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Halides-based Electrophiles Mediated Epoxide Ring-opening Reactions of α,β-Epoxysulfoxides in C_6-series : Deoxygenation versus Dehydration and an Overall 1,2-Keto Transposition

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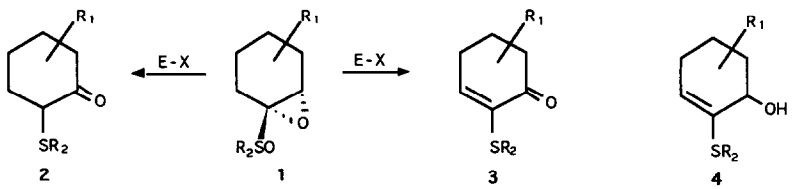
Abstract : New syntheses of α-thiosubstituted carbonyl compounds with the carbonyl carbon being the one that originally does not carry the sulfoxide group from six-membered ring α,β-epoxysulfoxides and several halides-based electrophiles are described. Mechanistic considerations for deoxygenation as well as dehydration reactions are also discussed. In addition, methodology for achieving 1,2-carbonyl transposition starting with isomerically pure cyclohexenyl sulfides derived from isophorone and cholestan-3-one is briefly reported.

Keywords : α ,β-epoxysulfoxide, β-keto sulfide, α-keto vinylthioether, halide-based electrophile, deoxygenation, dehydration, thionium ions, 1,2-keto transposition.

Acyclic and spirobicyclic α,β-epoxysulfoxides, most often prepared by base-mediated cyclization of α-halo-β-hydroxy sulfoxides[1], have been shown to undergo thermal and acid-catalyzed rearrangements to carbonyl derivatives[2]. Their reactions with nucleophilic reagents at the β-carbon to the sulfinyl group have also been well studied[3]. As a consequence of studies related to deoxygenation of sulfoxides and epoxides and in view of the possibility of selective manipulation of the two functional groups in α-sulfinyloxiranes, the question of how such compounds behave under deoxygenating conditions is of interest. We wish to disclose herein the results obtained in reactions of sulfinylated (cyclohexan-1,2-oxides) **1** with halides-based electrophiles which led to the discovery of new selective syntheses of β-keto sulfides **2** and α-keto vinylthioethers **3**.

eq (1)



2 1 3 4

Results

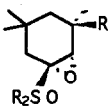
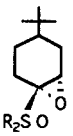
A recent exhaustive review by Madesclaire has listed reagents that can be used for the deoxygenation of sulfoxides to sulfides[4]. Some of the recommended reagents such as boron, silicon and phosphorus based derivatives are also capable of deoxygenating epoxides[5]. Low valent transition metals (e.g.Ti^{II}) also reduce both the sulfoxide and epoxide groups[6]. To the best of our knowledge, there is only one procedure which relies on deoxygenation of acyclic and spirobicyclic α,β-epoxysulfoxides employing the $TiCl_4$-Zn system[7] in ether. The reaction usually stops at the vinylsulfide stage, although partial reduction to the corresponding α,β-epoxysulfide has also been encountered. By submitting some of the title compounds to this system (4 equiv), allylic alcohols **4** (eq 1) were mainly produced but hydrolysis of the thioenol ether moiety was a major side reaction.

Others preliminary experiments in which the hindered epoxysulfoxide **1a** was treated under Pummerer-like conditions ($(CF_3CO)_2O$, CH_3SO_3H catalytic, CH_2Cl_2, rt) were also promising as a 3 : 2

mixture of O-trifluoroacetylated allylic alcohol **4a** and enone **3a** could be cleanly formed (entry 1, Table I). Consequently, we first focused our attention to select different reaction conditions with $(CF_3CO)_2O$ as the electrophile to achieve the highest selectivity. As can be seen from the table I, the $(CF_3CO)_2O$/NaI system[8,9], which proved considerably more reactive, gave similar competing reactions.

TABLE I

Dependence of O-protected allylic alcohol vs. enone product ratio upon F_3COI composition in the reactions with α,β-epoxysulfoxides **1 a-d**

entry	substrate 1	substrate-reagent ratio (mmol) $(CF_3CO)_2O$/NaI/addendum*	yield(%)[a] TFA allylic alcohol 4	yield(%)[a] enone 3
1	a  R_1 R_1=R_2=Me	1 : 2 : 0 : (ε $MeSO_3H$)[b]	60	40
2		1 : 2 : 2	40	60
3		1 : 2 : 8	60	40
4		1 : 2.5 : 0.5	25	75
5	b R_1=Me, R_2=C_6H_5	1 : 2.5 : 0.5	35	65
6	c R_1=H, R_2=Me	1 : 2.5 : 0.5	30	70
7	d 	1 : 2.5 : 0.5	15	70[d]
8		1 : 2.5 : 0 : (1 I_2)[b]	40	60

* *additionnal compound*

a) Products identies were surmised from the ^1H NMR spectra and ratios were estimated from the integration of these spectra and CG analysis b) No appreciable reaction was observed with $(CF_3CO)_2O$ alone c) 85 % isolated yield for enones 3a-c after saponification, acidification and further oxidation with MnO_2 and preparative TLC plates d) Material balance was 4-t-butylcyclohexanone

There are several significant features : (1) A two-fold or greater excess of the electrophile was necessary for the success of these transformations and the reaction is clean and complete in a few minutes ; (2) The reaction courses are dependent on the amount of sodium iodide used. Surprisingly, either a catalytic amount of CH_3SO_3H or a large excess of NaI exhibit the same moderate selectivity (entries 1 and 3, respectively). In contrast, by lowering the amount of iodide anion (from 8 to an half-equiv), the product distribution shifts to give more enone **3a** in 75 % selectivity (entry 4). Comparison of data in entries 4 and 5 reveals that methyl or phenylsulfinyl cyclohexan-1,2-oxides react with almost equal selectivity ; (3) With the 4-t-butyl derivative **1d**, it was found by GLC analysis that the above conditions afforded a substantial amount of simple 4-t-butylcyclohexanone besides the main product (entry 7). Possible sources of this ketone by-product will be considered latter ; (4) The possibility that the observed reactions could be due in part or entirely to iodine normally liberated in a deoxygenating process has been checked in the last entry ; (5) Although the $(CF_3CO)_2O$/NaI system failed to give nearly quantitative dehydration, the overall yield of the desired enones **3a-d** could be improved as follows : in each a-d set, the crude reaction mixture (saying the O-trifluoroacetylated allylic alcohol **4**) was exposed to sodium hydroxide at 100°C and further oxidation,

after acidification, with MnO_2 in CH_2Cl_2 at 25°C[10] led to the desired enone **3** in isolated yields indicated in footnote c (Table I).

We have now found that highly selective reactions - deoxygenation or dehydration - could occur with bicyclic α-sulfinyloxiranes **1** and selected halides-based electrophilic systems. The particular reactivity of these reagents is summarized in table II. While methods A-D yield almost exclusively α-thiosubstituted ketones **2**, methods E and F afford predominantly α-thiosubstituted enones **3**. A brief description of the individual systems is given below[11] :

- Methods A and B consist in a combination of soft nucleophile iodide ion and hard electrophile boron trifluoride etherate[12] or chlorotrimethylsilane[13] in dry acetonitrile, respectively.

