Stereocontrolled synthesis of *E*-homoallylic sulfides with 1,4,5 related chiral centres using the [2,3] sigmatropic rearrangement of sulfonium ylides[1]

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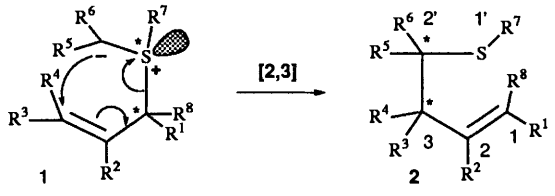
***E*-Homoallylic sulfides with 1,4,5 related chiral centres have been synthesised in a stereocontrolled way. An aldol condensation sets up the stereochemistry. Lactonisation with 1,2 arylsulfanyl migration followed by reduction and sulfur-assisted dehydration converts the aldols stereospecifically into allylic sulfides with 1,2 related chiral centres. Sulfonium salts are generated from the allylic sulfides at low temperature, and are deprotonated to give sulfonium ylides which undergo [2,3] sigmatropic rearrangement in good yield to give *E*-homoallylic sulfides with 1,4,5 related chiral centres. The 1,4 relative stereochemistry results from stereospecific chiral transfer and is directly related to the allylic sulfide 1,2 relative stereochemistry. High 4,5 diastereoselectivity is also observed. An explanation for the observed stereoselectivity is provided.**

Introduction

We developed an effective low-temperature method of generating sulfonium salts and ylides from simple allylic sulfides so as to carry out [2,3] sigmatropic rearrangements in high yields.[2] We wished to use this method to investigate and exploit the stereochemical aspects of the [2,3] sigmatropic rearrangement. In the [2,3] sigmatropic rearrangement of sulfonium ylide **1** to homoallylic sulfide **2**, a C–S bond is broken and a C–C bond formed (Scheme 1). The sulfonium ylide **1** contains three pieces of stereochemical information: a double bond geometry, a chiral centre at C(1) and a chiral centre at S. Following [2,3] sigmatropic rearrangement the resulting homoallylic sulfide **2** also contains three pieces of stereochemical information: a double bond geometry, a chiral centre at C(3), and a chiral centre at C(2′). This gives rise to six possible types of stereocontrol:[3] control of the product double bond geometry; C(1) to C(3) chiral transfer; S to C(2′) chiral transfer; S to C(3) chiral transfer; diastereoselectivity at C(3) in relation to chiral centres present elsewhere in the molecule; and C(2′)/C(3) diastereoselectivity. Let us consider these types of stereocontrol in order beginning with control of the double bond geometry.

When an open chain sulfonium ylide rearranges to give a disubstituted or trisubstituted (R^8 = H) double bond the *E* double bond geometry predominates.[4] The selectivity is particularly high when R^1 and/or R^4 are large on account of high allylic 1,3 strain.[5] On the other hand, in ring expansions/contractions the product double-bond geometry is dictated largely by product ring size.[6]

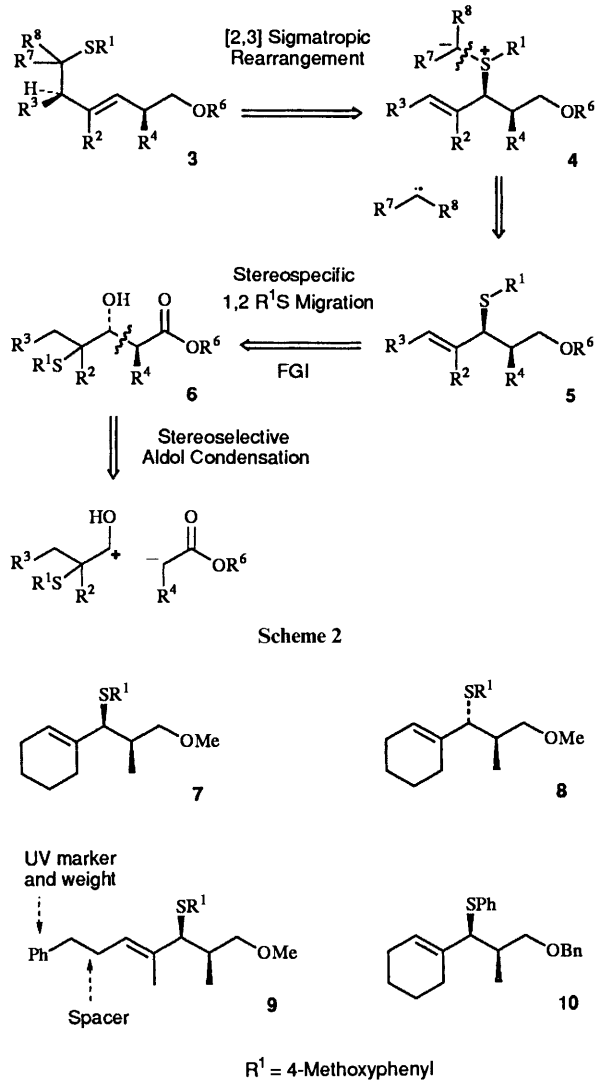
Many [2,3] sigmatropic rearrangements have been shown to be stereospecifically suprafacial and so to give quantitative C(1) to C(3) chiral transfer for a given product double-bond geometry.[7,8] 1,3 Chiral transfer in the sulfonium ylide rearrangement has been demonstrated in ring contractions,[9] and for migration over the surface of a ring,[10] but there has been only one example of 1,3 chiral transfer in a truly open chain compound.[11] Moreover, although in all these examples the rearrangement proceeded suprafacially, there has been no proof prior to the work that we now report that the course of the reaction is stereospecific rather than stereoselective.[1] Chiral transfer from S to C(2′) and from S to C(3) has been demonstrated in systems where there is no chiral centre at C(1).[12] An interesting development in this area is chiral induction at C(3) using a chiral auxiliary attached to an achiral sulfur.[13]



Scheme 1

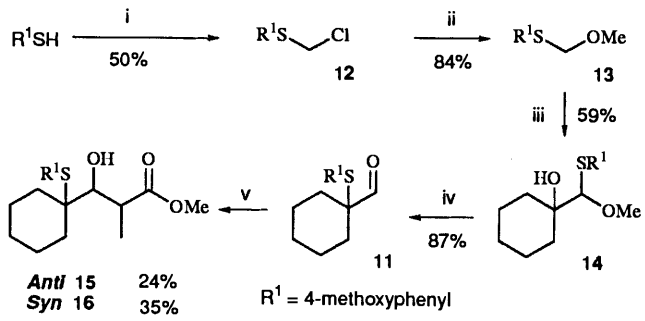
High C(2′)/C(3) diastereoselectivities have been observed in some ring contractions and ring expansions,[14] but the ring plays an important role in diastereoselectivity in these constrained systems. Prior to our work,[1] there was only one example of good diastereoselectivity in the rearrangement of an open chain sulfonium ylide.[11] In cases where there is no chiral centre at C(1) the diastereoselectivity has been very poor.[15] We hoped to induce good C(2′)/C(3) diastereoselectivity in open chain compounds using our low temperature conditions for the [2,3] sigmatropic rearrangement[2] and made no attempt to control the chirality at sulfur.

We have developed a method for the stereocontrolled synthesis of diols with 1,4 related chiral centres across an *E* double bond using the [2,3] sigmatropic rearrangement of allylic sulfoxides.[7] We hoped to build on this work and to develop a similar method to make *E*-homoallylic sulfides **3** with 1,4,5 related chiral centres by the [2,3] sigmatropic rearrangement of sulfonium ylides **4** derived from allylic sulfides **5** (see the retrosynthetic analysis, Scheme 2). Previously, we have shown that the precursor allylic sulfides **5** can be synthesised stereospecifically from aldols **6** by 1,2 PhS migration (R^1 = Ph).[16] By investigating the [2,3] sigmatropic rearrangement of sulfonium ylides derived from *syn* allylic sulfide **7** and *anti* allylic sulfide **8** (Fig. 1), we hoped to prove the stereospecificity of C(1) to C(3) chiral transfer and to find out whether good and predictable C(2′)/C(3) diastereoselectivities could be obtained in open chain compounds. The cyclohexenyl ring that connects C(2) and C(3) should not add an extra constraint to the system since the relationship between the substituents on these atoms is already fixed by the double bond and the transition state for [2,3] sigmatropic rearrangement is believed to be early.[17] To confirm that this ring does not affect the stereochemical outcome of the rearrangement we intended



Scheme 2

Fig. 1



Scheme 3 *Reagents and conditions:* i, (a) NaH, THF, RT, 1 h, (b) CH_2BrCl, 2 h 30 min; ii, NaOMe MeOH, 2 h 10 min, RT; iii, (a) BuLi, THF, −30 °C, 32 min, (b) cyclohexanone, 30 min; iv, $SOCl_2$, Et_3N, CH_2Cl_2, 0 °C, 1 h 25 min; v, MeCH=C(OLi)OMe, THF, −78 to −45 °C, 4 h

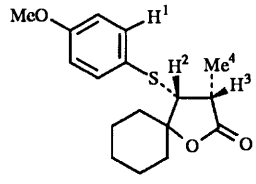


Fig. 2

Table 1 Difference NOE experiments on *syn* lactone **18**

Nucleus irradiated (ppm)	Multiplicity	NOE enhancement[a] 1-H	2-H	3-H	4-Me
2-H (3.63)	doublet	s	—	s	*
3-H (3.01)	double quartet	w	s	—	s
4-Me (1.41)	doublet	m	*	s	—

* = no NOE. [a] s = strong NOE, m = medium NOE, w = weak NOE.

to synthesise *syn* allylic sulfide **9** which has no ring (Fig. 1). The phenyl group in the allylic sulfide **9** was chosen to give the compound low volatility and as a UV marker. It is separated from the double bond by a spacer to avoid conjugation. The 4-methoxyphenylsulfanyl group was chosen as its sulfur atom is more nucleophilic than that of the phenylsulfanyl group and it has been shown to be more effective in the sulfonium salt forming reaction that precedes ylide formation and rearrangement;[2] its aromatic signals in the ^1H NMR spectra are distinctive, it has a strong UV absorption and we wished to see whether it affected the 1,2 arylsulfanyl migration. The *syn* allylic sulfide **10** bearing a phenylsulfanyl group was to be used for comparison.

Results and discussion

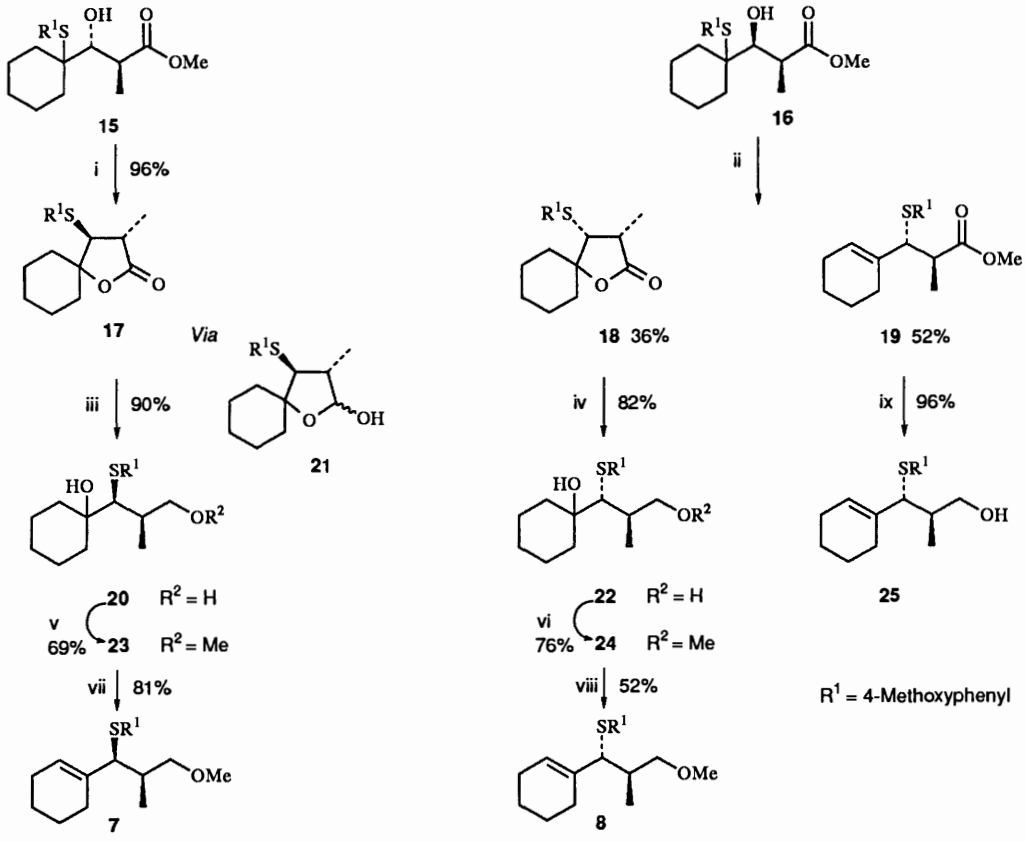
Synthesis of the allylic sulfides

Allylic sulfides **7** and **8** could be made from α-arylsulfanyl aldehyde **11** (Scheme 3, R^1 = 4-methoxyphenyl). To make this aldehyde, 4-methoxybenzenethiol was alkylated with bromochloromethane to give chloromethyl sulfide **12** and the chloride displaced by methoxide to give methoxy methyl sulfide **13**. Deprotonation of the latter with butyllithium at −30 °C and reaction with cyclohexanone gave alcohol **14** in moderate yield. The temperature of deprotonation is critical to the success of this reaction. Finally, rearrangement[18] of the alcohol **14** gave the aldehyde **11**.

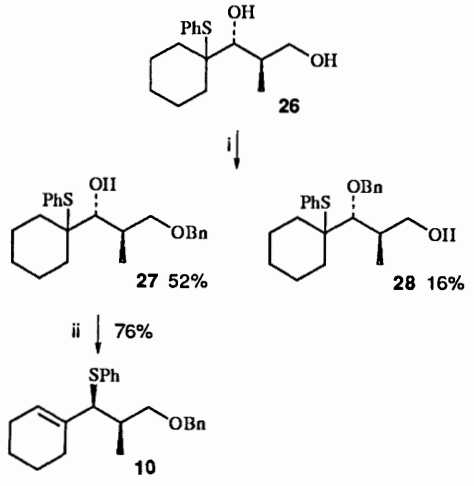
Since we wished to make both *syn* allylic sulfide **7** and *anti* allylic sulfide **8** we carried out an unselective aldol condensation on α-arylsulfanyl aldehyde **11** to give *anti* aldol **15** and the *syn* aldol **16** (Scheme 3); the latter could be separated by chromatography and their stereochemistry assigned by the shift of the methyl signal *Me*CH in the ^{13}C NMR (δ_{MeCH} 18.0 for *anti* aldol **15** and 14.3 ppm for *syn* aldol **16**).[19]

An interesting alternative to our usual synthesis[16] of allylic sulfides is lactonisation followed by reduction to the 1,3 diol, monoprotection and sulfur-assisted dehydration. The *anti* aldol **15** cyclised stereospecifically to the *anti* lactone **17** when heated under reflux in dichloromethane with catalytic acid (Scheme 4), but when the *syn* aldol **16** was subjected to similar conditions a mixture of *syn* lactone **18** and *anti* allylic sulfide **19** was obtained. The formation of the *syn* lactone **18** is slow due to steric interaction between the methyl and the 4-methoxyphenylsulfanyl groups in the transition state and so dehydration competes. Such competition can also take place in the cyclisation of *anti* aldols when the ester group is large.[16,20] The effect of the product 3,4 stereochemistry parallels that observed in tetrahydrofuran formation.[21] The stereochemistry of *syn* lactone **18** was proven by NOE (Fig. 2, Table 1) thus confirming the assignment of the aldols **15** and **16**.

