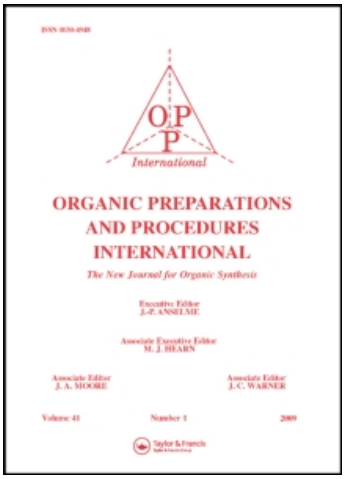

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SULFANYLATION REACTIONS OF CARBONYL COMPOUNDS AND CARBOXYLIC ACID DERIVATIVES EMPLOYING SULFUR ELECTROPffIlES. A REVIEW

Blanka Wladislaw[a]; Liliana Marzorati[a]; Claudio Di Vitta[a]
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INTRODUCTION

The presence of a sulfur functionality in the framework of organic molecules opens the possibility of several synthetic transformations.[1a-c] In particular, the usefulness of α-sulfur-substituted carbonyl or carboxy derivatives was demonstrated by Trost[1d-f] in his seminal papers, published in the late seventies. This class of compounds can be prepared by (*i*)-nucleophilic attack of a sulfur species on α-halocarbonyl derivatives, or (*ii*)-*via* electrophilic sulfur reagents and enols, enolates or enolate equivalents (sulfanylation reaction). The latter method presents the advantage of avoiding the need of preparation of halogenated precursors, and stands as the method of choice for some fundamental steps in several organosulfur based synthetic routes. However, over the last 25 years, this conceptually simple approach has been translated into a wide variety of experimental conditions, sulfanylating agents, catalysts, additives etc. In addition, the growing interest in stereo-defined compounds broadened the scope of this transformation and, in more recent years, several examples of diastereo- and enantioselective sulfanylation reactions can be found in the literature.

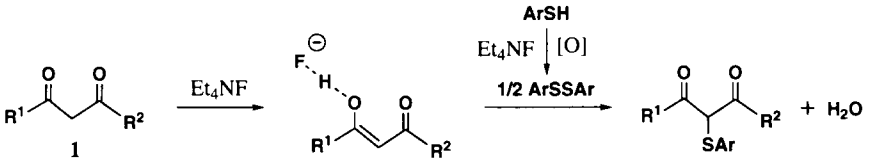
This review, covering work from 1979 to 2006, will describe a broad spectrum of examples of sulfanylation reactions, and special emphasis will be given to advances concerning the following aspects: (*i*) atom economy; (*ii*)-catalytic methods; (*iii*)-mono- *versus bis*-sulfanylation; (*iv*)-regio- and chemoselectivity and (*v*)-stereoselectivity. Reactions are presented in three substrate-oriented Tables. Entries of *Table 1* refer to those reactions for which no stereochemical outcome was reported.[2-55] All entries in *Table 2* and some in *Table 3* are examples of stereoselective sulfanylation reactions.[16,26,37,49,52,56-86,93,95,96,99] For entries in *Table 3*, all sulfanylation reactions[3,16,37,52,87-102] were performed using enolate equivalents, instead of carbonyl or carboxy derivatives.

I. ATOM ECONOMY METHODS

For classical sulfanylating agents such as disulfides, sulfanyl halides, sulfenamides, etc., a substancial mass of these reagents is wasted as a leaving group. To avoid this drawback, alternative sulfanylative methods were developed.

1. in situ Air Oxidation of Thiols or Thiolates[30,35,53,54]

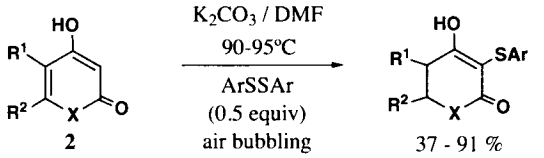
Ester and ketone enolates, to be reacted with disulfides, can be prepared quantitatively by deprotonation with LDA in anhydrous THF, in the absence of oxygen gas. However, for the deprotonation of compounds with more favorable pKas, such as β-dicarbonyl compounds, organic ammonium fluorides or K_2CO_3 are successfully used, and the resulting enolates can be sulfanylated using one equivalent of thiols or half equivalent of disulfides, respectively. In these cases, the presence of oxygen is beneficial, allowing the *in situ* generation of disulfides, either from added thiols or from liberated thiolates. As an example, the sulfanylation of propane-1,3-diones (**1**) is performed by using Et_4NF and equimolar quantities of thiol and of the β-dicarbonyl compound.[30] In this case, sulfanylation occurs *via* the β-dicarbonyl-tetraethylammonium fluoride monosolvate, that is prepared by mixing Et_4NF and **1** in DMF. After removal of solvent, a DMF solution of thiol is added dropwise to a cold solution of the solvate. At room temperature, a significant amount of free fluoride ions is present in solution, and the secondary hydrogen-bonding between fluoride and the thiol molecule will provide the driving force for air oxidation of the thiol to disulfide (*Scheme 1*, Entries 41, 50, 53 and 57, *Table 1*).



R^1 = Me, Ph, OEt; R^2 = OEt, Ph;

Scheme 1

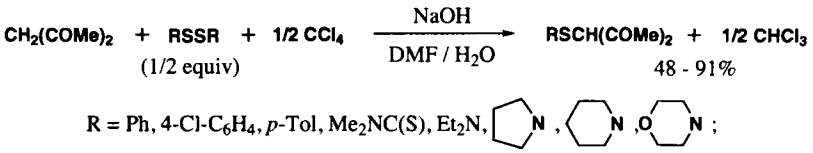
If a half equivalent of disulfides is used for the sulfanylation of β-dicarbonyl compounds, continuous air bubbling into the reaction mixture will be necessary to ensure the oxidation of any liberated thiolate anion into the corresponding disulfide.[53,54] Good results are obtained for the monosulfanylation of cyclic compounds **2** using this methodology, provided the reaction is conducted at 90-95°C (*Scheme 2*, Entries 93, 95, 97-99, 101, 103, 105, *Table 1*).



R^1 = H; R^2 = Me; = R^1 = R^2 ; = R^1 = R^2 ; X = NMe, O, NPh, NH;

Scheme 2

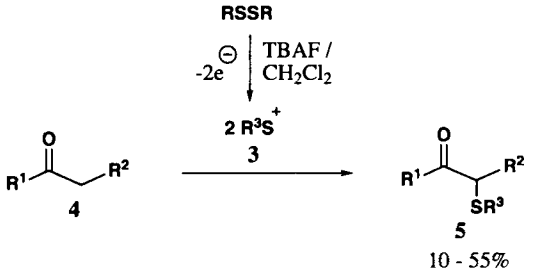
Alternatively, the solvent CCl_4 can play the role of oxidant[35] (*Scheme 3*, Entry 59, *Table 1*).



Scheme 3

2. Electrochemical Generation of the Sulfanylating Agent

In a very innovative approach, the new sulfanylating agents RS^+ (**3**; sulfenium cations) are generated by electrochemical oxidation of the corresponding disulfides, dissolved in CH_2Cl_2.[12] Upon reaction of these electrophilic sulfur reagents with the aliphatic ketones **4**, α-monosulfanylated products **5** are prepared in moderate yields in a two-step procedure (*Scheme 4*, Entries 13, 43, *Table 1*). In the first step, the organic disulfide is oxidized for about 15 h in



R = Me, Ph; R^1 = Pr, Me, Ph; R^2 = Me, Et, Pr, CO_2Et

Scheme 4

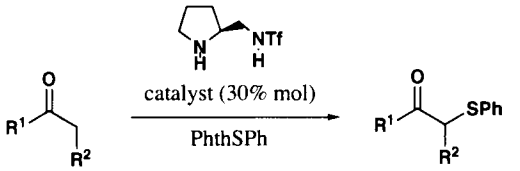
an H-type cell, on a platinum foil. In the second step, after the electrolysis is stopped, the solution of **3** is used for the direct quench of ketones **4**. The monosulfanylated products **5** are isolated in yields ranging from 10 to 55%.

II. CATALYTIC METHODS

Carbonyl compounds prone to aldol condensation, are usually sulfanylated *via* their enamines or silyl enol ethers (see *Table 3*), requiring a multistep preparative sequence. This drawback can be circumvented using catalytic methods for the α-sulfanylation of unmodified carbonyl compounds. Although examples of such methodologies are still rare in the literature, a recent report on a direct organo-catalytic reaction deserves mention: ketones and aldehydes are sulfanylated, in moderate to good yields, with N-phenylthiophthalimides in the presence of 20 mol% of pyrrolidine trifluoromethanesulfonamide[100] (*Scheme 5*, Entries 32, 33, *Table 3*).

Accordingly, phase-transfer catalysis (PTC), can be utilized in the sulfanylation of organic compounds bearing acidic methylene groups.[11,49,50,51,55,74,75,103,104] Under these milder

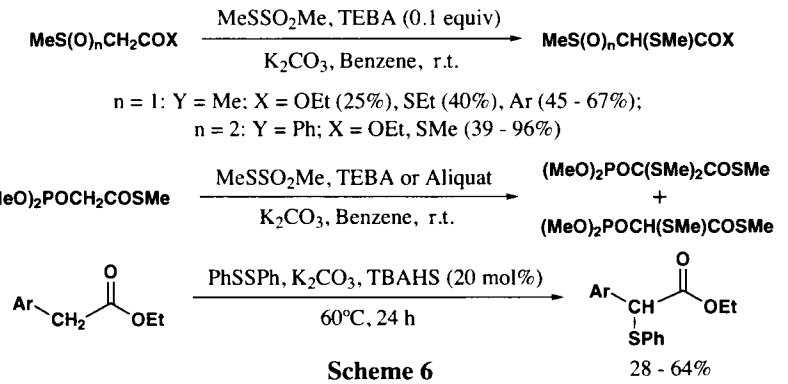
conditions, these substrates can be deprotonated at the interface of a solid and a liquid phase or at the boundary of two liquid phases. Common systems are composed by a solid base



R^1 = H, R^2 = Et, *i*-Pr, *n*-Bu, *n*-Pen, *n*-Hex, *n*-Hep, *n*-Oct
or R^1 and R^2 =$(CH_2)_4$, CH_2-CH_2-O-CH_2, CH_2-CH_2-N(Me)-CH_2

Scheme 5

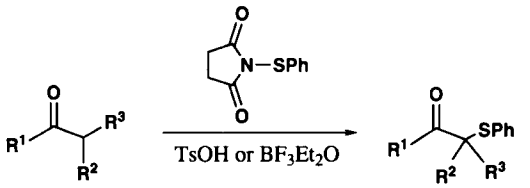
or a concentrated aqueous solution of sodium hydroxide in contact with a liquid organic phase containing the organic reactants.[105,106] After the deprotonation step, the phase-transfer catalyst, usually a quaternary ammonium salt, transfers the enolate to the organic phase, where the sulfanylation reaction takes place. Some examples of sulfanylation reactions, performed in a solid/liquid system,[11,49,50,51,55,74] are presented in *Scheme 6* (Entries 12, 84, 87, 108, 111, *Table 1* and Entry 25, *Table 2*).



Scheme 6

Acid-catalyzed sulfanylation reactions of enols are by far less common than those of the corresponding enolate versions. Such methodology was shown to be strongly dependent on the enol content of the carbonyl or carboxy derivative. For example, the sulfanylation of acylsilanes, aldehydes and ketones with N-(phenylthio)succinimide, in the presence of TsOH or boron trifluoride etherate,[101] is a quite successful reaction in the case of acylsylanes, but lower yields are obtained for the same reaction applied to other carbonyl compounds (*Scheme 7*, Entry 34, *Table 3*).

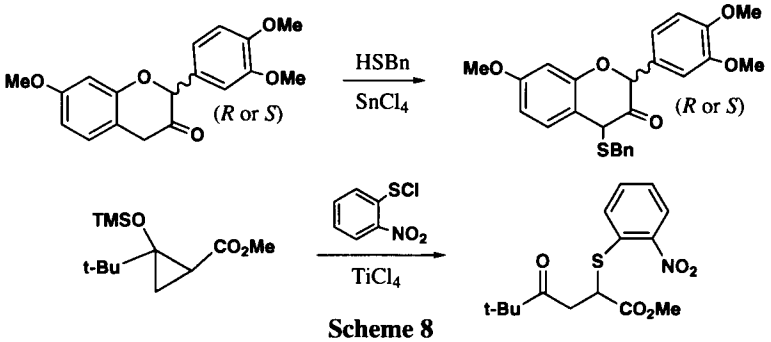
To our knowledge, only two other reports on the Lewis acid catalyzed sulfanylation of enols can be found in the literature, and they refer to $SnCl_4$[107] and $TiCl_4$[108] promoted reactions (*Scheme 8*).



R^1 = $SiPh_2Me$, TBS or TMS; R^2= H, Me, $(CH_2)_4Br$, $(CH_2)_3Br$,$(CH_2)_2CHMeBr$,$CHMe(CH_2)_3Br$, $(CH_2)_4Br$, n-Bu; R^3 = H } yields 80 - 92%

R^1 = H, Me, *n*-Ph; R^2 = *n*-Pr, *n*-Bu; R^3 = H, Me; } yields 19 - 68%

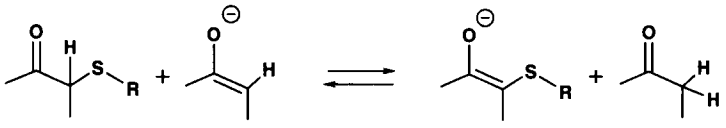
Scheme 7



Scheme 8

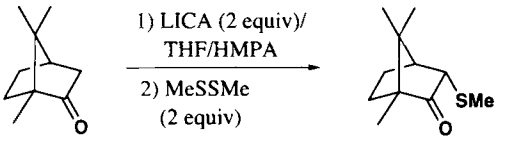
III. *mono- versus bis*-SULFANYLATION

Due to the increased acidity of the monosulfanylated product relative to the starting carbonyl compound, the following acid-base equilibrium can be set up if basic conditions are used:



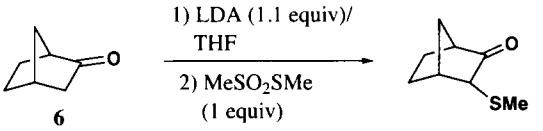
The consequences of this equilibrium are: (i) low yield of the monosulfanylated product due to the consumption of the original enolate and (ii) the possibility of formation of *bis*-sulfanylated by-products.