- Method C refers to diphosphorus tetraiodide[14] in dry dichloromethane.

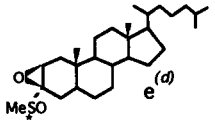
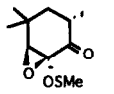
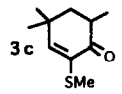
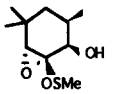
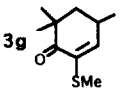
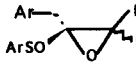
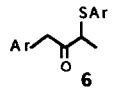
- Method D : the hydriodic acid is generated catalytically *in situ* from triphenylphosphine iodine in moist acetonitrile[15].

- Methods E and F are related to iodophosphonium[16] and chlorodimethylsulfonium[17] species, respectively. The former are generated by activation of tris(dimethylamino)phosphine with iodine and the latter by mixing chlorotrimethylsilane and dimethylsulfoxide, both in dry acetonitrile.

Operating on the assumption that an α-sulfinyloxirane of type **1** could undergo reactions via either sulfuranes (or their halosulfonium ion analogs) or protected *vic*-halohydrins intermediates, the exact molar ratio of substrat/reagent necessary for stoichiometric syntheses of final products **2/3** is generally used as shown in table II. The reactions proceed very well in most cases under the conditions A-F. However, reactions of 4-t-butyl-1-methylsulfinyl cyclohexan-1,2-oxides **1d** with BF_3-Et_2O/NaI (meth. A) and $(Me_2N)_3P/I_2$ (meth. E) give ketone **2d** and enone **3d** respectively, along with significant amount of 4-t-butyl cylohexanone by-product. This simple ketone arises from a formal reduction of the starting sulfinyl epoxide and its formation suggests that nucleophilic attack of iodide anion occurred to some extent at the β-carbon of the epoxide ring followed by desulfinylation (see scheme V). Interestingly, when **1d** was subjected to the conditions D and F, instead of A and E respectively, the ratio of products was considerably shifted in favor of the desired compounds (entries 5 and 9). The TMCS/DMSO system (meth. F) is the best one examined for enone synthesis. All the reactions, except the one with the system E for which heating is required and prolonged reaction times needed , are very clean and complete within few min at room temperature.

In an analogous way, diastereomeric 3-methylsulfinyl cholestan-2,3-oxides **1e** also undergo ready reactions when submitted to the conditions D and F (entries 10 and 11) ; the yields of epoxide ring-opened products **2e** and **3e** ranged from 70 to 80 %. Finally, on addition to Me_3SiCl/NaI system (meth. B), vicinal keto and hydroxy epoxysulfoxides **1f** and **1g** were converted into regioisomeric enones **3f** (=**3c**) and **3g**, respectively. Although the mechanistic details of these latter reactions are speculative and far from resolved up to now, the results in hand are consistent with initial deoxygenation of sulfoxide moiety. The resulting α-sulfenyloxirane having a proximate keto group would simply deoxygenate under the influence of the liberated iodine, while the other with an hydroxyl group would undergo rearrangement to afford a β-hydroxy-α-methylsulfenyl ketone intermediate that is usually quite unstable to undergo dehydration[18]. Of course, one must be cautioned that these pictures are oversimplified since alternative routes involving initially α-ring opening reactions may also be envisioned. Mandal *et al* [19] have speculated that the deoxygenation of α-keto-oxiranes to α,β-unsaturated carbonyl compounds proceeded through formation of α-iodohydrins.

TABLE II

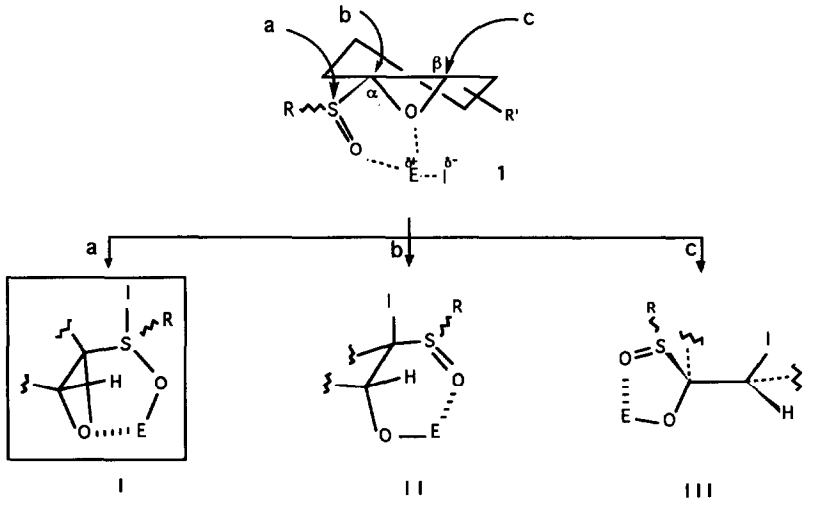
Entry	substrate 1	reagents[a]	Method	products (%)[b] ketone 2	enone 3
1	a/b/c	(2) $BF_3.Et_2O$/NaI	A	95	
2		(2) "Me_3SiI"	B	95	
3		(1/2) P_2I_4	C	90	
4		(2) "HI"	D	95	
5	d		A → D	65 → 90[c]	
6	a/b/c	(1) $(Me_2N)_3P/I_2$	E	15	80
7	d		E		55[c]
8	a	(3) Me_3SiCl/DMSO	F		95
9	d		F		90
10			D	70	
11	e[d]		F		75
12	 f		A		 3c
13	 g		B		 3g
14	 h		E	 5	 6

a) amount given as millimoles per millimoles of substrate. b) except with the method E, reactions were carried at room temperature and yields refer to isolated material by TLC plates. Products were identified by spectroscopic methods. c) 4-t-butylcyclohexanone as the main side-product. d) based on mechanistic considerations, the stereochemistry of these epoxides is suspected to be 2β-3β

Preliminary attempts to extend the reactions shown in eq (1) to acyclic epoxysulfoxides failed. However, in the last entry of table II, we have found that reaction of phenylsulfinyl oxiranes **1h** (derived originally from acetaldehyde by a Darzens reaction) with the $(Me_2N)_3P/I_2$ reagent occurred only on prolonged exposure to give a mixture of 1-phenylbutan-2-one **5** and its 3-phenylthio analogue **6**, the yields of which were nearly equal. It is also worthing to note that these compounds were identical to those derived by attack of phenylthiolate anion β to the phenylsulfinyl group[20] on **1h**. An interesting facet of the reactions at hand is that the rate enhancement observed with α-sulfinyl cyclohexene oxides relative to acyclic ones clearly shows the importance of conformational factors in promoting preferentially α-ring opening reactions.

