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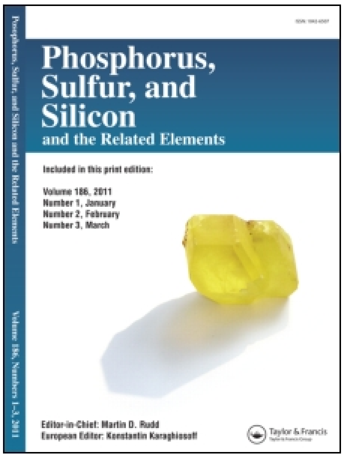

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Sulfonium Ylides. Application to the Synthesis of Optically Active Epoxides

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SULFONIUM YLIDES. APPLICATION TO THE SYNTHESIS OF OPTICALLY ACTIVE EPOXIDES

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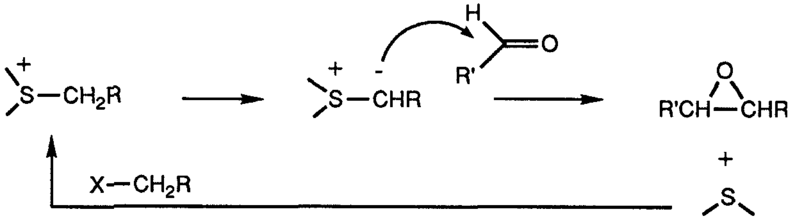
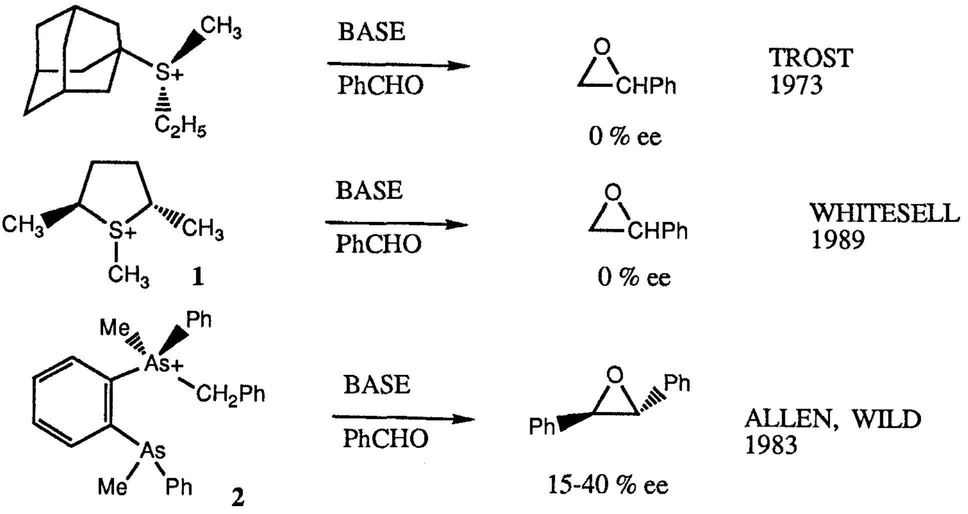
Abstract. The transfer of benzylidene groups from S-benzylsulfonium salts obtained from several optically active thiolanes and thianes to aldehydes and ketones yields optically active epoxides with high enatiomeric purity. In contrast, methylene transfer via the same auxiliaries leads to inactive epoxides. It is proposed that the difference in behaviour between these systems is best explained by assuming a 2+2 cycloaddition mechanism rather than the more commonly proposed nucleophilic anti-periplanar addition for the reaction of a sulfur ylide with a carbonyl component.

INTRODUCTION

Several years ago we became interested in the possibility of using optically active sulfur ylides for the preparation of enantiomerically enriched and possibly enatiomerically pure epoxides. The importance of epoxides in organic synthesis is well recognized and excellent routes to optically active epoxides, most notably the Sharpless epoxidation of allylic alcohols and related reactions, are available.[1] These methodologies typically involve the formation of carbon-oxygen bonds. In contrast, a carbon-carbon and a carbon-oxygen bond is formed in the reaction of a carbonyl compound with a sulfur ylide. The general scheme for this transformation using trimethylsulfonium methylide, whose reactivity was first carefully investigated by Corey and Chaykovsky,[2] is shown below.



The possibility that optically active epoxides might be accessed via sulfur ylides was first investigated by Trost in 1973.[3] Unfortunately, reaction of the ylide obtained from adamantylethylmethyl sulfonium tetrafluroborate with benzaldehyde furnished racemic styrene oxide. Whitesell reported even more discouraging results. The ylide obtained from **1** also afforded essentially racemic styrene oxide upon reaction with benzaldehyde.[4] There was however some encouraging data available concerning substituted ylides. Transfer of a benzylidene group from the optically active arsonium salt **2** via the benzyl ylide afforded trans-stilbene oxides with substantial asymmetric induction.[5]

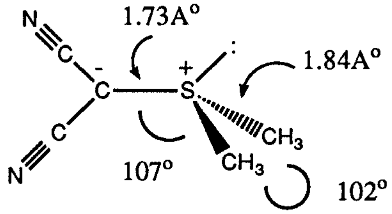


Prior to discussing our results it is perhaps useful to review relevant aspects of sulfonium salt and sulfur ylide structure and chemistry, including the possible mechanisms of the epoxide forming reaction.[6]

Sulfonium salts undergo stereomutation by a variety of mechanisms including (a) dealkylation-realkylation, (b) C-S heterolysis to a sulfide and a carbocation and again reversal of this process, and (c) pyramidal inversion. For the sulfonium salts studied by us pathways (a) and (b) are unlikely due to the choice of nonnucleo-philic counterions, the absence of substituents other than benzyl which would favour C-S bond cleavage and the use of a rather non-polar CH_2Cl_2 as solvent. Additionally, cyclic trialkyl sulfonium salts such as **1** typically require up to 50 h at 100°C in water as solvent for complete racemization. These observations, coupled with the design of the sulfide auxiliaries, which can yield only one, or strongly favour one sulfonium salt, allow us to conclude that sulfonium salt racemization should not come into play in this discussion.