As pointed out by Trost,[1e,f] in the case of ketones, a 2:1 base to ketone ratio should be used to avoid both mentioned drawbacks. In fact, (+)-camphor is monosulfanylated in 40% yield [62] by quenching a THF solution of lithium ketone enolate with MeSSMe, in the presence of excess of base (*Scheme 9*, Entry 10, *Table 2*).



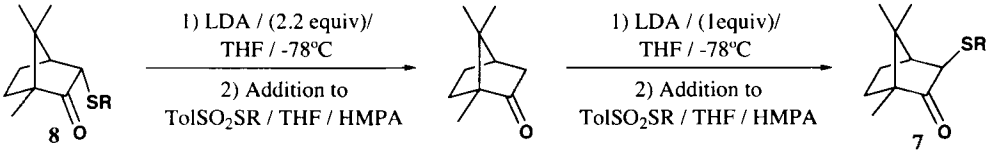
Scheme 9

However, the need to use two equivalents of base is still controversial. In this sense, the bicyclic ketone **6**, structurally related to (+)-camphor, can be sulfanylated in good yield by direct addition of the more reactive sulfanylating agent $MeSO_2SMe$ to one equivalent of the pre-formed enolate[15] (*Scheme 10*, Entry 64, *Table 1*).



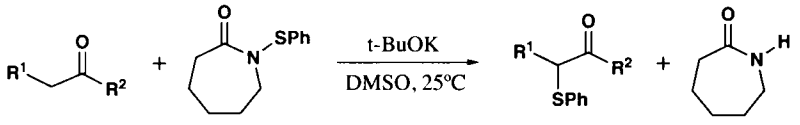
Scheme 10

Additionally, a literature survey shows that even for the less reactive disulfides, the use of one equivalent of base leads to good results[2,52,66,67,68,72,78] (Entries 1, 4, 90, 91, *Table 1*; Entries 14-18, 22, 30, 31, *Table 2*). However, the stereochemical outcome of the sulfanylation reaction can be dependent on the stoichiometry. For example, when the sulfanylation of (+)-camphor is performed by adding a solution of the enolate to different thiolsulfonates (inverse quench), the *exo* **7** isomers can be prepared selectively in good yields (61-86%) using one equivalent of base, whereas the thermodynamically more stable derivatives **8** are produced (yields ranging from 73-98%) in the presence of 2.2 equivalents of base[59] (*Scheme 11*, Entries 6, 7, *Table 2*).



Scheme 11

The relative proportion of *mono-* to *bis*-sulfanylated products can be improved by controlling the ratio of substrate to sulfanylating agent. For example, using **9** as the limiting reagent, a series of ketones can be monosulfanylated[6] in 80-97% yield (*Scheme 12*, Entry 7, *Table 1*).

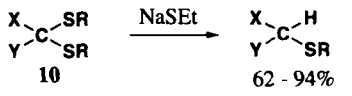


9

$R^1 = H$; R^2 = Me, *t*-Bu, Ph, 2-Naph
or $R^1 = R^2 = -(CH_2)_4-$

Scheme 12

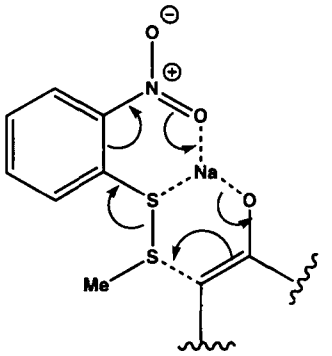
However, the opposite strategy, *i. e.* the use of excess of sulfanylating agent, can successfully employed as reported by Grossert and Dubey[7] (Entry 8, *Table 1*). According to these authors, the initially formed *bis*-sulfanylated compound **10** will be cleanly reduced to the *mono*-sulfanylated analog by treatment with NaSEt/excess of NaOEt or NaH in EtOH or THF (*Scheme 13*). It should be mentioned that this method, as applied to the monosulfanylation of sulfones, proved to be equally effective.[109,110]



X = COPh, Y = SO_2Me; R = Me, Et; X = Y = CO_2Et, R = Ph;
X = COMe, Y = CO_2Et; R = Ph; X = COPh, Y = H, R = Et

Scheme 13

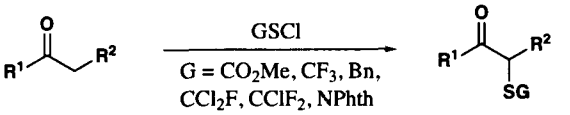
Useful reagents for *bis*-sulfanylation are N-phenylthiophthalimide[7] and 2-nitrophenyl alkyldisulfides (MNPDS).[10] Compared to other disulfides, MNPDS shows an enhanced reactivity due to the presence of the 2-nitrophenylthio group that probably activates not only the S-S bond, but also the sodium enolate in the transition state[10] (*Fig. 1*, Entries 11, 66, 67, *Table 1*).



"Double activated" Transition State for the sulfanylation of enolates using MNPDS

Fig. 1

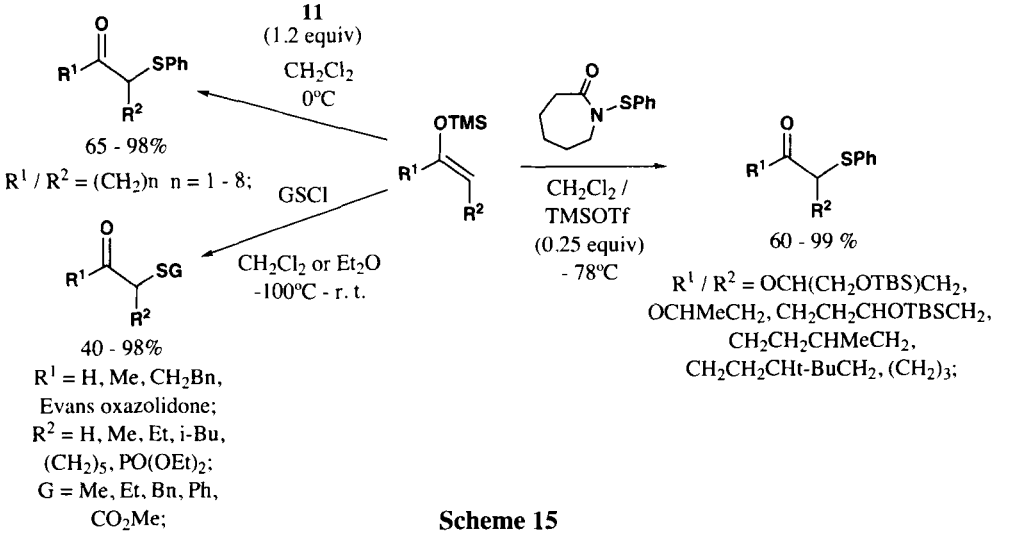
An obvious strategy for precluding *bis*-sulfanylation is to avoid the use of base. Under these conditions monosulfanylation can be achieved using (i) enols and sulfanyl chlorides[3,4,5,31,42,47,48] (*Scheme 14*, Entries 2, 3, 5, 6, 14, 42, 52, 74, 75, 82, 106, 107, *Table 1*) or (ii)



R^1 = H, Me, Bu, Ar, OEt, Ph, NHPh.
R^2 = H, Me, Bn, *n*-Pr, COMe, CO_2Et, CONHPh, COPh, C(NPh)Ph, C(NPh)Me

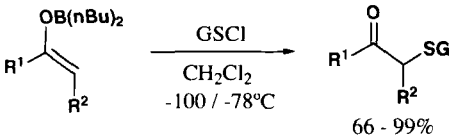
Scheme 14

silyl enol ether and sulfanyl chlorides[3,88,89,95] (*Scheme 15*, Entries 2, 3, 4, 15, 16, *Table 3*) or



Scheme 15

PhS(NTs)N(Ts)SPh[94] (**11**; *Scheme 15*, Entries 9, 21, *Table 3*) under neutral conditions, or N-phenylsulfanylcaprolactam with Lewis acid activation[92] (*Scheme 15*, Entries 6, 7, 14, *Table 3*) or (iii) enol borinates and sulfanyl chlorides[96] (*Scheme 16*, Entries 16, 18 - 20, *Table 3*).



R^1 = Et, *i*-Pr, *n*-Bu, *i*-Bu, *n*-Pen, Ph, Evans oxazolidone;
R^2 = H, Me, Et, *n*-Pr, *n*-Bu;
R^1/ R^2 = $CHMe(CH_2)_3$, $CH_2CHMe(CH_2)_2$
G= Ph, $(CH_2)_2CO_2Me$

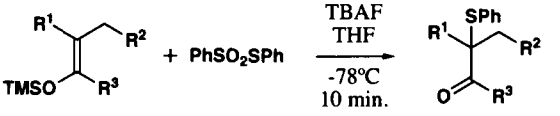
Scheme 16

IV. REGIO- AND CHEMOSELECTIVITY

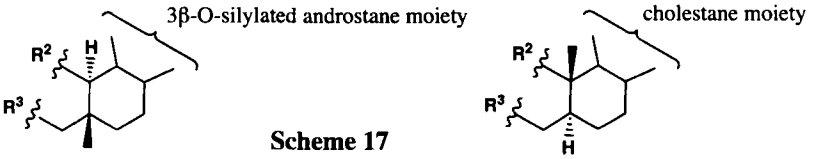
The problem of regioselectivity does not exist for esters, lactones, amides and lactams. However, the sulfanylation of unsymmetrical ketones might lead to mixtures of regioisomers. Regiospecifically generated lithium enolates are usually sulfanylated with less than 100% regioselectivity, due to a rapid proton transfer, equilibration and sulfanylation of the thermodynamically more stable enolate. For example, when the kinetically generated lithium enolate of 2-methylcyclohexanone is treated with PhSSPh, a mixture of 2-methyl-6-phenylthiocyclohexanone (80%) and 2-methyl-2-phenyl-thiocyclohexanone (20%) is obtained in 87% yield.[1f]

As for ketones, their transformation into regio-defined silyl enol ethers is a prerequisite to attain complete regioselectivity. *In situ* deprotection of these enolate equivalents with tetrabutyl-ammoniun fluoride (TBAF) generates the very reactive ammonium enolates that are readily

trapped by 3-phenylsulfanyl-2-(N-cyanoimino)thiazolidine[16] (Entries 10, 22, *Table 3*) or $PhSO_2SPh$[87] (Entries 1 and 12, *Table 3*). This method affords high yields of regioselectively sulfanylated ketones, as exemplified in *Scheme 17*.

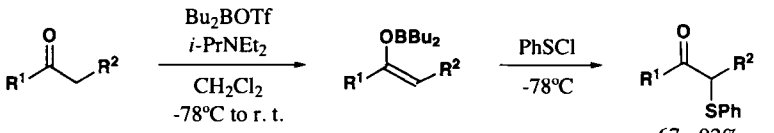


R^1 = H, Me; R^2 = OEt; R^3 = n-C_7H_{15};
R^2 / R^3 = $(CH_2)_3$, $CHMeCH_2CH_2$, CH_2CH_2CHt-Bu



Scheme 17

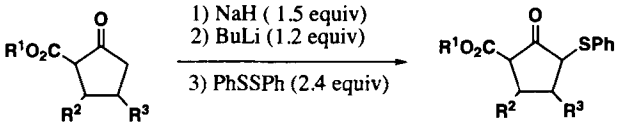
An alternate methodology to counteract enolate equilibration is the treatment of kinetically generated enol borinates with active sulfanylating agents at low temperature. For example, open-chain and cyclic unsymmetrical ketones can be monosulfanylated at the less substituted side in good yields and ≥ 85% regioselectivity,[96] *via* the corresponding enol borinates and sulfanyl chlorides (*Scheme 18*, Entries 18-20, *Table 3*).



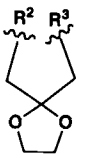
R^1 = *i*-Pr, *i*-Bu; R^2 = H, Me

Scheme 18

Chemoselective sulfanylation of 1,3-dicarbonyl compounds can be controlled by using the appropriate ratio base to substrate. Thus, if one equivalent of base is used for deprotonation, the more stable enolate will be generated, leading to sulfanylated products at C-2. However, sulfanylation of *bis*-metallated 1,3-dicarbonyl compounds with diphenyl disulfide occurs chemoselectively at the less substituted γ-carbon (Entries 25, 26, 30, 31, *Table 1*). These *bis*-metallated species can be generated either by using two equivalents of a strong base or one equivalent of NaH, followed by one equivalent of BuLi,[23,25] as illustrated in *Scheme 19*.



R^1 = Me, Et; R^2 = R^3 = H;



Scheme 19

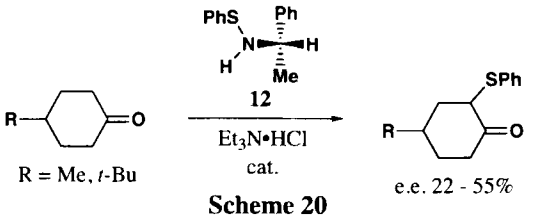
V. STEREOSELECTIVE SULFANYLATION REACTIONS

Several sulfur-containing molecules present a specific bioactivity strongly dependent of strict stereochemical requirements.[111,112] Additionally, in asymmetric synthetic transformations, the introduction of a thioether functionality might have a crucial role in the face differentiation of neighboring reactive groups.[76,113]

Stereoselectivity in sulfanylation reactions has been achieved *via* classical and innovative approaches. In this review, a special emphasis will be given to methodologies that make use of chiral sulfanylating reagents or catalysts or that are based on the chiral auxiliary concept. Examples of diastereoselectivity arising from substrate chirality can be found in *Table 2* (except Entries 14-17, 26-30, 44) and in *Table 3* (except Entries 16 and 17), but will not be mentioned nor discussed in this text.