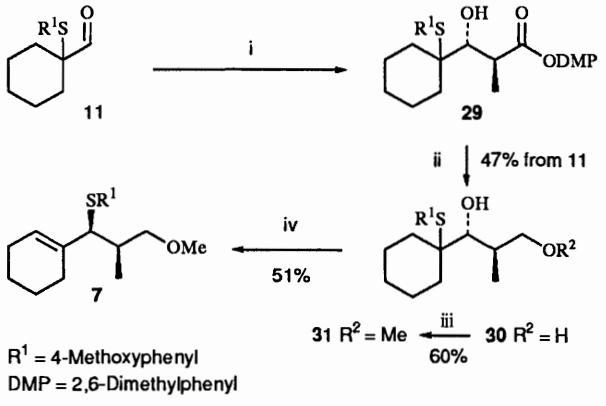
Reduction of *anti* lactone **17** to the *syn* diol **20** with lithium aluminium hydride was slow and the hemiacetal intermediate **21** (1:1 mixture of anomers) could be isolated (Scheme 4). However, the *syn* lactone **18** was reduced rapidly with lithium aluminium hydride at 0 °C to give the *anti* 1,4 diol **22**. This illustrates the greater stability of the 3,4 *anti* configuration relative to the 3,4 *syn* configuration in the cyclic hemiacetals. Monomethylation[22] of each of the diols **20** and **22** proceeded smoothly to give the corresponding alcohols **23** and **24**. The *syn*



Scheme 4 *Reagents and conditions:* i, TsOH (0.2 equiv.), CH_2Cl_2, reflux, 9 h 30 min; ii, TsOH (0.2 equiv.), CH_2Cl_2, reflux, 4 h 30 min; iii, $LiAlH_4$ (1.4 equiv.), THF, 3 h 30 min, RT; iv, $LiAlH_4$ (1.4 equiv.), THF, 1 h, 0 °C; v, (a) 50% $NaOH_{(aq.)}$ (1.3 equiv.), Bu_4NI (1.0 equiv.), CH_2Cl_2, 50 min, RT, (b) $(MeO)_2SO_2$ (1.5 equiv.), 0 °C then RT, 24 h; vi, (a) 50% $NaOH_{(aq.)}$ (2.6 equiv.), Bu_4NI (1.9 equiv.), CH_2Cl_2, 30 min, RT, (b) $(MeO)_2SO_2$ (3 equiv.), 0 °C then RT, 21 h; vii, TsOH (0.2 equiv.), CH_2Cl_2, reflux, 12 min; viii, TsOH (0.2 equiv.), CH_2Cl_2, reflux, 1 h 50 min; ix, $LiAlH_4$ (1.0 equiv.), 0 °C to RT, Et_2O, 6 h



Scheme 5 *Reagents and conditions:* i, (a) NaH (1.15 equiv.), THF, RT, 30 min, (b) Bu_4NI (0.01 equiv.), BnBr (1.05 equiv.), 1 h 50 min; ii, TsOH (0.2 equiv.), CH_2Cl_2, reflux, 6 min



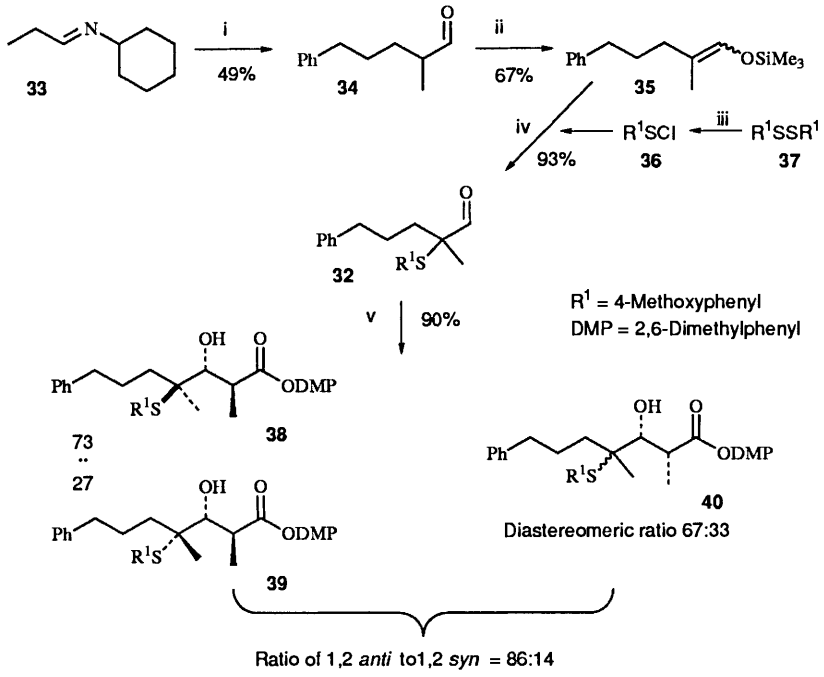
Scheme 6 *Reagents and conditions:* i, MeCH=C(OLi)ODMP, THF, −78 to −45 °C, 13 min; ii, $LiAlH_4$, THF, RT, 1 h 45 min; iii, (a) 50% $NaOH_{(aq.)}$ (1.3 equiv.), Bu_4NI, CH_2Cl_2, RT, 35 min, (b) $(MeO)_2SO_2$ (1.5 equiv.), 0 °C then RT, 24 h; iv, TsOH (cat.), PhH, reflux, 5 min

alcohol **23** was rapidly dehydrated under acid catalysis to give *syn* allylic sulfide **7**. The dehydration of the *anti* alcohol **24** required a very much longer time at reflux in dichloromethane to give the *anti* allylic sulfide **8**. It seems that the dehydration of the *syn* alcohol **23** is sulfur-assisted but that of the *anti* alcohol **24** is not.

The allylic sulfide **19** could be reduced to alcohol **25**, but methylation under the same conditions as above failed. Since a sulfonium ylide could be generated from allylic sulfide **19**, reduction and protection was not pursued further.

The lactonisation, reduction, monoprotection and dehydration route is effective in the case of the *anti* aldol **15** and has the advantage that the monoprotection is of a primary alcohol in the presence of a tertiary alcohol rather than in the presence of a secondary alcohol as is the case in our traditional route. This is worth noting as benzylation[23] of the known[16] *anti* diol **26** was not completely regioselective giving both the secondary alcohol **27** and the primary alcohol **28** (Scheme 5). The monobenzylated alcohol **27** was converted into the allylic sulfide **10** using acid catalysis.

We also made *syn* allylic sulfide **7** in a stereoselective manner using Heathcock's *anti* selective aldol reaction (Scheme 6).[24] Reaction of the lithium enolate of 2,6-dimethylphenyl propionate with α-arylsulfanyl aldehyde **11** proceeded with 90 : 10 diastereoselectivity but the aldol product **29** decomposed on silica and could only be isolated in 30% yield. Following our usual approach,[7,16] the crude aldol **29** was reduced and the purified *anti* diol **30** (47% from the aldehyde) was



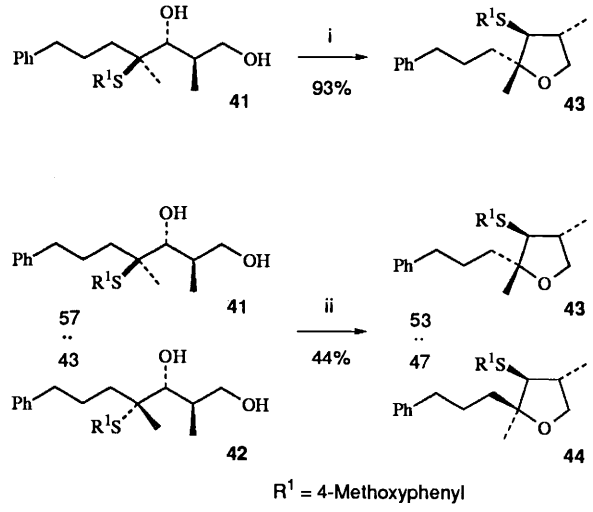
Scheme 7 *Reagents and conditions:* i, (a) LDA (1 equiv.), hexane–ether (3:4), 0 °C, 1 h 35 min, (b) $PhCH_2CH_2CH_2Br$ (1 equiv.), 0 °C to RT, then 65 h, (c) 2 mol dm^{-3} $HCl_{(aq.)}$ (6 equiv.), reflux, 2 h; ii, TMSCl (1.2 equiv.), Et_3N (2.4 equiv.), DMF, 80 °C, 22 h; iii, SO_2Cl_2 (1 equiv.), THF, RT, 1 h 20 min; iv, R^1SCl (1 equiv.), THF/CH_2Cl_2, −78 °C to RT, 4 h; v, *E*- MeCH=C(OLi)ODMP, THF, −78 °C, 11 min

monomethylated[22] on the primary hydroxyl to give alcohol **31**. 1,2 Aryl sulfanyl migration then gave *syn* allylic sulfide **7**.

Allylic sulfide **9** was synthesised from aldehyde **32** (Scheme 7). Alkylation of the metallated enamine derived from imine **33** gave aldehyde **34**. Silyl enol ether **35** (*E*:*Z*, 63:37) was prepared from aldehyde **34**, and added to a solution of the sulfenyl chloride **36** (formed by the action of sulfuryl chloride on disulfide **37**) to give aldehyde **32**.

Heathcock's *anti* selective aldol condensation[24] on the aldehyde gave a mixture of aldols in 90% yield. The 2,3 selectivity of 86:14 *anti–syn* is comparable to that observed for other aldols.[7,16] Since the steric effects of the methyl group and methylene chain are similar there was only a moderate preference (73:27) for the *anti,anti* aldol **38** over the *anti,syn* aldol **39** (Scheme 7). This is consistent with Roush's analysis of 3,4 stereoselectivity.[25] The ratio of 3,4 diastereoisomers of the 2,3 *syn* aldols **40** was 67:33, but they were not assigned. Chromatography gave *anti,anti* aldol **38** as a pure crystalline solid in 30% yield. Assignment of the 2,3 *anti* stereochemistry to each of the aldols **38** and **39** was made using the chemical shift of the methyl signal *Me*CH in the ^{13}C NMR (δ_{MeCH} 18.7 for both aldols **38** and **39**; in each case, the signal for the two methyls attached to the phenyl ring was in the region 16.7–16.8 ppm).

Lithium aluminium hydride reduction of ester **38** gave diol **41** in 65% yield. A similar yield of a mixture of the diols **41** and **42** was obtained from the reduction of a mixture of the 2,3 *anti* aldols **38** and **39**. Acid-catalysed cyclisation[16,21] of the pure *anti,anti* diol **41** gave *anti, anti* tetrahydrofuran **43** in 93% yield (Scheme 8). The stereochemistry was confirmed by NOE (Fig. 3, Table 2). Cyclisation of a 57:43 mixture of 2,3 *anti* aldols **38** and **39** gave a 53:47 mixture of tetrahydrofurans **43** and **44** in 44% yield. Assignment of the *anti,syn* stereochemistry to tetrahydrofuran **44** was made by comparison of the coupling constant J_{AB} between CH^AS and CH^BMe of 10.7 Hz with the coupling constant J_{AB} of *anti,anti* tetrahydrofuran **43** and other similar tetrahydrofurans of known stereochemistry. The 3,4 *anti* tetrahydrofurans have a coupling constant J_{AB} in the range 10.4–10.9 Hz, while 3,4 *syn* tetrahydrofurans have a coupling constant J_{AB} in the range 7.6–8.9 Hz.[16,26,27] Assignment of the stereochemistry of tetrahydrofurans **43** and **44** confirmed assignment of aldols **38**, **39** and **40**.



Scheme 8 *Reagents and conditions:* i, TsOH (0.2 equiv.), CH_2Cl_2, reflux, 1 h; ii, TsOH (0.2 equiv.), CH_2Cl_2, reflux, 24 min

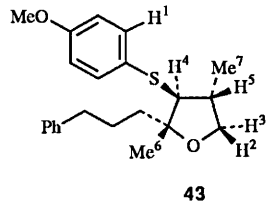


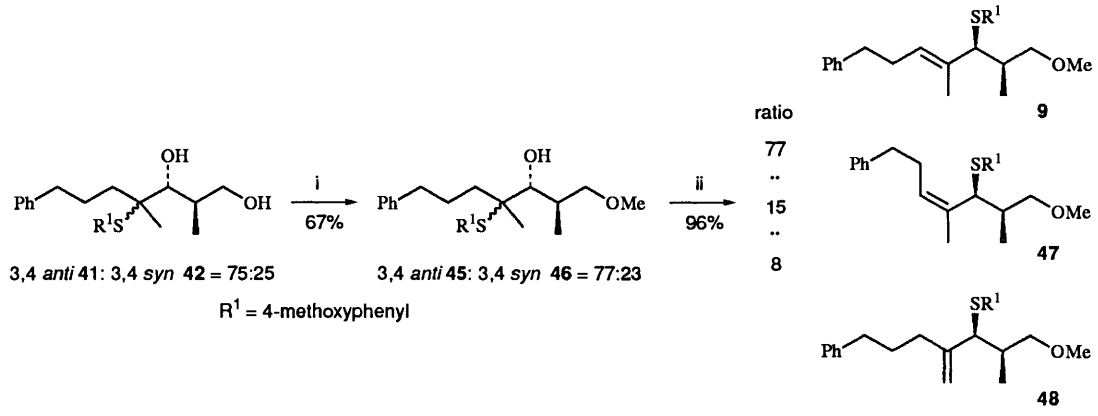
Fig. 3

Monomethylation[22] of a mixture of diols **41** and **42** gave a similar mixture of *anti,anti* alcohol **45** and *anti,syn* alcohol **46** (Scheme 9). This mixture was heated under reflux in benzene with catalytic acid for 9 min to give a (77:15:8) mixture of *E-endo* allylic sulfide **9**, *Z-endo* allylic sulfide **47** and *exo* allylic sulfide **48**. No carbocyclisation of the phenyl ring onto the episulfonium ion was observed.[27] The same reaction when carried out on a mixture of slightly different composition (a ratio of *anti,anti* to *anti,syn* of 82:18) in dichloromethane with a much longer reflux time (1 h) gave the allylic sulfides in a similar ratio to that above (**9**:**47**:**48**, 81.5:13.5:5) but less

Table 2 Difference NOE experiments on *anti,anti* tetrahydrofuran **43**

Nucleus irradiated (ppm)	Multiplicity	NOE enhancement[a]						
		1-H	2-H	3-H	4-H[4]	5-H	6-Me	7-Me
1-H (7.39)	doublet	—	*	*	w	*	w	w
2-H (3.96)	triplet	*	—	s	*	m	*	*
3-H (3.27)	triplet	*	s	—	w	*	*	w
4-H (2.74)	doublet	m	*	*	—	*	*	w
5-H (2.28)	multiplet	*	m	*	*	—	m	m
6-Me (1.21)	singlet	m	*	*	w	m	—	*
7-Me (1.09)	doublet	*	*	m	m	w	*	—

* = no NOE. [a] s = strong NOE, m = medium NOE, w = weak NOE.



Scheme 9 *Reagents and conditions:* i, (a) 50% $NaOH_{(aq.)}$ (1.3 equiv.), Bu_4NI (1.0 equiv.), CH_2Cl_2, 30 min, RT, (b) $(MeO)_2SO_2$ (1.5 equiv.), 0 °C then RT, 21 h; ii, TsOH (0.2 equiv.), benzene, heat to reflux (9 min), and reflux 2 min

cleanly with impurities including 17% 4-methoxybenzenethiol. Purification of the latter mixture by chromatography gave the *E-endo* allylic sulfide **9** and the *exo* allylic sulfide **48** as a (93:7) mixture in 56% yield.

[2,3] Sigmatropic rearrangements

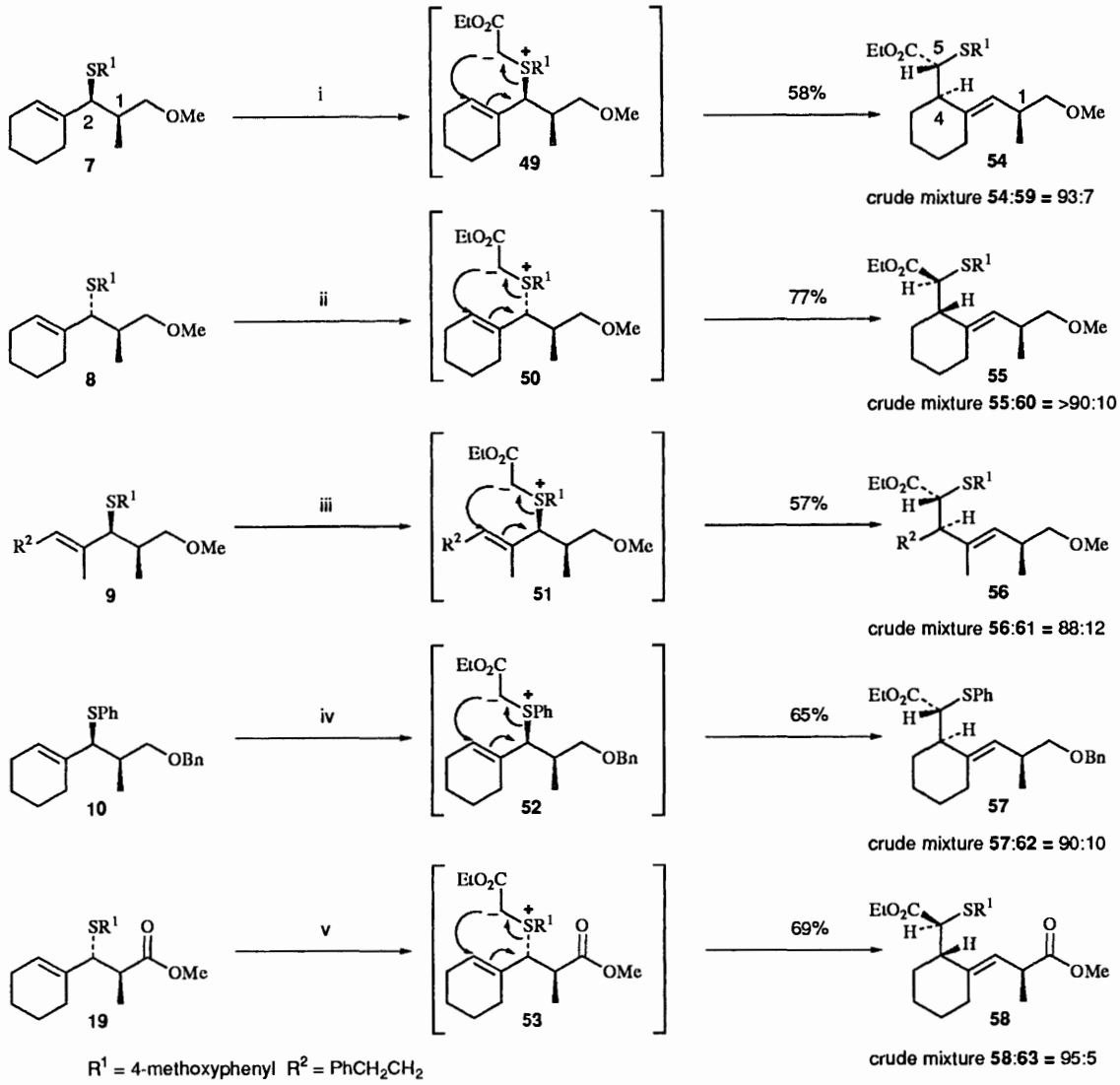
Sulfonium salts were prepared at low temperature from allylic sulfides **7**, **8**, **9**, **10** and **19** (Scheme 10).[1,2] The salts were not isolated but were treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the sulfonium ylides **49**, **50**, **51**, **52** and **53**, respectively. These rearranged spontaneously to give the homoallylic sulfides **54**, **55**, **56**, **57** and **58**, respectively (isolated yields after purification are given in Scheme 10). The only significant impurities in the crude products before they were purified by chromatography (ratio given in Scheme 10) were the epimers at the carbon attached to sulfur **59**, **60**, **61**, **62** and **63** (Scheme 11 and Fig. 4). Other impurities (with olefinic signals in the ^1H NMR spectra of the crude products) were present in only trace quantities. An exception was the rearrangement of sulfonium ylide **51** which gave an impurity, tentatively assigned to the rearrangement product of *exo* allylic sulfide **48**, as up to 9% of the homoallylic sulfide products. Purification by chromatography gave each of the homoallylic sulfides **54**–**58** in > 89% purity and in the yields shown (Scheme 10). Purities are based on the assumption that any olefinic signals in the ^1H NMR spectra belonged to compounds with molecular masses equal to that of the homoallylic sulfides.

