Enantioselective Routes to Sulfoxides Based Upon the Use of Carbanionic Leaving Groups

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Keywords: Carbanions / Asymmetric catalysis / Leaving groups / Sulfoxides

Several carbanionic leaving groups can be easily displaced from the sulfinyl group by organometallic reagents. The reaction follows a highly stereoselective course of inversion of configuration. Provided that a ready route to the precursor sulfinyl compound is available (e.g. an enantioselective oxidation of the corresponding sulfide), the process can be transformed into an easy and versatile procedure for the stereoselective synthesis of sulfoxides.

1. Introduction

The search for new methods leading to enantiomerically pure sulfoxides represents a synthetic theme of high interest because these chiral compounds are valuable intermediates[1,2] that have been widely used in asymmetric synthesis.[3,4]

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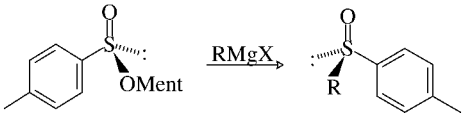
The Andersen procedure can be considered the classical method for the synthesis of chiral non-racemic sulfoxides.[5] This reaction is based upon the attack of organometallic reagents on a menthyl sulfinate. The nucleophilic species attacks the stereogenic sulfur centre, causing the stereocontrolled displacement of the menthoxide anion (Scheme 1).



Scheme 1

However, in spite of its widespread use, this procedure has been restricted practically to the synthesis of aryl or alkyl *p*-tolyl sulfoxides. Indeed, the starting sulfinate is obtained from a mixture of epimers at the sulfur centre, which

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MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

can be resolved by crystallisation, and a detailed protocol for the procedure is available in only a few cases, one of these being represented by menthyl *p*-toluenesulfinate.[6]

Menthyl alkanesulfinates, which would be necessary for the synthesis of dialkyl sulfoxides, cannot be easily prepared enantiomerically pure at the sulfur centre. Over the years, different leaving groups have been suggested as a way for extending the process to the synthesis of dialkyl sulfoxides. Several sulfinates have been introduced in which the leaving group is derived from a chiral alcohol different from menthol. In this respect, useful substrates are alkanesulfinates of *trans*-2-phenylcyclohexanol[7] or diacetoneglucose.[8] At least in principle, these sulfinates could yield dialkyl sulfoxides upon reaction with alkyl Grignard reagents and this was clearly shown by Alcudia et al. in the case of the alkanesulfinates of diacetoneglucose.[8] Dialkyl sulfoxides were also obtained from *N*-(alkylsulfinyl)oxazolidinones.[9]

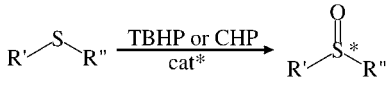
Another strategy leading to chiral sulfoxides is based upon the consecutive displacement of two equal (oxygen) or different (oxygen and nitrogen) leaving groups from a suitable sulfinyl compound. In the Kagan methodology,[10] a chiral cyclic sulfite was submitted to two sequential reactions with organometallic reagents to give enantiomerically pure sulfoxides, including dialkyl sulfoxides. However, the first step of the procedure is not always regioselective and the ratio between the two resulting sulfinates depends upon the organometallic reagent used.

A cyclic sulfamidite prepared from ephedrine has been used by Wudl et al.[11] In a first step, Grignard reagents are used to cleave the sulfur−oxygen bond. The subsequent reaction of the intermediate sulfinilamide with organolithium compounds yielded the desired sulfoxides. However, the reaction is not fully stereoselective in the sulfur−nitrogen bond cleavage, a drawback which was later overcome by using organoaluminium compounds.[12]

Very recently, improved protocols of this double displacement strategy have been reported. Garcia Ruano et al.[13] introduced the use of an *N*-acylated sulfamidite prepared from norephedrine. Organometallic reagents were used to cleave first the sulfur-nitrogen bond and then the sulfur-oxygen bond. Several sulfoxides, including a couple of examples of the dialkyl type, were reported. Similar lines have also been followed by Senanayake et al.[14] using an *N*-sulfonyl-sulfamidite formed from norephedrine.

All the above strategies require the separation of diastereomers or, at least, the use of a stoichiometric amount of the chiral compound necessary for the production of the starting material, a process which is not always straightforward.

An alternative approach to chiral non-racemic sulfoxides is the direct oxidation of the corresponding sulfides. The transformation can be easily performed by a variety of microbiological[15] and chemical processes.[16] In this context, special mention should be made of the oxidation devised by Kagan et al.,[17] and Modena and Di Furia et al.[18] who have used a modified Sharpless alkyl hydroperoxide/diethyl tartrate/Ti^{IV} system with or without added water (Scheme 2).