1. Chiral Sulfanylating Agents

The reactivity of sulfanylating agents containing the N-S bond has been fully exploited, and some new examples include chiral versions. In a first report on an asymmetric sulfanylation reaction,[80] enantiomerically enriched α-phenylsulfanylcyclohexanones were obtained upon reaction of the parent carbonyl compounds with sulfenamide **12** (*Scheme 20*, Entry 35, *Table 2*). These sulfanylations are carried out in the presence of a catalytic amount of Et_3N•HCl (7 mol%), and best *e.e.* results are obtained by conducting the reaction in refluxing benzene.

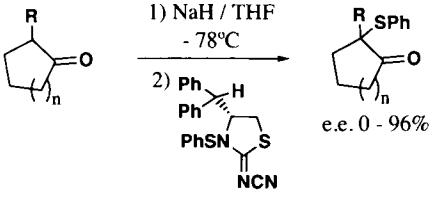


R = Me, *t*-Bu

e.e. 22 - 55%

Scheme 20

The chiral 4-diphenylmethyl-3-phenylsulfanyl-2-(N-cyanoimino)thiazolidine (**13**) is also an effecient asymmetric agent, and can be employed for the sulfanylation of aliphatic β-ketoesters, cyclic diketones or cyanoketones[16] (*e.e.* 3-96%, Entries 29, 33, 34, *Table 2*). In this case, cyclanones are treated with NaH at -78°C in THF, in order to generate the sodium enolates, which are directly quenched with 1.2 equivalents of **13**, at -78°C (*Scheme 21*).



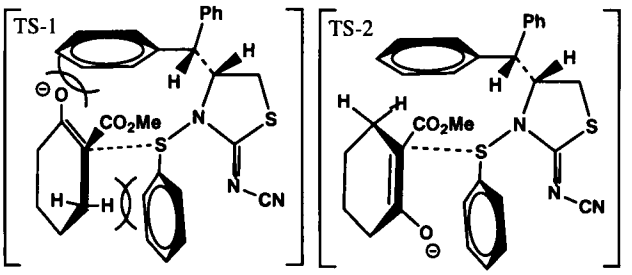
13

e.e. 0 - 96%

R = CO_2Et, COMe, COt-Bu, COPh, CN, CO_2Me, CO_2i-Pr, CO_2Ph;
n = 1 - 4

Scheme 21

The X-ray structural analysis and molecular modeling calculations for the sulfanylating agent **13** (*Fig. 2*) led to the proposal of a transition state (TS) model for the highly enantioselective sulfanylation of the 2-carbomethoxycyclohexanone[16] (*e.e.* 96% for R = CO_2Me, Entry 33, *Table 2*).



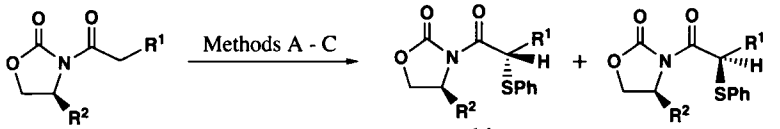
Transition states for the sulfanylation of 2-carbomethoxycyclohexanone using 13

Fig. 2

Two diastereomeric TS corresponding to the possible approaches of the phenylsulfanyl group to the enantiotopic faces of the enolate were suggested (*Fig. 2*). The observed *S*-enantioselectivity could be explained on the basis of steric effects, since TS-2 is less hindered than TS-1. It should be mentioned that the chiral 4-diphenylmethyl-2-(N-cyanoimino)thiazolidine can be recycled.

2. Use of Chiral Auxiliaries

As for the asymmetric sulfanylations using chiral auxiliaries, the Evans chiral oxazolidones,[79,95,96] chiral imidazolidin-2-ones,[78] and SAMP or RAMP[66,67] proved to be quite useful for the enolate face-diastereoselection. The efficiency of the Evans chiral auxiliaries was investigated by Paterson[95,96] and Warren,[79] as summarized in *Scheme 22* (Entry 32, *Table 2* and Entry 16, *Table 3*).



14

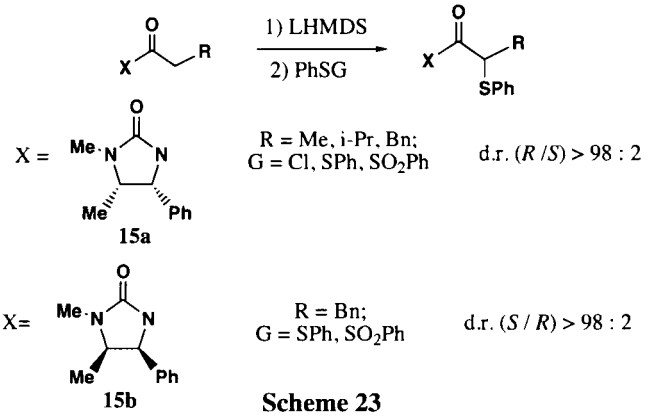
Method A- R^1 = Et, *n*-Pr, *i*-Pr, *t*-Bu; R^2 = Bn	97%	3%
Method B- R^1 = Me; R^2 = *i*-Pr	83 - 92%	17 - 8%
Method C- R^1 = Me; R^2 = *i*-Pr	88%	12%

Method A: 1) LDA; 2) PhSSPh / - 78°C; Method B: 1) LDA; 2) ClTMS (-78°C) or ClTBS (-100°C); 3) PhSCl; Method C: 1) Bu_2BOTf / $iPrNEt_2$; 2) PhSCl

Scheme 22

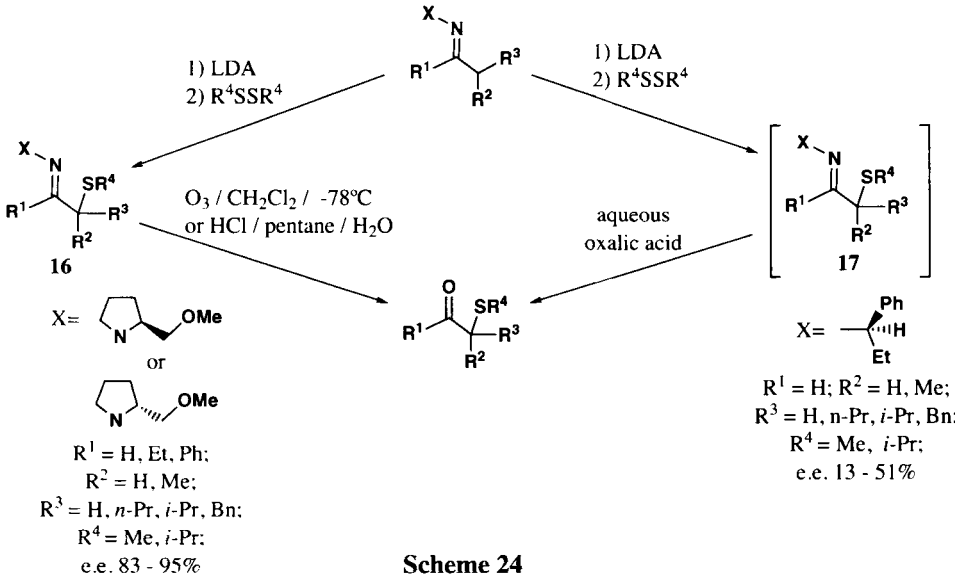
It should be mentioned that, although the prepared sulfanylated imides of *S* configuration (**14**) are obvious potential precursors of enantiopure aldehydes by partial reduction using Red-Al^R, this procedure results in racemization, while reduction to alcohols with $LiBH_4/H_2O$ preserves the stereochemical integrity at C-2. However, the oxidation of the intermediate alcohols requires a careful choice of oxidant to avoid racemization in this step. For this transformation, the Dess-Martin method is superior to the Swern oxidation. Very good yields and enantiomeric excesses are obtained for aldehydes prepared by this sequence.[79]

Imidazolinones **15a,b** both in enantiomerically pure forms, can also be used as covalently bonded chiral auxiliaries for the sulfanylation of lithium enolates[78] (*Scheme 23*, Entries 30 and 31, *Table 2*). Due to the facile preparation of both enantiomerically pure imidazolinones **15a,b**, this method is not limited to the preparation of one stereoisomer of the sulfanylated imides. It should also be mentioned that the chiral auxiliary is easily removed by reductive cleavage using $LiEt_3BH$.[78]



Scheme 23

The preparation of enantiomerically enriched α-sulfanylated carbonyl compounds can be also performed by reaction of chiral lithium azaenolates with disulfides. Aldehydes and ketones can be transformed into chiral hydrazones[66] or chiral imines[67] upon reaction with SAMP and RAMP or (R)-(+)-α-phenylethylamine, respectively. Sulfanylation reactions of SAMP and RAMP hydrazones[66] **16** (*Scheme 24*, Entries 14, 15, *Table 2*) are more stereoselective compared to those of imines[67] **17** (*Scheme 24*, Entries 16, 17, *Table 2*). However, when the cleavage of the



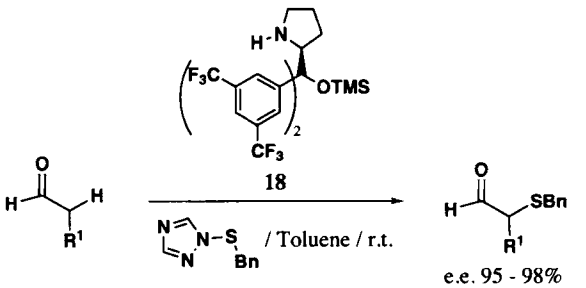
Scheme 24

C=N bond in SAMP hydrazones **16** is performed with HCl, in a two-phase system, low yields and virtual complete racemization is observed. Therefore, for these hydrazones a standard cleavage protocol, using ozone, should be used to liberate the corresponding carbonyl compound.[66]

3. Asymmetric Catalytic Methods

Only recently, reports on asymmetric catalytic sulfanylation reactions have appeared in the literature. In such cases, the catalyst might play one of the following roles: (i) a chiral auxiliary generating a transient chiral substrate, (ii) a chiral base generating a face-shielded enolate, (iii) a complexing agent, (iv) a chiral phase-transfer agent under PTC conditions. The following examples highlight some of these catalytic features.

Until few years ago, all practical methods for the preparation of enantiomerically pure α-sulfanylated aldehydes were multi-step procedures, involving chiral auxiliaries, as exemplified previously in *Schemes 22-24*. However, in 2005 an organo-catalytic method for the enantioselective sulfanylation of such substrates was reported. Under optimized conditions, a series of 2-monosubstituted acetaldehydes can undergo α-sulfanylation in the presence of 1-benzylsulfanyl-1,2,4-triazole, and the silylated prolinol **18** as catalyst.[77] Typically, a 30% excess of sulfanylating agent (0.33 mmol) is added to a mixture of aldehyde and amine **18** (as catalyst; 10 mol%) in toluene (0.5 mL), and the mixture is stirred at room temperature (*Scheme 25*, Entry 28, *Table 2*). The crude sulfanylated products are reduced *in situ*, yielding the corresponding chiral alcohols with high enantioselectivity.[77]

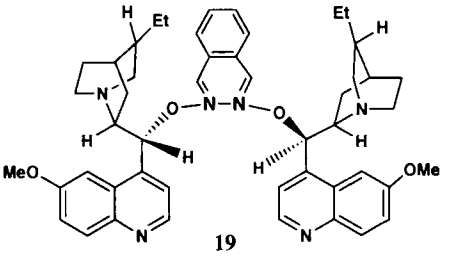


R^1 = Me, Et, *i*-Pr, *t*-Bu, Allyl, Ph, Bn

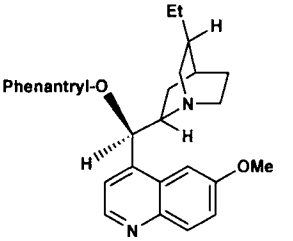
Scheme 25

The stereochemical course of the reaction can be rationalized[77] by assuming that, due to steric hindrance, the electrophile attacks the *Si* face of a postulated enamine intermediate, formed by reaction of the aldehyde and the amine catalyst **18**, yielding products of *S* configuration (*Fig. 3*).