The geometry of stabilized sulfur ylides has been determined by X-ray structural analysis. Data show that the geometry about the sulfur is nearly tetrahedral and that it does not change significantly in going from sulfonium salt to sulfur ylide. The carbon-sulfur bond length is slightly shorter, by about 0.1 A° in the ylide compared to that of sulfonium salts. Not surprisingly, the ylide carbon is planar in such ylides. e.g. Fig. A. The plane made by the ylide carbon and its two substituents bisects the Me-S^+-Me angle and the sulfur and carbon lone pair orbitals are orthogonal to each other. Ab initio studies show a pronounced minimum for this arrangement; maxima were found when these two adjacent lone pairs have dihedral angles of 0° and 180°.

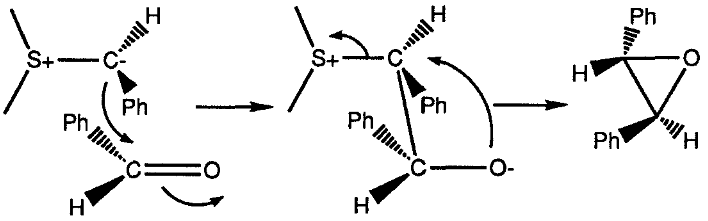
Fig A



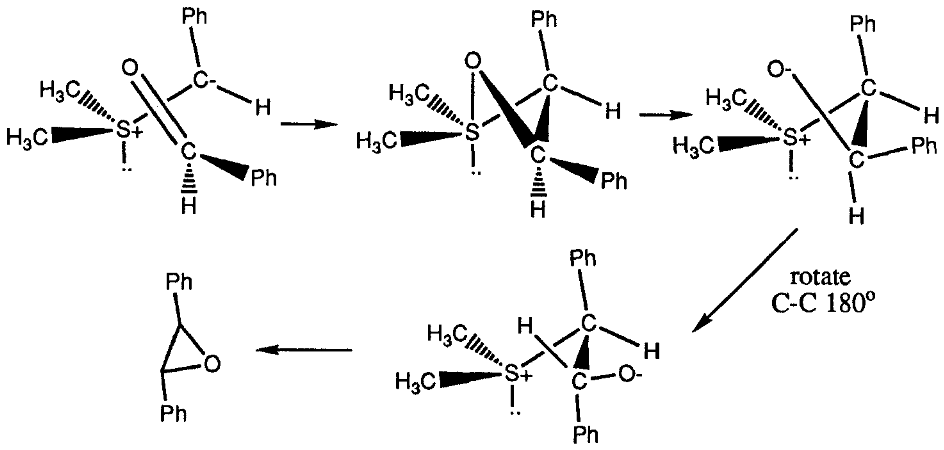
Experimental data obtained from rigid thiolanium cations show that α-hydrogens which are nearly orthoganal to the sulfur lone pairs exchange much faster than those which are co-planar. Sulfur ylides undergo stereomutation at sulfur more rapidly than the corresponding sulfonium salts. Again this of little concern due to the choice of the auxiliaries as discussed above.

Johnson and cowokers first proposed that epoxide formation from the reaction of a sulfur ylide and a carbonyl component involved nucleophilic attack of the ylide carbon on the carbonyl carbon in a head to tail fashion to generate an anti-betaine.[7] This can be converted directly into epoxide via an intramolecular S_N2, with the oxide acting as nucleophile and the sulfide as leaving group. Generation of betaines by deprotonation of preformed β-hydroxy sulfonium salts has shown that for non-stabilized ylides, including benzyl ylides, that betaines once formed are converted rapidly to epoxides and do not fragment to their ylide and carbonyl components.[8] It has also been proposed that betaines may result from a symmetry allowed π2s + π2a cycloaddition to give initially a 1,2-oxathietane. This intermediate must subsequently undergo C-S bond cleavage and a 180° rotation in order to arrive at the trans-betaine required for cyclization.[9]

BETAINE INTERMEDIATE



CYCLOADDITION MECHANISM



The observation that S-benzylsulfonium salts react with benzaldehyde to give mainly trans-stilbene oxide is compatible with both mechanisms. In the case of the head to tail addition the pathway leading to the trans-epoxide is sterically preferred. Similarly, in analogy with the formation of the cis-disubstituted oxaphosphatanes from non-stabilized phosphorus ylides and aliphatic aldehydes.[10] A $\pi 2s + \pi 2a$ approach will favour the cis-3,4 disubstituted oxathietane and hence eventual formation of the trans-epoxide.

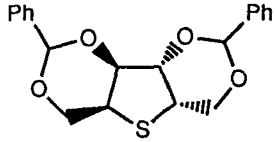
Theoretical studies of the $H_2S^+\text{-}CH_2^- + CH_2{=}O$ system[11] have shown that the sulfurane intermediate having an apical oxygen should form rapidly via a 2+2 cycloaddition, although no oxathietanes have been observed experimentally. The theoretical argument against this mechanism comes from the next step which according to the calculations is prohibitive, requiring nearly 40 Kcal/mol. Rather than open to a betaine, the oxathietane should revert to the the reactants. The head to tail addition to give the trans-betaine directly was calculated to be very favourable (10.6 Kcal/mol); this structure is according to the calculations, not a true intermediate but a transition state which leads directly to the observed epoxides.