Scheme 2

The Uemura group[19,20] has adopted a catalytic procedure based upon the use of hydroperoxides in the presence of a complex between titanium isopropoxide, optically pure 1,1′-bi-2-naphthol (BINOL) and water.

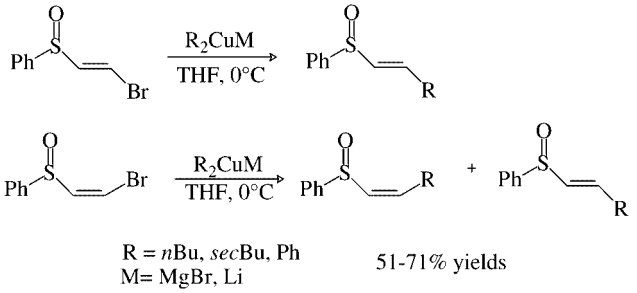
These reactions appear to be different from a mechanistic point of view. The Modena−Di Furia and Kagan procedures yield a low amount of the corresponding sulfone, while the Uemura system gives a high amount of the same product. When the BINOL system was used, the high *ee* values of the resulting sulfoxide were due to a combination of an enantioselective oxidation with an over-oxidation process occurring with kinetic resolution. However, since part of the sulfoxide must be consumed in the kinetic resolution process, the overall yields were not high.

Furthermore, independently of the catalytic system used, the enantioselective oxidation does not appear to be of general validity, particularly high *ee* values being obtained only in a number of cases dealing with aryl alkyl sulfoxides. As a consequence, the enantioselective oxidation of dialkyl sulfides through the same procedure cannot be considered a viable route to enantiomerically pure dialkyl sulfoxides.

Finally, it is worth noting that alkyl *tert*-butyl sulfoxides have been obtained by a procedure which combines the two types of strategies described above and based upon the oxidation process and the heteroatom substitution, respectively. (*R*)-*tert*-Butyl *tert*-butanethiosulfinate has been produced by an enantioselective oxidation of di-*tert*-butyl sulfide, and then this compound reacted with alkyl Grignard reagents to give alkyl *tert*-butyl sulfoxides.[21]

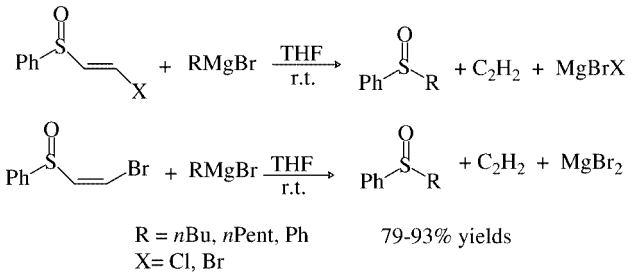
2. Reactions with Halovinyl Sulfoxides

In connection with our work on the cross-coupling reactions between 2-halovinyl sulfoxides and organometallic reagents, we found that the expected product resulting from carbon-carbon bond formation can be obtained by using organocopper compounds (Scheme 3).[22]



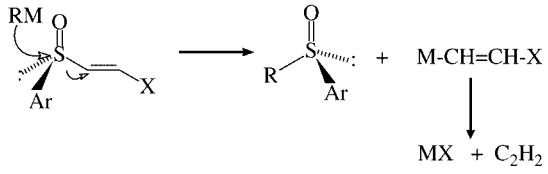
Scheme 3

However, Grignard reagents give products in which the halovinyl moiety has been displaced, with formation of the corresponding diaryl or aryl alkyl sulfoxides (Scheme 4).



Scheme 4

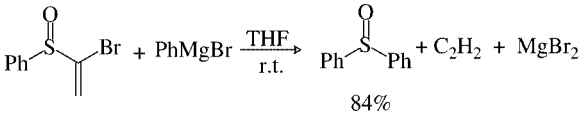
On the basis of the obtained results, a likely mechanism was considered to involve attack at the sulfur centre, with the displacement of the halovinyl moiety, which then decomposes to give acetylene (Scheme 5).



Scheme 5

In this type of process, the use of organolithium compounds appears to be less satisfactory in terms of reaction yields (43−47%).

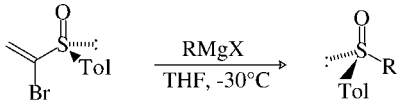
1-Halovinyl aryl sulfoxides have also been studied with similar reagents.[23] The Grignard reagent was found to attack the sulfur centre, with displacement of the halovinyl group (Scheme 6).