Control over the relative stereochemistry of the 1,4 related chiral centres was complete (numbering as indicated in Scheme 10): the 1,2 *syn* allylic sulfide **7** gave the 1,4 *syn* homoallylic sulfide **54**, while the 1,2 *anti* allylic sulfide **8** gave the 1,4 *anti* homoallylic sulfide **55**. In neither case was any trace of an *E*-homoallylic sulfide with the opposite 1,4 stereochemistry detected in the crude mixture. This is the first proof that C(1) to C(3) (numbering as in Scheme 1) chiral transfer is stereospecifically suprafacial for this rearrangement. The cyclohexenyl ring cannot play a major role in controlling the rearrangement as sulfonium ylide **51**, which lacks this ring, gave homoallylic sulfides **56** and **61** with no 1,4 *anti* isomers detectable in the crude mixture.

The selectivity for the *E*-double bond is well precedented but we also found a remarkable degree of control over the 4,5 stereochemistry (numbering as in Scheme 10). The ^1H NMR of the crude mixtures showed > 90:10 diastereoselectivity in favour of the 4,5 *anti* compounds **54**, **55**, **57** and **58**. The cyclohexenyl ring of the sulfonium ylides **49**, **50**, **52** and **53** should not introduce an additional constraint to rotation about the bonds of the 5-membered ring transition state (Scheme 1) since C(2) and C(3) are already linked by a double bond and the transition state is believed to be early.[17] This was confirmed by the almost equally good diastereoselectivities observed in the formation of homoallylic sulfide **56**. Equilibration experiments (Scheme 11) show that there is little difference in the thermodynamic stability of the 4,5-*syn* and 4,5-*anti* isomers and therefore the preference for the 4,5 *anti* stereochemistry must be kinetic. Interconversion of the homoallylic sulfides under basic conditions was slow at room temperature: 1,4 *syn*, 4,5 *anti* homoallylic sulfide **54** (95% pure) when stirred with sodium ethoxide (3.5 equiv.) gave little change in compound composition after 2 h.

The nature of the C(2')/C(3) diastereoselectivity (*i.e.* the 4,5 *anti* selectivity) can be explained using the folded envelope transition state proposed by Wu and Houk (Fig. 5).[17] Of the two possible envelope conformations **64** and **65**, the eclipsed substituent (R^1 and CO_2Et) orientation across the developing C(2')-C(3) bond disfavours **65**. Weinreb and co-workers observed the same type of diastereoselectivity in the rearrangement of a sulfonium ylide with a *Z*-double bond.[11]

The configuration at S is unknown and is not required to explain the configuration at C(3), which is set up by chiral transfer from C(1). It may be unimportant or it may invert. It is considered unimportant in our explanation of the C(2')/C(3) diastereoselectivity given above. If the configuration at S were stable and important in the C(2')/C(3) diastereoselectivity, then



Scheme 10 *Reagents and conditions:* i, (a) N_2CHCO_2Et (1.6 equiv.), HBF_4 (1.6 equiv.), CH_2Cl_2, < −72 °C, 11 min, (b) DBU (2.7 equiv.), 20 min, (c) AcOH (3 equiv.); ii, (a) N_2CHCO_2Et (1.6 equiv.), HBF_4 (1.6 equiv.), CH_2Cl_2, −55 °C, 10 min, (b) DBU (2.7 equiv.), −50 to −35 °C, 16 min, (c) $HCl_{(aq.)}$; iii, (a) N_2CHCO_2Et (1.6 equiv.), HBF_4 (1.6 equiv.), CH_2Cl_2, −54 °C, 15 min, (b) DBU (2.7 equiv.), −52 to −29 °C, 22 min, (c) $HCl_{(aq.)}$; iv, (a) N_2CHCO_2Et (1.6 equiv.), HBF_4 (1.6 equiv.), CH_2Cl_2, < −72 °C, 15 min, (b) DBU (2.7 equiv.), −78 to −35 °C, 45 min, (c) $HCl_{(aq.)}$; v, (a) N_2CHCO_2Et (1.6 equiv.), HBF_4 (1.6 equiv.), CH_2Cl_2, < −72 °C, 11 min, (b) DBU (2.7 equiv.), 30 min, (c) AcOH (4.4 equiv.)

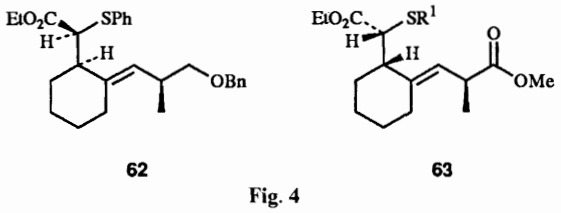


Fig. 4

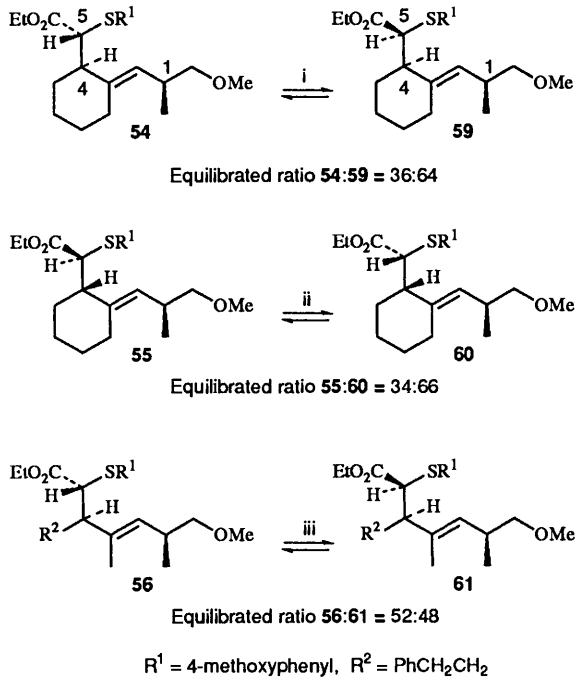
it would have to be determined by the configuration of the chiral centre at C(1). Under these circumstances one of the conformers **66** or **67** of the allylic sulfide must be alkylated preferentially in our system and the other conformer must be alkylated selectively in the system investigated by Weinreb and co-workers (Fig. 6).[11] This possibility cannot be excluded as in our previous work[2] we found that when the alkylation and rearrangement was carried out on allylic sulfides lacking a chiral centre at C(1) there was little diastereoselectivity, albeit at higher temperature.

Our low-temperature conditions for the generation of sulfonium salts and ylides allow formation of thermally unstable sulfonium salts, avoid side reactions, and give rise to good and predictable C(2′)/C(3) selectivities. The conditions do not affect ester groups or the stereochemical integrity of epimerisable centres (see reaction of allylic sulfide **19**). The phenylsulfanyl group which we previously showed to be less nucleophilic than the 4-methoxyphenylsulfanyl group[2] is sufficiently nucleophilic under the optimised conditions to give good yields of homoallylic sulfide from allylic sulfide.

Assignment of stereochemistry and further reactions

The rearrangement of the sulfonium ylides derived from *syn* allylic sulfide **5** and *anti* allylic sulfide **6** showed that the rearrangement is stereospecifically suprafacial (suprafacial from precedent) so that once the stereochemistry of the double bond is determined the 1,4 stereochemistry can be assigned. The epimerisation experiments demonstrated that the pairs of homoallylic sulfides **54** and **59**, **55** and **60** and **56** and **61**, differ only in their 4,5 stereochemistry. The ^1H NMR, ^{13}C NMR, APT, IR and MS data of all the major products were obtained. The minor product **61** was also isolated but the ^1H NMR data for the homoallylic sulfides **59** and **60** were derived from the spectra of the equilibrated mixtures.

The 4,5 stereochemistry and the double bond geometry were assigned from the spectral data of homoallylic sulfides **54**, **55**, **57** and **58**, which bear a cyclohexyl ring. The COSY spectrum of the *anti,anti* homoallylic sulfide **55** allowed the assignment of this compound's one-dimensional ^1H NMR spectrum (Fig. 7, Table 3). By comparison with this, the ^1H NMR spectra of



Scheme 11 *Reagents and conditions:* i, NaOEt (4.4 equiv.), EtOH, RT, 3 d; ii, NaOEt (3.3 equiv.), EtOH, RT, 3 d; iii, NaOEt (4.5 equiv.), EtOH, RT, 3 d

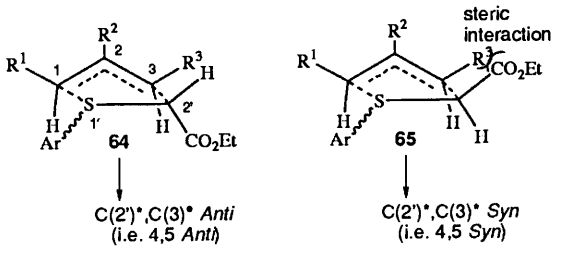


Fig. 5

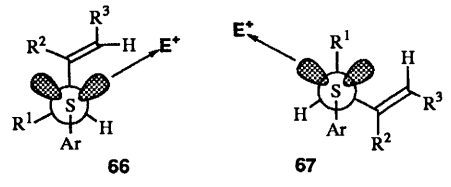


Fig. 6

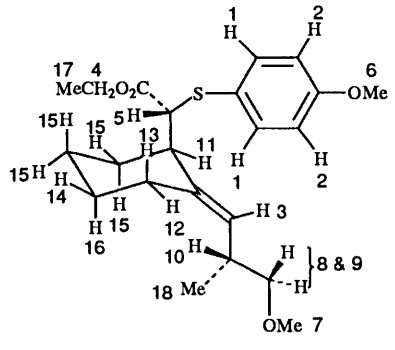


Fig. 7

homoallylic sulfides **54**, **57**, **58**, **59** and **60** could also be assigned using the great similarity in the shape and chemical shift of the signals.

The conformation of the *anti,anti* homoallylic sulfide **55** is shown in Fig. 7. Hydrogen atom 11 shows no diaxial coupling and so is assigned equatorial. The same applies to all the homoallylic sulfides which bear a cyclohexyl ring. Clearly, the 1,3

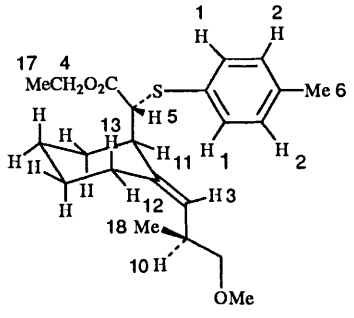


Fig. 8

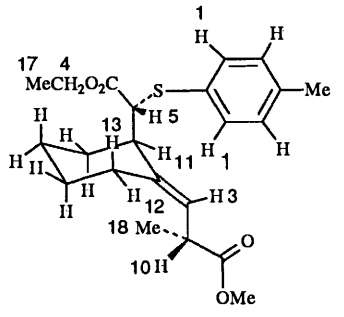


Fig. 9

diaxial interactions of hydrogen atoms 15 and 13 with the bulky secondary sulfide group are less unfavourable than the 1,3 allylic strain that would occur between hydrogen atom 3 and the same group if it were equatorial.[5] Axial hydrogen 13 shows a long-range coupling to hydrogen 3, which confirms its assignment.

In the ^{1}H NMR spectrum of homoallylic sulfide **55** the vicinal coupling constant $J_{5,11}$ is 11.6 Hz. This indicates that these hydrogen atoms are at approximately 180° to each other in the preferred conformation as illustrated in Fig. 7. This conformation has the large 4-methoxyphenylsulfanyl group orientated away from hydrogen atoms 15 and 13 so minimising 1,3 diaxial interactions. Similarly, in the ^{1}H NMR spectra of compounds **54**, **57** and **58** this coupling constant lies in the range of 11.6–11.8 Hz. Unfortunately, the CHS signals in the ^{1}H NMR spectra of homoallylic sulfides **59** and **60** were obscured by other signals, so the coupling constants were not obtained.

The major products of [2,3] sigmatropic rearrangement, homoallylic sulfides **54** and **55**, have almost identical ^{1}H NMR spectra; they differ only in the signals that correspond to hydrogens 8 and 9 in each case. This indicates that they have the same double-bond geometry and the same 4,5 stereochemistry. The epimerisation products, homoallylic sulfides **59** and **60**, also have ^{1}H NMR spectra similar to each other but markedly different from those of sulfides **54** and **55**, particularly in the chemical shift of the olefinic proton.

NOE experiments were carried out on *syn,anti* allylic sulfide **54** (Fig. 8, Table 4). Irradiation of olefinic hydrogen atom 3 (Fig. 8) of homoallylic sulfide **54** gave rise to an NOE enhancement of the equatorial hydrogen atom 11, which proves that the double bond geometry is *E*. This is further confirmed by the observation that equatorial hydrogen atom 12 shows an NOE enhancement when the allylic hydrogen atom 10 is irradiated. The 4,5 stereochemistry could not be assigned from these data.

NOE experiments on homoallylic sulfide **58** (Fig. 9, Table 5) proved that the double bond geometry of this compound is also *E*: NOE enhancements were detected between equatorial hydrogen atom 11 and olefinic hydrogen atom 3, and between equatorial hydrogen atom 12 and hydrogen atom 10. NOE

Table 3 COSY assignment of the 1D ^{1}H NMR of *anti,anti* homoallylic sulfide **55**

Assignment	Multiplicity	δ (ppm)	Assignment	Multiplicity	δ (ppm)
1	d	7.39	10	septet	2.74
2	d	6.81	11	br d	2.59
3	d	5.12	12	dt	2.40
4	AB dq	4.00	13	dt	1.89
5	d	3.93	14	m	1.8
6	s	3.78	15	m	1.6
7	s	3.33	16	m	1.3
8	dd	3.31	17	t	1.08
9	t	3.16	18	d	1.01

Table 4 Difference NOE experiments on *syn,anti* homoallylic sulfide **54**

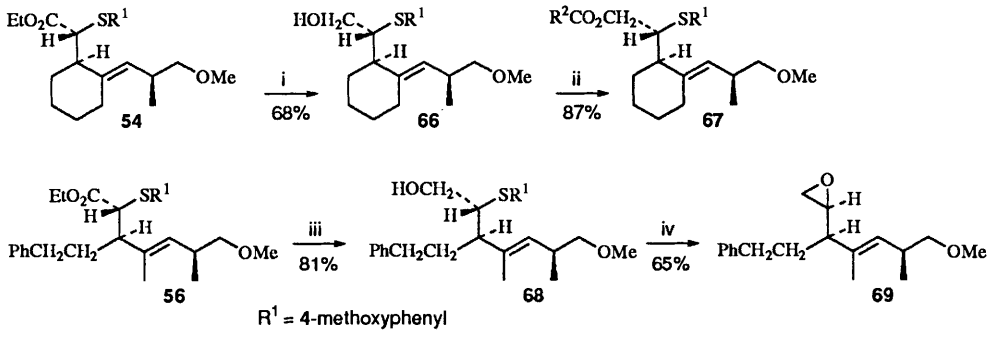
Nucleus irradiated (ppm)	Multiplicity	Nuclear Overhauser enhancements[a]											
		1-H	2-H	3-H	4-H	5-H	10-H	11-H	12-H	13-H	6-Me	17-Me	18-Me
1-H (7.37)	d	—	s	*	*	w	*	*	*	*	– ve	*	*
3-H (5.11)	d	*	*	—	*	*	*	m	*	*	*	*	*
4-H (3.98)	q	*	*	*	—	*	*	*	*	*	*	m	*
5-H (3.94)	d	m	*	w	*	—	*	*	*	w	*	*	*
10-H (2.74)	dsextet	*	*	*	*	*	—	*	m	*	*	*	m

* = no NOE. [a] s = strong NOE, m = medium NOE, w = weak NOE.

Table 5 Difference NOE experiments on *anti,anti* homoallylic sulfide **58**

Nucleus irradiated (ppm)	Multiplicity	NOE enhancement[a]									
		1-H	3-H	4-H	5-H	10-H	11-H	12-H	13-H	17-Me	18-Me
3-H (5.36)	d	w	—	*	m	*	s	*	*	*	m
4-H (3.99)	q	w	*	—	*	*	*	*	*	s	*
5-H (3.89)	d	m	w	*	—	*	*	*	w	*	*
10-H (3.43)	dq	*	m	*	*	—	*	m	*	*	s
11-H (2.61)	br d	*	s	*	*	*	—	*	*	*	*
12-H (2.37)	dt	*	*	*	*	m	*	—	s	*	*
13-H (1.93)	td	*	*	*	s	*	*	s	–	*	*

* = no NOE. [a] s = strong NOE, m = medium NOE, w = weak NOE.



Scheme 12 *Reagents and conditions:* i, $LiAlH_4$, Et_2O, −7 to 8 °C, 4 h, then RT, 5 h 30 min; ii, R^2COCl (1.4 equiv.), DMAP (1.4 equiv.), CH_2Cl_2, RT, 15 min; iii, $LiAlH_4$, Et_2O, 1 h 50 min, RT, iv, (a) Me_3OBF_4 (3.1 equiv.), CH_2Cl_2, RT, 1 h 25 min, (b) $NaOH_{(aq.)}$ (57 equiv.), 3 h

enhancements were also detected between hydrogen atom 5 and axial hydrogen atom 13, and between hydrogen atom 5 and olefinic hydrogen atom 3, but no NOE was observed between 5 and any of the other ring hydrogens. Together with the large vicinal coupling constant between hydrogen atoms 5 and 11, this confirms that the hydrogen atom 5 lies as illustrated in Fig 9. Therefore, the NOE enhancement from olefinic hydrogen atom 3 to the hydrogen 1 of the aryl ring proves the 4,5 stereochemistry is *anti*. Assignment of the 4,5 stereochemistry in other compounds is on the assumption that the stereoselectivity is in the same direction.

The epimerisation experiments (Scheme 11) showed that homoallylic sulfides **56** and **61** differ only in their 4,5 stereochemistry. The stereochemical assignment of these compounds was based on the demonstrated suprafacial stereospecificity and from the above precedent for 4,5 *anti* stereochemistry.

In summary, complete assignment of 1,4,5 stereochemistry and the double bond geometry has been possible using ^{1}H NMR techniques together with epimerisation experiments and the knowledge that C(1) to C(3) chiral transfer is stereospecific.

The synthetic possibilities of the homoallylic sulfides were briefly explored (Scheme 12). Reduction of ester **54** to the alcohol **66** and esterification gave a crystalline derivative **67**. Reduction of ester **56** gave alcohol **68** which could be converted into the epoxide **69** by using the conditions of Sharpless and co-workers.[28]

In conclusion, the [2,3] sigmatropic rearrangement of sulfonium ylides allows stereocontrolled synthesis of homoallylic sulfides with 1,4,5 related chiral centres across an *E*

double bond in good yield. The 1,4 relationship is formed stereospecifically from the 1,2 related chiral centres originally introduced by an aldol condensation; C(1) to C(3) chiral transfer (transition state numbering as in Scheme 1) in this [2,3] sigmatropic rearrangement has been proven to be stereospecifically suprafacial for the first time. The reaction is also highly selective for the 4,5 *anti* stereochemistry when carried out using our low-temperature conditions.