Chiral bases are useful reagents for the direct enantioselective α-sulfanylation of activated C-H bonds, as demonstrated by Jorgensen and his group.[81] These authors reported on the sulfanylation of 1,3-dicarbonyl compounds using some *cinchona* alkaloids derivatives, acting as bases at the initial catalytic deprotonation step (Entries 36-40, *Table 2*). These sulfanylation reactions are conducted in apolar medium, using 1-sulfanyl[1,2,4]triazoles as sulfanylating agents (*Scheme 26*). *Cinchona* alkaloids **19-21** are the best performing catalytic bases for such reactions.[81]



19



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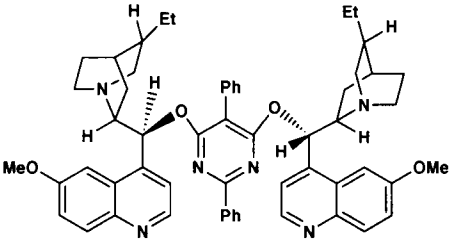
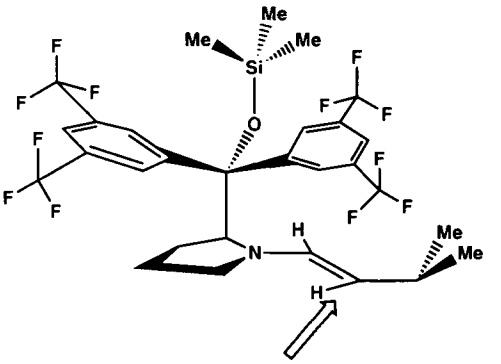


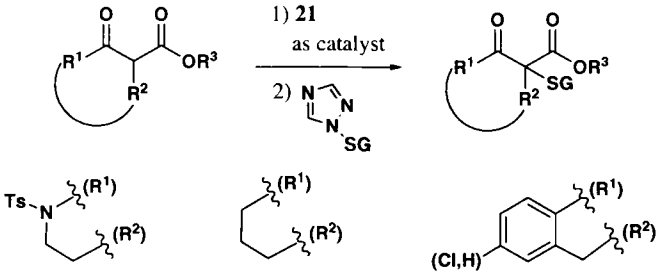
21



sulfur
electrophile attack

Electrophilic attack to the enamine formed by reaction of isobutyraldehyde and 18

Fig. 3

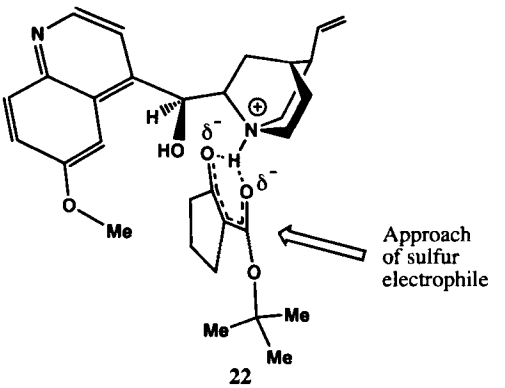


R^3 = Me, Et, *i*-Pr, *t*-Bu, Bn; G= Bn, *i*-Pr, 2,4-dinitrophenyl

Scheme 26

In a typical experimental procedure, the dicarbonyl compound is added to a solution of the dried catalyst (10 mol%) in dry toluene, under a N_2 atmosphere, at temperatures ranging from -30 to -40°C. This mixture is then treated with the sulfanylating agent, and stirred further at the same temperature,[81] yielding the sulfanylated cyclanones in 66-95% yield and 51-89% *e.e.*

The stereochemical outcome of these reactions was attributed[81] to a preferential attack of the electrophile to the less hindered face of the tightly hydrogen bonded intermediate **22** (*Fig. 4*).

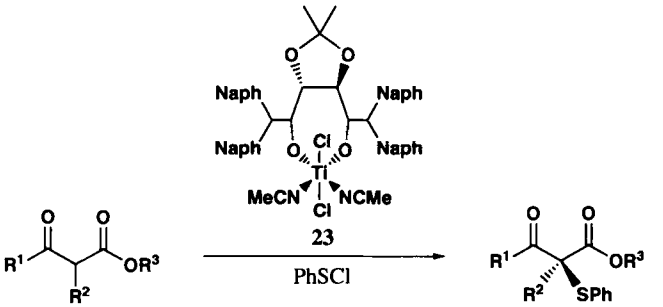


22

Approach of the sulfur electrophile to 22

Fig. 4.

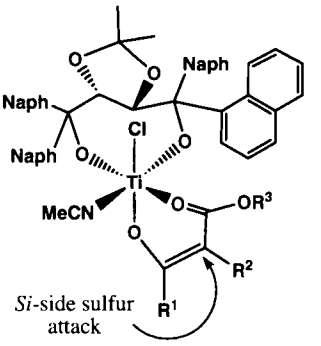
Metal complexes can be also used to achieve enantioselectivity. Ti(TADDOLates) are well known efficient chiral catalysts,[114] and can be successfully employed in the enantioselective sulfanylation of β-ketoesters.[84] This method works best for substrates bearing a bulky ester group, and consists in mixing the β-ketoester, the sulfanylating agent, and 5 mol% of catalyst **23** in toluene, at room temperature (*Scheme 27*. Entry 44, *Table 2*).



R^1 = Me, Et; R^2 = Me; $R^1 = R^2 = (CH_2)_3$; R^3 = Et, Am, *t*-Bu, Ar

Scheme 27

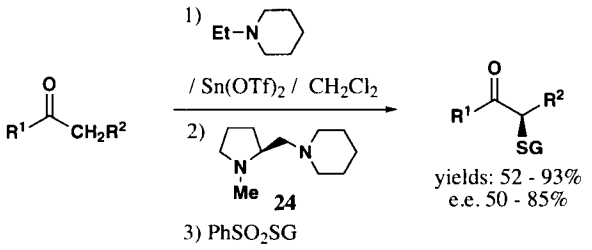
It should be noted that the absolute configuration of the product can be predicted if one assumes that the intermediate formed in this reaction is the same as that for previously reported halogenation and hydroxylation reactions.[84] By virtue of the shielding of the *Re* enantioface by one of the two face-on naphthyl groups, in the major diasteromeric intermediate containing the (*R,R*)-configured TADDOL, *S*-configured products are obtained (*Fig. 5*).



Attack to the Si enantioface of the titanium enolate

Fig. 5

Along the same line, the reaction of sulfur electrophiles with Sn(II), in the presence of chiral diamine ligands, affords chiral β-ketosulfides. As reported in 1986, the tin enolates of ketones can be made to react with thiolsulfonates, in the presence of the chiral diamine **24**,[76] to give (*R*)-β-ketosulfides in moderate to good *e.e.* (*Scheme 28*, Entries 26, 27, *Table 2*).

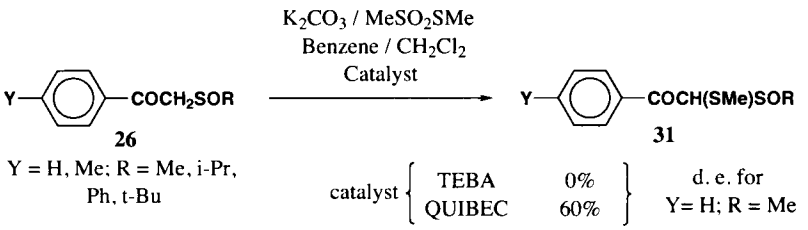


R^1 = Ph, *i*-Pr, *t*-Bu; R^2 = Me, Et, Bn; G= Naph, Ph;

Scheme 28

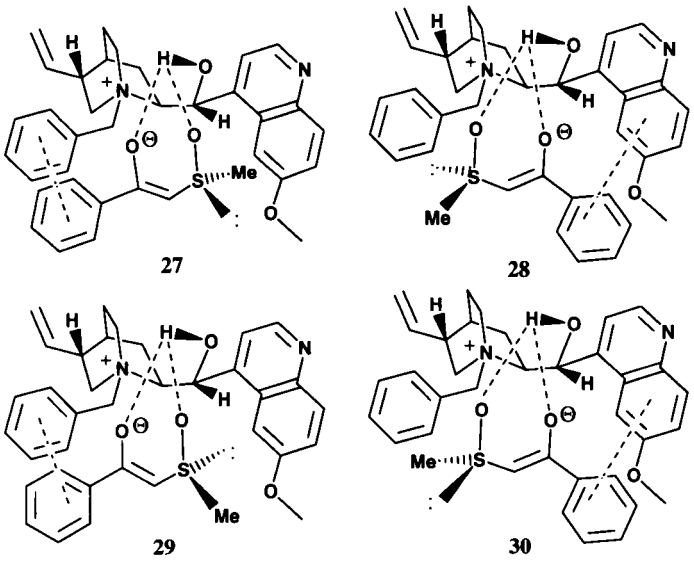
The bulkiness of thiolsulfonate contributes to increasing enantioselectivity, $NaphSO_2SPh$ being the best sulfanylating agent for this reaction.[76]

The chiral PTC catalyst[75] QUIBEC (N-benzylquininium chloride) promotes diastereoselective sulfanylation of racemic α-methyllsulfinylacetophenone (**25**), in a solid-liquid two-phase system (*Scheme 29*, Entry 25, *Table 2*).



Scheme 29

In this reaction, four possible diastereoisomeric ions-pairs **27-30** can be formed, in which the Z enolate of **26** (Y = H; R = Me) and the catalyst are tightly associated *via* hydrogen bonding and π-π interactions (*Fig. 6*).



Ion-pairs for racemic enolate of 26 (Y = H; R = Me) and QUIBEC

Fig. 6

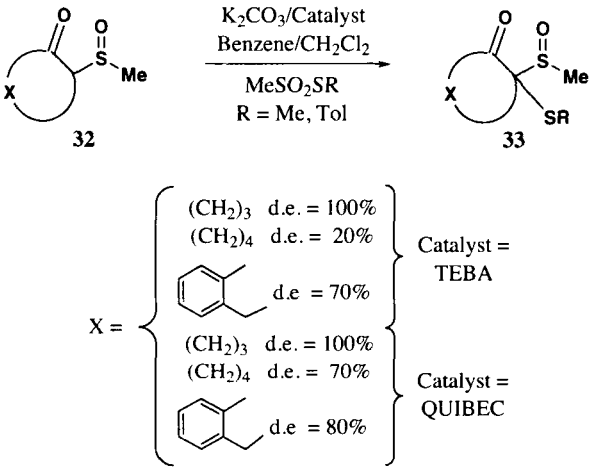
The stereochemical outcome of the sulfanylation of these intermediates, formed at the interface of the PTC system, can be summarized as follows:

Catalyst group which interacts with aromatic ring of enolate of **26** (Y = H; R = Me)	Enolate face blocked by catalyst	Configuration of sulfur at the enolate of **26** (Y = H; R = Me)	sulfanylated product **31** (Y = H; R = Me)
Benzyl	*Si*	*R*	S_RC_R
	Si	*S*	S_SC_R
Quinolyl	*Re*	*R*	S_RC_S
	Re	*S*	S_SC_S

The relative configuration of the major isolated diastereoisomer of **31** (*Scheme 29*, Y = H; R = Me) is $S_s{}^*C_s{}^*$.[75] This result suggests that the observed diastereoselectivity in the sulfanylation of the racemic **26** (*Scheme 29*, Y = H; R = Me), is due to a preferential attack of sulfur elec-

trophile at the unblocked faces of the ion-pairs **27** and **30**, in which the lone pair of the sulfinyl group is directed to the front, giving free access to the sulfanylating agent.

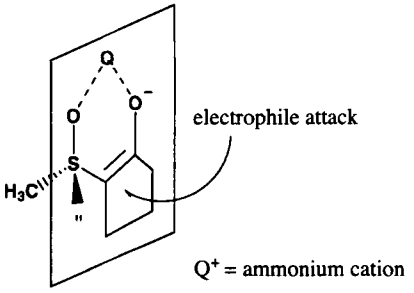
The sulfanylation of cyclic β-ketosulfoxides[82,83] is more diastereoselective as compared to the same reaction for the open chain analogs, due to restricted mobility of the cyclic structure. Therefore, when 2-methylsulfinylcyclopentanone, 2-methylsufinylhexanone and 2-methylsufinylindan-1-one (**32**, *Scheme 30*) are submitted to PTC sulfanylation using TEBA or some chiral catalysts, the corresponding α-sulfanylated β-ketosulfoxides **33** (R = Me, X = $(CH_2)_3$) are obtained as mixtures of diastereoisomers, except for the five-membered derivative **32** (*Scheme 30*, Entry 43; X = $(CH_2)_3$, *Table 2*).



Scheme 30

By substituting $MeSO_2STol$ for $MeSO_2SMe$, it is possible to prepare the solid $C_S{}^*S_S{}^*$ sulfanylated cyclopentanone sulfoxide **33** (*Scheme 30*; R = Tol, X = $(CH_2)_3$), that proved to be of $C_S{}^*S_S{}^*$ configuration by the X-ray analysis. This result is in accordance with those for some open-chain β-ketosulfoxides **26** (*Scheme 29*, Y = H, R = Me, i-Pr, t-Bu, Ph),[75] thus confirming the previous assumption that, upon formation of a tight ion-pair enolate/catalyst, the electrophilic attack occurs at the enolate face opposite to the methyl substituent at the sulfinyl group[82] (*Fig. 7*).

For analogous experiments, employing TEBA or QUIBEC and the indanone sulfinyl derivative **32** (*Scheme 30*, X = C_6H_4-CH_2, Entry 43 for indanone, *Table 2*), a decrease in diastereoselectivity is observed.[83] In this case, the enolate negative charge would be more dispersed, due to conjugation, leading to a looser interaction with the catalyst. Finally, in the case of cyclohexanone **32** (*Scheme 30*, X = $(CH_2)_4$) an even larger decrease in diastereoselectivity is observed (Entry 43, X = $(CH_2)_4$, *Table 2*), probably due to the increased mobility of the ring in comparison to the five-membered derivatives.[83]



Enolate / catalyst ion-pair for 32 (X = $(CH_2)_3$)

Fig. 7

It should be mentioned that in the sulfanylation of β-ketosulfoxydes, catalysts bearing a free OH group (N-benzylquininium and N-anthracenylquinidinium chlorides) are more efficient than those in which the OH group has been alkylated, such as O-benzyl-N-anthracenylquinidinium bromide. This result suggests that, in the case of β-ketosulfoxides, hydrogen bonding of the OH group to the carbonyl and sulfinyl oxygens is vital for diastereoselection.[83]

VI. TABLES

Table 1. Non-stereoselective Sulfanylation Reactions

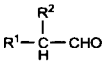
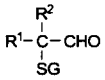
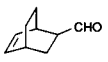
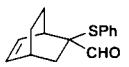
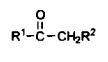
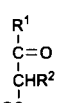
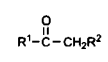
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)					Ref.
1		PhSSPh / KH	1/1/1	THF/r.t.		R^1	R^2	G	(%)	2
						Me	Me	Ph	42	
						Et	Et	Ph	82	
						Et	n-Bu	Ph	67	
						Me	s-Bu	Ph	81	
						-$(CH_2)_5$-		Ph	75	
						- CH_2CH=$CH(CH_2)_2$ -		Ph	58	
						Ph	Me	Ph	83	
						Me	C_9H_{19}	Ph	60	
						- $(CH_2)_7$ -		Ph	48	
2		MeO_2CSCl	1/1	$CHCl_3$/25°C to 35°C		Bn	H	CO_2Me	62	3
3		BnSCl	*	CCl_4		Me	Me	Bn	76	4
4		PhSSPh / KH	1/1/1.05	THF				48%		2
5		MeO_2CSCl	1/1	$CHCl_3$/25°C to 35°C		R^1	R^2	G	(%)	3
						Me	Me	CO_2Me	55	
						t-Bu	H	CO_2Me	65	
						p-ClC_6H_4	H	CO_2Me	72	
						Tol	H	CO_2Me	68	
						Me	p-$MeOC_6H_4$	CO_2Me	68	
						Me	CO_2Et	CO_2Me	72	
						Me	Bn	CO_2Me	68	
						Bu	Pr	CO_2Me	74	
6		F_3CSCl	1/1-1.4	-80°C to -20 °C		Me	H	CF_3	86	5
						Me	Me	CF_3	82	

Table 1. Continued...