Scheme 6

The possibility of displacing carbanionic leaving groups from sulfoxides has a few precedents in the literature, in particular in the work of Johnson,[24] Durst,[25] Hojo[26] and Furukawa.[27] However, in the cases where stereochemistry was studied, the optically active starting sulfoxides were obtained by the Andersen procedure and the results observed did not appear of special interest with respect to the possibility of setting up a novel enantioselective procedure leading to sulfoxides.

In our laboratories, the investigation of the stereochemical aspects of these reactions was performed with (*S*)-1-bromovinyl *p*-tolyl sulfoxide. This compound was obtained from *p*-tolyl vinyl sulfoxide, which, in turn, was prepared by an Andersen procedure. When this sulfoxide was reacted with Grignard reagents, the attack of the organometallic species at the sulfur stereogenic centre caused the release of a carbanionic leaving group, which led to full inversion of configuration (Scheme 7).



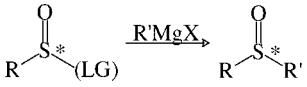
73-86% yields

R = Et, *n*Pr, *i*Pr, *n*Bu, Ph

Scheme 7

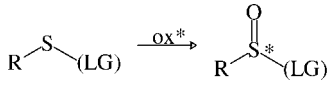
3. The Synthetic Project

Our work on the reaction between 1- or 2-halovinyl sulfoxides and Grignard reagents, with the smooth displacement of a carbanionic leaving group, was for us a clear indication of the possibility of devising a route to sulfoxides based upon the use of carbanionic leaving groups. We reasoned that a sulfinyl compound bearing a carbanionic leaving group (LG) could easily be transformed into a variety of sulfoxides according to Scheme 8.



Scheme 8

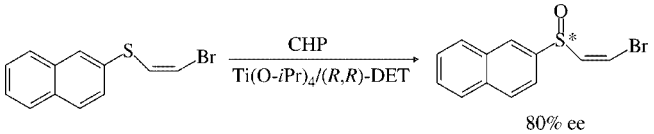
In principle, the necessary sulfinyl compound could be obtained by an enantioselective oxidation of the corresponding sulfide (Scheme 9).



Scheme 9

At the outset, the critical point of the synthetic project was considered to be the need for a high enantioselectivity in both oxidation and displacement steps.

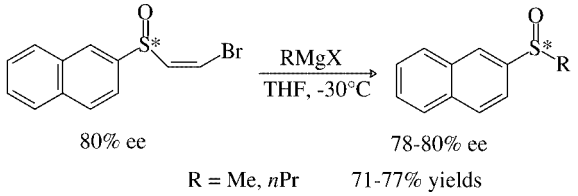
2-Naphthyl 2-bromovinyl sulfoxide appeared to be a good candidate for testing the validity of our strategy.[23] This compound was obtained in 80% *ee* by an enantioselective oxidation with cumene hydroperoxide in the presence of a stoichiometric amount of a complex between titanium isopropoxide and (*R*,*R*)-diethyl tartrate (Scheme 10).



80% ee

Scheme 10

The sulfoxide was then reacted with alkyl Grignard reagents to obtain alkyl 2-naphthyl sulfoxides with almost the same enantiomeric purity (Scheme 11).

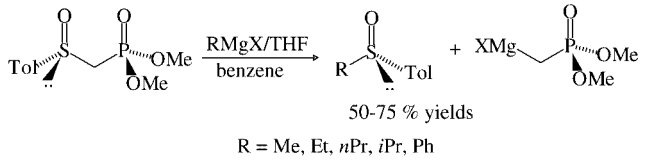


Scheme 11

At this point of our research, rather than improving the method based upon halovinyl sulfoxides, it appeared more convenient to turn our attention towards other sulfinyl compounds bearing potential carbanionic leaving groups.

3.1 Studies of Sulfinylmethylphosphonates

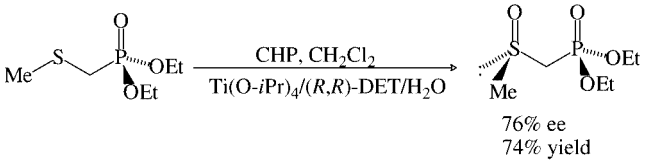
During an investigation of the Horner–Wadsworth–Emmons olefination of sulfinyl compounds,[28] we observed another displacement of a carbanionic leaving group.[29] Dimethyl (*S*)-(*p*-tolylsulfinyl)methylphosphonate was treated with aryl or alkyl Grignard reagents, with the formation of the corresponding aryl or alkyl *p*-tolyl sulfoxides and the release of the anion of dimethyl methylphosphonate as a new carbanionic leaving group (Scheme 12).