The results described in this paper dealing with asymmetric induction in the transfer of both benzylidene and methylene groups to aldehydes and ketones appear to fit best the cycloaddition pathway rather than the nucleophilic antiperiplanar addition mode.

RESULTS

In our initial studies we concentrated on the use of C_2 symmetric thiolanes as chiral sulfide auxiliaries. The advantages of C_2 symmetry in auxiliaries is well recognized. In the case of the sulfur ylides such geometry would ensure that only one sulfonium salt could be formed, and from it probably mainly one ylide. Such a situation would likely increase the possibility of observing a high ee in the product epoxides.

The initial target molecules chosen were the thiolanes **3**, **4** and **5**; the first two are readily available from D-mannitol while **5** was prepared via a series of classic reactions starting with adipic acid and resolving the material at the thiolane-2,5-dicarboxylic acid, **6** stage.[12] In the case of **3**, all attempts to alkylate at sulfur failed and resulted either in the recovery of starting material or ring opened products. Benzylation of **4** and **5** was accomplished using benzyl bromide and silver perchlorate in CH_2Cl_2 to give the sulfonium salts **7** and **8**, respectively.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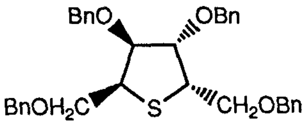
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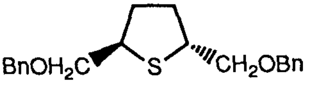
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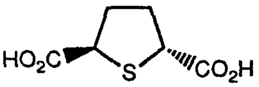
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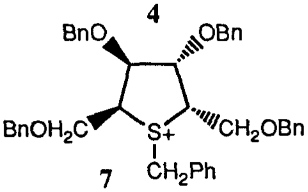
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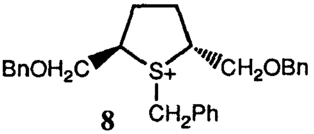

8

NMR investigation of the sulfonium salt **8** in CH_2Cl_2 showed that indeed only a single salt had formed; expectedly, this salt unlike its precursor no longer showed C_2 symmetry. Reaction of **8** with NaOH under phase transfer conditions in the presence of aromatic aldehydes gave R,R-trans-stilbene oxides (75% ee) in 30-50% yield; 80% of the thiolane auxiliary was recovered and showed no loss of optical activity. Similar results were obtained with the sulfonium salt **7**. These examples represented the first successful transfers of a benzylidene group from an optically active sulfonium salt with greater than 50% ee.

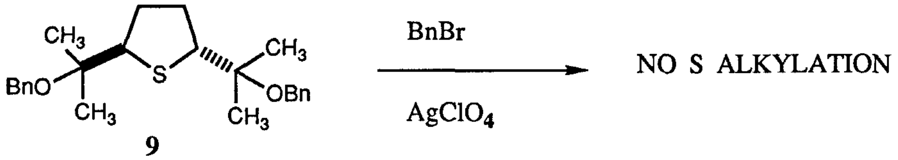
7 $\xrightarrow[\text{NaOH, PTC}]{\text{ArCHO, CH}_2\text{Cl}_2}$  + THIOLANE **4**

R,R, 45-55% 80% ee — 80-88 % recov.

8 $\xrightarrow[\text{NaOH, PTC}]{\text{ArCHO, CH}_2\text{Cl}_2}$  + THIOLANE **5**

R,R, 45-55% 75% ee — 50-60% recov.

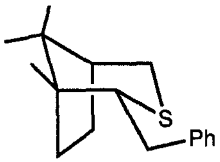
In principle, larger substituents at C-2 and C-5 in thiolanes should increase the ee's of the product epoxides. Unfortunately, attempted S-alkylation of the thiolane **9** with $PhCH_2Br/AgClO_4$ was unsuccessful yielding bibenzyl as the only identifiable product.



At this point it was clear that benzylidene and possibly other alkylidene groups could be transferred to carbonyl compounds with significant asymmetric induction. A number of difficulties had also become obvious, the most serious being efficient access to optically pure thiolane auxiliaries. Simple trans-2,5-dialkylthiolanes are not particularly easily available in enantiomerically pure form and furthermore are, as for example 2,5-dimethylthiolane, for the most part extremely unpleasant to work with. Those derived from D-mannitol or tartaric acid are easily prepared in optically active form and have no significant odour. However due to the presence of the many oxygen atoms, the sulfur nucleophilicity is low thus making the generation of sulfonium salts a formidable task.

We therefore decided that suitably designed non-C_2 symmetric sulfide auxiliaries could be of value in the synthesis of optically active epoxides. The requirements of such an auxiliary would be similar to those of the C_2 symmetric thiolanes, that is, alkylation should yield only one sulfonium salt and upon subsequent deprotonation mainly one ylide. To ensure high sulfur nucleophilicity the structure should be devoid of other electronegative heteroatoms.

The thiane **10** was considered to be an ideal candidate since alkylation would be expected to give only the equatorially oriented sulfonium salt **11**, deprotonation of which should give preferentially the ylide **12**. In this structure the large phenyl groups are opposed only by hydrogen atoms. Attack on the ylide by a carbonyl compound could realistically occur only from the back, that is the si face of the ylide, hereby fixing the stereochemistry of the ylide carbon as S. Trans epoxides formed by this route would have S,S and cis epoxides S,R stereochemistry.