Experimental

When the ^{13}C NMR spectrum was obtained on the 400 MHz machine, attached proton tests (APT) were carried out. In the APT, a positive deflection of the signal indicates that the carbon atom is attached to one or three hydrogen atoms and this is indicated by an 'a' (above) after the ^{13}C NMR frequency in ppm. A negative deflection of the signal indicates that the carbon atom is attached to none or two hydrogen atoms and this is indicated by a 'b' (below) after the ^{13}C NMR frequency in ppm. When the ^{13}C NMR spectrum was obtained on the 300 MHz machine, DEPT was used instead of APT; the result is the same except that carbon atoms with no hydrogens attached do not appear in the spectrum. An asterisk after the frequency of a signal in the ^{1}H NMR spectrum indicates that the hydrogen exchanged when the sample was shaken with D_2O. Room temperature is abbreviated to RT.

(1′*RS*,2′*SR*)-1-[3′-Methoxy-1′-(4-methoxyphenylsulfanyl)-2′-methylpropyl]cyclohexene 7

Toluene-*p*-sulfonic acid monohydrate (59.2 mg, 0.311 mmol) was added to a stirred solution of the *syn* alcohol **23** in dry dichloromethane (7.8 cm^3), under argon, with light excluded, and the mixture heated to reflux (4 min); it was then heated under reflux for 12 min. After the mixture had been cooled in an ice-bath it was quenched with saturated aqueous sodium hydrogen carbonate (25 cm^3) and extracted with dichloromethane (15 cm^3). Work-up and separation of the mixture by flash column chromatography on silica gave the syn-*allylic sulfide* **7** (389.1 mg, 81%) as an oil; $R_F(CH_2Cl_2)$ 0.42; ν_{max}(smear)/cm^{-1} 1595 (Ar), 1575 (Ar), 1495 (Ar) and 825 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.27 (2 H, d, *J* 8.8, ArH), 6.78 (2 H, d, *J* 8.8, ArH), 5.12 (1 H, br s, =CH), 3.78 (3 H, s, MeOAr), 3.34 (1 H, dd, *J* 4.3 and 9.2, CH_ACH_BOMe), 3.27 (1 H, d, *J* 9.6, CHS), 3.27 (3 H, s, $MeOCH_ACH_B$), 3.08 (1 H, dd, *J* 7.0 and 9.2, CH_ACH_BOMe), 2.33–2.19 [1 H, br d, *J* 17.5, $(CH_2)_4$], 2.07–1.39 [8 H, $(CH_2)_4$ and CHMe] and 1.18 (3 H, d, *J* 6.7, *Me*CH); δ_C(400 MHz; $CDCl_3$) 159.15b, 135.86a, 135.13b, 126.25b, 125.70a, 113.89a, 76.20b, 62.87a, 58.79a, 55.24a, 35.26a, 25.23b, 24.34b, 22.75b, 22.52b and 16.06a; *m/z* 306 (11, M^+), 167 (19, $M^+ - MeOC_6H_4S$), 166 (19, $M^+ - MeOC_6H_4SH$), 140 (100, $MeOC_6H_4SH$), 135 (100, $M^+ - MeOC_6H_4S$ and MeOH) and 121 (91, $M^+ - MeOC_6H_4S$ and MeOMe) (Found: M^+, 306.1647. $C_{18}H_{26}O_2S$ requires *M*, 306.1654).

(1′*RS*,2′*SR*)-1-[3′-Methoxy-1′-(4-methoxyphenylsulfanyl)-2′-methylpropyl]cyclohexene 7

Toluene-*p*-sulfonic acid monohydrate (313 mg, 1.65 mmol, 0.2 equiv.) was added to a stirred solution of the alcohol **31** (16.5 mg, 50.8 μmol) in dry benzene (0.25 cm^3), under argon, with light excluded, and the mixture heated to reflux (5 min). After the mixture had been heated under reflux for 5 min it was cooled in an ice-bath, filtered through a short silica column with dichloromethane as eluent and evaporated under reduced pressure. Flash column chromatography of the residue yielded the *syn* allylic sulfide **7** (8.0 mg, 51%) as an oil the spectra of which were identical with those described above.

(1′*RS*,2′*RS*)-1-[3′-Methoxy-1′-(4-methoxyphenylsulfanyl)-2′-methylpropyl]cyclohexene 8

Under similar conditions but with the reaction carried out in dry dichloromethane and a period of heating under reflux of 1 h 50 min converted alcohol **24** into anti *allylic sulfide* **8** (192.4 mg, 52%); this was isolated as an oil after purification by flash column chromatography on silica eluting with hexane–diethyl ether (15:1 to 5:1); $R_F(CH_2Cl_2)$ 0.45; ν_{max}(smear)/cm^{-1} 1595 (Ar), 1575 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.27 (2 H, d, *J* 8.7, ArH), 6.78 (2 H, d, *J* 8.8, ArH), 5.06 (1 H, br m, =CH), 3.77 (3 H, s, *Me*OAr), 3.63 (1 H, dd, *J* 3.6 and 9.2, CH_AH_BOMe), 3.47 (1 H, dd, *J* 6.3 and 9.2, CH_AH_BOMe), 3.35 (3 H, s, MeO), 3.28 (1 H, d, *J* 10.5, CHS), 2.26 [1 H, br d, *J* 17.2, $(CH_2)_4$], 2.20–1.40 [8 H, m, $(CH_2)_4$ and CHMe] and 0.93 (3 H, d, *J* 6.8, *Me*CH); δ_C(400 MHz; $CDCl_3$) 159.21b, 136.04a, 134.67b, 128.21b, 128.15a, 113.87a, 75.99b, 61.96a, 58.91a, 55.24a, 35.37a, 25.23b, 23.81b, 22.73b, 22.54b and 16.25a; *m/z* 306 (34%, M^+), 167 (33, $M^+ - MeOC_6H_4S$), 140 (94, $MeOC_6H_4SH$), 135 (100, $M^+ - MeOC_6H_4S$ and MeOH), 121 (87, $M^+ - MeOC_6H_4S$ and MeOMe) (Found: M^+, 306.1683. $C_{18}H_{26}O_2S$ requires *M*, 306.1653).

[2*RS*,3*SR*,(*E*)]-7-Methoxy-5-(4-methoxyphenylsulfanyl)-4,6-dimethyl-1-phenylhept-3-ene 9

Toluene-*p*-sulfonic acid monohydrate (38.3 mg, 0.201 mmol) and alcohols **45** and **46** (2.7:1) (404.8 mg, 1.04 mmol) were heated under reflux for 1 h in dry dichloromethane (10.5 cm^3), under argon and with light excluded. After being cooled in an ice-bath, the mixture was filtered through a short silica column with dichloromethane as eluent and evaporated under reduced pressure. Repeated flash column chromatography of 97% of the mixture on silica (40 g) eluting with hexane–ethyl acetate (16:1) yielded the *allylic sulfide* **9** (209.6 mg, 56%) as an oil of 93% purity; R_F(dichloromethane) 0.33; ν_{max}(smear)/cm^{-1} 1595 (Ar), 1570 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.27–7.12 (5 H, m, 2 of C_6H_4OMe and 3 of PhH), 7.06 (2 H, d, *J* 6.9, PhH), 6.78 (2 H, d, *J* 8.7, C_6H_4OMe), 4.93 (1 H, t, *J* 7.1, CH=), 3.77 (3 H, s, *Me*OAr), 3.31 (1 H, d, *J* 9.8, CHS), 3.24 (1 H, obscured, CH_ACH_BOMe), 3.24 (3 H, s, $MeOCH_2$), 3.01 (1 H, dd, CH_ACH_BOMe), 2.44 (1 H, dt, *J* 13.7 and 7.9, CH_AH_BPh), 2.37 (1 H, dt, *J* 13.8 and 7.1, CH_AH_BPh), 2.16 (2 H, q, *J* 7.5, CH_2CH=), 1.95 (1 H, m, CHMe), 1.61 (3 H, s, *Me*C=) and 1.18 (3 H, d, *J* 6.7, *Me*CH); δ_C(250 MHz; $CDCl_3$) 159.22b, 142.04b, 135.78a, 133.13b, 128.29a, 128.23a, 128.08a, 126.11b, 125.72a, 114.05a, 76.09b, 64.43a, 58.77a, 55.27a, 35.45b, 35.22a, 29.51b, 16.05a and 12.26a; *m/z* 370 (9.2%, M^+), 230 (7.2, M – $MeOC_6H_4SH$), 199 (20, M – $MeOC_6H_4S$ and MeOH), 140 (30, $MeOC_6H_4SH$) and 91 (100, $PhCH_2$) (Found: M^+, 370.1955. $C_{23}H_{30}O_2S$ requires *M*, 370.1967).

(1′*RS*,2′*SR*)-1-[3′-Benzyloxy-2′-methyl-1′-(phenylsulfanyl)-propyl]cyclohexene 10

In the same way, a mixture of toluene-*p*-sulfonic acid monohydrate (20.6 mg, 0.108 mmol) and *anti* β-hydroxy sulfide **27** (185 mg, 0.50 mmol) in dry dichloromethane (2.4 cm^3) were heated to reflux (7 min) and refluxed for 6 min. Filtration and flash column chromatography on silica (30 g) eluting with hexane–diethyl ether (30:1) gave syn *allylic sulfide* **10** (134 mg, 76%) as an oil; R_F[hexane–diethyl ether (10:1)] 0.43; ν_{max}(smear)/cm^{-1} 3060 (=CH) 3030 (PhH), 2980–2830 (CH), 1585 (Ph), 750 (Ph), 740 (C=CH) and 700 (Ph); δ_H(250 MHz; $CDCl_3$) 7.36–7.14 (10 H, m, Ph), 5.29 (1 H, br s, =CH), 4.47 (1 H, d, *J* 12.1, CH^AH^BPh), 4.43 (1 H, d, *J* 12.1, CH^AH^BPh), 3.54 (1 H, d, *J* 9.1, CHS), 3.45 (1 H, dd, *J* 4.6 and 9.1, CH^DH^EOBn), 3.24 (1 H, dd, *J* 6.6 and 9.1, CH^DH^EOBn), 2.23 [1 H, br d, *J ca.* 16, $(CH_2)_5$], 2.08 (1 H, m, CHMe), 1.96–1.68 [3 H, m, $(CH_2)_5$], 1.63–1.35 [4 H, m, $(CH_2)_5$] and 1.20 (3 H, d, CH*Me*); δ_C(400 MHz; $CDCl_3$) 138.60b, 136.16b, 135.15b, 132.74a, 128.35a, 128.27a, 127.55a, 127.44a, 126.57a, 125.81a, 73.59b, 73.05b, 61.25a, 35.74a, 25.21b, 24.65b, 22.74b, 22.46b and 15.91a; *m/z* 352 (19%, M^+), 243 (11, M – PhS) and 91 (100, $PhCH_2$) (Found: M^+, 352.1874. $C_{23}H_{28}OS$ requires *M*, 352.1861).

1-(4-Methoxyphenylsulfanyl)cyclohexanecarbaldehyde 11

Thionyl chloride (3.2 cm^3, 44.1 mmol) was added, over 25 min,

to a stirred solution of the alcohol **14** (11.8 g, 41.8 mmol) and triethylamine (99%; 6.2 cm^3, 44.0 mmol) in dry dichloromethane (42 cm^3) under nitrogen at −2 °C, the temperature of the mixture not rising above 9 °C. The resulting mixture was stirred for 1 h between −5 and −2 °C and then quenched with ice cold *water (20 cm³)*. Aqueous hydrochloric acid (2 mol dm^{-3}; 50 cm^3) was added to the mixture which was then extracted with dichloromethane (1 × 20 cm^3, 3 × 50 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the residue was separated by flash column chromatography on silica (300 g) eluting with hexane–diethyl ether (8:1–5:1). The impure fractions were rechromatographed to yield the *aldehyde* **11** (9.10 g, 87%) as a cream-coloured solid, mp < 30 °C; R_F(dichloromethane) 0.48; ν_{max}(smear)/cm^{-1} 3010 (ArH), 2940–2800 (CH), 2710 (CH of aldehyde), 1715 (C=O), 1595 (Ar), 1570 (Ar), 1495 (Ar) and 830 (*para* disubstituted benzene); δ_H(300 MHz; $CDCl_3$) 9.27 (1 H, s, O=CH), 7.30 (2 H, d, *J* 8.7, ArH), 6.83 (2 H, d, *J* 8.8, ArH), 3.80 (3 H, s, MeO), 1.89–1.75 [4 H, m, $(CH_2)_5$], 1.66–1.52 [3 H, m, $(CH_2)_5$] and 1.44–1.29 [3 H, m, $(CH_2)_5$]; δ_C(300 MHz; $CDCl_3$) 194.47a, 160.89, 138.76a, 119.44, 114.49a, 59.97, 55.31a, 30.35b, 25.50b and 23.06b; *m/z* 250 (34, M^+), 221 (85, M − CHO), 140 (86, $MeOC_6H_4SH$), 139 (94, $MeOC_6H_4S$) and 59 (100) (Found: M^+, 250.1006. $C_{14}H_{18}O_2S$ requires *M*, 250.1028).

Chloromethyl (4-methoxyphenyl) sulfide 12

Sodium hydride (80% suspension in oil; 5.48 g, 0.183 mol) was added to a stirred solution of 4-methoxybenzenethiol (25.1 g, 0.174 mol) in dry THF (1.0 dm^3) under nitrogen at RT. After being stirred for 1 h, the mixture was treated with bromochloromethane (98%; 12.5 cm^3, 0.183 mol) and stirred for a further 2.5 h. The mixture was then filtered through Kieselguhr eluting with diethyl ether and evaporated under reduced pressure. The resultant oil was distilled to give the slightly impure chloride (16.4 g, 50%) as an oil, bp 96 °C at 0.3–0.4 mmHg; δ_H(300 MHz; $CDCl_3$) 7.52 (2 H, d, *J* 8.7, ArH), 6.93 (2 H, d, *J* 8.8, ArH), 4.87 (2 H, s, CH_2Cl) and 3.84 (3 H, s, MeO); δ_C(300 MHz; $CDCl_3$) 160.36, 134.85a, 123.45, 114.86a, 55.42a and 53.13b; *m/z* 190 (29%, M^+ with ^{37}Cl), 188 (68, M^+ with ^{35}Cl), 153 (79, M − Cl) and 139 (100, M − CH_2Cl).

Methoxymethyl 4-methoxyphenyl sulfide 13

Sodium methoxide (5.01 g, 90.0 mmol) was added to a stirred solution of the chloride **12** (16.3 g, 86.4 mmol) in methanol and the resulting mixture stirred at RT for 2 h 10 min before removal of the solvent under reduced pressure. The residue was dissolved in water (200 cm^3) and extracted with diethyl ether (200 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The resultant yellow oil was distilled *in vacuo* to yield the *title compound* **13** (13.4 g, 84%) as an oil, bp 86 °C at 0.3–0.4 mmHg; R_F[hexane–diethyl ether (10:1)] 0.39; ν_{max}(smear)/cm^{-1} 1595 (ArH), 1570 (ArH) and 830 (*para* disubstituted benzene); δ_H(300 MHz, $CDCl_3$) 7.43 (2 H, d, *J* 8.8, ArH), 6.86 (2 H, d, *J* 8.7, ArH), 4.85 (2 H, s, SCH_2O), 3.79 (3 H, s, ArOMe) and 3.45 (3 H, s, CH_2OMe); δ_C(300 MHz, $CDCl_3$) 159.36, 133.69a, 126.01, 114.62a, 79.29b, 56.00a and 55.37a; *m/z* 184 (100%, M^+), 154 (28, M − CH_2O), 139 (41, M − CH_2OMe) and 45 (89, M − $MeOCH_2$) (Found: M^+, 184.0560. $C_9H_{12}O_2S$ requires *M*, 184.0558).

1-[Methoxy(4-methoxyphenylsulfanyl)methyl]cyclohexanol 14

Butyllithium (2.5 mol dm^{-3} solution in hexane; 29 cm^3, 72.5 mmol) was added over 7 min to a stirred solution of the sulfide **13** (13.3 g, 72.1 mmol) in dry THF (80 cm^3) under nitrogen, the temperature being maintained at −45 to −28 °C. After being stirred for 25 min the now brown–yellow solution was treated with cyclohexanone (7.5 cm^3, 72.2 mmol); it immediately turned pale yellow. Stirring was continued for a further 30 min with the temperature being allowed to rise to −20 °C; the reaction was then quenched by addition of saturated aqueous ammonium chloride (200 cm^3) to the mixture which was then extracted with diethyl ether (3 × 200 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the mixture separated by repeated flash column chromatography on silica (424 g) eluting with hexane–diethyl ether (9:1–4:1) to give the *alcohol* **14** (12.01 g, 59%) as an oil; R_F[hexane–diethyl ether (3:1)] 0.36; ν_{max}(smear)/cm^{-1} 3510 (OH), 1595 (Ar), 1570 (Ar), 1495 (Ar) and 830 (*para*-disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.46 (2 H, d, *J* 8.9, ArH), 6.83 (2 H, d, *J* 8.9, ArH), 4.32 (1 H, s, CHS), 3.79 (3 H, s, ArO*Me*), 3.42 (3 H, s, CHO*Me*), 2.24 (1 H, very br s, OH), 1.78–1.46 [9 H, m, $(CH_2)_5$] and 1.27–1.08 [1 H, m, $(CH_2)_5$]; δ_H(300 MHz; $CDCl_3$) 159.47, 135.29a, 126.39, 114.74a, 104.89a, 74.19, 57.90a, 55.37a, 33.24b, 32.76b, 25.76b, 21.76b and 21.40b; *m/z* 282 (26%, M^+), 143 (62, M − $MeOC_6H_4S$) and 140 (100, $MeOC_6H_4SH$) (Found: M^+, 282.1279. $C_{15}H_{22}O_3S$ requires *M*, 282.1289).