Scheme 12

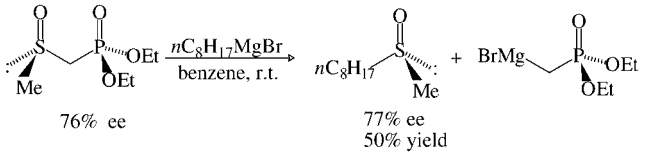
This reaction also occurred with full inversion of configuration. The organometallic reagent could either metallate the substrate at the methylene group or displace the carbanionic leaving group, but it was possible to drive the reaction towards a prevailing displacement by a suitable choice of the reaction solvent. In this respect, we found that benzene was superior to THF in terms of isolated yields of the desired chiral sulfoxides.

Originally, chiral dimethyl (*p*-tolylsulfinyl)methylphosphonate was prepared according to the Andersen procedure.[30] However, since the corresponding diethyl (arylthio-) or (alkylthio)methylphosphonates are commercially available, we evaluated the possibility of producing the starting material for this carbon-for-carbon substitution by an enantioselective oxidation. Diethyl (*R*)-(methylsulfinyl)-methylphosphonate was obtained with 76–80% *ee* by a hydroperoxide oxidation in the presence of a titanium/diethyl (*R*,*R*)-tartrate (DET) complex at −20 °C (Scheme 13).[31]



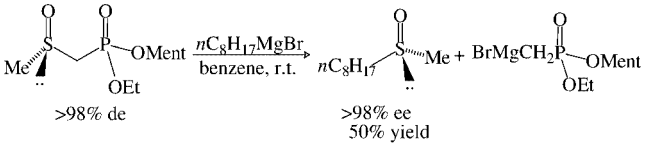
Scheme 13

The same enantiomeric purity was measured after the displacement of the anion of diethyl methylphosphonate by a Grignard reagent (Scheme 14)



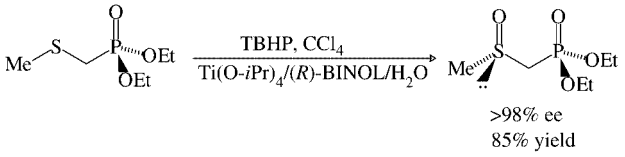
Scheme 14

Furthermore, when an ethyl menthyl (S_S)-(methylsulfinyl)-methylphosphonate (> 98% *de*), obtained by oxidation of the corresponding sulfide, was subjected to the displacement with alkyl Grignard reagents, a dialkyl sulfoxide (> 98% *ee*) was produced (Scheme 15).[31]



Scheme 15

A remarkable improvement of the procedure was achieved by introducing a new chiral ligand into the titanium complex involved in the enantioselective oxidation.[32] When (*R*)-BINOL was used in conditions different from those used by the Uemura group,[19,20] an enantioselective oxidation in high yields and very high enantiomeric purity occurred at room temperature. In particular, diethyl (*S*)-(methylsulfinyl)methylphosphonate was obtained in 85% yield and in greater than 98% *ee* (Scheme 16).

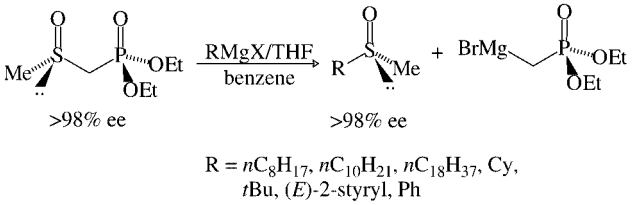


Scheme 16

High values of enantioselectivity were also obtained when (ethylthio)- or (phenylthio)methylphosphonate were oxidised (91% and 94% *ee*, respectively). Therefore, the enantioselective catalytic oxidation of (alkylthio)- or (phenylthio)methylphosphonates with a titanium/BINOL complex

represents a simple and straightforward route to precursors of sulfoxides with high enantiomeric purity. The process is easy, uses a small amount of the chiral auxiliary, works at room temperature and leads to sulfinyl derivatives in which the amount of undesired sulfone is minimal. This result could suggest that the oxidation is a genuine fully enantioselective process, without a significant contribution from kinetic resolution. The separation of the products from the chiral ligand is very simple, and, consequently, it should be possible to scale up the procedure to a multigram scale.