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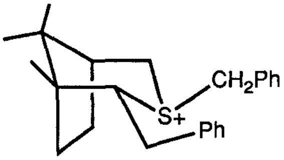

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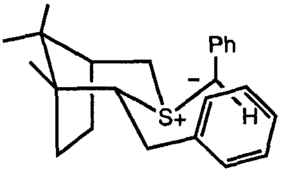
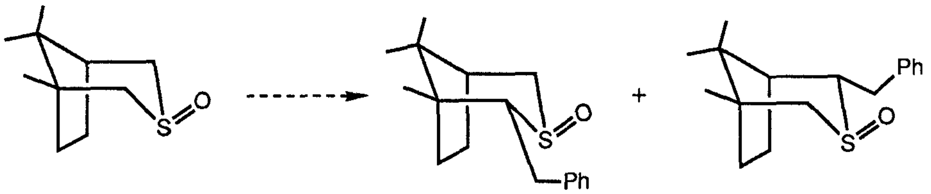


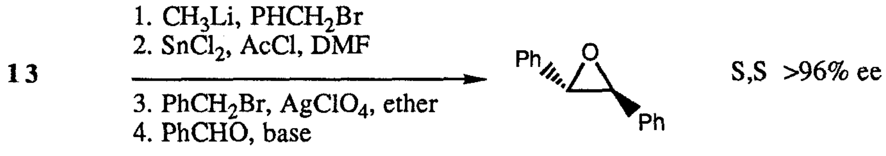
12

Access to this auxiliary was expected starting with commercially available (+)-camphoric acid. Based on the work of Marquet and coworkers[13] in the early 1970's dealing with the methylation of 4-t-butylthiane-S-oxides, we expected that benzylation of the equatorial sulfoxide **13** would result in a mixture of the equatorially substituted sulfoxides **14** and **15**. At this stage obtaining a mixture was considered advantageous since the thianes obtainable by reduction of **14** and **15** should lead to enantiomeric epoxides.

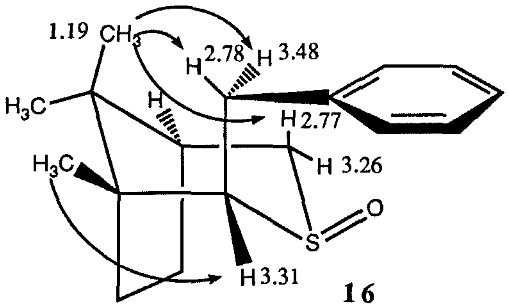


13 **14** **15**

Benzylation of **13** did indeed give two isomeric α-benzylated sulfoxides in a 64% yield and a 2:1 ratio. The major isomer was shown by nmr to be the more desirable 2-substituted isomer; its proton nmr spectrum appeared consistent with **14**. This sulfoxide was reduced with $SnCl_2$/acetyl chloride in DMF to give a sulfide which was subsequently benzylated and the benzylidene group transferred to benzaldehyde under the usual basic conditions. Much to our delight the trans-stilbene oxide obtained had the predicted S,S configuration and had an enantiomeric purity of > 96%.



In order to confirm the expected key structure **14**, the 2-benzylated sulfoxide was subjected to an X-ray structure determination. Surprisingly this material did not have structure **14** but that of the axially substituted sulfoxide **16**.[14] A series of HOMCOR and nOe experiments were in complete agreement with the X-ray determined structure and indicted that the solution conformation was virtually identical with that of the solid. The key data is summarized below; the arrows indicate significant nOe enhancements upon selective irradiarion of the three methyl groups. Similar nmr studies allowed us to show that the isomeric sulfoxide had structure **16a**. The complete characterization of structures **16** and **16a** created two interesting problems. Why the unusual and sterically unfavourable axial alkylation of **13**, and how can one now explain the high ee and S,S configuration of the trans-stilbene oxide obtained using the thiane auxiliary obtained form **16**?



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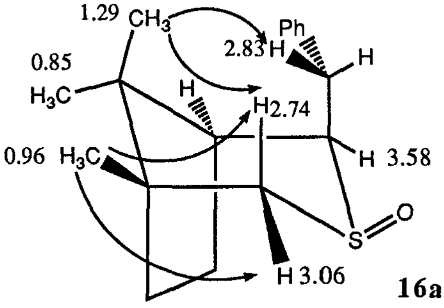
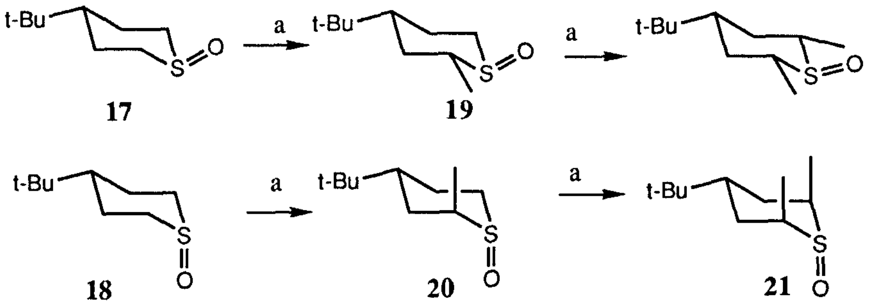