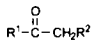
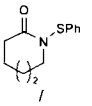
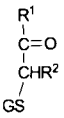
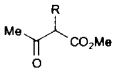
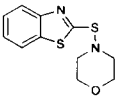
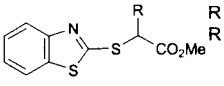
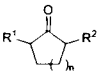
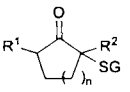
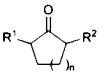
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
7		 / t-BuOK	3/1/3.3	DMSO/25°C	R^1 R^2 G (%) Me H Ph 62 t-Bu H Ph 81 Ph H Ph 83 Naph H Ph 30	6
8		PhthNSEt / t-BuOK	1/2/2	DMSO	Ph H Et 76[b]	7
9			1/1/2	DMSO	Ph SEt Et 81[b]	7
		$TolSO_2SG$ / LDA	1/1/1	THF / HMPA -60 °C	Ph H Bu 88 Ph H Bn 85 Ph H $(CH_2)_3CO_2Et$ 79 Ph H Allyl 74 Ph Et Et 96 Ph Et C_5H_{11} 98 Ph Et Bn 92	8
10		$PhSO_2SPh$ / LDA	*	THF/-78°C	TMS Bn Ph 62	9
11		 / NaH	1/2.2-2.4/2.4	THF	 MeO Bn Me 70[b] MeO p-MeOBn Me 57[b] MeO i-Bu Me 57[b]	10
12		PhSSPh / K_2CO_3	1/1/2	60°C /TBAHS as catalyst	EtO Ph Ph 63 EtO p-$MeOC_6H_4$ Ph 60 EtO p-ClC_6H_4 Ph 51 EtO p-$NO_2C_6H_4$ Ph 28 EtO a-Naph Ph 64 EtO p-MeC_6H_4 Ph 60	11
13		GSSG	1/1	Electro-chemical oxidation	C_3H_7 C_2H_5 Ph 26 Ph Me Ph 55 Ph Me Me 54 Ph C_2H_5 Me 53 Ph C_3H_7 Me 50	12
14		FCl_2CSCl $F_2ClCSCl$ F_3CSCl	1/1 1.5/1 1/1.3	-80°C	Me COMe FCl_2C 75 Me COMe F_2ClC 72 Me COMe F_3C 83	5
15			1 / 1	MeOH or EtOH reflux	 R = H 92% R = C_6H_{13} 98%	13
16		$TMS(CH_2)_2STs$ / LDA	*	THF -78°C	 R^1 R^2 n G (%) H H 1 CH_2CH_2TMS 90 H H 2 CH_2CH_2TMS 76 Bn H 2 CH_2CH_2TMS 75	14
17		$MeSO_2SMe$ / LDA	1/1/1.1	THF -10°C to -80°C	H H 1 Me 92 H H 2 Me 87 H H 3 Me 89 H H 8 Me 88 Me H 2 Me 69	15

Table 1. Continued...

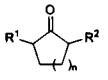
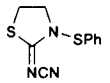
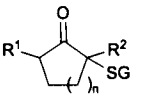
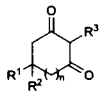
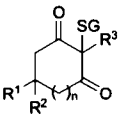
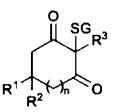
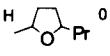
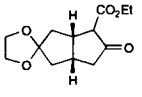
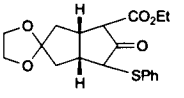
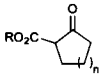
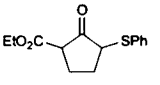
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
18		 / LDA	1/1.2/2	-78°C		16
					R^1 R^2 n G (%) H H 1 Ph 59 H H 2 Ph 76 H H 3 Ph 49	
19		 / t-BuOK	3/1/3.3	DMSO	H H 2 Ph 82	6
20		$PhSO_2SPh$ / LICA	1/1.1/1.2	-78°C ñ r.t.	R^1 R^2 n G (%) OMe H 2 Ph 93 H OMe 2 Ph 1	17
21		GSCl / NaH	1/2/2	THF		18
					R^1 R^2 R^3 n G (%) H H SPh 1 Ph 87 H H SMe 1 Me 75	
			1/1.2/1		R^1 R^2 R^3 n G (%) H H Me 0 Ph 89 H H H 1 Ph 86 H Me H 1 Ph 83 Me Me H 1 Ph 85 Me Me H 1 Ph 83 H H Me 1 Ph 86 H H CH_2CO_2Et 1 Ph 83	18
22		 /Py	1/1/*	CH_2Cl_2	Me Me H 1 cholest-5-en-3β-yl 54	19
23		 /Et_3N	1/1/1	Benzene reflux		20
					R^1 R^2 R^3 n G (%) H H H 1 Ph 97 H H H 0 Ph 62	
			1/1.1-2.0/1		H H Me 0 Ph 90 H H i-Pr 0 Ph 97	22
24			1/1/1.2	CH_2Cl_2	H H  0 Ph 70	21
25		PhSSPh / LDA	1/2.4/2.4	THF 0°C ! r.t.	 69	23
26		PhSSPh / 1) NaH 2) BuLi	1/2.4/1.5 and 1.2	THF 0°C ! r.t.	 85	23

Table 1. Continued...

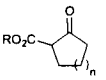
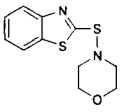
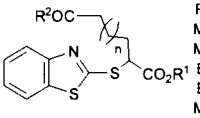
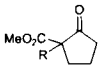
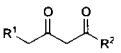
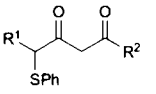
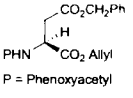
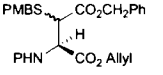
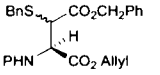
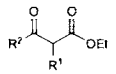
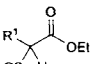
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
27		PhSCl / NaH	1/1/1	THF 0°C	 R: Me, Et, Et; n: 1, 2, 4; (%): 93, 85, 95	18
28			1 / 1	MeOH or EtOH reflux	 R^1: Me, Me, Et, Et, Me; R^2: OMe, OEt, OMe, OEt, OMe; n: 1, 1, 1, 1, 2; (%): 99, 73, 92, 58, 99	13
			1 / 1	Benzene or CH_2Cl_2	Me,  n: 1; (%): 97 or 87	13
29		PhSSPh / NaI (additive)	1/1/1	HMPA 165 to 175 °C	 R: H, Me; (%): 47, 49	24
30		PhSSPh / NaH and BuLi	1/1.5/1.2 and 1	THF	 R^1: H, H, H, Me, H, -CH_2CH_2-; R^2: MeCO, EtO, Me_2N, MeCO, Me; (%): 72, 65, 52, 72, 76, 61	25
31		PhSSPh / LDA	1/1/2.4	THF -15°C to 0°C	H, MeCO, 78 H, EtO, 64 H, Me_2N, 52 Me, MeCO, 47 H, Me, 79 -CH_2CH_2-, 47	25
32	 P = Phenoxyacetyl	$PMBSSO_2Tol$ / LHMDS	1/*/2	THF -78°C	 PMB = p-$MeOCH_2C_6H_4CH_2$	96%	
33		$BnSO_2SBn$ / LHMDS	1/*/2	THF -78°C		77%	26
34		GSO_2SG / EtONa	1/1/1.1-1.9	EtOH r.t.	 R^1: n-$C_{10}H_{21}$, Bn, CH_2CH=CH (n-C_5H_{11}), Bn; R^2: Me, Me, Me, Me; G: Me, Me, Me, Ph; (%): 98, 99.5, 92, 92	27
35		GSSG / EtONa	1/2-3/1.5		Bn, Me, Me, 15 Bn, Me, Ph, 75 n-$C_{10}H_{21}$Ph, Me, Ph, 92 CH_2CH=CH(n-C_5H_{11}), Me, Ph, 94	27
36		$MeSO_2SMe$ / NaH	1/2/2	DMSO r.t.	H, OH, Me, 64[b] Me, OH, Me, 55[b] Ph, OH, Me, 59[b]	28

Table 1. Continued...

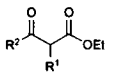
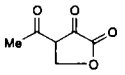
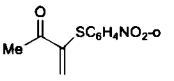
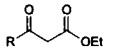
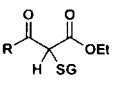
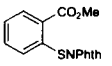
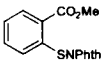
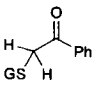
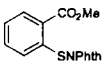
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
37		PhthNSMe / NaH			R^1 H: R^2 OH, G Me, (%) 64[b]; R^1 Ph: R^2 OH, G Me, (%) 66[b]	
38		MeSSMe / NaH			H: OH, Me, 58[b]	
39		o-$O_2NC_6H_4SCl$ / $KHCO_3$	1/0.43/1	1) base/ethanol 2) solvent removal 3) sulfanylating agent/THF 4) base/water	 92%	29
40		PhthNSPh / Et_3N	1/2/2	CH_2Cl_2 r.t.	 R = Me, G = Ph, 93%[b]	7
41		PhSH / Et_4NF	1/1/1	DMF r.t.	R Me: G Ph, (%) 86	30
42		GSCl	1/1.3	-80°C to 24°C	Me: FCl_2C 72; Me: F_2ClC 67; Me: F_3C 96	5
			1/1.2	-30°C to r.t.	Ph: CF_3 59	31
43		PhSSPh	1/1	Electrochemical oxidation	Me: Ph 10	12
44		 / NaH	1/0.67/1	THF r.t.	Me:  88	32
45		 / NaI (additive)	1/1/1	HMPA 165-175 °C	 Ph: Ph 36	24
46		$MeSO_2SMe$ / EtONa	1/1.2-2.5/1.2-2.1	EtOH r.t.	 R: G (%) 33; $n-C_{10}H_{21}$ Me 90; Bn Me 70; $(n-C_5H_{11})CH=CHCH_2$ Me 88; Ph Me 92; $CH_2CH_2CO_2Et$ Me 73; $CH(CH_3)CH_2CO_2Et$ Me 77; $CHPhCH_2CO_2Et$ Me 75	
		$PhSO_2SPh$ / EtONa	1/1.0-1.2/1.0-1.2	EtOH r.t. to 50°C	$n-C_{10}H_{21}$ Ph 90; Bn Ph 83; Ph Ph 90	33
47		 / NaH	1/0.67/1	THF r.t.	H:  78	32

Table 1. Continued...

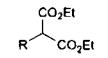
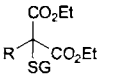
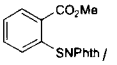
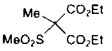
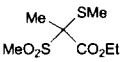
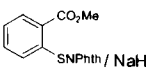
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
48		$F_2ClCSCl$ F_3CSCl	1/3.5 1/3	115°C -50°C to 107°C	R G (%) H CF_2Cl 4.7(44)[b] H CF_3 51.5 (15.5)[b]	34 34
49		PhthNSPh / Et_3N	1/2/2	CH_2Cl_2 r.t.	 H Ph 94[b]	7
50		PhSH / Et_4NF	1/1/1	DMF r.t.	H Ph 78	30
51		PhSSPh / NaI (additive)	1/1/1	HMPA 165-175 °C	 R^1 R^2 R^3 (%) Bu H Et 40 Bn H Et 46 Pr Me Et 60 Me Me Et 71 Bn Bn Et 66	24
52		F_3CSCl	1/1.2	$CHCl_3$	 X Y G (%) COPh $CONHPh$ CF_3 72 COMe $CONHPh$ CF_3 75	31
53		PhSH / Et_4NF	1/1/1	DMF	COPh COMe Ph 78 COPh COPh Ph 84	30
54		 / NaH	1/0.67/1	THF r.t.	COPh COMe  73 CN CO_2Et  74	32
55		PhSSPh / NaI (additive)	1/1/1	HMPA 165 to 175 °C	CN CO_2Et Ph 23	24
56		$MeSO_2SMe$ / DABCO (additive)	1/1.1/5	Toluene; 1)DABCO / reflux 2) $MeSO_2SMe$ / r. t.	 68 %	28
57		GSH / Et_4NF	1/1/1	DMF r.t.	 R G (%) H Ph 81 H p-$NO_2C_6H_4$ 41 H p-MeC_6H_4 85 H pyridine 68	30
58		 / NaH	1/0.67/ 1	THF r.t.	H  81	32

Table 1. Continued...