In the second step, the chiral non-racemic sulfinylmethylphosphonate was treated with an alkyl, alkenyl or aryl Grignard reagent with the displacement of the methylphosphonate anion and the production of the chiral non-racemic sulfoxide (Scheme 17).[32]



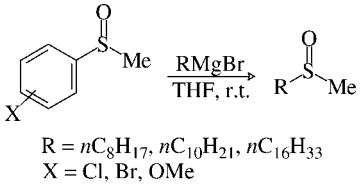
Scheme 17

The isolated yields of the sulfoxides prepared were moderate (43−50%), due to the competing metallation of the starting material by the organometallic compound. However, this drawback was overcome since the unchanged sulfinylmethylphosphonate could be recovered and re-used. Furthermore, for some cases, we devised a procedure for recovering the metallated species in situ, by methylation of the carbanion and subsequent reaction with fresh Grignard reagent. Using this procedure, an improvement of the yields was obtained (61−86% isolated yields).

Summing up, the strategy described above represents a convenient method for the synthesis of a variety of methyl sulfoxides with high *ee*'s.

3.2 Substituted Aryl Groups as Carbanionic Leaving Groups

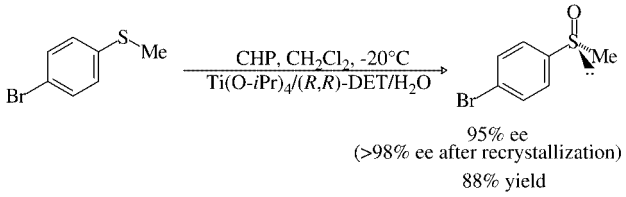
After a preliminary study on substituted aryl methyl sulfoxides, we found that anisyl methyl sulfoxides or haloaryl methyl sulfoxides could react with alkyl Grignard reagents with displacement of the whole aryl group and the formation of alkyl methyl sulfoxides (Scheme 18).[33]



Scheme 18

The reaction of *o*-, *m*- and *p*-anisyl methyl sulfoxides with alkylmagnesium bromide gave low isolated yields (up to 48%) of the corresponding alkyl methyl sulfoxide, due to the concurrent formation of side products; *o*-, *m*- and *p*-halophenyl methyl sulfoxides yielded satisfactory isolated yields (64−82%) of the alkyl methyl sulfoxide. When the reactivity order was evaluated, no significant reactivity difference was observed between *p*-chloro- and *p*-bromophenyl methyl sulfoxides, or *m*-bromo- and *p*-bromophenyl methyl sulfoxides. However, *o*-bromophenyl methyl sulfoxide was found to be about twice as reactive as *m*- or *p*-bromophenyl compounds.

The stereochemical analysis of these reactions was performed by using chiral non-racemic substrates which were prepared by a cumene hydroperoxide enantioselective oxidation of the prochiral sulfides in the presence of a complex of titanium with diethyl tartrate. High enantioselectivities (80−97% *ee*) and good yields (67−94%) of chiral sulfoxides were obtained. In particular, *p*-bromophenyl methyl sulfoxide with a high *ee* value was easily obtained by an enantioselective oxidation (95% *ee*) and then it was recrystallised to give the enantiomerically pure sulfoxide (Scheme 19).



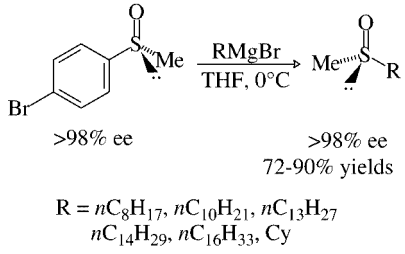
Scheme 19

The enantiomerically enriched aryl methyl sulfoxides were reacted with alkyl Grignard reagents. This reaction occurred with inversion of configuration and the enantiomeric excess of the resulting sulfoxides was found to be very close to the value measured for the starting material. The reactions could be driven towards the complete displacement of the carbanionic leaving group, with limited amounts of side products.

Due to the higher *ee* values, *p*-bromophenyl methyl sulfoxide became the most useful starting material from a synthetic point of view. Indeed, alkyl Grignard reagents were reacted with (*R*)-*p*-bromophenyl methyl sulfoxide with formation of alkyl methyl sulfoxides in high yield and with complete inversion of configuration. In particular, we focused on long chain alkyl methyl sulfoxides, which were needed in our investigations for their use as components of chiral metallomesogens.[34] The (*S*)-alkyl methyl sulfoxides were obtained with high enantiomeric purity (> 98%), and in good isolated yields (72−90%, Scheme 20).[33]

The reaction was also performed with secondary alkyl Grignard reagents. However, a low conversion was obtained in the reaction of tertiary alkyl Grignard reagents with *p*-bromophenyl methyl sulfoxide. Furthermore, aryl organomagnesium reagents reacted sluggishly. As a result, a partial racemisation was observed in the obtained aryl methyl sulfoxide.