Mechanisms

The halides-based electrophiles mediated reactions of sulfoxides[4] and epoxides[5] generally proceed via an addition-elimination mechanism. Accordingly, the results summarized in tables I and II can be rationalized by reference to scheme I. In this scheme, we speculate that both oxygen atoms in α,β-epoxysulfoxides tend to bind to the electrophilic component of the reagent[21]. Once such complexation has occurred, halide ion attack may then take place at the three contiguous sites. The importance of internal chelation in the primary adducts I-III should depend upon the nature of E (*vide infra*).

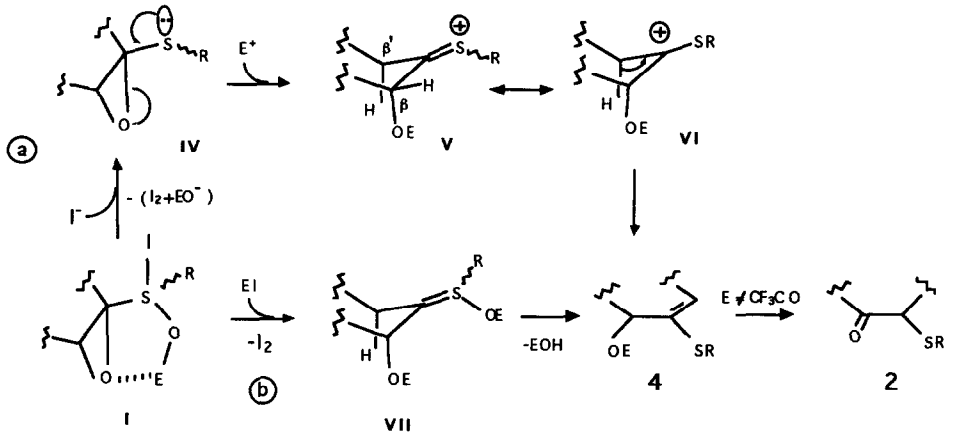


Scheme I : Mechanistic aspects for halides-based electrophiles addition to α,β-epoxysulfoxides 1

At this point, the question of any intrinsic regiochemical preference within the ring opening appears to be of synthetic importance since it allows a ready access to carbonyl derivatives with high positional selectivity. With α-sulfinyloxiranes derived from acyclic system, oxirane cleavage occurs predominantly at Cβ, i.e. at the least substituted carbon atom (entry 14, table II). This seems to indicate that destabilisation of an electron-deficient α-carbon by the electron withdrawing group and steric hindrance associated at this position promote β-attack[22]. In contrast, α-epoxysulfoxides fused to six-membered ring display a very strong orientational preference for ring-opening at carbon α to sulfur atom[23] suggesting that product distribution would largely be the result of conformational control.

The deoxygenating reaction: In agreement with all the facts cited above, the overall reduction of the sulfinyl group in α-sulfinyloxiranes **1** may be confidently assumed to follow scheme II. Within this scheme, it is anticipated that primary adducts such as α-epoxysulfuranes I should serve as suitable precursors for the formation of O-protected allylic alcohols **4** and further, possibly ketones **2**. Two reaction pathways can be devised for this purpose. In one of them, the unstable tetracoordinate sulfurane I (or its iodosulfonium salt) may give rise to an epoxysulfide IV in presence of a second molecule of iodide ion. Species of this type have been invoked as intermediates in a number of reactions [7,24] and even isolated occasionally[25]. Their involvement in six-membered ring vinylsulfides-ozone reactions and their remarkable regioselective ring opening to allylic alcohols have also been established[26]. It is, therefore, reasonable to assume that

regiocontrolled cleavage of the epoxide IV and selective removal of the β'-axial proton in the ensuing thionium ion V occur as depicted in path a. Alternatively, the proximate oxirane ring in sulfurane I[27] can be viewed to be capable of diverting the classical elimination step (path b). The geometrical condition for the success of this second reaction course requires an anti-periplanar orientation of the bounded iodine atom and C_α- O bond in I. The available evidence does not allow a definitive choice between these two routes.

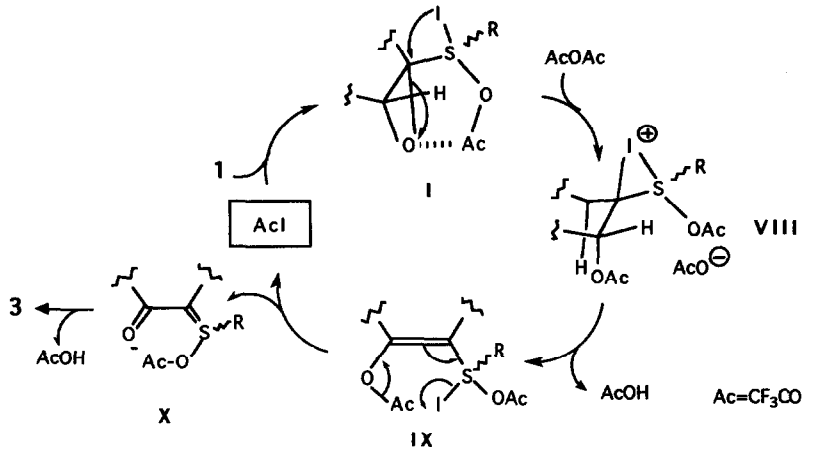


Scheme II : Schematic of competitive mechanisms for a deoxygenating process

The dehydration reaction : The most striking difference in reactivity from the tabulated data is that the tendency towards α-thiosubstituted cyclohexenones **3** occurs with three out of seven tested halides-based electrophiles, *viz.* the $(CF_3CO)_2O$/cat. NaI, $(Me_2N)_3P/I_2$ and Me_2SO/Me_3SiCl systems ; the last being the best one examined for eliminative deoxygenation. Also significant are the results reported for the 4-t-butyl derivative **1d** ; no trace of 4-t-butyl cyclohexanone by-product could be detected with the latter reagent (entry 9, table II). Mechanistically and in connection with the results previously discussed, several special comments are appropriate.

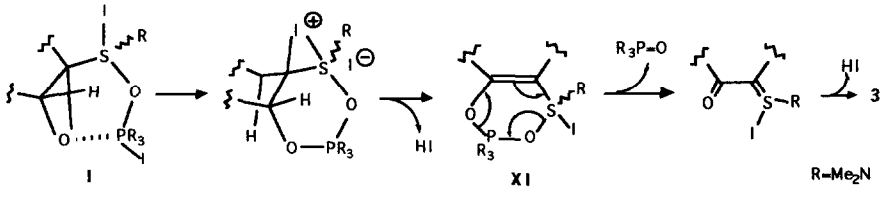
In our opinion, there is a correlation between the dehydrating action and ability of the reagent to chelate both sulfinyl and oxiranyl groups in substrates **1**. Moreover, the ease of dehydration product formation seems also to be related to the fact that the solution which is initially almost neutral turned strongly acidic in a short time. This can be most dramatically demonstrated in the reactions with the $Ph_3P/I_2/\varepsilon H_2O$ and $(Me_2N)_3P/I_2$ systems in a polar solvent like acetonitrile (meth. D and E, respectively). While in the former "HI" is generated catalytically *in situ* in the absence of water the second $(Me_2N)_3P$, I_2 reagent seems to operate [28] with a completely different mechanism, an enone being formed (compare entries 4 and 6, table II). Since the preference for one or other product is apparently connected with the abilities of the reagents to engage internal coordination to the flanking oxygen atoms in α-sulfinyloxiranes **1**, it may be assumed that the dehydration process must involve strongly chelated or even cyclic intermediates.