Methyl 3-hydroxy-3-[1-(4-methoxyphenylsulfanyl)cyclohexyl]-2-methylpropionate 15, 16

Methyl propionate (2.8 cm^3, 29.1 mmol) was added over 5 min to a stirred solution of LDA [made from butyllithium (1.6 mol dm^{-3} solution in hexane; 19.5 cm^3, 31.2 mmol) and diisopropylamine (4.4 cm^3, 31.1 mmol)] in dry THF (150 cm^3), under argon, and cooled in a CO_2–acetone bath. After being stirred for 30 min at < −68 °C the mixture was treated with a solution of the aldehyde **11** (7.02 g, 28 mmol) in dry THF (10 cm^3), added slowly and washed in with THF (5 cm^3). Stirring was continued for 4 h with the temperature rising gradually to −45 °C. After this the reaction was quenched by the addition of saturated aqueous ammonium chloride (100 cm^3) and water (100 cm^3) to the mixture which was then extracted with diethyl ether (3 × 200 cm^3). The combined extracts were washed with hydrochloric acid (3 mol dm^{-3}; 200 cm^3) and the aqueous layer back-extracted with diethyl ether (400 cm^3). The combined ethereal extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the mixture was separated by flash column chromatography on silica (600 g) with dichloromethane–methanol (800:1 to 200:1) as eluent. Impure fractions were rechromatographed. This yielded the anti (2RS,3SR)-*aldol* **15** (2.28 g, 24%) as an oil; R_F[CH_2Cl_2–MeOH (400:1)] 0.19; ν_{max}(smear)/cm^{-1} 3470 (OH), 1740 (C=O, conformer without hydrogen bonding), 1710 (C=O, conformer with hydrogen bonding), 1595 (Ar), 1570 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.37 (2 H, d, *J* 8.7, ArH), 6.82 (2 H, d, *J* 8.7, ArH), 4.18 (1 H, br s, OH), 3.79 (3 H, s, OMe), 3.71 (3 H, s, OMe), 3.48 (1 H, dq, *J* 1.9 and 7.3, C*H*Me), 3.25 (1 H, br s, C*H*OH), 2.05–1.03 [10 H, m, $(CH_2)_5$] and 1.34 (3 H, d, *J* 7.3); δ_C(400 MHz; $CDCl_3$) 178.14b, 160.24b, 138.44a, 121.32b, 114.23a, 79.30a, 58.90b, 55.25a, 51.94a, 37.10a, 30.61b, 29.75b, 25.74b, 21.89b, 21.67b and 17.97a; *m/z* 338 (5.4%, M^+), 221 [53, M^+ − CH(OH)CH(Me)CO_2Me], 199 (19, M^+ − $MeOC_6H_4S$), 181 (41, M^+ − $MeOC_6H_4S$ and H_2O) and 140 (100, $MeOC_6H_4SH$) (Found: M^+, 338.1564. $C_{18}H_{26}O_4S$ requires *M*, 338.1552) and the syn (2RS, 3RS)-*aldol* **16** (3.35 g, 35%) as plates, mp 84.5–85.5 °C (from hexane); R_F[CH_2Cl_2–MeOH (400:1)] 0.16; ν_{max}(Nujol mull)/cm^{-1} 3520 (OH), 1720 (C=O), 1590 (Ar), 1570 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.42 (2 H, d, *J* 8.6, ArH), 6.84 (2 H, d, *J* 8.7, ArH), 3.80 (3 H, s, MeOAr), 3.73 (1 H, d, *J* 5.7, CHOH), 3.63 (3 H, s, MeOCO), 2.97 (1 H, qn, *J* 6.5, C*H*Me), 2.01–1.12 [10 H, m, $(CH_2)_5$] and 1.28 (3 H, d, *J* 7.0, *Me*CH); δ_C(400 MHz; $CDCl_3$) 176.80b, 160.40b, 138.48a, 120.59b, 114.39a, 74.32a, 60.99b, 55.25a, 51.79a, 40.37a, 30.90b, 30.16b, 25.92b, 21.86b and 14.32a; *m/z* 338 (2.1%, M^+), 221 [19, M^+ − CH(OH)CH(Me)CO_2Me], 181 (19, M^+ − $MeOC_6H_4S$ and H_2O) and 140 (100, $MeOC_6H_4SH$) (Found: C, 64.0; H, 7.7; S, 9.4%; M^+, 338.1524. $C_{18}H_{26}O_4S$ requires C, 63.88; H, 7.74; S, 9.47%; *M*, 338.1552).

(3*RS*,4*SR*)-4-(4-Methoxyphenylsulfanyl)-3-methyl-1-oxaspiro[4.5]decan-2-one 17

By the same procedure as for **9** above, a solution of toluene-*p*-

sulfonic acid monohydrate (170.3 mg, 0.895 mmol) and the alcohol **15** (1.55 g, 4.58 mmol) in dry dichloromethane (23 cm^3) was heated under reflux for 9 h 30 min to give, after filtration, the anti *lactone* **17** (1.35 g, 96%) as needles, mp 124–126 °C (from hexane–ethyl acetate); $R_F(CH_2Cl_2)$ 0.32; ν_{max}(Nujol mull)/cm^{-1} 1770 (C=O), 1595 (Ar), 1575 (Ar), 1495 (Ar) and 825 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.43 (2 H, d, *J* 8.8, ArH), 6.85 (2 H, d, *J* 8.9, ArH), 3.80 (3 H, s, MeO), 2.94 (1 H, d, *J* 12.3, CHSAr), 2.65 (1 H, dq, *J* 12.3 and 7.0, CHMe), 1.99–1.90 [1 H, m, $(CH_2)_5$], 1.85–1.51 [8 H, m, $(CH_2)_5$], 1.27 (3 H, t, *J* 7.0, MeCH) and 1.25–1.08 [1 H, m, $(CH_2)_5$]; δ_C(400 MHz; $CDCl_3$) 176.52b, 160.00b, 135.64a, 124.22b, 114.87a, 86.85b, 63.25a, 55.35a, 41.32a, 36.18b, 31.68b, 25.10b, 22.40b, 21.44b and 13.86a; *m/z* 306 (53%, M^+), 180 (100, M − CO_2 and C_6H_{10}) and 140 (23, MeO-C_6H_4SH) (Found: C, 66.5; H, 7.2; S, 10.6%; M^+, 306.1268. $C_{17}H_{22}OS$ requires C, 66.64; H, 7.24; S, 10.46%; *M*, 306.1289).

(3*SR*,4*SR*)-4-(4′-Methoxyphenylsulfanyl)-3-methyl-1-oxaspiro[4.5]decan-2-one 18 and (2*SR*,3*SR*) methyl 3-(cyclohex-1′-enyl)-3-(4″-methoxyphenylsulfanyl)-2-methylpropionate 19

In the same way, a solution of toluene-*p*-sulfonic acid monohydrate (313 mg, 1.65 mmol) and the aldol **16** (2.79 g, 8.23 mmol) in dry dichloromethane (20 cm^3), was heated under reflux for 4 h 30 min. Filtration and flash column chromatography on silica eluting with dichloromethane gave the *lactone* **18** (1.303 g, 52%) as prisms, mp 65–67 °C (from hexane–diethyl ether); R_F(dichloromethane) 0.25; ν_{max}(Nujol mull)/cm^{-1} 1770 (C=O), 1595 (Ar), 1495 (Ar) and 830 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.36 (2 H, d, *J* 8.8, ArH), 6.85 (2 H, d, *J* 8.9, ArH), 3.80 (3 H, s, MeO), 3.63 (1 H, d, *J* 9.0, CHS), 3.01 (1 H, dq, *J* 9.0 and 7.7, C*H*Me), 1.96–1.50 [9 H, m, $(CH_2)_5$], 1.41 (3 H, d, *J* 7.7, *Me*CH) and 1.32–1.12 [1 H, m, $(CH_2)_5$]; δ_C(400 MHz; $CDCl_3$) 177.90b, 159.48b, 133.93a, 125.28b, 114.94a, 87.34b, 59.62a, 55.35a, 39.31a, 36.79b, 34.15b, 24.86b, 22.64b, 21.96b and 13.81a; *m/z* 306 (63%, M^+), 180 (100, M^+ − CO_2 and C_6H_{10}) and 140 (52, $MeOC_6H_4SH$) (Found: M^+, 306.1295. $C_{17}H_{22}O_3S$ requires *M*, 306.1290); and the *allylic sulfide* **19** (934.9 mg, 36%) as an oil; R_F(dichloromethane) 0.46; ν_{max}(smear)/cm^{-1} 1740 (C=O), 1595 (Ar), 1575 (Ar), 1495 (Ar) and 840 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.28 (2 H, d, *J* 8.7, ArH), 6.78 (2 H, d, *J* 8.7, ArH), 5.07 (1 H, br s, C=CH), 3.78 (3 H, s, ArMe), 3.74 (3 H, s, CO_2Me), 3.43 (1 H, d, *J* 11.6, CHS), 2.66 (1 H, dq, *J* 11.6 and 6.8, C*H*Me), 2.25 [1 H, vbr d, *J ca.* 17, $(CH_2)_4$], 1.96–1.40 [7 H, m, $(CH_2)_4$] and 1.08 (3 H, d, *J* 6.9, *Me*CH); δ_C(400 MHz; $CDCl_3$) 175.88b, 159.57b, 136.54a, 133.11b, 126.99a, 125.11b, 113.90a, 61.53a, 55.23a, 51.74a, 42.20a, 25.23b, 23.76b, 22.65b, 22.44b and 16.59a; *m/z* 320 (41%, M^+), 181 (28, M^+ − $MeOC_6H_4S$), 149 (36, M^+ − $MeOC_6H_4S$ and MeOH), 140 (100, $MeOC_6H_4SH$) and 121 (66, M^+ − $MeOC_6H_4S$, MeOH and CO) (Found: M^+, 320.1459. $C_{18}H_{24}O_3S$ requires *M*, 320.1446).

(2*SR*,3*RS*)-3-(1-Hydroxycyclohexyl)-3-(4-methoxyphenylsulfanyl)-2-methylpropan-1-ol 20

Lithium aluminium hydride (95%; 58.4 mg, 1.46 mmol) and the *anti* lactone **17** (378.4 mg, 1.23 mmol) in dry THF (6 cm^3) were stirred at RT for 3.5 h after which the reaction was quenched with ice. Aqueous potassium sodium tartrate (0.5 mol dm^{-3}; 200 cm^3 solution) and aqueous sodium hydroxide (10% solution; 30 cm^3) were added to the mixture which was then extracted with diethyl ether (2 × 100 cm^3) and then dichloromethane (3 × 100 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Flash column chromatography of the residue on silica (26 g) with dichloromethane–methanol (50:1) as eluent yielded the syn *diol* **20** (345.2 mg, 90%) as plates, mp 86–87 °C; R_F[dichloromethane–methanol (50:1)] 0.20; ν_{max}(Nujol mull)/cm^{-1} 3280 (OH), 1595 (Ar), 1575 (Ar), 1495 (Ar) and 820 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.44 (2 H, d, *J* 8.9, ArH), 6.80 (2 H, d, *J* 8.9, ArH), 3.77 (3 H, s, MeO), 3.75 (1 H, dd, *J* 9.2 and 10.5, CH_AH_BOH), 3.58 (1 H, dd, *J* 4.9 and 10.6, CH_AH_BOH), 3.42 (1 H, d, *J* 2.1, CHS), 2.39 (1 H, m, C*H*Me), 1.84 (2 H, br s, OH), 1.78–1.08 [10 H, m, $(CH_2)_5$] and 1.01 (3 H, d, *J* 6.8, *Me*CH); δ_C(400 MHz; $CDCl_3$) 158.65b, 133.09a, 128.51b, 114.70a, 74.85b, 66.68b, 64.21a, 55.29a, 37.60b, 35.96a, 35.05b, 25.61b, 22.14b and 12.95a; *m/z* 310 (1.9%, M^+), 212 (100, M^+ − $C_6H_{10}O$) and 140 (76, $MeOC_6H_4SH$) (Found: M^+, 310.1575. $C_{17}H_{26}O_3S$ requires *M*, 310.1603).

(2*RS* and 2*SR*,3*RS*,4*SR*)-4-(4-Methoxyphenylsulfanyl)-3-methyl-1-oxaspiro[4.5]decan-2-ol 21

In the same way, reduction of the *anti* lactone **17** (119.3 mg, 0.389 mmol) for 2 h at 4–15 °C and then for 1 h 10 min at RT gave *syn* diol **20** (89.5 mg, 74%) and the *hemiacetal* **21** (22.7 mg, 18%) as a 1:1 mixture of anomers *anti anti* (A) and *syn anti* (B); R_F[dichloromethane–methanol (50:1)] 0.47; δ_H(250 MHz; $CDCl_3$) 7.42 (2 $H^{A\ or\ B}$, d, *J* 8.8, ArH), 7.41 (2 $H^{A\ or\ B}$, d, *J* 8.8, ArH), 6.81 (2 $H^{A\ and\ B}$, d, *J* 8.8, ArH), 5.23 (1 H^B, br s, C*H*OH), 5.00 (1 H^A, t, *J* 4.6, CHOH), 3.79 (3 $H^{A\ and\ B}$, s, MeO), 3.48 (1 H^A, d, *J* 4.4, CHO*H*), 3.00 (1 $H^{A\ or\ B}$, d, 12.4, CHS), 2.91 (1 H^B, d, *J* 2.4, CHO*H*), 2.66 (1 $H^{A\ or\ B}$, d, *J* 11.3, CHS), 2.18 (1 $H^{A\ and\ B}$, m, C*H*Me), 1.80–1.46 [10 $H^{A\ and\ B}$, m, $(CH_2)_5$], 1.17 (3 $H^{A\ or\ B}$, d, *J* 6.8, CH*Me*) and 1.13 (3 $H^{A\ or\ B}$, *J* 6.8, CH*Me*); δ_C(400 MHz; $CDCl_3$) 159.38b, 159.27b, 135.04a, 134.88a, 126.26b, 125.98b, 114.55a, 114.52a, 102.77a, 97.31a, 85.15b, 65.74a, 63.37a, 55.30a, 47.66a, 44.20a, 38.72b, 36.90b, 33.92b, 32.69b, 25.61b, 25.47b, 23.02b, 22.93b, 21.91b, 21.80b, 15.74a and 11.84a; *m/z* 308 (30%, M^+), 210 (48, M − $C_6H_{10}O$) and 140 (100, $MeOC_6H_4SH$) (Found: M^+, 308.1443. $C_{17}H_{24}O_3S$ requires *M*, 308.1446).

(2*RS*,3*RS*)-3-(1-Hydroxycyclohexyl)-3-(4-methoxyphenylsulfanyl)-2-methylpropan-1-ol 22

In the same way, reduction of the *syn* lactone **18** (32.2 mg, 0.105 mmol) with cooling in an ice-bath for 1 h followed by quench, work-up and flash column chromatography on silica (3.5 g) with dichloromethane–methanol (50:1) as eluent gave the anti *diol* **22** (26.6 mg, 82%) as prisms, mp 112.5–115 °C (ethyl acetate); R_F[dichloromethane–methanol (50:1)] 0.25; ν_{max}(Nujol mull)/cm^{-1} 3230–3130 (OH), 1595 (Ar), 1570 (Ar), 1495 (Ar) and 830 (*p*-disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.38 (2 H, d, *J* 8.8, ArH), 6.81 (2 H, d, *J* 8.9, ArH), 3.78 (3 H, s, MeO), 3.74 (1 H, dd, *J* 9.4 and 12.0, CH_ACH_BOH), 3.44* (2 H, br s, OH), 3.38 (1 H, dd, *J* 3.0 and 12.2, CH_ACH_BOH), 3.05 (1 H, d, *J* 1.5, CHS), 2.59 (1 H, m, C*H*Me), 2.04–1.95 [2 H, m, $CH_{eq.}COH$ of $(CH_2)_5$, signal not wide enough to be axial protons], 1.70–1.16 [8 H, m, $(CH_2)_5$] and 1.11 (3 H, d, *J* 6.9, *Me*CH); δ_C(400 MHz; $CDCl_3$) 158.75b, 133.34a, 128.62b, 114.64a, 74.89b, 69.59a, 64.76b, 55.30a, 38.28b, 35.38a, 34.88b, 25.56b, 22.26b, 22.05b and 18.86a (Found: C, 65.8; H, 8.4; S, 10.6. $C_{17}H_{26}O_3S$ requires C, 65.77; H, 8.44; S, 10.33%).

(1′*RS*,2′*SR*)-1-[3′-Methoxy-1′-(4″-methoxyphenylsulfanyl)-2′-methylpropyl]cyclohexanol 23

Aq. sodium hydroxide (50%; 0.270 cm^3, 3.38 mmol) was added to a solution of the *syn* diol **20** (801.6 mg, 2.58 mmol) and tetrabutylammonium iodide (98%; 0.985 g, 2.61 mmol) in dry dichloromethane (2.6 cm^3) over 5 min and the mixture stirred at RT for 50 min. Cooling in an ice-bath was followed by addition of dimethyl sulfate (0.370 cm^3, 3.90 mmol) over 50 min. The ice-bath was removed and the mixture was stirred for 24 h at RT before treatment with concentrated aqueous ammonia (3 cm^3). The mixture was then stirred for 35 min after which it was poured into water (100 cm^3) and extracted with dichloromethane (3 × 100 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The mixture was separated by flash column chromatography on silica with

dichloromethane–methanol (200:3) as eluent; the impure fractions were then combined and separated on silica with dichloromethane–methanol (10:1) as eluent, to yield the syn *alcohol* **23** (576.0 mg, 69%, 91% on unrecovered starting material) as an oil; R_F[MeOH–CH_2Cl_2 (1:50)] 0.55; ν_{max}(smear)/cm^{-1} 3490 (OH), 1595 (Ar), 1575 (Ar), 1495 (Ar) and 825 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.39 (2 H, d, *J* 8.8, ArH), 6.80 (2 H, d, *J* 9.0, ArH), 3.77 (3 H, s, MeOAr), 3.54 (1 H, t, *J* 9.5, CH_AH_BOMe), 3.43 (1 H, d, *J* 2.1, CHS), 3.25 (3 H, s, *Me*OCH_2), 3.23 [1 H, dd (partially obscured), *J* 9.2 and 4.6, CH_AH_BOMe], 2.46 (1 H, m, C*H*Me), 1.99* (1 H, br s, OH), 1.79–1.06 [10 H, m, $(CH_2)_5$] and 0.98 (3 H, d, *J* 6.9, *Me*CH); δ_C(400 MHz; $CDCl_3$) 158.44b, 132.67a, 128.92b, 114.52a, 76.41b, 74.74b, 63.90a, 58.27a, 55.27a, 37.88b, 34.97b, 33.25a, 25.63b, 22.15b and 12.99a; *m/z* 324 (5.2%, M^+), 226 (100, $M^+ - C_6H_{10}O$), 194 (32, $M^+ - C_6H_{10}O$ and MeOH) and 140 (87, $MeOC_6H_4SH$) (Found: M^+, 324.1758. $C_{18}H_{28}O_3S$ requires *M*, 324.1760).