A comparison between the present procedure and the approach based upon the use of the anion of dialkyl methyl-



Scheme 20

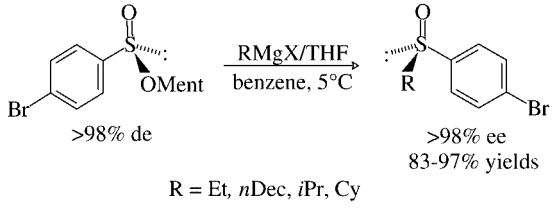
phosphonates as leaving group reveals that the two methodologies can be considered complementary for the synthesis of alkyl methyl sulfoxides.

4. Synthesis of Chiral Non-Racemic Dialkyl Sulfoxides by a Two Displacement Procedure

4.1 One Carbon-for-Oxygen Displacement Coupled with a Carbon-for-Carbon Displacement

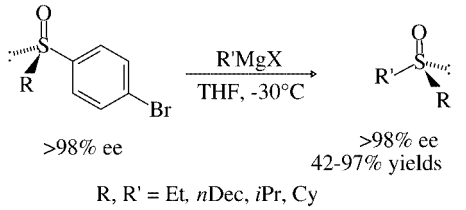
In the Introduction section, we referred to the two-displacement strategy which permits the synthesis of sulfoxides through a sequential substitution of the two heteroatom leaving groups present on the sulfur atom by organometallic reagents.[10−14]

We wanted to evaluate the possibility of inserting the use of carbanionic leaving groups into this strategy. To this end, we decided to combine our carbanionic leaving group approach with the classical displacement of the menthoxide anion from a suitable menthyl sulfinate.[35] After preliminary tests, menthyl *p*-bromobenzenesulfinate appeared to be a good candidate for a two-step synthesis of chiral sulfoxides. Indeed, this substrate reacted with Grignard reagents, undergoing a carbon-for-oxygen substitution followed by a carbon-for-carbon substitution. Accordingly, menthyl (*S*)-*p*-bromobenzenesulfinate in benzene was reacted with alkyl Grignard reagents in THF. Only the substitution of the menthoxide ion occurred. The formation of alkyl *p*-bromophenyl sulfoxides was found to take place in high yield (83−97%), high enantiomeric purity (>98% *ee*) and with inversion of configuration (Scheme 21).



Scheme 21

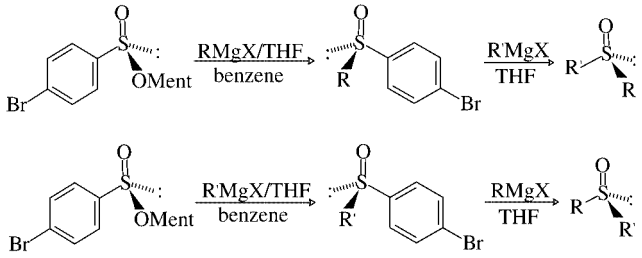
The second step of the procedure — the carbon-for-carbon substitution at the alkyl *p*-bromophenyl sulfoxide — was performed with alkyl Grignard reagents in THF, yielding the target dialkyl sulfoxide in good yields and with the same enantiomeric purity as the starting material (>98% *ee*, Scheme 22).



Scheme 22

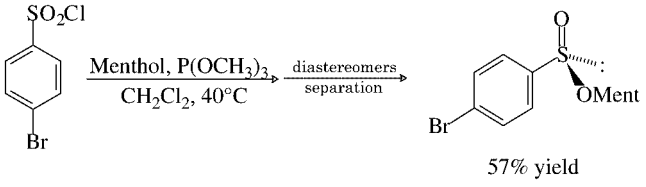
In this step, better yields were achieved when an *n*-alkyl *p*-bromophenyl sulfoxide was the substrate (76−97%), whereas *sec*-alkyl *p*-bromophenyl sulfoxides gave lower yields (42−60%).

Following the same procedure, both enantiomers of the desired sulfoxide could be obtained from the same substrate simply by choosing the right order of introduction of the alkyl substituents (Scheme 23).