On the basis of these observations and others, the course of the overall transformation can be tentatively depicted as in schemes III and IV, respectively with the TFAA/cat.NaI and $(Me_2N)_3P/I_2$ systems. The pathway followed by the reagent formed from the combination of dimethylsulfoxide with trimethyl chlorosilane (meth. F) is expected to be closely parallel to the one reported in scheme IV.



Scheme III : A possible reaction pathway for the iodide-catalyzed dehydration of 1 with trifluoroacetic anhydride

The hypothesis which led to the use of trifluoroacetic anhydride in combination with a small amount of sodium iodide was that CF_3COI might be regenerated as depicted in scheme III. In no case, however, was the iodide anion found to be reducible to catalytic. The structural arrangement within the presumed α-epoxysulfurane I, formerly obtained by the addition of CF_3COI to **1**, is also seen to be properly predisposed for conversion to dehydrated product **3**. Thus, the iodine atom bound to sulfur in I may participate [29] in the ring-opening of the epoxide, the ensuing iodonium ion VIII being further stabilized by deprotonation. As already pointed out, the directionality of this removal is probably settled by the geometry of the molecule. If the β'-axial proton is abstracted, this must be accompagnied by a 1,3-hydrogen shift. The resulting trifluoroacetylated enol IX that bears a β-sulfurane moiety cis to the $OCOCF_3$ group would simply give the reactive Pummerer-like[30] intermediate X along with trifluoroacetyl iodide. The final step of the overall process consists in the loss of a second molecule of trifluoroacetic acid from X. Other variants cannot, at this point, be excluded. We have checked in separate experiments that α-sulfinylcyclohexanones which are isomeric with epoxides **1** were not apparently playing a role in the dehydration reaction.

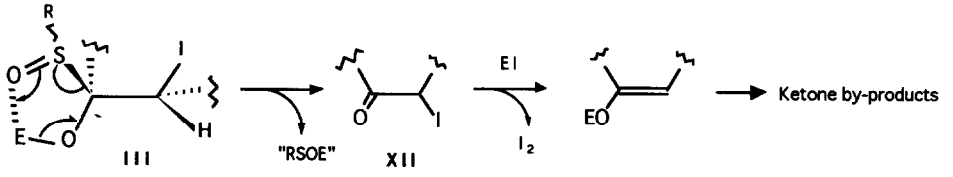


Scheme IV : A reasonable mechanism for stoichiometric dehydration of 1 by $(Me_2N)_3P^+I, I^-$ in dry CH_3CN

As shown in scheme IV, the reaction with the $(Me_2N)_3P/I_2$ system should proceed through an unsaturated six-membered ring intermediate XI containing pentacoordinated phosphorus. This will happen if the mechanism so far considered can, in theory at least, operate here. XI is viewed to be ideally set up for giving keto-sulfenium like species. The question that remains is why the ring closure with concomitant loss

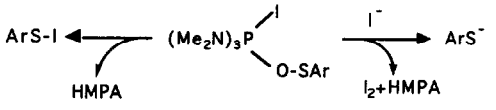
of HI is slow. The overall transformation is concerned with the conversion of one equivalent of tris-dimethylaminophosphine to its oxide. Hydrogen iodide formed may also act as a reducing agent.

The desulfinylation reaction : A plausible mechanism that rationalized the formation of ketone by-products is shown below. The initially formed O-protected α-sulfinyl iodohydrin III, arising from attack of iodide anion β- to the sulfinyl group in **1**, may collapse to an α-iodo ketone intermediate XII. Earlier, Olah *et al* [31] have demonstrated that α-halogenated ketones are quite susceptible to reductive dehalogenation ; hydrolytic conversion of the resulting enolethers leading the parent ketones. The possibility that *vic*-iodohydrin III may eliminate "RSOE" along with molecular iodide in the presence of a second molecule of EI reagent with a net *syn* stereochemistry cannot be excluded.



Scheme V : The desulfinylation reaction

With acyclic α-sulfinyloxiranes **1h** (entry 14, table II), 1-phenyl-3-phenylthio butan-2-one **6** was found coexisting with the simpliest ketone **5** by reaction with $(Me_2N)_3P/I_2$ system in dry CH_3CN. The mechanism for the formation of **6** is of some interest and may imply several competing pathways . By analogy with scheme V, nucleophilic attack at the β-position is followed by elimination of $(Me_2N)_3P(I)OSPh$. Once such phosphorylated species are formed they can act either as a source of benzenesulfenyl iodide or benzenethiolate anion, depending on the amount of iodide ion (eq 2). In the latter situation, 1-phenyl-3-iodo-butan-2-one intermediate and/or the starting material **1h** are suitable substrate for nucleophilic displacement.



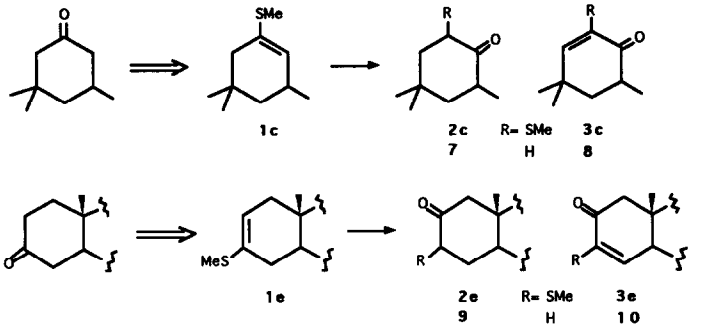
(eq 2)

In conclusion, we are led to believe that thionium ions appended with adjacent O-protected hydroxy and keto groups might account for the deoxygenation and dehydration reactions respectively ; the final stabilization step being β'-proton abstraction. Extensive studies to learn about the scope and mechanism of these novel and interesting transformations remain to be carried out.

1,2-ketone transposition

Among the large number of methods available for transposing carbonyl groups by one carbon, those which rely on vinylsulfides as last materials have been extensively studied and a review appeared recently[32]. In an attempt to extend the synthetic utility of vinylsulfides and to promote the chemistry of α-sulfinyl cyclohexene oxides, we describe below a 1,2-carbonyl transposition where the vinylsulfide is built at the first stage of the sequence and may function as a ketone and enone progenitor at the β-position. Isophorone and cholestan-3-one constitute the starting materials and the key step of the overall process is concerned with the conversion of the corresponding vinylsulfides to β-ketosulfides **2c** or **2e**. The efficient generation of such versatile intermediates[33] by the ozone-mediated epoxidation of vinylsulfides in C6-series allowed us to

describe the syntheses of the saturated ketones **7** and **8** as well as those of enones **9** and **10** in acceptable yields and in a few steps. Reductive cleavage or oxidative thermal elimination of the α-substituent complete the sequence.