(1′*RS*,2′*RS*)-1-[3′-Methoxy-1′-(4″-methoxyphenylsulfanyl)-2′-methylpropyl]cyclohexanol 24

Aq. sodium hydroxide (50%; 0.385 cm^{-3}, 4.81 mmol) was added to a solution of the *anti* diol **22** (572.1 mg, 1.84 mmol) and tetrabutylammonium iodide (98%; 1.33 g, 3.52 mmol) in dry dichloromethane (2.77 cm^3) and the mixture stirred at RT for 30 min. Cooling in an ice-bath was followed by addition of dimethyl sulfate (0.523 cm^{-3}, 5.53 mmol) over 50 min. After removal of the ice-bath, the mixture was stirred at RT for 21 h. After being quenched, work-up of the mixture as for **23** above and flash column chromatography on silica (61 g) with dichloromethane–methanol (40:1) as eluent and then on silica (68 g) with dichloromethane–methanol (80:1) as eluent gave the anti *alcohol* **24** (454.3 mg, 76%) as an oil; R_F[dichloromethane–methanol (50:1)] 0.62; R_F[hexane–ethyl acetate (3:1)] 0.34; ν_{max}(smear)/cm^{-1} 3400 (OH), 1595 (Ar), 1575 (Ar), 1495 (Ar) and 830 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.40 (2 H, d, *J* 8.9, ArH), 6.79 (2 H, d, *J* 8.9, ArH), 4.16 (1 H, s, OH), 3.77 (3 H, s, ArOMe), 3.71 (1 H, d, *J* 9.3, CH_AH_BOMe), 3.35 (3 H, s, CH_2OMe), 3.21 (1 H, dd, *J* 4.2 and 9.5, CH_AH_BOMe), 2.99 (1 H, br d, *J* 1.5, CHS), 2.61 (1 H, m, C*H*Me), 2.14 [1 H, m, $(CH_2)_5$], 1.85–1.10 [9 H, m, $(CH_2)_5$] and 1.02 (3 H, d, *J* 6.9); δ_C(400 MHz; $CDCl_3$) 158.50b, 133.40a, 129.77b, 114.45b, 75.02b, 73.29b, 69.22a, 58.68a, 55.26a, 37.37b, 36.48b, 33.45a, 25.87b, 22.35b, 22.28b and 18.85a; *m/z* 324 (3.2%, M^+), 226 (100, $M^+ - C_6H_{10}O$), 194 (33, $M^+ - C_6H_{10}O$ and MeOH) and 140 (54, $MeOC_6H_4SH$) (Found: M^+, 324.1739. $C_{18}H_{28}O_3S$ requires *M*, 324.1759).

(2*RS*,3*RS*)-3-(Cyclohex-1′-enyl)-3-(4″-methoxyphenylsulfanyl)-2-methylpropanol 25

By a method similar to that for **20**, lithium aluminium hydride (95%, 98.7 mg, 2.47 mmol) and the ester **19** (806.2 mg, 2.51 mmol) were stirred in dry ether (12.5 cm^3) for 6 h with the temperature of the mixture rising from 0 °C to RT. After being quenched, work-up of the mixture followed by flash column chromatographic separation on silica (84 g) with dichloromethane–methanol (50:1) as eluent gave the *alcohol* **25** (701.4 mg, 96%) as an oil; R_F[CH_2Cl_2–MeOH (50:1)] 0.43; ν_{max}(smear)/cm^{-1} 3390 (OH), 3050 (=CH), 3000–2800 (CH), 1595 (Ar), 1575 (Ar), 1495 (Ar), 850 (*para* disubstituted benzene) and 800 (C=CH); δ_H(250 MHz; $CDCl_3$) 7.28 (2 H, d, *J* 8.8, ArH), 6.79 (2 H, d, *J* 8.8, ArH), 5.03 (1 H, br s, =CH), 3.81 (2 H, secondary ABX system, CH_AH_BOH), 3.78 (3 H, s, MeO), 3.23 (1 H, d, *J* 10.7, CHS), 2.28 [1 H, br d, *J* 17.5, $(CH_2)_4$], 1.97–1.41 (8 H, m, $(CH_2)_4CH_XMe$) and 0.92 (3 H, d, *J* 6.9, *Me*CH_X); δ_C(400 MHz; $CDCl_3$) 159.43b, 136.19a, 134.66b, 128.22a, 125.59b, 113.99a, 66.67b, 63.01a, 55.24a, 38.98a, 25.20b, 23.71b, 22.70b, 22.51b and 16.13a; *m/z* 292 (26, M^+) and 140 (100, $MeOC_6H_4SH$) (Found: M^+, 292.1510. $C_{17}H_{24}O_2S$ requires *M*, 292.1497).

(1*RS*,2*RS*)-3-Benzyloxy-1-[1′-(phenylsulfanyl)cyclohexyl]-2-methylpropan-1-ol 27 and (1*RS*,2*RS*)-3-benzyloxy-3-[1′-(phenylsulfanyl)cyclohexyl]-2-methylpropan-1-ol 28

Sodium hydride (60% dispersion in oil; 60.5 mg, 1.51 mmol) was added to a stirred solution of the diol **26** (370.7 mg, 1.32 mmol) in dry THF (7.3 cm^3), under argon, at 4 °C; the temperature of the mixture was allowed to rise to RT. After 30 min tetrabutylammonium iodide (98%; 5.1 mg, 13.9 μmol) was added to the mixture and followed after 4 min by benzyl bromide (165 mm^3, 1.39 mmol); the mixture was then stirred for a further 1 h 50 min. After this the reaction was quenched by addition of saturated aqueous ammonium chloride (25 cm^3) to the mixture which was then extracted with diethyl ether (3 × 25 cm^3). The combined extracts were then dried ($MgSo_4$) and evaporated under reduced pressure. The residue was separated by flash column chromatography on silica (66 g) eluting with dichloromethane to give *secondary alcohol* **27** (252.5 mg, 52%) as needles, mp 53–55.5 °C; R_F[dichloromethane–methanol (100:1)] 0.58; ν_{max}(Nujol mull)/cm^{-1} 3440 (OH), 3080–3040 (PhH), 1585 (Ph), 1575 (Ph) and 1500 (Ph); δ_H(250 MHz; $CDCl_3$) 7.51 (2 H, m, SPh), 7.36–7.23 (8 H, m, Ph and PhS), 4.52 (1 H, d, *J* 11.9, CH_AH_BPh), 4.49 (1 H, d, *J* 11.8, CH_AH_BPh), 3.66 (2 H, d, *J* 4.9, CH_2OBz), 3.61* (1 H, s br, OH), 3.31 (1 H, d br, sharpened by D_2O shake, *J* 2.8, C*H*OH), 2.33 (1 H, m, C*H*Me), 1.99–1.17 [10 H, m, $(CH_2)_5$] and 1.12 (3 H, d, *J* 7.0, Me); δ_C(400 MHz; $CDCl_3$) 138.14b, 137.11a, 130.91b, 128.68a, 128.66a, 128.37a, 127.73a, 127.63a, 79.31a, 73.63b, 73.35b, 61.56b, 33.78a, 30.74b, 25.93b, 22.03b, 21.92b and 19.45a; *m/z* 370 (0.17, M^+), 261 (1.4, M^+ – PhS), 243 (4.6, M^+ – PhS and H_2O), 225 (2.5, M^+ – PhS and 2 × H_2O), 191 (27, $PhSC_6H_{10}$) and 91 (100, $PhCH_2$) (Found: C, 74.75; H, 8.2; S, 8.8%; M^+, 370.1999. $C_{23}H_{30}O_2S$ requires C, 74.55; H, 8.16; S, 8.65%; *M*, 370.1966); and the *primary alcohol* **28** (77.1 mg, 16%) as an oil; R_F[dichloromethane–methanol (100:1)] 0.29; ν_{max}(smear)/cm^{-1} 3420 (OH), 3060 (PhH), 3040 (PhH), 1670, 1580 (Ph) and 1500 (Ph); δ_H(250 MHz; $CDCl_3$), 7.58–7.54 (2 H, m, SPh), 7.36–7.23 (8 H, m, Ph and SPh), 4.59 (2 H, s, CH_2Ph), 3.82 (1 H, dd, *J* 4.3 and 11.4, CH_ACH_BOH), 3.73 (1 H, dd, *J* 6.0 and 11.4, CH_ACH_BOH), 3.38 (1 H, d, *J* 2.8, C*H*OCH_2Ph), 2.59 (1 H, m, C*H*Me), 2.35* (1 H, br s, OH), 2.03–1.38 [9 H, m, $(CH_2)_5$], 1.25 [1 H, m, $(CH_2)_5$] and 1.16 (3 H, d, *J* 7.2, Me); δ_C(400 MHz; $CDCl_3$) 137.74b, 136.85a, 131.99b, 128.55a, 128.49a, 128.40a, 127.90a, 127.81a, 90.99a, 66.04b, 59.83b, 35.79a, 32.08b, 31.54b, 25.75b, 21.82b and 19.49a; *m/z* 370 (0.15, M^+), 311 (0.21, M^+ – $HOCH_2CH(Me)$; only possible for this regioisomer), 261 (1.3, M^+ – PhS), 201 [2.5, M^+ – $HOCH_2CH(Me)$ and PhSH], 191 (52, $PhSC_6H_{10}$) and 91 (100, $PhCH_2$) (Found: M, 370.1950. $C_{23}H_{30}O_2S$ requires *M*, 370.1966).

(2*RS*,3*SR*)-2,6-Dimethylphenyl 3-hydroxy-3-[1-(4-methoxyphenylsulfanyl)cyclohexyl]-2-methylpropionate 29

With similar conditions to those used in the synthesis of the diol **30** below, but with isolation of the aldol by chromatography on silica eluting with hexane–ether gave *aldol* **29** (30%) as cubes, mp 98–99 °C; R_F(dichloromethane) 0.16; ν_{max}(Nujol mull)/cm^{-1} 3470 (sharp, OH), 1725 (C=O), 1595 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.42 (2 H, d, *J* 8.8, SAr), 7.05 (3 H, s, Ar), 6.85 (2 H, d, *J* 8.8, SAr), 3.81 (3 H, s, MeO), 3.77 (1 H, dd, *J* 1.5 and 2.5, C*H*OH), 3.36 (1 H, d, *J* 2.4, OH), 2.19 (6 H, s, Me_2Ar), 2.10–1.45 [10 H, m, $(CH_2)_5$, C*H*Me], 1.57 (3 H, d, *J* 7.4, CH*Me*) and 1.30–1.10 [1 H, m, $(CH_2)_5$, C*H*Me]; δ_C(250 MHz; $CDCl_3$) 175.20b, 160.41b, 147.69b, 138.56a, 130.25b, 128.79a, 126.04a, 121.09b, 114.40a, 79.01a, 59.57b, 55.32a, 37.91a, 30.39b, 30.18b, 25.85b, 21.79b, 21.69b, 18.88a and 16.76a; *m/z* 428 (0.6%, M^+), 289 (9, M – $MeOC_6H_4S$), 271 (16, M – $MeOC_6H_4S$ and H_2O), 221 (24, $MeOC_6H_4SC_6H_{10}$), 149 (26, M – $MeOC_6H_4S$, H_2O and $Me_2C_6H_3OH$), 140 (100, $MeOC_6H_4SH$) and 122 (67, $Me_2C_6H_3OH$) (Found: M^+, 428.2010. $C_{25}H_{32}O_4S$ requires *M*, 428.2022).

(1*RS*,2*RS*)-1-[1-(4-Methoxyphenylsulfanyl)cyclohexyl]-2-methylpropane-1,3-diol 30

2,6-Dimethylphenyl propionate (102.1 mg, 0.572 mmol) in dry THF (1.0 cm^3) was added over 8 min to a stirred solution of LDA [made from butyl lithium (1.5 mol dm^{-3} solution in hexane; 0.400 cm^3, 0.6 mmol) and diisopropylamine (84 mm^3, 0.599 mmol)] in dry THF (2.6 cm^3), under argon, and cooled in a solid CO_2–acetone bath. Stirring was continued at < −72 °C for 22 min after which a solution of the aldehyde **11** (137.1 mg, 0.548 mmol) in dry THF (1.0 cm^3) was added to the mixture over 5 min. After a further 8 min, the reaction was quenched by addition of saturated aqueous ammonium chloride (100 cm^3) to the mixture which was then allowed to warm to RT. Aqueous hydrochloric acid (1 mol dm^{-3} solution; 15 cm^3) was then added to the mixture after which it was extracted with diethyl ether (20 cm^3) and then dichloromethane (20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residual mixture was dissolved in dry THF (2.8 cm^3) and lithium aluminium hydride (95%; 22.8 mg, 0.570 mmol) was added to the solution which was then stirred for 1 h 45 min before being quenched and worked up as for the alcohol **20**. The mixture was separated by flash column chromatography on silica to yield the anti *diol* **30** (78.8 mg, 46%) as prisms, mp 67–68 °C; ν_{max}(Nujol mull)/cm^{-1} 3340 (OH), 3190 (OH), 1595 (Ar), 1570 (Ar), 1495 (Ar) and 830 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.39 (2 H, d, *J* 8.7, ArH), 6.85 (2 H, d, *J* 8.7, ArH), 3.81 (3 H, s, MeO), 3.67 (1 H, dd, *J* 3.9 and 11.3, CH_ACH_BOH), 3.64 (1 H, dd, *J* 6.3 and 11.3, CH_ACH_BOH), 3.17 (1 H, d, *J* 4.9, C*H*OH), 2.09–1.93 (2 H, m, 2 × $CH_{eq.}$), 1.85–1.48 (5 H, m, 3 × $CH_{eq.}$, 2 × $CH_{ax.}$), 1.41–1.08 (3 H, m, 3 × $CH_{eq.}$) and 0.86 (3 H, d, *J* 7.0, *Me*CH); δ_C(400 MHz; $CDCl_3$) 160.56b, 138.54a, 120.16b, 114.54a, 79.02a, 66.69b, 62.65b, 55.34a, 34.58a, 30.02b, 28.79b, 26.30b, 21.87b, 21.68b and 18.57a; *m*/*z* 310 (0.48%, M^+), 221 [5.5, M^+ − CH(OH)CH(Me)CH_2OH], 140 (61, $MeOC_6H_4SH$), 86 (68) and 84 (100) (Found: C, 65.9; H, 8.6; S, 10.5%; M^+, 310.1601. $C_{17}H_{26}O_3S$ requires C, 65.77; H, 8.44; S, 10.33%; *M*, 310.1603).

(2*RS*,3*RS*)-3-Methoxy-1-[1′-(4″-methoxyphenylsulfanyl)-cyclohexyl]-2-methylpropan-1-ol 31

In the way as for the alcohol **23**, the *anti* diol **30** (31.2 mg, 0.100 mmol) gave anti *alcohol* **31** (19.6 mg, 60%) as an oil after flash column chromatography on silica with hexane–ethyl acetate (6:1) as eluent; R_F[hexane–ethyl acetate (4:1)] 0.35; ν_{max}(smear)/cm^{-1} 3381 (OH), 1592 (Ar), 1569 (Ar), 1492 (Ar) and 826 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.42 (2 H, d, *J* 8.7, ArH), 6.83 (2 H, d, *J* 8.7, ArH), 3.79 (3 H, s, *Me*OAr), 3.57 (1 H, d, *J* 4.2, C*H*OH), 3.57 (1 H, dd, *J* 4.3 and obscured 9.3, CH_ACH_BOMe), 3.51 (1 H, dd, *J* 5.7 and 9.3, CH_ACH_BOMe), 3.33 (3 H, s, *Me*OCH_2), 3.26 (1 H, br s, OH), 2.25 (1 H, m, C*H*Me), 1.94–1.47 [8 H, m, $(CH_2)_5$], 1.40–1.32 [1 H, br d, *J* 8.6, $(CH_2)_5$], 1.28–1.16 [1 H, m, $(CH_2)_5$] and 1.08 (3 H, d, *J* 7.1, *Me*CH); δ_C(400 MHz; $CDCl_3$) 160.19b, 138.58a, 121.31b, 114.19a, 78.93a, 76.07b, 61.11b, 58.91a, 55.26a, 33.57a, 30.52b, 30.41b, 25.97b, 22.03b, 21.92b and 19.32a; *m*/*z* 324 (0.7%, M^+), 221 [15, M^+ − CH(OH)CH(Me)CH_2OMe], 167 (15, M^+ − $MeOC_6H_4S$ and H_2O), 140 (52, $MeOC_6H_4SH$), 86 (65) and 84 (100) (Found: M^+, 324.1755. $C_{18}H_{28}O_3S$ requires *M*, 324.1760).

2-(4-Methoxyphenylsulfanyl)-2-methyl-5-phenylpentanal 32

Sulfuryl chloride (97%; 0.93 cm^3, 11.2 mmol) was added to a stirred solution of the disulfide **37** (3.14 g, 11.3 mmol) in dry THF, with light excluded, under argon, and stirring continued at RT for 1 h 20 min. After being cooled in an ice-bath, this solution was added to a stirred solution of the silyl enol ethers **35** (5.60 g, 22.5 mmol) in dry dichloromethane (12 cm^3) under argon, cooled in a solid CO_2–acetone bath, over 8 min. The resulting solution was allowed to warm to RT over 4 h after which it was evaporated under reduced pressure. The residue was separated by flash column chromatography on silica (268 g) eluting with hexane–ethyl acetate (12:1–10:1) to yield the α-*thioaldehyde* **32** (6.56 g, 93%) as needles, 48.5–51.5 °C (from hexane–ethyl acetate); R_F[hexane–ethyl acetate (12:1)] 0.23; ν_{max}(Nujol mull)/cm^{-1} 1715 (C=O), 1590 (Ar), 1495 (Ar), 830 (*para* disubstituted benzene) and 755 and 700 (monosubstituted benzene); δ_H(250 MHz; $CDCl_3$) 9.25 (1 H, s, CHO), 7.32–7.15 (7 H, m, Ph and 2 of C_6H_4OMe), 6.79 (2 H, d, *J* 8.8, C_6H_4OMe), 3.78 (3 H, s, *Me*OAr), 2.71–2.52 (2 H, m, CH_2Ph), 1.97–1.47 (4 H, m, CH_2CH_2CS) and 1.21 (3 H, s, MeCS); δ_C(400 MHz; $CDCl_3$) 194.97a, 160.83b, 141.58b, 138.69a, 128.38a, 125.95a, 119.90b, 114.48a, 59.32b, 55.24a, 35.99b, 33.17b, 26.13b and 17.55a; *m*/*z* 314 (30%, M^+), 145 (100, M − HCO and $MeOC_6H_4SH$), 140 (98, $MeOC_6H_4SH$) and 139 (59, $MeOC_6H_4S$) (Found: C, 72.7; H, 7.0; S, 10.35%; M^+, 314.1344. $C_{19}H_{22}O_2S$ requires C, 72.58; H, 7.05; S, 10.20%; *M*, 314.1341).