Scheme 23

The possibility of transforming this double displacement sequence into a convenient route to dialkyl sulfoxides was strictly dependent upon the availability of the starting material. Menthyl *p*-bromobenzenesulfinate was prepared starting from a sulfinic acid derivative.[36,37] Following a literature report dealing with similar cases,[38] we found that it was possible to produce the compound on a larger scale by reacting natural menthol and *p*-bromophenylsulfonyl chloride, with the addition of trimethyl phosphite as a reducing agent. A mixture of diastereomers was obtained, the predominant one being the stereoisomer with the (*S*)-configuration at the stereogenic sulfur centre (Scheme 24).



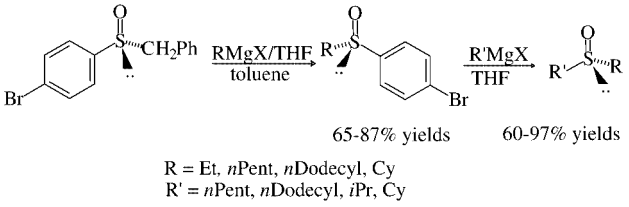
Scheme 24

The mixture of menthyl *p*-bromobenzenesulfinates was separated by crystallisation. A further amount of the (*S*)-stereoisomer could be recovered upon treatment of the mother liquor, enriched in the (*R*)-stereoisomer, with HCl (57% overall yield).[35]

4.2 Two Carbon-for-Carbon Displacements

In order to avoid the separation of the diastereomers, we considered it convenient to elaborate a strategy based upon two sequential carbon-for-carbon displacements. After the usual preliminary investigation, benzyl *p*-bromophenyl sulfoxide was the sulfinyl compound chosen for the reaction with organometallic reagents.[39] The possibility of displacing the *p*-bromophenyl group was already known from our previous work, whereas the decisive advantage was offered by the possibility of displacing the benzyl moiety at a faster rate than the *p*-bromophenyl moiety.

In fact, in preliminary experiments, we observed that the controlled reaction of this material with 1.5 equivalents of alkyl Grignard reagent caused the displacement of only the benzyl group, yielding the alkyl *p*-bromophenyl sulfoxide, without the displacement of the *p*-bromophenyl moiety. The isolated alkyl *p*-bromophenyl sulfoxide was then subjected to reaction with different Grignard reagent, as described in the previous sections. Both displacements were conducted at −30 °C. The execution of the synthetic plan is shown in



Scheme 25

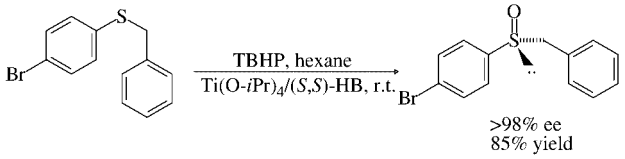
Scheme 25 with (*R*)-benzyl *p*-bromophenyl sulfoxide. The isolated yields are good and the reactions occur under complete stereochemical control (Scheme 25).

As in the case of the two-displacement procedure starting with menthyl (*S*)-*p*-bromobenzenesulfinate (see Scheme 23), both enantiomers of the required sulfoxide could be obtained by choosing the suitable substitution sequence.

The success of the whole synthetic procedure depends upon the ready availability of the starting material. Therefore, we considered of fundamental importance to investigate the production of (*R*)-benzyl *p*-bromophenyl sulfoxide by asymmetric oxidation.[39]

In preliminary work, we oxidised benzyl *p*-bromophenyl sulfide with *tert*-butyl hydroperoxide in the presence of a catalytic amount of a complex between titanium and BINOL, according to our previously reported procedure.[32] By using this method, it was possible to obtain the enantiopure desired sulfoxide but only in a 34% yield. A high amount of the corresponding sulfone was formed together with the sulfoxide and, very likely, the high enantiomeric purity of the product was due to a combination of a mechanism of enantioselective oxidation, followed by a kinetic resolution in the subsequent step. Lower enantiomeric purities were observed in the enantioselective oxidation with hydroperoxides in the presence of a complex between titanium and diethyl tartrate (up to 57% *ee*).

Better results were obtained by using *tert*-butyl hydroperoxide in the presence of a complex between titanium and (*S*,*S*)-hydrobenzoin (HB, 1,2-diphenyldiol, or stilbene diol), a chiral ligand which is commercially available and not expensive. Other groups[40,41] had already used this oxidation system, but we have modified the reaction conditions previously used (temperature, time, solvents and reaction ratios) significantly, in order to obtain the best enantioselectivity in the oxidation of benzyl *p*-bromophenyl sulfide. As a result of our efforts, by using (*S*,*S*)-(HB), (*R*)-benzyl *p*-bromophenyl sulfoxide was obtained in a high isolated yield (85%) and in high enantiomeric purity (>98% *ee*, Scheme 26).



