol) in dichloromethane (0.5ml) was added to a solution of the sulfide **4** (30µl, 0.22mmol) and trifluoroacetic acid (18µl, 0.22mmol) in dichloromethane (0.5ml). The reaction was monitored by TLC and potassium iodide test. Both indicated the presence of unreacted oxaziridine **3** after 24 h of stirring at r.t.. The reaction mixture was diluted with CH_2Cl_2 and washed with aqueous HCl (5%). The organic layer was washed (water and brine) and then dried (Na_2SO_4) and concentrated *in vacuo*. The sulfoxide **6** was isolated by preparative TLC. Yield 50%; ee 42% (HPLC), $[\alpha]_D$ -44 (c 1.33, acetone), S enantiomer (lit[14] data for the enantiomerically pure (R)-*p*-tolylmethylsulfoxide $[\alpha]_D$ +145.5, acetone). Entry 2: A solution of the oxaziridine **3** (120mg, 0.51mmol) in methylene chloride (1ml) was added to a solution of the sulfide **4** (75µl, 0.56mmol) and methanesulfonic acid (35µl, 0.53mmol) in methylene chloride (1ml). A negative potassium iodide test was immediately observed. The reaction mixture was diluted with

CH_2Cl_2, washed with aqueous NaOH (5%). The organic layer was washed with water and brine, dried (Na_2SO_4) and concentrated *in vacuo*. The sulfoxide was isolated by preparative TLC. Yield 64%; ee 44% (HPLC), S enantiomer.

Table 2. Oxygen transfer reactions to p-tolylmethylsulfide with oxaziridine 3 (entries 1,4,5,6): The acid, trifluoroacetic acid (9µl, 1.2 equivalent) or methanesulfonic acid (6.8µl, 1.05 equivalent) was added at r.t. to a solution of the oxaziridine **3** (24mg, 0.1mmol) and the sulfide **4** (15µl, 0.11mmol) in deuterated chloroform (0.5ml). The reactions were monitored by ^{1}H NMR. *Reactions of oxaziridine 3 with acids* (entries 2 and 7): The acid, trifluoroacetic acid (9µl, 1.2 equivalent) or methanesulfonic acid (6.8µl, 1.05 equivalent) was added at r.t. to a solution of the oxaziridine **3** (24mg, 0.1mmol) in deuterated chloroform (0.5ml). The reactions were monitored by ^{1}H NMR. *Reaction of oxaziridine 3 with trifluoroacetic acid in presence of sulfoxide* (entry 3): Trifluoroacetic acid (9µl, 1.2mmol) was added at r.t. to a solution of the oxaziridine **3** (24mg, 0.1mmol) and the sulfoxide **6** (15mg, 0.1mmol) in deuterated chloroform (0.5ml). The reaction was monitored by ^{1}H NMR. In these reactions the conversions were determined by integration of the following ^{1}H NMR signals: **4**→**6**: the C_{Ar}-Me groups [**4**: δ 2.3ppm (s) and **6**: δ 2.41ppm (s)]; the **3**→**x** conversions (**x** = **3**, **5**, **12**, **13**): the C_3-Me groups [**3**: δ 1.34ppm (d) J 6.7Hz; **5**: δ 1.5ppm (d) J 6.7Hz, **12**: δ 1.55ppm (d) J 6.8Hz, **13**: δ 2.67ppm (s)]. The conversions **4**→**6** in table 2 were calculated multiplying the actual conversions (determined by NMR) by the factor 1.1 (which comes from the initial molar ratio **4**:**3** = 1.1:1) to allow them to be easily compared to corresponding conversions **3**→**5**.

Oxygen transfer to sulfides with oxaziridine 3 *(table 3).* A solution of the oxaziridine **3** (118mg, 0.5mmol) in methylene chloride (1ml) was added to a solution of the sulfide (0.52mmol) and methanesulfonic acid (33.5µl, 0.52mmol) in methylene chloride (1ml). The reaction mixtures were stirred 5-10 minutes at r.t. and then, diluted with CH_2Cl_2 and washed with diluted aqueous NaOH solution (entries 1-3, 12) or diluted HCl solution (entries 4-11). The organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The sulfoxides were purified by preparative TLC. The following results were obtained: *entry 1*: yield 64%; ee 44% (HPLC). *entry 2*: yield 48%; ee 25% (HPLC), $[\alpha]_D$ -43 (c 0.75, ethanol 95%), S-enantiomer (lit[14] data for the enantiomerically pure (R)-sulfoxide $[\alpha]_D$ +180, ethanol 95%). *entry 3*: yield 82%; ee 7% (^{1}H NMR), $[\alpha]_D$ +17 (c 0.13, ethanol 95%), R enantiomer (lit[14] data for the enantiomerically pure (R)-sulfoxide $[\alpha]_D$ +190, ethanol 95%). *entry 4*: yield 57%; ee 26% (HPLC), $[\alpha]_D$ -31 (c 1.34, acetone), S enantiomer (lit[24] data for the (R)-sulfoxide with >98% optical purity $[\alpha]_D$ +118). *entry 5*: yield 61%; ee 35% (^{1}H NMR), $[\alpha]_D$ -42 (c 0.72, chloroform), S enantiomer (lit[25] data for the (R)-sulfoxide with 80% optical purity $[\alpha]_D$ +105, chloroform). *entry 6*: yield 68%; ee 40% (^{1}H NMR), $[\alpha]_D$ -38 (c 0.83, acetone), S enantiomer (lit[26] data for the enantiomerically pure (R)-sulfoxide $[\alpha]_D$ +107.9, c 2.4 acetone). *entry 7*: yield: 50%; ee 32% (HPLC), $[\alpha]_D$ -54 (c 0.7, chloroform), S enantiomer (lit[27] data for the enantiomerically pure (R)-sulfoxide $[\alpha]_D$ +178.3, chloroform). *entry 8*: yield 76%; ee 5% (HPLC). *entry 9*: yield 80%; ee 7% (HPLC). *entry 10*: yield 57%; ee 22% (HPLC). *entry 11*: yield 77%; ee 35% (^{1}H NMR). *entry 12*: yield 68%; ee 21% (HPLC), $[\alpha]_D$ -48 (c 0.91, ethanol), S enantiomer (lit[28] data for the enantiomerically pure (S)-sulfoxide $[\alpha]_D$ -200.1, c 1.5 ethanol).

Oxygen transfer to p-tolylmethylsulfide a with oxaziridinium 15 *(table 4). Reaction in dichloromethane* (entry 1): To a solution of *p*-tolylmethylsulfide **4** (70µl, 0.52mmol) in methylene chloride (2.5ml) was added a solution of the oxaziridinium **15**[13] (178mg, 0.53mmol) in methylene chloride (2.5ml). A negative potassium iodide test was observed immediately. The solvent was evaporated. The sulfoxide **6** was isolated by preparative TLC. Yield 60%; ee 35% (HLPC), S enantiomer. *Reactions in benzene or pentane* (entries 2 and 3): The oxaziridinium salt **15** (24mg, 0.07 mmol) was added to a solution of *p*-tolylmethylsulfide **4** (10µl, 0.07mmol) in the corresponding solvent (1ml). A negative KI test was observed immediately and the solvent was evaporated. The sulfoxide **6** was isolated by preparative TLC. Entry 2 (*benzene*): Yield 76%; ee 37% (HPLC), S enantiomer. Entry 3 (*pentane*): Yield 93%; ee 37% (HPLC), S enantiomer.

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