2-Methyl-5-phenylpentanal 34

A solution of the imine **33** (16.0 g, 0.116 mol) in dry diethyl ether (110 cm^3) was added over 1 h 10 min to a stirred solution of freshly made lithium diisopropylamide (0.116 mol), in hexane–diethyl ether (77.5 cm^3, 100 cm^3) at 0–5 °C. After 26 min, a solution of 1-bromo-3-phenylpropane (18.0 cm^3, 98%, 0.116 mol) in diethyl ether (110 cm^3) was added to the mixture over 18 min. The cooling bath was removed and the mixture stirred at RT for 65 h. The reaction was quenched by addition of aqueous hydrochloric acid (2 mol dm^{-3}; 350 cm^3) to the mixture and heating under reflux for 2 h, under argon. After the mixture had cooled to RT, the aqueous layer was separated from the diethyl ether layer and extracted with diethyl ether (3 × 250 cm^3). The combined diethyl ether solution extracts were washed with a mixture of brine (75 cm^3) and saturated aqueous sodium hydrogen carbonate (25 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was distilled with a few crystals of quinol to give the aldehyde [29] **34** (10.01, 49%) as an oil, bp 76–86 °C at 2.5–3.0 mmHg; δ_H(250 MHz; $CDCl_3$) 9.60 (1 H, d, *J* 1.9, CHO), 7.31–7.15 (5 H, m, Ph), 2.63 (2 H, t, *J* 7.4, PhCH_2), 2.35 (1 H, dsextet, *J* 1.9 and 6.8, C*H*Me), 1.82–1.60 [3 H, m, $(CH_2)_2$], 1.47–1.33 [1 H, m, $(CH_2)_2$] and 1.09 (3 H, d, *J* 7.0, Me).

2-Methyl-5-phenyl-1-trimethylsiloxypentene 35

The aldehyde **34** (9.58 g, 54.3 mmol) was added to a stirred solution of trimethylsilyl chloride (8.3 cm^3, 65.4 mmol) and triethylamine (18 cm^3, 0.129 mol) in dry DMF (35 cm^3) at RT and washed in with more DMF (5 cm^3). The mixture was heated to 80 °C, stirred for 22 h, and then allowed to cool to RT. Light petroleum (bp 30–40 °C) (250 cm^3) was added to the mixture which was then washed with cool (5 °C) aqueous hydrochloric acid (3 mol dm^{-3}; 2 × 40 cm^3), cool, saturated aqueous sodium hydrogen carbonate (50 cm^3) and finally cool brine (50 cm^3). After being dried ($MgSO_4$), the mixture was evaporated under reduced pressure and the residue distilled *in vacuo* to give the *silyl enol ethers* **35** (9.05 g, 67%) as a *cis* (A) and *trans* (B) (37:63) mixture as an oil, bp 102 °C at 0.5 mmHg; ν_{max}(smear)/cm^{-1} 3100 (HC=), 3070 (HC=), 3040 (PhH), 2960–2850 (CH), 1675 (C=C), 1605 (Ph), 1500 (Ph), 1255 (Si-Me), 880 (R_2C=CH, unusually high), 840 ($SiMe_3$) and 750 and 700 (monosubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.31–7.14 (5 H^A and 5 H^B, m, PhH), 6.05 (1 H^A and 1 H^B, s, CH=), 2.60 (2 H^A, unsymmetric t, *J* 7.7, CH_2Ph), 2.57 (2 H^B, unsymmetric t, *J* 7.7, CH_2Ph), 2.14 (2 H^A, unsymmetric t, *J* 7.6, CH_2C=), 1.93 (2 H^B, unsymmetric t, *J* 7.3, CH_2C=), 1.76–1.63 (2 H^A and 2 H^B, m, CH_2CH_2Ph), 1.59 (3 H^B, d, *J* 1.3, MeC=), 1.53 (3 H^A, d, *J* 1.3, MeC=), 0.17 [9 H^B, s, Me_3Si] and 0.16 [9 H^A, s, Me_3Si]; δ_C(400 MHz; $CDCl_3$) 142.97 d^A, 142.68b^B, 133.61a^B, 133.22a^A, 128.45$a^{A\ and\ B}$, 128.25a^B, 128.19a^A, 125.61a^B, 125.52a^A, 117.75b^B, 117.40b^A, 35.73b^A, 35.34b^B, 33.40b^B, 29.74b^B, 29.20b^A, 28.29b^A, 17.02a^A and 12.58a^B (the last two signals identify A and B as *cis* and *trans* respectively[30]); *m*/*z* 248

(11, M^+), 143 (37, M − $PhCH_2CH_2$) and 73 (100, Me_3Si) (Found: M^+, 248.1610. $C_{15}H_{24}OSi$ requires *M*, 248.1596).

Bis(4-methoxyphenyl) disulfide 37

Aqueous potassium hydroxide (> 85%; 3.63 g, 55–65 mmol) and potassium *ferri*cyanide (98%; 20.9 g, 62 mmol) in water (75 cm^3) was added to a rapidly stirred emulsion of 4-methoxybenzenethiol (97%, 4.47 g, 30.9 mmol) in water over 50 min. The mixture, which went from yellow *via* green to black–dark green, was then extracted with ethyl acetate (100 cm^3), further diluted (to 250 cm^3) with water and then extracted with more ethyl acetate (2 × 200 cm^3). The combined black–green extracts were dried ($MgSO_4$) and evaporated under reduced pressure and then filtered through silica eluting with dichloromethane. Flash column chromatography of the residue on silica (192 g) with hexane–ethyl acetate (8:1) yielded the disulfide[31] **37** (4.01 g, 93%) as plates, mp 36–37 °C; R_F[hexane–ethyl acetate (8:1)] 0.24; ν_{max}(Nujol mull)/cm^{-1} 1590 (Ar), 1575 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.39 (4 H, d, *J* 8.8, *meta* protons of 2 × $MeOC_6H_4$), 6.83 (4 H, d, *J* 8.8, *ortho* protons of 2 × $MeOC_6H_4$) and 3.79 (6 H, s, 2 × MeO); δ_C(400 MHz; $CDCl_3$) 159.91b, 132.67a, 128.42b, 114.61a and 55.36a; *m*/*z* 278 (29%, M^+), 140 (67, $MeOC_6H_4SH$), 139 (100, $MeOC_6H_4S$) and 125 (41, HOC_6H_4S) (Found: M^+, 278.0431. $C_{14}H_{14}O_2S_2$ requires *M*, 278.0435).

(2*RS*,3*SR*,4*RS* and 4*SR*) 2′,6′-Dimethylphenyl 3-hydroxy-4-(4″-methoxyphenylsulfanyl)-2,4-dimethyl-7-phenylheptanoate 38, 39

A solution of the aldehyde **32** (2.0 g, 6.36 mmol) in dry THF (10 cm^3) was added over 10 min to a solution of the lithium enolate of 2,6-dimethylphenyl propionate (freshly prepared) in THF–hexane (40 cm^3, 4.3 cm^3), under argon, and cooled in a solid CO_2–acetone bath, with the temperature maintained < −65 °C. After 11 min, the reaction was quenched by addition of aqueous hydrochloric acid (1 mol dm^{-3}; 30 cm^3) to the mixture which was then allowed to warm to RT when it was extracted with diethyl ether (3 × 100 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (30 cm^3) and brine (30 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Flash column chromatography of the residue on silica (270 g) of 99.2% of the mixture, eluting with hexane–diethyl ether (4:1), gave pure anti,anti (2RS,3SR,4RS)-*aldol* **38** (0.95 g, 30%) as plates, mp 98–99 °C (ethyl acetate–hexane); R_F(dichloromethane) 0.27 and R_F[hexane–diethyl ether (4:1)] 0.22; ν_{max}(Nujol mull)/cm^{-1} 3520 (OH sharp), 1725 (C=O), 1590 (Ar), 1570 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.33–7.17 (7 H, m, Ph and protons *ortho* to S in SC_6H_4OMe), 7.06 (3 H, s, $OC_6H_3Me_2$), 6.79 (2 H, d, *J* 8.7, protons *meta* to S in SC_6H_4OMe), 3.80 (3 H, s, MeO), 3.55 (1 H, dq, *J* 2.9 and 7.3, C*H*Me), 3.48 (1 H, d, *J* 2.9, C*H*OH), 2.62 (2 H, t, *J* 7.5, CH_2Ph), 2.18 (6 H, s, $OC_6H_3Me_2$), 2.12–1.62 (4 H, m, CH_2CS, CH_2CH_2Ph), 1.55 (3 H, d, *J* 7.3, CH*Me*) and 1.14 (3 H, s, MeCS); δ_C(400 MHz; $CDCl_3$) 175.07b, 160.46b, 147.67b, 142.39b, 138.64a, 130.23b, 128.79a, 128.60a, 128.34a, 126.07a, 125.77a, 121.11b, 114.32a, 78.68a, 57.91b, 55.30a, 38.73a, 36.20b, 35.75b, 26.19b, 21.84a, 18.70a and 16.74a; *m*/*z* 370 (7.1%, $M^+ - HOC_6H_3Me_2$), 353 (M − $MeOC_6H_4S$), 285 [9.5, $Ph(CH_2)_3CH(Me)SC_6H_4OMe$], 140 (92, $MeOC_6H_4SH$), 122 (82, $HOC_6H_3Me_2$) and 91 (100, $PhCH_2$) (Found: C, 73.3; H, 7.4; S, 6.7%; $M^+ - HOC_6H_3Me_2$, 370.1595. $C_{30}H_{36}O_4S$ requires C, 73.14; H, 7.37; S, 6.51%; $C_{22}H_{26}O_3S$ requires *M*, 370.1603). The mixed fractions of the aldols **38** and **39** were rechromatographed to remove a lower running impurity, eluted with dichloromethane, to give a (52:44:5) mixture of the aldol **38**, anti,syn (2RS,3SR,4SR)-*aldol* **39** (0.91 g, 29%), and one of the 2,3 *syn* isomers, as crystals. The NMR spectra of *anti,syn* (2*RS*,3*SR*,4*SR*) aldol **39** could be derived from those of the mixture; δ_H(250 MHz; $CDCl_3$) 7.36 (2 H, d, *J* 8.8, ArS), 7.33–7.17 (5 H, m, Ph), 7.05 (3 H, s, $Me_2C_6H_3$), 6.81 (2 H, d, *J* 8.7, ArS), 4.09 (1 H, d, *J* 6.7, OH), 3.81 (3 H, s, MeO), 3.51–3.45 (1 H, obscured, C*H*OH), 3.37 (1 H, dq, *J* 3.7 and 7.2, C*H*Me), 2.67–2.51 (2 H, obscured, CH_2Ph), 2.19 (6 H, s, MeC_6H_3), 2.09–1.32 [4 H, m, $(CH_2)_2$] and 1.51 (3 H, d, *J* 7.7, 1 peak coincident with Me of **38**); δ_C(400 MHz; $CDCl_3$) 174.18b, 160.50b, 147.84b, 142.17b, 138.72a, 130.29b, 128.73a, 128.44a, 128.40a, 125.99a, 125.89a, 121.12b (coincident with peak of **38**), 114.33a (coincident with peak of **38**), 78.75a, 58.53b, 55.31a (coincident with peak of **38**), 39.62a, 36.29b, 35.66b, 26.53b, 21.41a, 18.65a and 16.79a; *m*/*z* 492 (0.19%, M^+), 370 (10, M − $Me_2C_6H_3OH$), 180 (41), 140 (74, $MeOC_6H_4SH$), 122 (100, $Me_2C_6H_3OH$) and 91 (74, $PhCH_2$) (Found: M^+, 492.2349. $C_{30}H_{36}SO_4$ requires *M*, 492.2334).

(2*RS*,3*RS*,4*SR*)-4-(4-Methoxyphenylsulfanyl)-2,4-methyl-7-phenylheptane-1,3-diol 41

In the same way as for alcohol **20**, lithium aluminium hydride (95%; 43.9 mg, 1.10 mmol) and the ester **38** (547.7 mg, 1.11 mmol) in dry THF (5.6 cm^3) were stirred at RT for 3.5 h. After being quenched and worked up the mixture was separated by flash column chromatography on silica eluting with dichloromethane–methanol (50:1) to yield the anti,anti *diol* **41** (269.7 mg, 65%) as a solid, mp 52.5–53 °C; R_F[dichloromethane–methanol (50:1)] 0.23; ν_{max}(Nujol mull) 3390 (OH), 3090–3030 (ArH), 1595 (Ar), 1495 (Ar) and 835 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.35 (2 H, d, *J* 8.7, ArH), 7.33–7.16 (5 H, m, Ph), 6.84 (2 H, d, *J* 8.7, ArH), 3.81 (3 H, s, MeO), 3.69 (1 H, dd, *J* 3.3 and 11.2, CH_AH_BOH), 3.62 (1 H, dd, *J* 6.3 and 11.2, CH_AH_BOH), 3.26 (1 H, d, *J* 5.3, C*H*OH), 2.62 (2 H, dd, *J* 6.3 and 8.3, CH_2Ph), 2.08–1.65 (5 H, m, CH_2CH_2CS and C*H*Me), 1.10 (3 H, s, MeCS) and 0.89 (3 H, d, *J* 7.0, CH*Me*); δ_C(400 MHz; $CDCl_3$) 160.57b, 142.22b, 138.78a, 128.45a, 128.37a, 125.84a, 120.29b, 114.38a, 80.11a, 67.00b, 59.87b, 55.33a, 36.52b, 34.79a, 33.78b, 26.64b, 23.04a and 18.22a; *m*/*z* 374 (0.7%, M^+), 285 [4.7, M − $HOCH_2C$-(Me)CHOH], 140 (100, $MeOC_6H_4SH$) and 91 (45, $PhCH_2$) (Found: M^+, 374.1939. $C_{22}H_{30}O_3S$ requires *M*, 374.1915).

(2*RS*,3*RS*,4*RS* and 4*SR*)-4-(4-Methoxyphenylsulfanyl)-2,4-methyl-7-phenylheptane-1,3-diol 41, 42

In the same way, a 3.5–5.5:1 mixture of the alcohols **38** and **39** (814.3 mg, 1.65 mmol) was reduced with lithium aluminium hydride (95%; 132.6 mg, 3.32 mmol) to give an inseparable 4.3:1 mixture of the anti,anti (2RS,3RS,4SR)-*diol* **41** (isomer A) and the anti,syn (2RS,3RS,4RS) *diol* **42** (isomer B) (479.4 mg, 63%) as a gum; R_F[dichloromethane–methanol (50:1)] 0.23; δ_H(250 MHz; $CDCl_3$) 7.35 (2 H^A, d, *J* 8.8, ArH), 7.32–7.19 (5 H^A, 7 H^B, m, Ph and ArH^B), 6.84 (2 H^A, d, *J* 8.7, ArH), 6.78 (2 H^B, d, *J* 8.8, ArH), 3.81 (3 $H^{A\text{ and }B}$, s, MeO), 3.76–3.57 (2 $H^{A\text{ and }B}$, m, CH_2OH), 3.26 (1 H^A, d, *J* 5.2, C*H*OH), 3.15 (1 H^B, d, *J* 4.7, C*H*OH), 2.96 (2 $H^{A\text{ and }B}$, s, OH), 2.70–2.50 (2 $H^{A\text{ and }B}$, m, CH_2Ph), 2.18–1.64 (5 H, m, $CH_2CH_2{}^{A\text{ and }B}CS$, $CH_2{}^ACH_2CS$ and $CH^{A\text{ and }B}$Me), 1.46 (1 H^B, unsymmetric dt, *J* 4.8 and *ca.* 13.9 and 12.1), 1.26–1.13 (1 H^B, m, CH_2), 1.17 (3 H^B, s, MeCS), 1.10 (3 H, s, MeCS), 0.93 (3 H^B, d, *J* 7.1, C*H*Me) and 0.89 (3 H, d, *J* 7.0, CH*Me*); δ_C(400 MHz; $CDCl_3$) 160.58b^A, 160.47b^B, 142.22b^A, 142.10a^B, 138.77a^A, 138.27a^B, 128.54a^B, 128.44a$^{A\text{ and }B}$, 128.36a^A, 125.92a^B, 125.84a^A, 120.33b$^{A\text{ and }B}$, 114.45a^B, 114.38a^A, 80.13a^A, 78.68a^B, 66.98b^A, 66.37b^B, 61.31b^B, 59.89b^A, 55.32a$^{A\text{ and }B}$, 36.52b^A, 36.07b^B, 34.82a$^{A\text{ and }B}$, 33.84b$^{A\text{ and }B}$, 26.62b^A, 26.18b^B, 23.04a$^{A\text{ and }B}$, 18.40a^B and 18.22a^A; *m*/*z* 356 (1.4%, $M^+ - H_2O$), 283 (3.5%, M − $PhCH_2$), 140 ($MeOC_6H_4SH$, 100) and 91 (34, $PhCH_2$) (Found: $M^+ - H_2O$, 356.1790. $C_{22}H_{28}O_2S$ requires *M*, 356.1790).