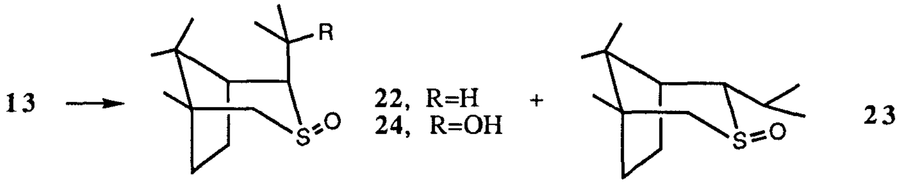
16a

Let us consider the α-lithio sulfoxide problem first. The structure and the stereochemistry of the reactions of α-lithio sulfoxides was a topic of considerable interest and some controversy in the 1970's. It is beyond the scope of this article to review much of this material. The key experimental observations most closely related to the situation involving the lithio derivatives of **13** were made by the Marquet group and have already been alluded to.[13] Methylation of the lithio derivatives of thiane-S-oxides **17** and **18** were shown to occur preferentially trans to the existing S=O bond forming **19** and **20**, respectively. The stereoelectronic effect in this alkylation, and presumably also a benzylation, is sufficiently strong to overcome the 1,3-diaxial interaction in **21**. In contrast, deuterium incorporation took place cis to the S=O bond upon quenching with sources of D+.



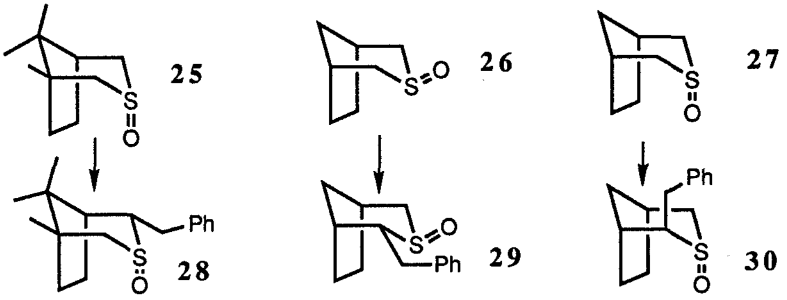
a) MeLi, THF then MeI

In the case of the lithio sulfoxide of **13**, other electrophiles such as isopropyl bromide, acetone and CH_3COOD gave similar stereochemical results: with isopropyl bromide the major product (40%) was the 4-axially substituted derivative **22** accompanied by a small amount of equatorially substituted **23**; with acetone 60% of **24** was formed, while deuteration gave an approximately 1:1 mixture of 2- and 4-monodeuterio derivatives of **13**.



In order to gain insight into the unusual behaviour of sulfoxide **13**, the isomer **25** and the analogs **26** and **27** which lacked the methyl substituents, in particular the C-8 endo methyl, were prepared and the stereochemistry of the reactions of the corresponding lithio derivatives with several electrophiles were studied. The results can be summarized as follows: Both benzylation and deuteration of **25** resulted in equatorial substitution giving, in the first instance, **28**. This result is again opposite that expected based on **18** as a model. In contrast, the lithio derivatives of the sulfoxides **26** and **27** mirrored the behavior of the t-butylthiane-S-oxides; benzylation occurred trans to the S=O bond to give **29** and

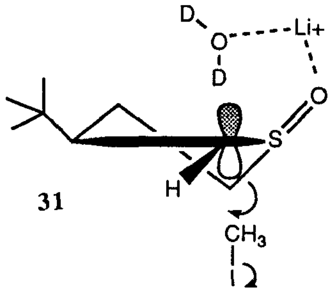
30, respectively, while deuteration gave the opposite stereochemical outcome.



Rationalization of these results in a satisfying manner is not obvious to us and an explanation may require considerable further experimental efforts. The structural assignments have been made with care and are, we believe, on firm ground. The attempted explanation, below, is qualitative at best.

It is apparent that the anomalous behaviour of the lithio derivatives from **13** and **25** when compared to those of the thiane-S-oxides studied by Marquet group is not due to the bicyclic nature of these compounds since **26** and **27** behave as expected based on **17** and **18**. The difference appears to be caused by the presence of the 8-endo methyl group. Based on extensive low temperature nmr studies, Marquet and co-workers concluded that the α-lithio derivatives of sulfoxides are planar (sp^2 hybridized) and existed as 4-membered ring chelates. Complexation of D_2O or CH_3CO_2D with the lithium should result in a syn delivery of D^+, (31). Alkylation occurs trans due the repulsive effects of the S^+-O^- dipole and the developing charge on the leaving group.[13]

For the lithio derivative of **13** the formation of a planar chelate is sterically unfavourable due to the presence of the endo methyl group at C-8. A potential way to explain the exclusive axial entry of electrophiles upon reaction of this lithio derivative is to suggest that that hybridization at the α-carbon be sp^3 with the lobe oriented axially and that the thiane ring retain its chair conformation. Marquet and coworkers suggested that their data indicated only a small difference in energy between the two types of hybridization.[13] Attack by electrophiles is only possibly fom the axial direction with retention since in an inversion process the path of the electrophile is blocked by the ethano bridge, **32**. A similar explanation holds for the axial sulfoxide if one opts for the equatorially oriented α-sp^3 hybridized species, **33**. Only equatorial approach is possible for electrophiles; axial attack is blocked effectively by the C-8 methyl group. Such an explanation is at odds with the theoretical calculations made by Wolfe, Rauk and Csizmadia since **32**, in which the carbanion is trans to the sulfur lone pair was calculated to represent an energy maximum; the same calculations conclude that **33** represents an energy minimum.[15]



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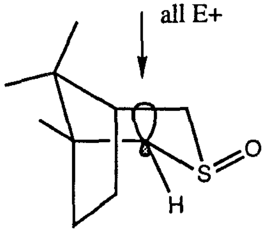