EXPERIMENTAL SECTION

General

All the reactions with electrophiles were performed under nitrogen atmosphere and monitored on analytical TLC plates (silica gel $60F_{254}$, 255μm) using ultraviolet light for visualization. The solvents were purified by the usual methods. The starting α-sulfinyl epoxides were generally used as a diastereomeric mixture after simple purification over silica gel rather than pure isomers which needed additional crystallizations.

With electrophilic reagents listed under methods A-E, the classical work-up was as follows : the reaction mixture was quenched with 10 % aqueous sodium thiosulfate solution (iodometric titration) to discharge the dark-brown color due to free iodine and extracted three times with ether. After washing the organic layers with water and brine, the final dried extracts (over $MgSO_4$) were evaporated *in vacuo* to leave a residue which was immediately submitted to GC analysis on a 3m x 3/8in. column packed with 5 % SE DC 550 on chromosorb GAW 60/80 using a Girdel 3000 chromatograph. Purification was also performed on silica gel plates with 1:1 hexane-ethyl acetate as the eluent.

IR and NMR spectra were recorded in CCl_4 unless otherwise stated.

Materials

α-Sulfinyl cyclohexene oxides **1a** to **1d** were prepared from the corresponding enolthioethers and ozone as described[26] previously. The syntheses of isomerically pure hydroxy and keto-epoxysulfoxides **1f** and **1g** will be reported later together with their stereochemistry. In the acyclic series, the epoxysulfoxides **1h** were prepared from 1-chloro-2-(phenylethyl)phenyl sulfoxide and acetaldehyde[20].

As an extension of our previous work, we describe below the preparation by the ozonation procedure of isomeric α-sulfinyl cholestene oxides **1e** from the corresponding vinylsulfide.

Preparation of 3-methylthiocholest-2-ene : In a 250 ml three necked flask equipped with a magnetic stirrer and two gaz inlet tubes, an ice-cooled solution of cholestan-3-one[34] (6 g, 15.5 mmoles) in 150 ml of dry toluene was treated by bubbling a gaz stream of hydrochloric acid and methanethiol for 1 h (the reaction was frequently checked by TLC). After the residual gazeous reagents have been removed *in vacuo*, the resulting reaction mixture was washed with a 2 % sodium carbonate solution, then twice with water and concentrated. The residue was mixed with 100 ml of methanol to afford 6.85 g of white crystals after they were dried over Büchner and rinsed with acetone : *3,3-Bismethylthiocholestane :* ^{1}H NMR δ 0.65 (s), 0.80 (s), 1.18 (s), 0.5 to 2.20 (m) (46H), 1.97 (s, 3H), 2.07 (s, 3H).

The crude dithioketal was dissolved in a mixture of dry dichloromethane and petroleum ether (100 ml) and the solution was vigorously stirred and cooled to -70°C. MCPBA (3.41 g, 1.15 equiv) was added and the solution was kept overnight. The reaction mixture was washed with sodium carbonate, twice with water, concentrated and well dried *in vacuo*. The sulfinyl derivative obtained was checked by TLC and NMR : *3-Methylsulfinyl-3-methylthiocholestane :* ^{1}H NMR δ 0.65 (s), 0.82 (br s), 0.90 (s), 0.4 to 2.240 (m) (46H), 2.02 (s, 3H), 2.55 (s, 3H).

This crude product was dissolved in toluene (100 ml) and heated to reflux in a 250 ml flask equipped with a Dean-Stark vessel during 2 h. The thermolysis was monitored by TLC until it was ended. The solution was then washed with sodium carbonate, twice with water and concentrated to deposit white

crystals (5.10 g, yield= 80 %). A pure sample was obtained by crystallization from a mixture of ethyl acetate and methanol. *3-Methylthiocholest-2-ene* : white prisms, mp= 129°C, ^{1}NMR δ 0.60 (s), 0.74 (s), 0.80 (s), 0.90 and 0.6 to 2.20 (m) (44 H), 2.17 (s, 3H), 5.13 to 5.46 (m, $W_{1/2}$ = 9 Hz, 1H).
Anal. Calc. for $C_{28}H_{48}S$: C, 81.09 ; H, 11.18 : S, 7.73. Found : C, 81.06 ; H, 11.29 ; S, 7.81.

Ozonation of 3-methylthiocholest-2-ene : The enolthioether (2g, 4.8 mmole) was treated with 2 equiv of ozone as described previously[26]. The flash chromatography over silica gel of the crude residue has supplied, among minor by-products, eluted portions from petroleum ether-ethyl acetate (60:40 to 50:50) which have been analysed as a mixture of epoxysulfoxides diastereomers. Pure analytical samples of each compound could be obtained by fractionnal recrystallization of the first and the last portions.
2,3-Epoxy-3-methylsulfinyl cholestane **1e** *(S_SSS or R_SRR)* : less polar isomer, white crystals, m.p= 164°C, IR : 1063 cm^{-1} (νSO); ^{1}H NMR ($CDCl_3$) δ 0.65 (s), 0.80 (s), 0.91 (s) and 0.3 to 2.3 (m) (44 H), 2.57 (s, 3H), 3.49 and 3.58 (d of br s, J= 5 Hz, $W_{1/2}$ = 2.5 Hz, 1H); (C_6D_6) δ 0.60 (s), 0.66 (s), 0.29 (s), 0.97 (s) and 0.2 to 2.0 (m) (44 H), 2.09 (s, 3H), 3.16 and 3.25 (d of br s, J= 5 Hz, $W_{1/2}$= 2.5 Hz, 1H) ; ^{13}C NMR δ 12.0, 12.6, 18.8, 21.2, 21.6, 22.6, 22.8, 23.9, 24.3, 28.1, 28.2, 28.6, 31.6, 33.6, 34.3, 35.8, 35.8, 36.3, 37.5, 38.2, 39.6, 40.0, 42.6, 53.7, 56.5, 52.3, 71.2.
Anal. Calc. for $C_{28}H_{48}O_2S$: C, 74.94 ; H, 10.78 ; S, 7.15. Found : C, 74.81 ; H, 10.61 ; S, 7.31.
2,3-Epoxy-3-methylsulfinyl cholestane **1e** *(R_SSS or S_SRR)* : most polar isomer, white crystals, m.p= 170°C, IR : 1070 cm^{-1} (νSO) ; ^{1}H NMR ($CDCl_3$) δ 0.64 (s), 0.78 (s) 0.86 (d, J= 6.6 Hz, 6H), 0.90 (d, J= 7.3 Hz, 3H) and 0.2 to 2.2 (m) (44 H for the all), 2.55 (s, 3H), 3.64 and 3.67 (d of br s, J= 5.9 Hz, $W_{1/2}$ = 2H, 1H) ; (C_6D_6) δ 2.08 (s, 3H), 3.72 and 3.82 (d of br s, J= 5.9 Hz, $W_{1/2}$ = 2 Hz, 1H) ; ^{13}C NMR δ 12.1, 13.0, 18.9, 21.2, 22.7, 22.9, 24.1, 24.4, 27.8, 28.2, 28.3, 28.7, 31.7, 33.4, 34.4, 35.9, 36.4, 37.9, 38.1, 39.8, 40.1, 42.7, 53.7, 54.7, 56.5, 56.6, 73.4.
Anal. Calc. for $C_{28}H_{48}O_2$: C, 74.94 ; H 10.78 ; S, 7.15. Found : C, 75.21 ; H, 10.85 ; S, 7,30.