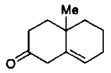
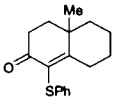
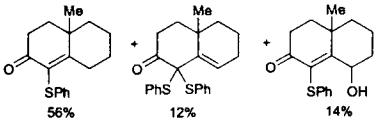
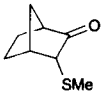
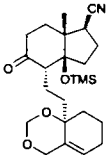
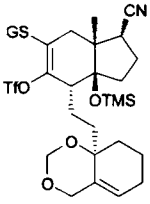
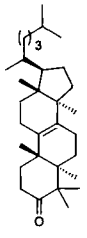
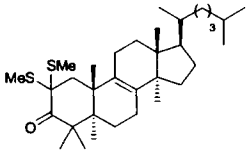
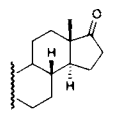
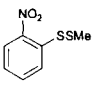
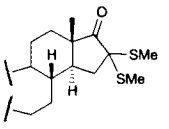
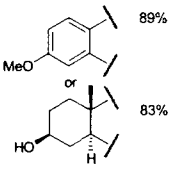
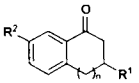
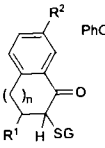
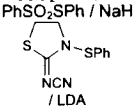
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
59		GSSG / NaOH	1/0.5/*	DMF / CCl_4 / H_2O	R G (%) H Ph 88 H p-ClC_6H_4 91 H p-MeC_6H_4 63 H  47 H  48 H $Me_2NC(S)$ 58 H $Et_2NC(S)$ 59 H  72	35
60		$MeSO_2SMe$ / EtONa	1/1.2/1.4	EtOH r.t.	 Bn Me 92 n-C_7H_{15} Me 94 n-$C_{12}H_{25}$ Me 92 Geranyl Me 90	36
61		$MeSO_2SMe$ / K_2CO_3	1/1.4/1.6	1)Me_2CO, reflux 2)MeOH, reflux	Bn Me 97 n-C_7H_{15} Me 95 n-$C_{12}H_{25}$ Me 95 Geranyl Me 89	36
62		PhSSPh / NaH	*	DME 25°C	 51%	37
63		$PhSO_2SPh$ / NaH	*	DME 25°C	 56% 12% 14%	37
64		$MeSO_2SMe$ / LDA	1/1/1.1	THF -10°C	 86%	15
65		MeSSMe or PhSSPh / KHMDS	*	THF -78°C 1)Base/ sulfanylating agent 2)Base/ $PhNTf_2$	 G (%) Me 90 Ph 95	38
66		 / NaH	1/*/2.2-2.4	THF r.t.	 84%	10

Table 1. Continued...

Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
67		 / NaH	1/*/2.2-2.4	THF	  89% 83%	10
68		PhSSPh /LDA	1/1.6/2.1	THF/-78°C		39
69		$TMS(CH_2)_2STs$/LDA	*	THF/-78°C		14
70		$MeSO_2SMe$ /LDA	1/1/1.2	THF/-10°C		15
71		$PhSO_2SPh$ / NaH	1/3/3	THF		40,41
72		 / LDA	1/1.2/2	THF/-78°C		16

	R^1	R^2	n	G	(%)
	$PhOCH_2CH_2$	OMe	0	Ph	84
	H	H	0	CH_2CH_2TMS	80
	H	H	1	Me	94
	H	H	1	Ph	70[b]
	H	H	1	Ph	41 (13)[b]

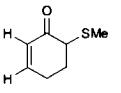
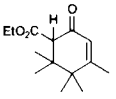
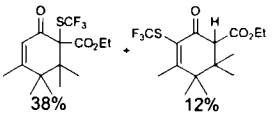
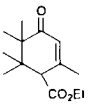
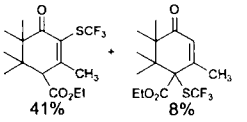
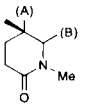
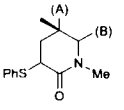
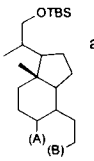
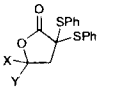
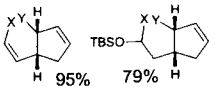
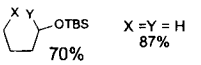
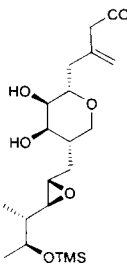
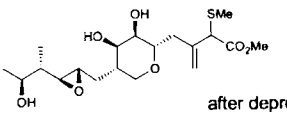
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
73		$MeSO_2SMe$ / LDA	1/1/1.2	THF -80°C	 71%	15
74		F_3CSCl	1/1	Pentane 0°C	 38% 12%	42
75		F_3CSCl	1/1	Pentane 0°C	 41% 8%	42
76		PhSSPh / LDA	1/1.2/4	THF -78°C to 0°C	  75% after desilylation	43
77		$PhSO_2SPh$ / LDA	1/2.1-2.8/ 1.2-3 for some cases	THF or THF / HMPA -78°C r.t.	  95% 79%  70% X =Y = H 87%	41 44 40
78		$MeSO_2SMe$ / LDA	1/5/1.5	THF	 70% after deprotection	45

Table 1. Continued...

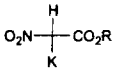
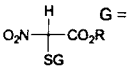
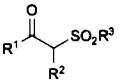
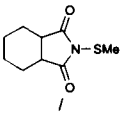
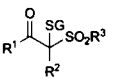
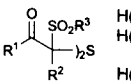
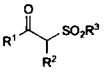
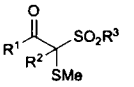
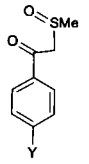
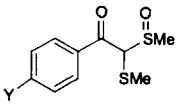
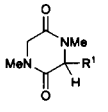
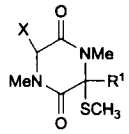
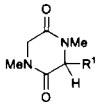
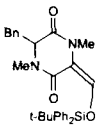
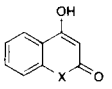
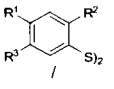
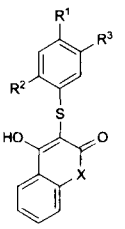
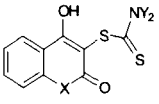
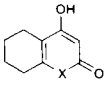
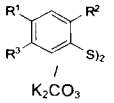
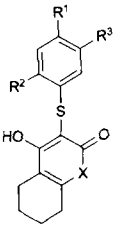
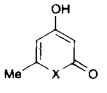
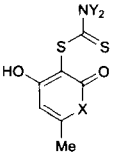
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
79		GSCl	*	THF 20°C, 2 h	 G = Ph or p-ClC$_6$H$_4$; R = Et or Bn 84-95%	46
80		 / t BuOK	*	DMSO	 R^1 R^2 R^3 G (%) Ph H Ph Me 90 Ph H Me Me 88	7
81		PhthNSEt / t-BuOK	*	DMSO	Ph SEt Me Et 87	
82		PhthNSCl PhthNSCl SuccNSCl	1/1 1/1.4 1/1.5	$CHCl_3$	 H(CF$_2$)$_3$ H Bn Phth 75 H(CF$_2$)$_3$ H Tol Phth 80 H(CF$_2$)$_3$ H Bn - 45	47 48 47
83		MeSSO$_2$Me / NaH	1/1.2/1.1	DMSO	 R^1 R^2 R^3 (%) OEt Me Ph 55 OEt Ph Ph 64	50
84		MeSSO$_2$Me / K_2CO_3	1/1.2/2.1	CH_2Cl_2 or Benzene r. t. TEBA as catalyst	OEt Me Ph 96 OEt Ph Ph 86 OEt Et Ph 70 OEt H Ph 75 OEt i-Pr Ph 39 OEt n-Hex Ph 86 OEt p-MeOC$_6$H$_4$ Ph 56 OEt p-ClC$_6$H$_4$ Ph 72 OEt p-NO$_2$C$_6$H$_4$ Ph 75 OEt p-MeC$_6$H$_4$ Ph 46	50
85		MeSSO$_2$Me or PhthNSMe / NaH	1/1/1.2 1/1/1.1	DMSO/r.t.	SEt Me Me 89 SEt H Me 60 SEt Bn Me 53	49
86		MeSSO$_2$Me / K_2CO_3	1/1/2	CH_2Cl_2 r. t. TEBA as catalyst	SMe H Ph 64 SMe Me Ph 81 SMe Et Ph 91 SMe Ph Ph 82	
87		MeSSO$_2$Me / K_2CO_3	1/1/2	Benzene/ CH_2Cl_2 r. t. TEBA as catalyst	 Y (%) H 67 Cl 45 Me 45 MeO 65	51
88		MeSSO$_2$Me / NaH	1/1/2	DMSO	Y (%) H 84 Cl 90 Me 58 MeO 45	51
89		MeSCl / Et_3N	1/1.3/1	THF/-100°C to 0°C	 R^1 X (%) CHO H 100	52

Table 1. Continued...

Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
90		MeSSMe / LDA	1/excess/ 1.2	THF/ -78°C	SMe 66%	
91		MeSSMe / LDA	1/5/1.15	THF/ -100°C	G (%) Me 82	52
92		Sulfur (monoclinic)/ LDA	1/2/1.15	THF/ -78°C	H 99[c]	
93		 / K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		53
94		$(Y_2NC(S)S)_2$ / K_2CO_3	1/1.1/2	DMF 90°C		53
95		 / K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		53
96		$(Y_2NC(S)S)_2$ / K_2CO_3	1/1.1/2	DMF 90°C		54

X	R^1	R^2	R^3	(%)
NMe	H	H	H	75
NMe	Cl	H	H	74
NMe	H	NO_2	H	64
NMe	H	CO_2H	H	87
NMe	Cl	Cl	Cl	82
NMe	NO_2	H	CO_2H	86
O	H	H	H	75
O	Cl	H	H	77
O	H	NO_2	H	57
O	H	CO_2H	H	91
NPh	H	H	H	49
NPh	Cl	H	H	41
NPh	H	NO_2	H	70
NPh	Cl	Cl	Cl	82
NBn	Cl	H	H	50
NH	Cl	Cl	Cl	75

X	Y	(%)
NMe	Et	74
NPh	Et	50
NPh	Me	56
O	Me	68

X	R^1	R^2	R^3	(%)
NPh	H	H	H	72
NPh	Cl	H	H	54
NPh	NO_2	H	H	51
NPh	H	NO_2	H	63
NPh	Cl	Cl	Cl	68

X	Y	(%)
O	Me	59
O	Et	48
NH	Me	51
NH	Et	46
NMe	Me	51
NMe	Et	52

Table 1. Continued...

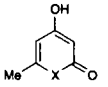
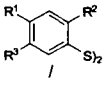
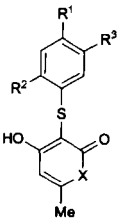
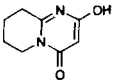
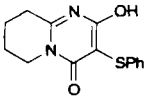
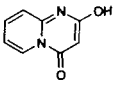
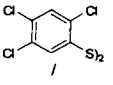
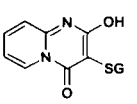
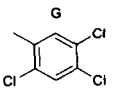
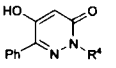
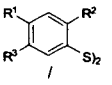
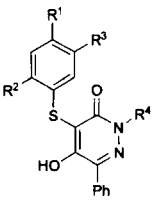
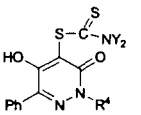
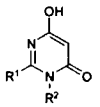
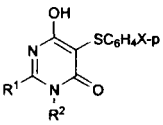
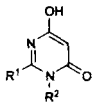
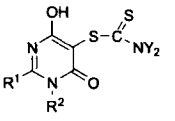
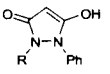
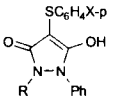
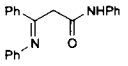
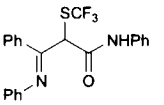
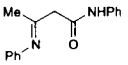
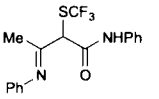
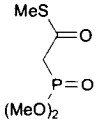
Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
97		 / K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		54
98		PhSSPh / K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		53
99		 / K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		53
100		$(Me_2NC(S)S)_2$ / K_2CO_3 $(Et_2NC(S)S)_2$ / K_2CO_3	1/1.1/2	DMF 90°C		53
101		 / K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		54
102		$(Y_2NC(S)S)_2$ / K_2CO_3	1/1.1/2	DMF 90°C		54
103		$(p\text{-}XC_6H_4S)_2$ / K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		54
104		$(Y_2NC(S)S)_2$ / K_2CO_3	1/1.1/2	DMF 90°C		54

Table 1. Continued...

Entry	Cmpd	Sulfanylating agent/base	Ratio	Conditions	Product (Yield %)	Ref.
105		$(p\text{-}XC_6H_4S)_2$ /K_2CO_3	1/0.5/1.5	DMF 90-95°C air (bubbled)		R: H, Ph, Ph; X: Me, Me, Et; (%): 65, 58, 66	54
106		F_3CSCl	1/1.2	$CHCl_3$		83%	31
107		F_3CSCl	1/3	$CHCl_3$		62%	31
108	$MeSOCH_2COY$	$MeSO_2SMe$ / K_2CO_3	1/1/2	Benzene/ TEBA as catalyst	$MeSOCHSMeCOY$	Y: OEt, SEt; (%): 25, 40	49
109		$MeSO_2SMe$ / NaH	1/1/1.2	DMSO		Y: OEt, SEt; (%): 31, 74	49
110		$MeSO_2SMe$ / K_2CO_3	1/1.5/2	Benzene	$(MeO)_2POCH(SMe)COSMe$ (%) = 0	$(MeO)_2POC(SMe)_2COSMe$ (%) = 63	55
111				Benzene/ TEBA	30	42	
				Benzene/ Aliquat	61	7	

a) ratio refers to the relation carbonyl compound / sulfanylating agent / base; b) bis-sulfanylated product; hydrogen at the sulfanylated carbon must be replaced by a GS group; c) after reduction; * not mentioned

Table 2. Stereoselective Sulfanylation Reactions

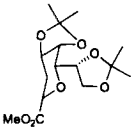
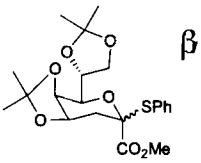
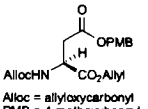
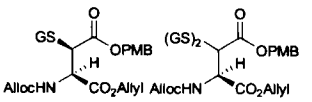
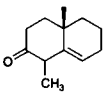
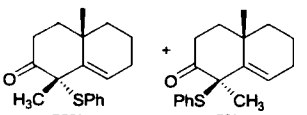
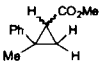
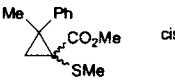
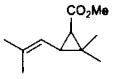
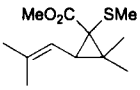
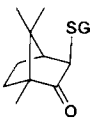
Entry	Cmpd	Sulafylating agent/base	Ratio	Conditions	Product (Yield%)	Ref.
1		PhSSPh / LDA	1/1.25/1.5	THF -50°C to r.t.	 51% $\beta\,\alpha$ = 85 : 15	56
2	 Alloc = allyloxycarbonyl PMB = 4-methoxybenzyl	TolSO$_2$SG / LHMDS	1/*/2	THF -78°C to -30 °C	 63 % 17 % G=2,4(MeO)$_2$C$_6$H$_3$CH$_2$	26
3		PhSO$_2$SPh / NaH	*	DME reflux	 58% 5%	37
4		MeSSMe / LDA	*	THF -78°C to 20°C	 87% cis / trans = 94 : 6	57
5		MeSSMe / LDA	1/5/3	THF -78°C	 61%	58
6	 (+)-camphor	TolSO$_2$SG / LDA	1/1.2/1	THF / HMPA -78°C	 G (%): Allyl 78; $CH_2CH{=}CHCH_3$ (E) 81; $CH_2CH{=}C(CH_3)_2$ 86; $CH_2CH{=}CHC_5H_{11}$ (E) 72; Me 74; n-Pr 61; Bn 80	59
7		TolSO$_2$SG / LDA	1/1.2/2.2	THF / HMPA -78°C	 Allyl 80; $CH_2CH{=}CHCH_3$ 77; $CH_2CH{=}C(CH_3)_2$ 75; $CH_2CH{=}CHC_5H_{11}$ (E) 78; Me 89; Et 75; Bn 73	59
8		TolSO$_2$SAllyl / LDA	1/2/3	THF / HMPA -78°C	G=Allyl endo / exo = 20 : 1 (quenching at r. t.) 77 % exo (quenching at -78 ° C)	60
9	(±)-camphor	PhSCl / BuLi	1/0.7/7	THF -72°C to r.t. or -20°C	G = Ph 40 % endo / exo 10 / 90 (at -78 °C) 35 / 65 (at - 20 °C)	61
10	(+)-camphor	MeSSMe / LICA	1/2/2	THF / HMPA	G=Me 40 %	62

Table 2. Continued...