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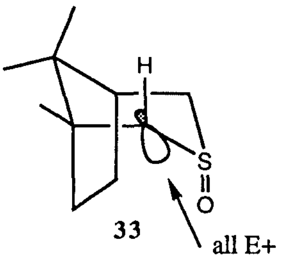
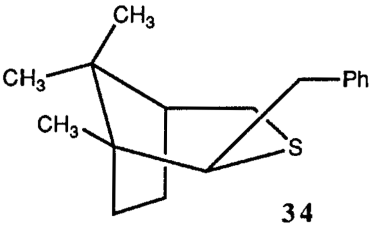


33

For **26** and **27**, the same explanations which the Marquet group provided for the behaviour of their compounds should hold. Formation of a planar α-anion and complexation of lithium to both carbon and oxygen is more feasible in **26** than in **13** due to the absence of the interfering methyl group in **26**. An explanation for the different behaviour of **25** and **27** based on differences in hybridization and complexation with lithium appears questionable since the environment about the axial S=O bond is very similar in both molecules.

Let us now return to the epoxide forming reactions starting with the sulfide auxiliary **34**, S-benzylation of which gave a salt whose nmr spectrum is consistent with the structure **35**. The alkyation trans to the 2-benzyl group was confirmed by nOe studies which showed a positive effect for H2$_{exo}$, H4$_{exo}$ and H7$_{endo}$ upon irradiation of the $>S^+-CH_2-Ph$ protons. Irradiation of the 8-endo methyl group strongly affected only the C2 benzylic hydrogens and H4$_{endo}$. Coupling constants of 3.5 and 0 Hz for H5-H4$_{exo}$ and H5-H4$_{endo}$, respectively, were interpreted as indicating torsional angles of about 50° and 85°, consistent with a half-chair conformation. In contrast, the C2 unsubstituted sulfonium salt related to **35** had torsional angles of 85° (J=0 Hz) and 45° (J= 3.9 Hz) for the same protons in agreement with a chair conformation. The coupling constants observed for H2$_{endo}$ and H_A (12.3 Hz) and H_B (3.4 Hz) in **35** help define the structure as drawn.



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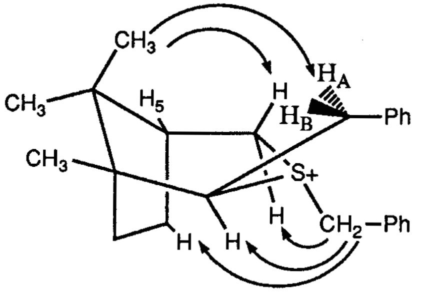
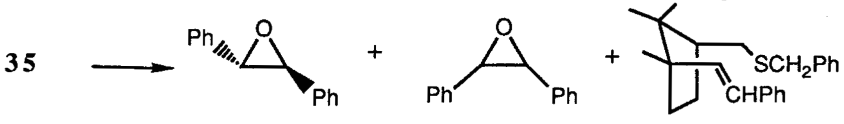


35

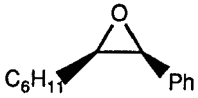
When the salt **35** was reacted with NaOH and benzaldehyde in CH_2Cl_2 in the presence of a PTC a 40% yield of S,S-trans-stilbene oxide, having ee>96% as measured by nmr using Eu(hfc)$_3$ as shift reagent, was isolated. This product was accompanied by 8% of cis-stilbene oxide and 20% of the elimination product **36**; 60% of the sulfide auxiliary was also recovered. Reaction of **35** under the same conditions with 4-methylbenzaldehyde gave the expected trans stilbene oxide in similar chemical yield and the same high ee.



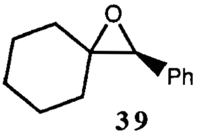
40%, S,S 8% **36** (20%)

Benzylidene transfer from **35** to cyclohexanecarboxaldehyde afforded a mixture of the trans and cis epoxides **37** and **38** in 9 and 14% isolated yields after a difficult chromatographic separation. Importantly, the ee's of these two epoxides, again determined by the nmr shift technique, were identical; the S configuration is assumed at each benzylic carbon. Cyclohexanone gave essentially optically pure S-**39**, albeit in only about 5% yield. Finally, reaction of the ylide derived from **35** with formaldehyde afforded styrene oxide 24% ee) in 50% yield. These results are summarized in the table below.

37



38

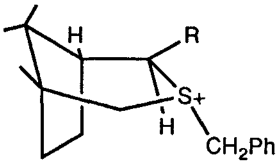


39

Table. Reactions of the ylide derived from **35** with aldehydes and ketones

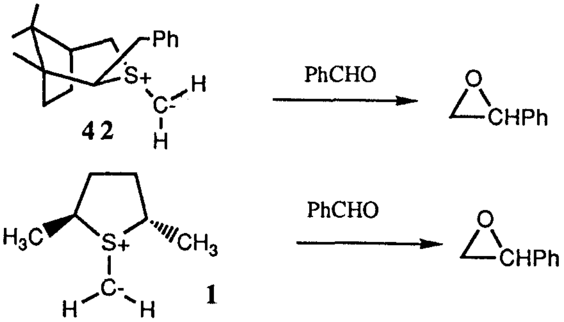
Carbonyl component	Epoxide stereochemistry	% ee
PhCHO	S,S	>96
4-MeC_6H_4CHO	S,S	>96
$C_6H_{11}CHO$	S,S (trans)	84
	S,R (cis)	84
cyclohexanone	S	>96
H_2CHO	S	24

As expected, the 4-axially substituted S-benzythiolanium salts **40** and **41** afforded epoxides having absolute stereochemistry opposite to those obtained from **35**.