Reactions of α,β-epoxysulfoxides with :

$TiCl_4$-Zn in ether[7] **:** Zn (4 mmol) was mixed with titanium(IV) chloride (4 mmol) in ether at room temperature. The solution was stirred for 3 min before the dropwise addition of the epoxysulfoxides **1a** (1 mmol) solution in methylene chloride. After the addition was completed, the solution was refluxed with stirring for additional 45 min. Water was added to the cooled reaction mixture and the aqueous solution was extracted with chloroform to give, after removal of the solvent, two main reaction products : the allylic alcohol **4a** and its corresponding hydrolysis product. These compounds were identified by comparison (GC, NMR) with authentic samples available in the laboratory.

$(CF_3CO)_2O$ / NaI in acetone[8] **:** A round bottom flask was charged with acetone (5 ml), epoxysulfoxide **1** (1 mmol) and sodium iodide (0.5 mmol) and then immersed in an ice bath. An acetone solution of trifluoroactic anhydride (2-2.5 mmol) was slowly added with stirring. On completion of the reaction (15 min) and after classical work-up, the crude clean reaction mixture was analysed by its ^{1}H NMR spectrum (CHO_2CF_3 signal near 4.7 ppm in $CDCl_3$) and GC runs (140 to 170°C).

As indicated in footnote c of the table I, the enones **3a-c** could be prepared in an overall yield of 80% by further submitting the above mixture to : (1) saponification (4N NaOH, 100°C, 30 min) ; (2) acidification to pH 3-4 (10 % H_2SO_4) followed by extraction with ether. The dried etheral extracts were evaporated *in vacuo* and the residue was dissolved in dry dichloromethane (5 ml) and vigorously stirred with MnO_2 (2 mmol) until the end of the reaction (TLC monitoring). The suspension was passed through celite (2 g) which was washed twice with CH_2Cl_2 and then concentrated to leave practically pure products.

Reactions of 1 with other halides-based electrophilic reagents:

BF_3-Et_2O / NaI in CH_3CN (method A)[18] **:** To a stirred solution of α-epoxysulfoxide **1** (1 mmol) and sodium iodide (300 mg, 2 mmol) in acetonitrile (4 ml) was added freshly distilled borontrifluoride etherate (250 µl, 2 mmol) via a syringue. After 10 min, work-up of the dark reaction mixture, followed by purification on TLC plates gave the α-sulfenyl carbonyl product in yields as indicated in Table II.

$ClSiMe_3$ / NaI in CH_3CN (method B)[13b] **:** Chlorotrimethylsilane (217 mg, 2 mmol) was added to a solution of the substrat **1** (1 mmol) and sodium iodine (300 mg, 2 mmol) in acetonitrile (4 ml), and the whole was stirred at room temperature. On completion of the reaction (*ca.* 15 min) the resulting mixture was taken up as in method A.

P_2I_4 in CH_2Cl_2 (method C)[14b] **:** α,β-epoxysulfoxide (1 mmol) in dichloromethane (1 ml) was added to a stirred suspension of diphosphorus tetraiodide (566 mg, 0.5 mmol) in CH_2Cl_2 (4 ml) at room temperature. The red-black solution was stirred for 10 min, hydrolyzed and worked-up as usual.

$(Ph)_3P$ / I_2 in moist CH_3CN (method D)[15] **:** A solution of iodine (1 mmol) in reagent-grade acetonitrile containing *ca.* 2 % of water was added dropwise to a solution of triphenylphosphine (1 mmol) in the same solvent (10 ml/100 mg Ph_3P). The brown colour of iodine immediately disappeared. The epoxysulfoxide (1 mmol) dissolved in CH_3CN was rapidly added and the mixture was stirred for 15 min. The pale yellow solution became quickly dark-brown due to free iodine and was worked-up as above.

$(Me_2N)_3P$ / I_2 in dry CH_3CN (method E)[16] : In a 10 ml flask equipped with a magnetic stirring bar and a reflux condenser, iodine (254 mg, 1 mmol) was suspended in acetonitrile (5 ml). To this stirred suspension, *tris*(dimethylamino)phosphine (165 mg, 1 mmol) and a solution of epoxysulfoxide (1 mmol) in acetonitrile (2 ml) were slowly added successively. Refluxing of the reaction mixture slowly resulted in the liberation of iodine, and the reaction was complete in 2 to 4 h as monitored by TLC. Work-up of the reaction mixture was as described above.

Me_3SiCl / DMSO in CH_3CN (method F)[17b] : To a stirred solution of **1** (1 mmol) in dry acetonitrile (4 ml), trimethylchlorosilane (3 mmol) and dimethylsulfoxide (3 mmol) were added successively. The reaction was kept at 10-15°C by external cooling. After 20 min, the mixture was poured into water (8 ml) and extracted with ether.

α-Alkylthio (or arylthio) ketones 2

These ketones were prepared according to the above methods (see details in Table II). Analytical samples of the pure ketones could be obtained by preparative GC or preparative TLC plates. The compounds **2a** to **2d** were previously reported[26].

3-Methylthiocholestan-2-one **2e** : white crystals, mp= 135°C, IR : 1690 cm^{-1} (νCO) ; ^1H NMR δ 0.57, 0.68, 0.73, 0.83 and 0.60 to 2.50 (m) (42H), 1.93 (s, 3H), 2.10 and 2.72 (AB system partially masked, J= 14 Hz, 2H), 3.07 (pseudo d d, $W_{1/2}$ = 8 Hz, 1H); ^{13}C NMR δ 208.2 (C2).
Anal. Calc. for $C_{28}H_{48}OS$: C, 77.73 ; H, 11.18. Found : C, 77.85 ; H, 11.21.