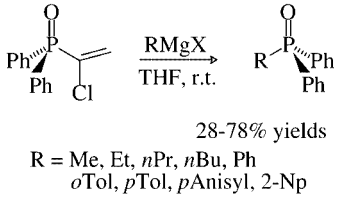
Scheme 26

When the reaction was performed in *n*-hexane, the produced sulfoxide was found to precipitate from the reaction media. After a simple recrystallisation, to remove traces of sulfone, the enantiopure sulfoxide (>98% *ee*) was ready for use. We had no difficulty in running the reaction on a 25-gram scale, and probably no difficulty should arise for a larger scale-up.

Finally, it is worth mentioning that, in this oxidation reaction, we observed a clear chiral amplification. Indeed, the use of a ligand with a given enantiomeric purity (e.g. 66% *ee*) led to the formation of a chiral product with a higher enantiomeric purity (e.g. 88% *ee*).

5. Extension of the Carbanionic Leaving Groups Strategy to the Synthesis of Phosphane Oxides

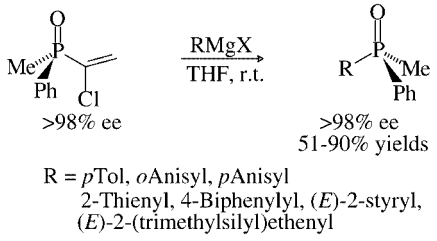
The use of carbanionic leaving groups in phosphorus chemistry was investigated in a joint work with Pietrusiewicz and co-workers. In a preliminary paper,[42] we found that alkyl or aryl Grignard reagents could react with (1-chlorovinyl)diphenylphosphane oxide, forming alkyl- or aryldiphenylphosphane oxides (isolated yields up to 78%; Scheme 27).



Scheme 27

The stereochemical investigation was performed on (*R*)-(1-chlorovinyl)methylphenylphosphane oxide. This compound was prepared by a straightforward synthetic sequence starting from (*S*)-(menthoxycarbonylmethyl)phenyl-

vinylphosphane oxide, a compound which could be obtained on a 20-gram scale.[43] Aryl or vinyl Grignard reagents reacted with (*R*)-(1-chlorovinyl)methylphenylphosphane oxide with formation of aryl- or vinylmethylphenylphosphane oxides and displacement of the whole chlorovinyl group. The reaction occurred with full inversion of configuration at the phosphorus centre to give a series of phosphane oxides in 51−90% isolated yields (Scheme 28).[44]



Scheme 28

These phosphane oxides had been previously prepared by an Andersen-like procedure, starting from menthyl methylphenylphosphinate,[45] a compound which is not easily available. Finally, it was found that, besides the halovinyl moiety, the methoxymethyl group could also be displaced by organometallic reagents.[46]

6. Conclusion

The carbanionic leaving group strategy outlined in this review permits the highly enantioselective synthesis of a variety of sulfoxides, mainly presenting a dialkyl structure. The catalytic enantioselective oxidation of sulfides is the most convenient procedure for preparing the precursor sulfinyl system. Therefore, all the problems connected with the preparation and the resolution of diastereomers can be avoided. The versatility of the procedure derives from the possibility of using a variety of leaving groups (halovinyl, dialkyl methylphosphonate, haloaryl and benzyl moieties). A similar approach can be adopted also in the synthesis of phosphane oxides and this increases the importance of the carbanionic leaving group strategy.

Further developments could enlarge the scope of the reaction. For instance, with a suitable choice of carbanionic leaving groups, it should be possible to extend the same methodology to the synthesis of any type of diaryl sulfoxide. Detailed mechanistic aspects, such as competition between ligand exchange and ligand coupling (observed in other related process[47]), also deserve attention in future work.

Finally, it seems rather easy to predict that a better knowledge of the displacement of carbanionic leaving groups from sulfinyl compounds will also be useful for the progress of investigations in which attention is focused on the fate of the leaving group.[48]

Acknowledgments

This work was financially supported in part by the Ministero dell'Istruzione, Università e Ricerca, Rome (National Project "Stereoselezione in Sintesi Organica. Metodologie e Applicazioni") and by the University of Bari.

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Received August 5, 2003
Early View Article
Published Online November 26, 2003