40 R= CH_2Ph
41 R=$CH(CH_3)_2$

The S-methylsulfonium salt **42** which by nmr has a structure analogous to **35**, when reacted with 4-chlorobenzdehyde under the usual conditions gave 4-chlorostyrene oxide in 50% yield. In contrast to the above results this product was obtained as an almost racemic mixture with the ee being less than 3% in favour of the S-isomer.



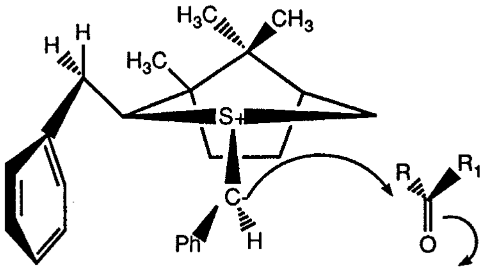
Less than 3 % ee

Less than 1 % ee

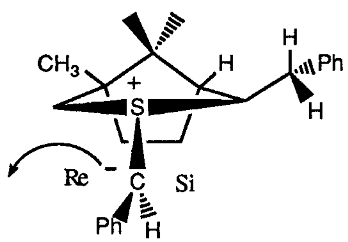
This result is reminiscent of Trost[3] and Whitesell[4] results which indicated that a methylene group could not be transferred via a sulfur ylide to a carbonyl compound with significant asymmetric induction.

The explanation for the symmetric induction observed in the reactions of the ylide derived from the sulfonium salt **35** is qualitatively quite straightforward via either the antiperiplanar or the 2+2 cycloaddition mechanism. Assuming that the ylide derived from **35** has structure **43**, attack by an aldehyde on the ylide carbon should occur preferentially from the back side (si face). This fixes the absolute configuration at that carbon as S. Any trans-stilbene formed from this approach would necessarily have S,S configuration. The observed absolute S configuration at the ylide benzylic carbon of all the remaining epoxides obtained from **43**, including both the cis and trans isomers obtained with cyclohexanecarboxaldehyde, is in agreement with this. The rather low ee found in the 4-chlorstyrene oxide formation indicates that the 2-benzyl group in **43** is unable to block completely the approach of this small molecule from the front (re face).

43

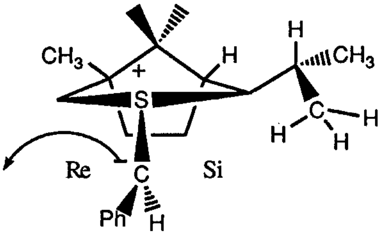


The lower ee's and the opposite absolute configurations of the epoxides obtained from the 4-substituted sulfonium salts can be similarly rationalized.



44 → R,R -trans- STILBENE OXIDE

34% ee

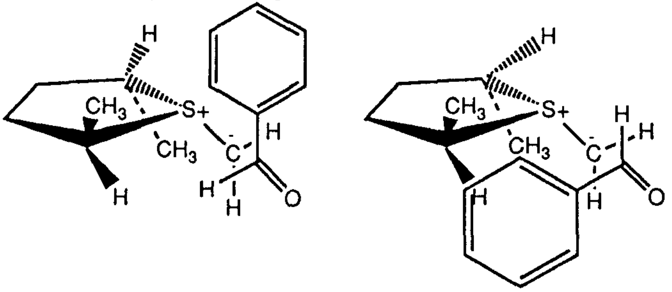


45 → R,R -trans- STILBENE OXIDE

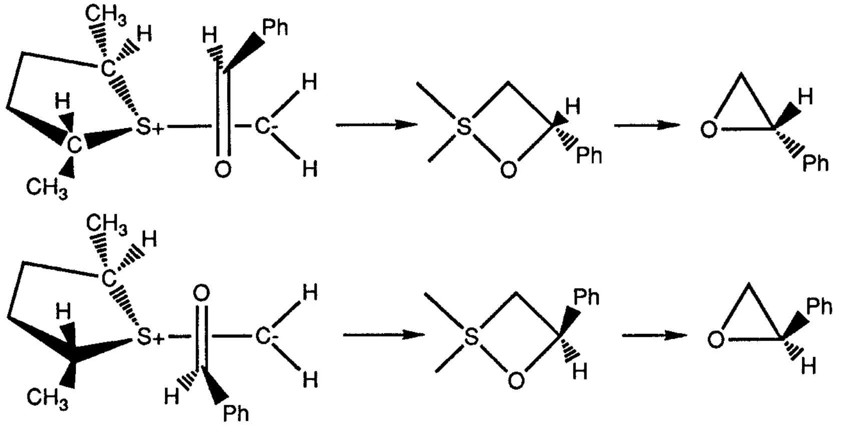
65% ee

Nmr data showed that the phenyl group in **44** lies above the C5 hydrogen and thus the si face of the ylide is shielded only by a hydrogen. This translates into a low, 35%, ee in the R,R trans-stilbene obtained. In **45**, shielding of the si face by a methyl group is more effective and the R,R isomer is produced in 65% ee.

The lack of asymmetric induction in the reaction of the methylene ylide **42** is hard to rationalize on the basis of an initial antiperiplanar head to tail betaine formation. Obviously, any asymmetry observed in the product must be due to facial selectivity at the carbonyl group since the methylene group of the ylide is not prochiral. Inspection of molecular models suggest that a significant bias ought to exist for the approach of benzaldehyde leading to S-styrene oxide; only a very marginal preference was found. An even larger facial bias ought to be realized in the reaction of the 'Whitesell' ylide derived from S-methyl-trans-2,5-dimethylthiolane (of the two possible approaches by benzaldehyde to the least hindered side of the ylide the one on the left leading to S-styrene oxide ought to be significantly favoured; molecular models show the difference more clearly), but again none was found.