α-Alkylthio (or arylthio) enones 3

4,4,6,6-Tetramethyl-2-methylthiocyclohex-2-en-1-one **3a** : colorless oil which crystallizes at r t, IR : 1680 cm^{-1} (νCO) ; ^1H NMR δ 1.20 (br.s, 12H), 1.80 (s, 2H), 2.16 (s, 3H) and 6.06 (s, 1H) ; ^{13}C NMR δ 14.1, 27.2, 31.2, 31.6, 33.9, 41.6, 48.9, 133.5, 146.7, 200.9.
Anal. Calc. for $C_{11}H_{18}OS$: C, 66.61 ; H, 9.15 ; S, 16.17. Found : C, 66.42 ; H, 9.12 ; S 16.15.
4,4,6,6-Tetramethyl-2-phenylthiocyclohex-2-en-1-one **3b** : white crystals, mp = 97°C, IR (KBr) : 1690 cm^{-1} (νCO) ; ^1H NMR δ 1.12 (s) and 1.18 (s) (12H) ; 1.72 (br.s, 2H), 6.20 (s, 1H), 7.0 to 7.80 (m, 5H) ; ^{13}C NMR δ 26.3, 27.4, 29.6, 30.7, 34.4, 42.1, 49.2, 125.4, 127.8, 129.0, 129.3, 131.2, 133.0, 153.5, 154.5, 199.9.
Anal. Calc. for $C_{16}H_{20}OS$: C, 73.80 ; H, 7.74 ; S, 12.32. Found : C, 73.82 ; H, 7.70 ; S= 12.03.
4,4,6-Trimethyl-2-methylthio cyclohex-2-en-1-one **3c** : colorless oil which crystallizes at r t, I.R : 1680 cm^{-1} (broad νCO) ; ^1H NMR δ 1.13 (d, J=6Hz, 3H), 1.17 (s, 3H), 1.20 (s, 3H), 1.40 to 2.00 (m, 2H), 2.14 (s, 3H), 2.25 to 2.95 (m, 1H), 5.98 (s, 1H) ; ^{13}C NMR δ 14.0, 15.2, 25.9, 31.3, 34.7, 38.1, 44.9, 135.1, 147.8, 198.2.
Anal. Calc. for $C_{10}H_{16}OS$: C, 65.17 ; H, 8.75 ; S, 17.40. Found : C, 65.29 ; H, 8.62 ; S, 17.77.
5-t Butyl-2-methylthiocyclohex-2-en-1-one **3d** : translucid needles, mp = 70°C, IR : 1680 and 1670 cm^{-1} (νCO) ; ^1H NMR δ 0.92 (s, 9H), 1.40 to 3.0 (m, 5H) ; 2.20 (s, 3H) ; 6.48 to 6.52 (d d, J= 6 Hz and J= 4 Hz, 1H). ^{13}C NMR δ 13.9, 27.0, 28.9, 32.3, 40.5, 45.4, 137.3, 139.9, 196.8.
Anal. Calc. for $C_{11}H_{18}OS$: C, 66.61 ; H, 9.15 ; O, 8.07 ; S, 16.17. Found: C, 66.63 ; H, 9.11 ; O, 8.34 ; S, 16.22.
3-Methylthiocholest-3-en-2-one **3e** : white crystals, mp = 122°C, IR : 1670 cm^{-1} (ν CO) ; ^1H NMR δ 0.60, 0.78, 0.81, 0.85 and 0.5 to 2.2 (m, 40H), 2.12 (s, 3H), 2.03 and 2.63 (AB system partially masked, J= 16 Hz, 2H), 6.12 (d, J= 2 Hz, 1H) ; ^{13}C NMR δ 12.2, 12.9, 13.8, 18.8, 21.2, 22.6, 22.8, 23.9, 24.2, 27.2, 28.1, 28.2, 31.9, 34.8, 35.8, 36.3, 39.6, 39.8, 41.1, 42.8, 48.3, 52.4, 53.3, 56.4, 136.8, 143.1, 196.1.
Anal. Calc. for $C_{28}H_{46}OS$: C, 78.09 ; H, 10.77. Found : C, 77.82 ; H, 10.77.
4,6,6-Trimethyl-2-methylthiocyclohex-2-en-1-one **3g** : colorless oil, I.R : 1680 cm^{-1} (ν CO) ; ^1H NMR δ 1.16 (s, 6H), 1.17 (d, J=6Hz, 3H), 1.40 to 2.10 (m, 2H), 2.50 to 3.10 (m, 1H), 6.10 to 6.30 (m, 1H); ^{13}C NMR δ 14.0, 21.6, 23.9, 25.4, 29.6, 42.0, 45.4, 135.6, 143.2, 200.8.
Anal. Calc. for $C_{10}H_{16}OS$: C, 65.17 ; H, 8.75 ; S, 17.40. Found: C, 65.51 ; H, 8.83 ; S, 17.48.

1,2-ketone transposition

Reductive sulfur removal[35] **of α-methylthioketones 2c and 2e** : To a vigorously stirred suspension of Raney Nickel catalyst (from Fluka, 1g washed twice with ethanol) in ethanol (10 ml) was added a solution of the methylthioketone (2 mmol) in a mixture of acetone / ethanol (10 ml). The mixture was heated to reflux for 12 hours and the reaction checked by TLC. The resulting mixture was then diluted with acetone and the catalyst cautiously removed by filtration. After evaporation *in vacuo*, the residue was taken up in ether, the extracts were washed with water and brine, dried and then concentrated. The crude ketones **7** and **9** were obtained in good yield (90%). Pure samples, prepared by GC for **7** or silica gel chromatography for **9** were identified by comparison of their spectroscopic data to those reported in the litterature[36,37].

Oxidative sulfur removal[38] **of α-methylthioketones 2c and 2e** : To a cooled (0°C) and vigorously stirred suspension of sodium metaperiodate (470 mg, 2.2 mmol) in a 9:1 methanol-water mixture (10 ml) was added a solution of the methylthioketone (2 mmol) in acetone / methanol (10 ml). The reaction mixture was stirred for 20 hours, then poured into water (20 ml) and extracted repeatedly with ether. The etheral

extracts were washed, dried and concentrated *in vacuo* to give the clean sulfoxide. The crude mixture was heated to reflux in dry toluene (5ml) and the reaction was monitored by GC (for **2c**) or TLC (for **2e**) and NMR analysis. Within a few hours was obtained a 70-30 mixture of the cleaved enones **8** and **10** and the dehydrated side-products **3c** and **3e**, respectively. Data of the analytical samples obtained by preparative GC for **8** or preparative TLC plate for **10** were identical to those reported in the litterature[39,40].