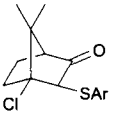
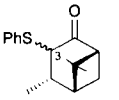
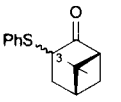
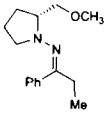
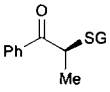
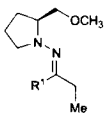
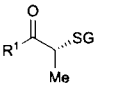
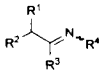
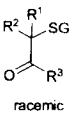
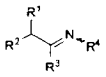
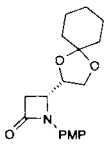
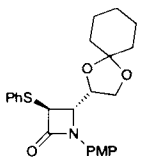
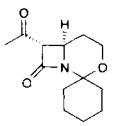
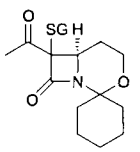
Entry	Cmpd	Sulafylating agent/base	Ratio	Conditions	Product (Yield%)	Ref.
11		$ArSO_2SAr$ / BuLi	1/1/1.1	THF	 58% Ar= p-ClC_6H_4	63
12		$PhSO_2SPh$ / LDA	1/1.1/1.2	THF -78°C to r.t.	 93% 3*S* / 3*R* = 4 / 6	64
13		$PhSO_2SPh$ / LDA	1/1.1/1.1	THF -78°C to r.t.	 3R 80% 3S 15%	65
14		GSSG / LDA	1/1/1.1	THF -100°C to r.t.	 G (%) ee (%): Me 56 92; i-Pr 56 95	66
15		GSSG / LDA	1/1/1.1	THF -100°C to r.t.	 R¹ G (%)[b] e.e.(%): Et Me 72 83; Et i-Pr 67 88; Ph Me 39 96; Ph i-Pr 53 87	66
16		GSSG / LDA	1/1/1	Et_2O -78°C	 racemic; R¹ R² R³ R⁴ G (%)[b]: Me Me H t-Bu Tol 94; H i-Pr H t-Bu Tol 93; H i-Pr H Me Tol 52; H $(CH_2)_4$ c-C_6H_{11} Me 93; H $(CH_2)_4$ c-C_6H_{11} Ph 87	67
17	 R^4 = (R)-(+)-α phenylethyl	GSSG / LDA	1/1/1	Et_2O -78°C	 R¹ R² R³ G (%)[b] e.e. (%): H i-Pr H Me 88 *; H i-Pr H Ph 92 *; H i-Pr H Tol 89 *; Ph Me H Me 93 *; Ph Me H i-Pr 91 13; Ph Me H Bn 79 *; Ph Me H Ph 95 42; Ph Me H Tol 94 51; H -$(CH_2)_4$- Me 92 *; H -$(CH_2)_4$- i-Pr 87 *; H -$(CH_2)_4$- Ph 92 *; H -$(CH_2)_4$- Tol 91 *	67
18		PhSSPh / LDA	1/1/1	THF -78°C to r.t.	 57%	68
19		$TolSO_2STol$/ Et_3N / $MeSO_2SMe$ / Et_3N	1/1/1.2	CH_2Cl_2 r.t. or 50°C	 G = Ph 76%; G= Me 83%	69, 70

Table 2. Continued...

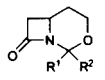
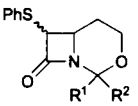
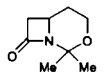
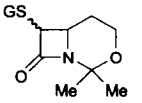
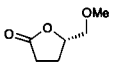
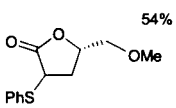
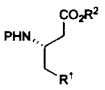
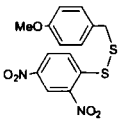
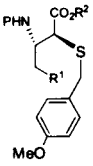
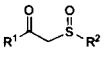
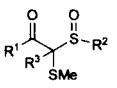
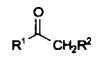
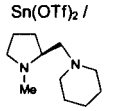
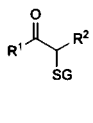
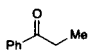
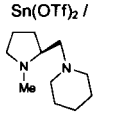
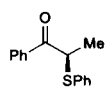
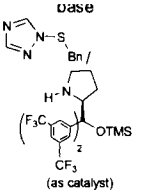
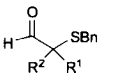
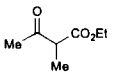
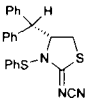
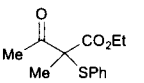
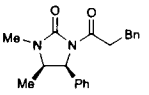
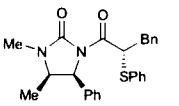
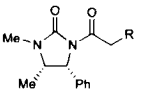
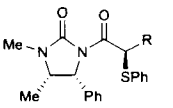
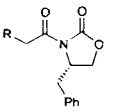
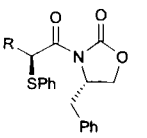
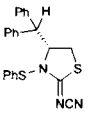
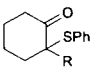
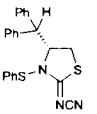
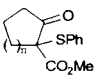
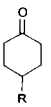
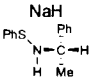
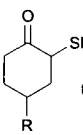
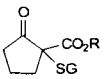
Entry	Cmpd	Sulafylating agent/base	Ratio	Conditions	Product (Yield%)	Ref.
20		PhSSPh / LDA	1/1/2.1	THF -78°C	 R¹ R² (%): Me Me 89 (trans); -(CH₂)₅- 72 (trans)	71
21		GSSG / LDA	1/1/2-2.5	THF -78°C	 G (%): 2-Pyridyl 75 (trans); $Me_2NC(=S)$ 66 (trans); Me trans / cis = 3	71
22		PhSSPh / LDA	1/1.3/1.2	THF / HMPA -78°C	 54%	72
23		 / LDA	1/1.4/2.4-3.4	THF -78°C	 P R¹ R² (%) anti : syn: Boc i-Pr Me 69 99 : 1; Boc Ph Me 68 >95 : 5; Boc CH_2OTBS Me 49 >95 : 5; Cbz CH_2SO_2NHt-Bu Me 57 >95 : 5; Cbz $(CH_2)_3NHBoc$ Me 69 >95 : 5; Boc CH_2CO_2t-Bu Me 24 >95 : 5; Boc CH_2CO_2t-Bu Allyl 20 >95 : 5	73
24		$MeSSO_2Me$ / NaH	*	DMSO	 R¹ R² η (%) d.e. (%): Ph Me 84 0; Ph Et 60 0; Ph i-Pr 63 0; Ph t-Bu 54 80; Ph Ph 66 20	74
			1/1/1.2		OEt Me 31 *; SEt Me 74 *	49
25		$MeSSO_2Me$ / K_2CO_3	1/1/2	Benzene/ CH_2Cl_2 r.t. TEBA as catalyst	R¹ R² (%) d.e. (%): Ph Me 57 0; Ph Et 66 0; Ph i-Pr 38 20; Ph t-Bu 73 100; Ph Ph 28 33	74
		$MeSSO_2Me$ / K_2CO_3	1/1/1	Benzene/ CH_2Cl_2 r.t. QUIBEC as catalyst	Ph Me 55 60; Tol Me 47 60	75
26		$PhSO_2SG$ / 	1/1.5-2/2-3	CH_2Cl_2 $Sn(OTf)_2$ / 	 R¹ R² G (%) e.e. (%): Ph Me Naph 78 85; Ph Et Naph 80 75; i-Pr Me Naph 72 50; t-Bu Me Naph 52 70; Me Ph 93 81; Bn Ph 91 82	76
27		PhSX / 	1/1.5/1.5-3	CH_2Cl_2 $Sn(OTf)_2$ / 	 X (%) e.e. (%): Cl 63 54; N-Succ 27 60; SO_2Ph 58 75; SO_2Naph 78 85	76

Table 2. Continued...

Entry	Cmpd	Sulafylating agent/base	Ratio	Conditions	Product (Yield%)	Ref.
28		base  (as catalyst)	1/1.3/0.1	Toluene		77
29		 / NaH	*	THF -78°C	 84%; 23% e.e.	16
30		PhSSPh / LHMDS $PhSO_2SPh$ / LHMDS	1/*/1	THF -78°C	 90% 93% d. e. > 96 %	78
31		PhSCl or PhSSPh or $PhSO_2SPh$ / LHMDS	1/*/1	THF -78°C	 82-97% R = Me, i-Pr, Bn d. e. > 96 %	78
32		PhSSPh / LDA	*	-78°C		79
33		 / NaH	*	THF -78°C		16
34		 / NaH	*	THF -78°C		16
35		 / Et_3N HCl (as catalyst)	catalyst used in 7 mol %	Benzene, THF, $CHCl_3$ or CCl_4		80
36		 / catalyst[d]	1/2/0.1	Toluene -30°C or r.t.		81

Product	R^1	R^2	(%)[c]	e.e. (%)
	i-Pr	H	81	98
	Me	H	60	95
	Et	H	85	96
	Bn	H	94	97
	Allyl	H	64	96
	t-Bu	H	83	95

Product	R	(%)	e.e. (%)
	CO_2Et	83	85
	COMe	88	71
	COt-Bu	75	48
	COPh	88	3
	CN	79	55
	CO_2Me	90	96
	CO_2i-Pr	86	77
	CO_2Ph	93	26

Product	n	(%)	e.e. (%)
	1	79	65
	3	76	22
	4	87	0

Product	R	(%)	optical yield (%)
	t-Bu	47-83	22-50
	Me	47-77	44-55

Product	R	G	(%)(e.e.)
	Et	Bn	91 (63)
	i-Pr	Bn	78 (71)
	t-Bu	Bn	88 (89)
	t-Bu	i-Pr	80 (79)
	t-Bu	2,4-dinitrophenyl	83 (83)

Table 2. Continued...

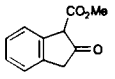
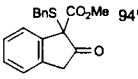
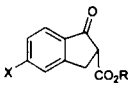
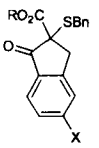
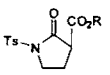
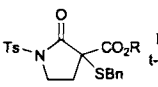
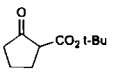
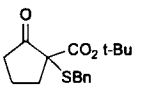
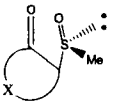
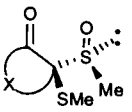
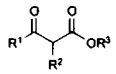
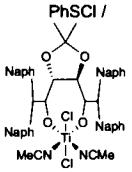
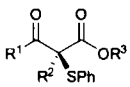
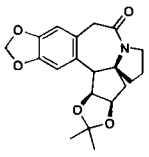
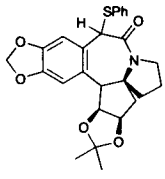
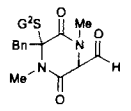
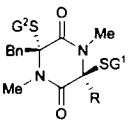
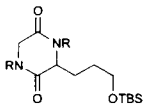
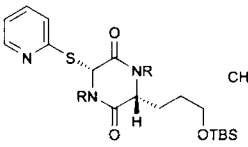
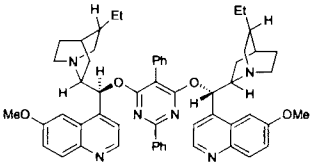
Entry	Cmpd	Sulafylating agent/base	Ratio	Conditions	Product (Yield%)	Ref.
37		 catalyst[d]	1/2/0.1	Toluene -30°C	 94%; e.e. 53%	81
38			1/2/0.1	Toluene -30°C or -40°C	 X R (%) e.e.(%) H Bn 84 60 Cl Me 95 51	81
39			1/2/0.1	Toluene -30°C or -40°C	 R (%) e.e. (%) Et 89 59 t-Bu 87 85	81
40			1/2/0.1	Toluene r.t.	 66%; 70% e.e.	81
41	 (±)	$MeSO_2SMe$ / LDA	1/1/1	THF	 X (%) d.e.(%) $(CH_2)_3$ 84 100 $(CH_2)_4$ 47 50	82
42		$MeSO_2SMe$ / K_2CO_3	1/1/2	Benzene/ CH_2Cl_2	$(CH_2)_3$ 39 100 $(CH_2)_4$ 0 0  0 0	83
43				Benzene/ CH_2Cl_2 TEBA as catalyst QUIBEC as catalyst NAQC[e] OBNAQB[f]	$(CH_2)_3$ 82 100 $(CH_2)_4$ 93 20  85 70 $(CH_2)_3$ 78 100 $(CH_2)_4$ 74 70  84 80 $(CH_2)_4$ 89 70 $(CH_2)_4$ 65 30	
44		PhSCl /  (as catalyst)	catalyst used in 5 mol%	Toluene r.t.	 R^1 R^2 R^3 (%)(e.e.) Me Me Et 94 (53) Me Me t-Am 80 (87) $(CH_2)_3$ t-Bu 84 (88) Me Me t-Bu 86 (88) Et Me t-Bu 80 (87) Et Me Ar 95 (86) Ar = 2,4,6-$(C_3H_7)_3C_6H_2CH$;	84
45		$PhSO_2SPh$ / LDA	1/4/2	THF / HMPA -78°C	 85%	85

Table 2. Continued...