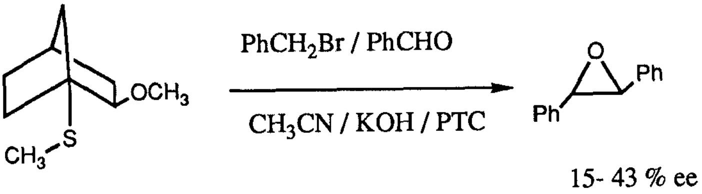
This brings into question the antiperiplanar mechanism of the sulfur ylide + aldehyde->epoxide (Corey-Chaykovsky) reaction. A $\pi 2s + \pi 2a$ concerted approach, similar to that leading to cis-oxaphosphatanes and eventually cis-alkenes in the salt-free Wittig reaction involving non-stabilized ylides and aliphatic aldehydes, has previously been proposed but refuted by theoretical calculations.[11] Nevertheless such a mechanism in which the aldehyde approaches the ylide orthogonally offers a reasonable explanation for the necessity of having a substituted ylide in order to observe asymmetric induction in the epoxide formation. As before attack of an aldeyhyde on **43** occurs preferentially from the back side. Orthoganal approach of the aldehyde with the oxygen either 'up' or 'down' appears to have very little steric bias, especially if the aldehyde carbon is tilted somewhat toward the ylide carbon and the oxygen towards the sulfur. A similar situation holds for the reaction of the ylide from **1** which because of its simplicity is used in the illustration below.



The above proposed concerted cylcoaddition results in preferential formation of a 1,2-oxathietane sulfurane. Conversion of this to the product epoxides requires S-O bond cleavage followed by a 180° rotation and finally cyclization. Admittedly this is, according to calculations by Volatran and Eisenstein a highly unfavourable path, and no experimental evidence exist for such oxathietanes as observable intermediates but it does offer at this point a plausible explanation for the stereochemistry observed in the reaction of the sulfur ylides with aldehydes described in this paper.

Finally it is important to place these results into perspective. We have shown that it is possible to produce optically active epoxides via the reaction of sulfonium ylides and carbonyl compounds. We have defined some of the required perameters with respect to the structure of the sulfide auxiliaries and have raised questions concerning the generally accepted antiperiplanar addition mechanism for the Corey-Chaykovsky reaction. From the synthesis point of view this methodology is far inferior to that of the catalytic epoxidations and cis hydroxylations of alkenes for producing optically active epoxides. It is most unfortunate that methylene transfer from S-methylsulfonuim salts to carbonyl compounds which affords terminal epoxides in excellent yields does not yet occur with asymmetric induction.

The possibility of carrying out these epoxidations catalytically with respect to the sulfide auxiliary has been investigated and realized in principle.[16] At present turnover rates based on sulfide are less than 3.



References:

1. Gao Y., Hanson R.M., Klunder J. M., Ko S.Y., Masamune H., Sharpless K.B. J. Am. Chem. Soc. **1987**, 109, 5765.
2. Corey E.J., Chaykovsky M. J. Am. Chem. Soc. **1962**, 84, 867, 3782.
3. Trost B. M., Hammen R.F. J. Am. Chem. Soc. **1973**, 95, 962.
4. Whitesell J. K. IUPAC Organic Synthesis Meeting, Nancy, France, **1988**.
5. Allen D.G., and Wild S.B. Organometallics. **1983**, 2, 394.
6. For a summary see Stirling C.J.M., The Chemistry of the Sulfonium Group; Patai S., ed.; John Wiley & Sons, New York, 1981.
7. Johnson A,W., Lacount R.B. J. Am. Chem. Soc. **1961**, 86, 417; Johnson A.W., Hruby V,J., Williams J.L. J. Am. Chem. Soc. **1964**, 86, 918.
8. Johnson. C. R., Schroeck C.W., Shanklin J.R. *J. Am. Chem. Soc.* **1973**, 95, 8424; Durst T., Van Den Elxen R., Nguyen C. H. J. Chem Soc. Chem. Commun. **1971**, 1334; Townsend J. M., Sharpless K. B. Tetrahedron Lett. **1972**, 3313.
9. See ref. 6, p361.
10. Vedejs E., Snoble K.A. J. Am. Chem. Soc. **1973**, 95, 5778; Vedejs Meir G. P., Snoble K.A. J. Am. Chem. Soc. **1981** 103, 2823; Vedejs E., Marth C.F., J. Am. Chem. Soc. **1988**, 110, 3948, and refs. therein.
11. Volatron F. Eisenstein O. J. Am. Chem. Soc. **1973**, 109, 1.
12. Breau L., Ogilvie W.W., Durst. *Tetrahedron Lett.* **1990**, 31, 35.
13. Bory S., Lett.R., Moreau B., Marquet A. Terahedron Lett. **1972** 4921; Bory S., Marquet A. Tetrahedron Lett. **1973**, 4155; Chassaing G. Lett R., Marquet A. Tetrahedron Lett. **1978**, 471; Chassaing G., Marquet.A. Tetrahedron **1978**, 34, 1399; Lett R., Chassaing G. Tetrahedron **1978**, 34, 2705.
14. Breau L., Durst T. Tetrahedron Asymmetry. **1991**, 2, 367.
15. Wolfe S., Stolow A., LaJohn L. A. Tetrahedron Lett. **1983**, 4071; and ref. therein
16. Furukawa N., Sugihara Y., Fujihara H. J. Org. Chem. **1989**, 54, 4222; Breau L. Ph.D. thesis. Univ. Of Ottawa. **1991**.