LITERATURE

1. Durst, T. *J. Am. Chem. Soc.* **1969**, *91*, 1034.
2. Durst, T.; Tin, K.C. *Tetrahedron Lett.* **1970**, 2369; Tavares, D.F.; Estep, R.E.; Blezard, M. *Tetrahedron Lett.* **1970**, 2373; Durst, T.; Tin, K.C.; de Reinach-Hirtzbach, F.; Decesare, J.M.; Ryan, M.D. *Can. J. Chem.* **1978**, *57*, 258 and references cited therein. Taber, D.F.; Gunn, B.P. *J. Org. Chem.* **1979**, *44*, 450.
3. Satoh, T.; Oohara, T.; Ueda; Y.; Yamakawa, K. *J. Org. Chem.* **1988**, *54*, 3130.
4. a) Madesclaire, M. *Tetrahedron*, **1988**, *44*, 6537. b) Grossert, J.S.; in "Chemistry of sulphones and sulphoxides", Eds. S. Patai, Z. Rappoport and C.J.M. Stirling, Wiley, London, 1988, p.925.
5. a) Wong, H.N.C.; Fok, C.C.M.; Wong, T. *Heterocycles*, **1987**, *26*, 1345. b) Kocienski, P. in "Comprehensive Organic Synthesis", Vol. 6, Ed. E. Winterfeldt, Pergamon Press, Oxford, 1991, P. 909-911..
6. Drabowicz, J.; Mikolajczyk, M. *Synthesis*, **1978**, 138; Mc Murry, J.E.; Silvesti, M.G.; Fleming, M.P.; Hoz, T.; Grayston, M.W. *J. Org. Chem.* **1978**, *43* , 3249.
7. Reutrakul, V.; Poochairatananon, P. *Tetrahedron Lett.* **1983**, 351.
8. For deoxygenation of epoxides with this reagent see : Sonnet, P.E. *J. Org. Chem.* **1978**, *43*, 1841 and Sarma, D.N.; Sharma, R.P. *Chem. Ind.(London)*, **1984**, 712. For deoxygenation of sulfoxides see : Drabowicz, J.; Oae, S. *Synthesis*, **1977**, 404.
9. Alkaline-halides in combination with CF_3CO_2H have been used for cleaving epoxides (a) and keto-oxiranes (b) : a) Larack, R.C. "Comprehensive organic transformations"; C.H. Publishers Inc.; New York, 1989, pp 508-510; Bajira, J.S.; Anderson, R.C. *Tetrahedron Lett.* **1991**, 2373; Paulsen, H.; Koebernick, W. *Chem. Ber.* **1977**, *110*, 2127. b) Begue, J.P.; Charpentier-Morize, M.; Mayer, M. *Bull. Soc. Chim. Fr.* **1970**, 2300.
10. Attenburrow, J.; Cameron, A.F.B.; Chapman, J.H.; Evans, R.M.; Hems, B.A.; Jansen, A.B.A.; Walker, T. *J. Chem. Soc.*, **1952**, 1094; Torii, S.; Inokuchi, T.; Ogawa, H. *J. Org. Chem.* **1979**, *44*, 3412.
11. Most of these systems have been used for deoxygenation of both epoxides and sulfoxides.
12. Palumbo, G.; Ferreri, C.; Caputo, R. *Phosphorus and Sulfur*, **1983**, *15*, 19; Vankar, Y.D.; Rao, C.T. *Tetrahedron Lett.* **1985**, 2717.
13. a) Caputo, R.; Mangoni, L.; Neri, O.; Palumbo, G. *Tetrahedron Lett.* **1981**, 3551. b) Olah, G.A.; Narang, S.C.; Gupta, B.G.B.; Malhotra, R. *Synthesis*, **1979**, 61. c) For a review on Me_3SiI reagent see : Olah, G.A.; Narang, S.C. *Tetrahedron*, **1982**, *38*, 2225.
14. a) Suzuki, H.; Fuchita, T.; Iwasa, A.; Mishina, T. *Synthesis*, **1978**, 905; Yamashita, M.; Tsunekawa, K.; Sugiura, M.; Oshikawa, T. *Synthesis*, **1985**, 65. b) Denis, J.N.; Krief, A. *Tetrahedron Lett.* **1979**, 3995; Suzuki, H.; Sato, N.; Osuka, A. *Chem. Lett.* **1980**, 143.
15. Garlaschelli, L.; Vidari, G. *Gazz. Chim. It.* **1987**, *117*, 251.
16. Olah, G.A.; Gupta, B.G.B.; Narang, S.C. *J. Org. Chem.* **1978**, *43*, 4503.
17. a) For an earlier review on DMSO reagents see : Mancuso, A.J.; Swern, D. *Synthesis*, **1981**, 165. b) Caputo, R.; Ferreri, C.; Palumbo, G. *Tetrahedron*, **1986**, *42*, 2369. c) Ghelfi, F.; Grandi, R.; Pagnoni, U.M. *J. Chem. Research (S)*, **1988**, 200.
18. Such compounds have been isolated and shown to give easily the corresponding enones. Results to be published later.
19. Mandal, A.K.; Mahajan, S.W. *Tetrahedron*, **1988**, *44*, 2293.
20. Satoh, T.; Kaneko, Y.; Isawa, T.; Sakata, K.; Yamakawa, K. *Bull. Chem. Soc. Jpn*, **1985**, *58*, 1983.
21. Castro, B.R. *Org. React.* **1983**, *29*, 1.
22. a) Parker, R.E.; Isaac, N.S. *Chem. Rev.* **1959**, *59*, 737. b) Rao, A.S.; Palnikar, S.K.; Kirtane, J.G. *Tetrahedron*, **1983**, *39*, 2323; Gorzynski-Smith, J. *Synthesis*, **1984**, 629.
23. This mode of oxirane cleavage does not agree with the report of reference 22a that electron-withdrawing groups inhibit attack on the adjacent carbon atom. Meanwhile, α-ring openings of α,β-epoxyketones are known.[9b, 17c, 18]
24. Lucetti, J.; Krief, A. *Synth. Commun.* **1983**, 1153; Verhé, R.; DeKimpe, N.; DeBuyck, L.; Schamp, N. *Synthesis*, **1984**, 46.
25. Tavares, D.F.; Estep, R.E. *Tetrahedron Lett.* **1973**, 1229; Cohen, T.; Kuhn, D.; Falck, J.R. *J. Am. Chem. Soc* **1975**, *97*, 4749.
26. Barillier, D.; Vazeux, M. *J. Org. Chem.* **1986**, *51*, 2276.
27. Simple sulfuranes have the leaving group and halogen atom in axial positions of a trigonal bipyramid structure.
28. Hydrogen halides or halogens are known to trigger the catalytic reduction of sulfoxides: Aida, T.; Akasaka, T.; Furukawa, N.; Oae, S. *Bull. Chem. Soc. Jpn*, **1976**, *49*, 1117.
29. March, J. "Advanced Organic Chemistry", third edition, Wiley, NY, 1985, p. 268 and references cited therein.
30. Durst, T. in "Comprehensive Organic Chemistry", vol 3, Ed. D. Neville Jones, Pergamon Press, NY, 1979, p.137-139
31. Olah, G.A.; Awanaghi, M.; Vankar, Y.D. *J. Org. Chem.* **1980**, *45*, 3531.
32. Kane, V.V.; Singh, V.; Martin, A.; Doyle, D.L. *Tetrahedron*, **1983**, *39*, 345.
33. Trost, B.M. *Acc. Chem. Res.* **1978**, *11*, 453 and *Chem. Rev.* **1978**, *78*, 363.
34. Bruce, W.F. *Org. Synth. Coll.*, Vol 2, Wiley, London, 1948, p.139.
35. Paterson, I.; Fleming, I. *Tetrahedron Lett.* **1979**, 995.
36. Barieux, J.J.; Gore, J. *Bull. Soc. Chim. Fr.* **1971**, 3978.
37. Fristad, W.E.; Bailey, J.R.; Paquette, L.A. *J. Org. Chem.* **1978**, *43*, 1620; *ibid*, **1980**, *45*, 3228.
38. Johnson, C.R. ; Keiser, J.E. *Org. Synth.* **1966**, *46*, 3412; Paterson, I.; Fleming, I. *Tetrahedron Lett.* **1979**, 2179.
39. Smith, H.A.; Huff, B.J.L.; Powers, W.J.; Caine, D. *J. Org. Chem.* **1967**, *32*, 2851; Torri, J.; Azzaro, M. *Bull. Soc. Chim. Fr.* **1978**, 283.
40. Mincione, E.; Ortaggi, G.; Sirna, A. *Synthesis*, **1977**, 773; Mimura, T.; Nakai, T. *Chem. Lett.* **1980**, 1099.

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