Entry	Cmpd	Sulafylating agent/base	Ratio	Conditions	Product (Yield%)	Ref.
46		MeSCl or Ph_3CSSCl / Et_3N	1/1.25/1.25 1/1/1	THF -100°C	 G¹ G² R: Me Me CH_2OH; $SCPh_3$ $SSCPh_3$ CHO	52
47		 / LDA	1/1.3/1.2-1.3	THF -78°C to r.t.	 R (%): Me 92; Bn 86; CH_2OMe 79	86

a) ratio refers to the relation carbonyl compound / sulfanylating agent / base; b) after hydrolysis; c) isolated as the corresponding alcohol after reduction; d) catalyst =



e) N-Anthracenylquinidinium chloride as catalyst; f) O-Benzyl-N-anthracenylquinidinium bromide as catalyst; * not mentioned.

Table 3. Sulfanylation Reactions of Enolate Equivalents

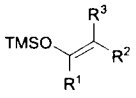
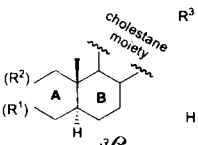
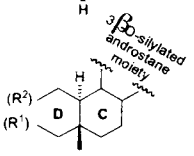
Entry	Cmpd	Sulfanylating agent/additive	Ratio	Conditions	Product (Yield%)	Ref.
1		$PhSO_2SPh$ / TBAF	1/1.2/1	THF -70°C	   $R^1 = OEt$ $R^2 = C_8H_{17}$	R³ G (%): cholestane moiety: H Ph 94; 3β-silylated androstane moiety: H Ph 74; H Ph 90	87
2		BnSCl	*	CH_2Cl_2	R^1 R^2 R^3 G (%): H Me Me Bn 85; H Et H Bn 79; H Et Me Bn 79; H i-Bu H Bn 86	88
3		MeSCl	*	Et_2O -40°C	Me Me $P(O)(OEt)_2$ Me 40	89
4		MeO_2CSCl	1/1	$CHCl_3$ 25°C to 35°C	CH_2Bn H H CO_2Me 73	3

Table 3. Continued...

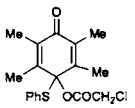
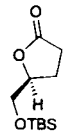
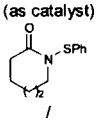
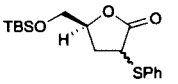
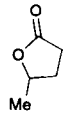
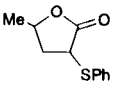
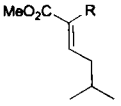
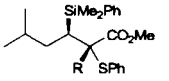
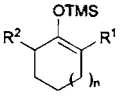
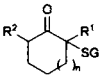
Entry	Cmpd	Sulfanylating agent/additive	Ratio	Conditions	Product (Yield%)	Ref.
5		 TMSOTf (as catalyst)	1/1/cat	MeCN -30°C	OMe H H Ph 99 OMe H Me Ph 100 OMe H Ph Ph 98 OMe H OMe Ph 99 Ph H H Ph 96 c-Pr H H Ph 81	90, 91
6		 TMSOTf (as catalyst)	1/1.25/1.25	1)LHMDS / -78°C 2) TMSCl / -78°C 3) sulfanylating agent 4) TMSOTf	 92% trans / cis = 9 : 1	92
7			1/1.25/1.25	1)LHMDS /-78°C 2)TMSCl /-78°C 3) sulfanylating agent 4)TMSOTf	 99% trans / cis = 3.7 : 1	92
8		PhSCl		1) $(PhMe_2Si)_2CuLi$ / THF / -78°C 2)TMSCl 3) PhSCl / THF / -78°C	 R (%) Me 55 H 47	93
9			1/1.2	CH_2Cl_2 0°C	 R^1 R^2 n G (%) H H 0 Ph 75 H H 1 Ph 70 H H 2 Ph 82 H H 3 Ph 92 H H 5 Ph 98 H H 7 Ph 86 H Me 1 Ph 85 Me H 1 Ph 76	94
10		 TBAF	1/1.2/1	-78°C	H H 0 Ph 45 (33)[b] H H 1 Ph 84 (12)[b] H H 2 Ph 95 Me H 1 Ph 76	16
11		 MeLi	1/1.2/2.2	-78°C	H H 0 Ph 44 (29)[b] H H 1 Ph 78 (6)[b] H H 2 Ph 79	16
12		$PhSO_2SPh$ / TBAF	1/1.2/1	THF -70°C	R^1 R^2 n G (%) H H 1 Ph 94 H Me 1 Ph 92 Me H 1 Ph 86	87

Table 3. Continued...

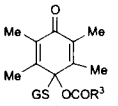
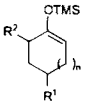
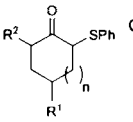
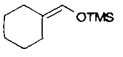
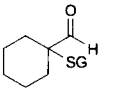
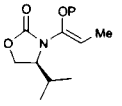
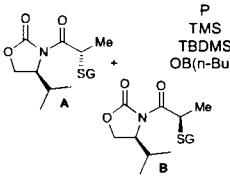
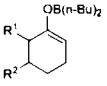
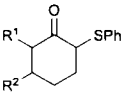
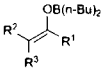
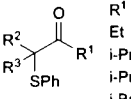
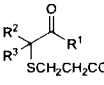
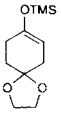
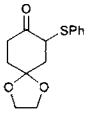
Entry	Cmpd	Sulfanylating agent/additive	Ratio	Conditions	Product (Yield%)	Ref.
13		 TMSOTf (as catalyst)	1/1/cat.	MeCN -30°C	R^1 R^2 R^3 n G (%) H H Me 0 Ph 98 H H Me 0 Me 94 H H Me 1 Me 94 R^1 R^2 R^3 n G (%) H H CH_2Cl 0 Ph 99 H H CH_2Cl 1 Ph 95 H H CH_2Cl 0 p-$MeOC_6H_4$ 99 H H CH_2Cl 0 p-$NO_2C_6H_4$ 100 H H CH_2Cl 1 Ph 95 H H CH_2Cl 1 p-$NO_2C_6H_4$ 96	90, 91 90 91
14		 TMSOTf (as catalyst)	1/1.25/0.25	CH_2Cl_2 -78°C	 R^1 R^2 n (%) (cis : trans) OTBS H 1 77 1 : 5.5 H Me 1 60 1 : 1 t-Bu H 1 68 1 : 1 H H 0 84	92
15		GSCl	*	CH_2Cl_2	 G (%) Me 97 Et 98 Bn 83 Ph 98	88
16		PhSCl	*	CH_2Cl_2 -78°C or -100°C	 P G A : B (%) TMS Ph 83 : 17 90 TBDMS Ph 92 : 8 83 $OB(n\text{-}Bu)_2$ Ph 88 : 12 70	95, 96
17		PhSCHClMe / $TiCl_4$	*	CH_2Cl_2 -23°C	P G A : B (%) TMS Ph 60 : 40 68 TES Ph 60 : 40 37	95
18		PhSCl	1/1	CH_2Cl_2 -78°C	 R^1 R^2 (%) Me H 84 H Me 83	96
19		PhSCl	1/1	CH_2Cl_2 -78°C	 R^1 R^2 R^3 (%) Et Me H 87 i-Pr Me Me 91 i-Pr Me H 92 i-Bu H H 67 i-Bu Me H 82 n-Bu n-Pr H 99 Ph H H 95 Ph Me H 99 Ph Et H 99	96
20		$MeO_2CCH_2CH_2SCl$	1/1	CH_2Cl_2 -78°C	 n-Pent n-Bu H 66 i-Bu Me H 69	96
21		$PhS(NTs)N(Ts)SPh$	1/1.2	CH_2Cl_2 0°C	 65%	94

Table 3. Continued...

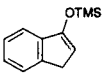
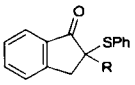
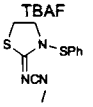
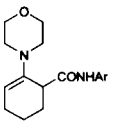
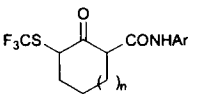
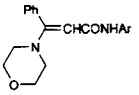
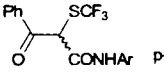
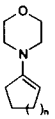
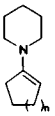
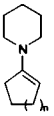
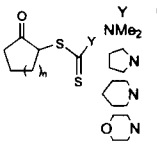
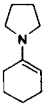
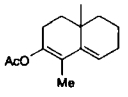
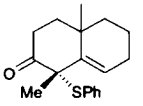
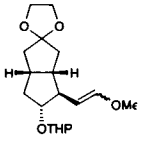
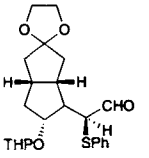
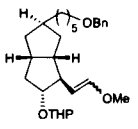
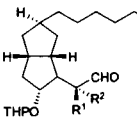
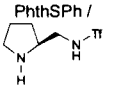
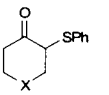
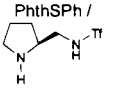
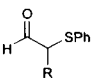
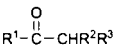
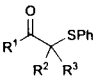
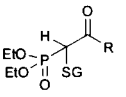
Entry	Cmpd	Sulfanylating agent/additive	Ratio	Conditions	Product (Yield%)	Ref.
22		 / TBAF	1/1.2/1	-78°C	 R: H (53%), SPh (28%)	16
		 / MeLi	1/1.2/2.2	-78°C	H (67%), SPh (13%)	16
23		F_3CSCl	1/1	Toluene / Pyridine -5°C to 0°C	 n: 1, Ar: Ph (16%); 1, p-ClC$_6$H$_4$ (21%); 2, Ph (45%); 2, p-ClC$_6$H$_4$ (27%)	97
24		F_3CSCl	1/1	Toluene / Pyridine r.t.	 Ar: Ph (43%), p-ClC$_6$H$_4$ (44%)	97
25		$TolSO_2SG$ / Et_3N	1/1/1.7	MeCN reflux	 n: 1, G: $C_{11}H_{23}$ (85%); 1, C_3H_7 (72%); 2, C_6H_{13} (70%); 2, Allyl (15%); 3, C_5H_{11} (73%)	98
26			1/1	0°C	1, Ph (72%); 2, Ph (83%); 3, Ph (85%)	16
27		$(YC(S)S)_2$ / Et_3N or NaOH or EtONa	*	CCl_4 / DMF / H_2O	 Y: NMe_2 (48%; 65%); (31%; 61%); (45%; 50%); (28%; 32%)	52
28		$TolSO_2SG$ / Et_3N	1/1/1.7	MeCN reflux	 G: C_3H_7 (67%), C_6H_{13} (68%)	98
29		$PhSO_2SPh$ / MeLi	1/*/2.2	THF r.t.		69% 37
30		PhSCl / K_2CO_3	1/excess/ 13	Toluene -78°C		91% 99
31		PhSCl / K_2CO_3	1/excess/ 13	Toluene -78°C	 R^1 R^2 G: SG H Ph (62%); H SG Ph (5%)	99

Table 3. Continued...

Entry	Cmpd	Sulfanylating agent/additive	Ratio	Conditions	Product (Yield%)		Ref.
32		PhthSPh / 	1/0.5/0.3	CH_3CN r. t.		X (%) CH_2 83 O 88 NMe 60	100
33		PhthSPh / 	1/0.5/0.3	CH_3CN r. t.		R (%) iPr 56 Et 56[d] C_4H_9 42[d] C_5H_{11} 52[d] C_6H_{13} 66 C_7H_{15} 63 C_8H_{17} 57[d] Me;Me 46	100
34		SuccNSPh / TsOH or BF_3•Et_2O	1/1/0.1	CH_3CN or CH_2Cl_2		R^1 R^2 R^3 (%) $SiPh_2Me$ $(CH_2)_4Br$ H 92 $SiPh_2Me$ $(CH_2)_3Br$ H 80 $SiPh_2Me$ $(CH_2)_2CHMeBr$ H 92 $SiPh_2Me$ $CHMe(CH_2)_3Br$ H 88 $SiPh_2Me$ Me H 90 TBS $(CH_2)_4Br$ H 83 TMS n-Bu H 86 H n-Bu H 19 H n-Pr Me 68 Me n-Bu H 24 n-Pr Me Me 22	101
35	$(EtO)_2POCH_3$	GSX / BuLi / RCN	1/1.2/1.1/1[e]	THF -78°C to -5°C to -78°C		R G X (%) Ph Ph SPh 75 Ph Ph Cl 83 p-ClC_6H_4 Ph SPh 80 Tol Ph SPh 80 p-ClC_6H_4 Me SO_2Me 50	102

a) ratio refers to the relation carbonyl compound / sulfanylating agent / additive; b) bis-sulfanylated product; c) after hydrolysis; d) in admixture with bis-sulfanylated product; e) ratio refers to the relation phosphonate / sulfanylating agent / BuLi / nitrile; *not mentioned

VII. CONCLUSIONS

The sulfanylation reaction stands as the most important method for the introduction of a sulfur atom at the α position of a carbonyl or carboxyl group, allowing several further synthetic transformations. In the last three decades new methods and sulfanylating agents have been developed, with a special emphasis on chiral, regiodefined and catalytic versions. In this sense this classical reaction has been updated following the modern trends of organic synthesis, that include the seach for milder, efficient and green methodologies.

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