(2*RS*,3*SR*,4*RS*)-3-(4′-Methoxyphenylsulfanyl)-2,4-dimethyl-2-(3″-phenylpropyl)tetrahydrofuran 43

In the same way as for **9** above, a solution of toluene-*p*-sulfonic acid monohydrate (5.6 mg, 29.2 μmol) and the diol **41** (41.6 mg, 0.111 mmol) in dry dichloromethane (0.55 cm^3) were heated under reflux for 1 h to give, after filtration, the anti,anti

tetrahydrofuran **43** (36.9 mg, 93%); R_F(dichloromethane) 0.35; ν_{max}(smear)/cm^{-1} 3080–3030 (ArH), 1595 (Ar), 1575 (Ar), 1495 (Ar), 830 (*para* disubstituted benzene) and 750 and 700 (phenyl); δ_H(250 MHz; $CDCl_3$) 7.39 (2 H, d, *J* 8.9, C_6H_4OMe), 7.29–7.07 (5 H, m, PhH), 6.82 (2 H, d, *J* 8.9, C_6H_4OMe), 3.96 (1 H, t, *J* 8.2, CH_AH_BO), 3.81 (3 H, s, MeO), 3.27 (1 H, t, *J* 8.7, CH_ACH_B), 2.74 (1 H, d, *J* 10.7, CHS), 2.47 (2 H, m, CH_2Ph), 2.28 (1 H, m, C*H*Me), 1.72–1.35 (4 H, m, $CH_2CH_2CH_2Ph$), 1.21 (3 H, s, MeCO) and 1.09 (3 H, d, *J* 6.5, CH*Me*); δ_C(400 MHz; $CDCl_3$) 159.41b, 142.48b, 135.23a, 128.38a, 128.21a, 126.00b, 125.64a, 114.51a, 85.10b, 71.66b, 63.54a, 55.32a, 40.34a, 39.92b, 36.30b, 25.64b, 22.70a and 16.16a; *m*/*z* 356 (11%, M^+), 194 [100, M – $Ph(CH_2)_3COMe$], 140 (44, $MeOC_6H_6SH$), 135 (91) and 91 (79, $PhCH_2$) (Found: M^+, 356.1788. $C_{22}H_{28}O_2S$ requires *M*, 356.1810).

(3*SR*,4*RS*)-3-(4′-Methoxyphenylsulfanyl)-2,4-dimethyl-2-(3″-phenylpropyl)tetrahydrofuran 43, 44

In the same way, a solution of toluene-*p*-sulfonic acid monohydrate (8.2 mg, 43.1 μmol) and the diols **41** and **42** (77.8 mg, 0.208 mmol) in dry dichloromethane (1.0 cm^3) were heated under reflux for 24 min. Filtration of the mixture followed by flash column chromatography on silica (7 g) eluting with hexane–ethyl acetate (8 : 1) gave the *anti,anti* tetrahydrofuran **43** (2.1 mg, 3%) as an oil {R_F[hexane–ethyl acetate (4 : 1)] 0.40, spectroscopically identical with sample **43** above}, a 54 : 46 mixture of the tetrahydrofurans **43** and **44** (28.4 mg, 38%), and syn,anti (2SR,3SR,4RS)-*tetrahydrofuran* **44** (2.3 mg, 3%) as an oil; R_F[hexane–ethyl acetate (4 : 1)] 0.36; δ_H(250 MHz; $CDCl_3$) 7.38 (2 H, d, *J* 8.8, C_6H_4OMe), 7.31–7.14 (5 H, m, PhH), 6.80 (2 H, d, *J* 8.8, C_6H_4OMe), 3.86 (1 H, t, *J* 8.3, CH_AH_BO), 3.79 (3 H, s, MeO), 3.31 (1 H, t, *J* 8.4, CH_ACH_B), 2.72 (1 H, d, *J* 10.7, CHS), 2.63 (2 H, unsymmetric t, *J* 7.3, CH_2Ph), 2.24 (1 H, m, C*H*Me), 1.80–1.50 (4 H, m, $CH_2CH_2CH_2Ph$), 1.09 (3 H, d partly obscured, *J* 5.5, CH*Me*) and 1.08 (3 H, s, MeCS).

(2*RS*,3*RS*,4*RS* and 4*SR*)-1-Methoxy-4-(4′-methoxyphenylsulfanyl)-2,4-dimethyl-7-phenylheptan-3-ol 45, 46

In the same way as for alcohol **22**, a (3.0 : 1) mixture of the 2,3 *anti* diols **41** and **42** (801.6 mg, 2.14 mmol) gave a (3.4 : 1) diastereoisomeric mixture of the 3,4 anti (2RS,3RS,4SR)-*alcohol* **45** (isomer A) and the 3,4 syn (2RS,3RS,4RS)-*alcohol* **46** (isomer B) (554.7 mg, 67%) as an oil after flash column chromatography on silica eluting with hexane–ethyl acetate (8 : 1); R_F[hexane–ethyl acetate (4 : 1)] 0.25; ν_{max}(smear)/cm^{-1} 3510 (OH), 1595 (Ar), 1570 (Ar), 1495 (Ar) and 830 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.33 (2 $H^{A\text{ and }B}$), 7.29–7.18 (5 $H^{A\text{ and }B}$, m, PhH), 6.80 (2 H^A, d, *J* 8.7, C_6H_4OMe), 6.78 (2 H^B, d, *J* 8.7, C_6H_4OMe), 3.80 (3 $H^{A\text{ and }B}$, s, *Me*OAr), 3.55 (1 H^A, dd, *J* 5.0 and 9.3, CH_AH_BOMe), 3.51 (2 H^B, obscured, CH_2OMe), 3.50 (1 H^A, dd, *J* 4.6 and 9.3, CH_AH_BOMe), 3.35 (1 H^A, d, *J* 3.6, C*H*OH), 3.314 (3 H^B, s, *Me*OCH_2), 3.306 (3 H^A, s, *Me*OCH_2), 3.27 (1 H^B, d, *J* 3.4, C*H*OH), 2.20–1.48 (5 H^A and 3 H^B, m, C*H*Me, CH_2CS, $PhCH_2CH_2{}^A$), 1.36–1.25 (2 H^B, m, $PhCH_2CH_2{}^B$), 1.14 (3 H^B, s, MeCS), 1.12 (3 H^A, s, MeCS), 1.08 (3 H^A, d, *J* 7.1, *Me*CH) and 1.06 (3 H^B, d, *J* 7.0, *Me*CH); δ_C(400 MHz; $CDCl_3$) 160.26$b^{A\text{ and }B}$, 142.44b^A, 142.34b^B, 138.84a^A, 138.71a^B, 128.52a^A, 128.31a^B, 125.79a^A, 125.73a^B, 121.54$b^{A\text{ and }B}$, 114.16a^B, 114.11a^A, 79.44a^A, 78.74a^B, 76.08b^A, 75.59b^B, 59.81b^B, 58.89$a^{A\text{ and }B}$, 58.75b^A, 55.28a^A, 36.40b^A, 36.26b^B, 36.13b^B, 35.93b^A, 34.03a^B, 33.69a^A, 26.41$b^{A\text{ and }B}$, 22.64a^A, 20.49a^B, 19.09a^B and 18.94a^A; *m*/*z* 388 (1.2%, M^+), 140 (100, $MeOC_6H_4SH$) and 91 (92, $PhCH_2$) (Found: M^+, 388.2088. $C_{23}H_{32}O_3S$ requires *M*, 388.2072).

(2*RS*,2′*SR*,2″*RS*,*E*)-Ethyl 2-[2′-(3″-methoxy-2″-methyl-1″-propylidenyl)cyclohexyl]-2-(4-methoxyphenylsulfanyl)ethanoate 54

Aliquots of ethyl diazoacetate (5 × 10 mm^3, 0.475 mmol) and then a pre-cooled solution of tetrafluoroboric acid–diethyl ether complex (1 : 1)† in dry dichloromethane (0.474 mmol in 4 additions) were added alternately over 7 min to a solution of the allylic sulfide **7** (89.0 mg, 0.290 mmol) in dichloromethane (0.6 cm^3) under argon with light excluded at −75 to −73 °C. After 4 min, DBU (96%, 120 mm^3, 0.770 mmol) was added to the mixture which was then stirred at the same temperature for 20 min. After this the reaction was quenched by addition of glacial acetic acid (50 mm^3, 0.87 mmol) to the mixture which was then poured into aqueous hydrochloric acid (1.0 mol dm^{-3}; 20 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure after which 90% of the mixture was separated by flash column chromatography on silica eluting with hexane–diethyl ether (2 : 1) to yield the *ester* **54** (52.8 mg, 51%, 95% pure) as an oil, together with a less pure mixture (26.5 mg, 26%). Separation of the latter by HPLC failed and returned a poor yield of the *ester* (6.3 mg, 6%; 90% pure); R_F[hexane–diethyl ether (2 : 1)] 0.46; ν_{max}(smear) 1730 (C=O), 1595 (Ar), 1575 (Ar), 1495 (Ar) and 830 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.37 (2 H, d, *J* 8.9, ArH), 6.79 (2 H, d, *J* 8.7, ArH), 5.11 (1 H, d, *J* 9.0, =CH), 3.98 (2 H, q, *J* 7.2, $MeCH_2O$), 3.94 (1 H, d, *J* 11.7, CHS), 3.76 (3 H, s, ArO*Me*), 3.32 (3 H, s, CH_2OMe), 3.22 (1 H, dd, *J* 6.7 and 9.2, CH_AH_BOMe), 3.16 (1 H, dd, *J* 7.4 and 9.1, CH_AH_BOMe), 2.74 (1 H, dsextet, *J* 8.9 and 6.8, C*H*Me), 2.59 (1 H, br d, *J* 11.5, $CH_{eq.}CHS$), 2.38 (1 H, dt, *J* 13.5 and 3.6, $CH_{eq.}H_{ax.}C$=), 1.87 (1 H, unsymmetric dt, *ca.* *J* 3.6 and 12.8, $CH_{eq.}H_{ax.}C$=), 1.80–1.48 [5 H, m, $(CH_2)_3$], 1.40–1.23 [1 H, m, $(CH_2)_3$], 1.07 (3 H, t, *J* 7.2, *Me*CH_2O) and 1.00 (3 H, d, *J* 6.7, CH*Me*); δ_C(400 MHz; $CDCl_3$) 172.33b, 159.85b, 137.34b, 136.05a, 128.55a, 124.19b, 114.30a, 78.11b, 60.74b, 58.74a, 55.27a, 53.30a, 46.20a, 32.21a, 31.37b, 27.84b, 25.63b, 22.02b, 17.95a and 14.03a; *m*/*z* 392 (10%, M^+), 226 (31, $MeOC_6H_4SCH_2CO_2Et$), 135 (90, M^+ – $MeOC_6H_4SCH_2CO_2Et$ and MeO•) and 110 (100, PhSH) (Found: M^+, 392.2024. $C_{22}H_{32}O_4S$ requires *M*, 392.2021).

Epimerisation of the homoallylic sulfide 54

A solution of the homoallylic sulfide **54** (7.8 mg, 19.8 μmol) and sodium ethoxide (from 2 mg of sodium, 87 μmol) in ethanol (1.5 cm^3) was stirred at RT, with light excluded, for 3 d. The reaction mixture was quenched with saturated ammonium chloride, and then extracted twice with diethyl ether and then twice with dichloromethane. The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a 64 : 36 mixture of the homoallylic sulfides **59** : **54** (7.2 mg, 93%). From the ^{1}H NMR spectrum of the mixture, the spectrum of the homoallylic sulfide **59** could be derived; δ_H(250 MHz; $CDCl_3$) 7.42 (2 H, d, *J* 9.0, ArH), 6.82 (2 H, d, *J* 8.8, ArH), 4.92 (1 H, *J* 9.0, C=CH), 3.98 (2 H, q, *J* 7.1, OCH_2Me), 3.81 (1 H, assumed d, second peak obscured by MeOAr, CHS), 3.79 (3 H, s, ArO*Me*), 3.29 (3 H, s, CH_2OMe), 3.15 (1 H, dd, *J* 6.5 and 9.2, CH_AH_BOMe), 3.09 (1 H, dd, *J* 7.3 and 9.2, CH_AH_BOMe), 2.62 (1 H, m, obscured, C*H*Me), 2.51 (1 H, dt, *J* 11.8 and 4.1, $CH_{eq.}CHS$), 2.28 (1 H, dt, *J* 14.1 and 4.1, $CH_{eq.}H_{ax.}C$=), 2.23–2.13 [1 H, m, $(CH_2)_3$], 1.98 (1 H, unsymmetric dt, averaged *J* 3.4 and 12.7, $CH_{eq.}H_{ax.}C$=), 1.80–1.22 [5 H, m, integration poor, $(CH_2)_3$], 1.13 (3 H, t, *J* 7.1, OCH_2Me) and 0.84 (3 H, d, *J* 6.7, CH*Me*).

(2*RS*,2′*SR*,2″*RS*,*E*)-Ethyl 2-[2′-(3″-methoxy-2″-methyl-1″-propylidenyl)cyclohexyl]-2-(4-methoxyphenylsulfanyl)ethanoate 55

Aliquots of ethyl diazoacetate (5 × 10 mm^3, 0.475 mmol) and then a pre-cooled solution of tetrafluoroboric acid–diethyl ether complex (1 : 1)† in dry dichloromethane (0.779 mol dm^{-3};

† Solutions in dichloromethane were made from tetrafluoroboric acid–diethyl ether complex 85% ex Aldrich.

2 × 200 mm^3, then 150 mm^3, then 50 mm^3) were added alternately over 6 min to a solution of the allylic sulfide **8** (92.4 mg, 0.301 mmol) in dichloromethane (0.6 cm^3), under argon, with light excluded, at −55 to −50 °C. After 4 min DBU (96%; 120 mm^3, 0.770 mmol) was added to the mixture the temperature of which was allowed to rise from −50 to −35 °C over 16 min. After this the reaction mixture was poured into aqueous hydrochloric acid (1.0 mol dm^{-3}; 30 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the residue was separated by flash column chromatography on silica (14 g) eluting with hexane–diethyl ether (2:1) to give the *ester* **55** (91.5 mg, 77%, 89% purity) as an oil; R_F[hexane–diethyl ether (2:1)] 0.34; ν_{max}(smear)/cm^{-1} 1735 (C=O), 1595 (Ar), 1500 (Ar) and 830 (*p*-disubstituted); δ_H(250 MHz; $CDCl_3$) 7.39 (2 H, d, *J* 8.8, ArH), 6.81 (2 H, d, *J* 8.8, ArH), 5.12 (1 H, d, *J* 9.0, C=CH), 4.00 (2 H, two q approx. 4 × 10^{-3} ppm apart, *J* 7.2 and *J* 7.1, CH_2Me), 3.93 (1 H, d, *J* 11.6, CHS), 3.78 (3 H, s, ArO*Me*), 3.33 (3 H, s, CH_2OMe), 3.31 (1 H, dd, *J* 5.5 and 9.2, CH_AH_BOMe), 3.16 (1 H, unsymmetric t, *J* 8.2 and 9.1, CH_AH_BOMe), 2.74 (1 H, m, C*H*Me), 2.59 (1 H, br d, *J* 11.6, $CH_{eq.}$CHS), 2.40 (1 H, dt, *J* 13.7 and 3.7, $CH_{eq.}H_{ax.}$C=), 1.89 (1 H, unsymmetric dt, averaged *J* 4.0 and 12.7, $CH_{eq.}H_{ax.}$C=), 1.80–1.69 [1 H, m, $(CH_2)_3$], 1.66–1.47 [4 H, m, $(CH_2)_3$], 1.38–1.22 [1 H, m, $(CH_2)_3$], 1.08 (3 H, t, *J* 7.1, OCH_2Me) and 1.01 (3 H, d, *J* 6.6, CH*Me*); δ_C(400 MHz; $CDCl_3$) 172.35b, 159.87b, 137.30b, 136.14a, 128.34a, 124.18b, 114.30a, 77.81b, 60.75b, 58.72a, 55.28a, 53.18a, 46.26a, 32.28a, 31.40b, 27.82b, 25.84b, 22.02b, 18.21a and 14.04a; *m/z* 392 (17%, M^+), 226 (30, $MeOC_6H_4SCH_2CO_2Et$), 135 (81, $M^+ - MeOC_6H_4SCH_2CO_2Et$ and MeO) and 110 (110, PhSH) (Found: M^+, 392.1994. $C_{22}H_{32}O_4S$ requires *M*, 392.2021).

Epimerisation of the homoallylic sulfide 55

A solution of the homoallylic sulfide **55** (92% purity; 7.6 mg, 17.9 μmol) and sodium ethoxide (from 1.5 mg of sodium, 64.3 μmol) in ethanol (1.2 cm^3) was stirred at RT, with light excluded, for 3 days. The reaction mixture was then quenched with saturated ammonium chloride, extracted twice with diethyl ether then twice with dichloromethane. The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a 66:34 mixture of the homoallylic sulfides **60**:**55** (87% purity). From the ^1H NMR spectrum of the mixture the ^1H NMR of the *homoallylic sulfide* **60** could be derived; δ_H(250 MHz; $CDCl_3$) 7.42 (2 H, d, *J* 8.8, ArH), 6.82 (2 H, d, *J* 8.8, ArH), 4.89 (1 H, *J* 8.9, C=CH), 3.98 (2 H, q, *J* 7.1, OCH_2Me), 3.80 (1 H, assumed d, second peak obscured by MeOAr of *trans* A, CHS), 3.79 (3 H, s, ArO*Me*), 3.25 (3 H, s, CH_2OMe), 3.08 (1 H, dd, *J* 5.9 and 9.1, CH_AH_BOMe), 3.00 (1 H, unsymmetric t, *J* 7.8 and 9.1, CH_AH_BOMe), 2.67–2.55 (1 H, m, obscured, C*H*Me), 2.50 (1 H, dt, *J* 11.9 and 4.3, $CH_{eq.}$CHS), 2.25 (1 H, dt, *J* 14.0 and 4.3, $CH_{eq.}H_{ax.}$C=), 2.18–1.87 [2 H, m, $CH_{eq.}H_{ax.}$C= and $(CH_2)_3$], 1.78–1.24 [5 H, m, integration poor, $(CH_2)_3$], 1.13 (3 H, t, *J* 7.1, OCH_2Me) and 0.91 (3 H, d, *J* 6.6, CH*Me*).

(2*RS*,3*SR*,6*SR*,*E*)-Ethyl 7-methoxy-2-(4-methoxyphenylsulfanyl)-4,6-dimethyl-3-(2′-phenylethyl)hept-4-enoate 56

Aliquots of ethyl diazoacetate (4 × 15 mm^3, 0.713 mmol, 1.6 equiv.) and then a pre-cooled solution of tetrafluoroboric acid–diethyl ether complex (1:1)† in dry dichloromethane (0.717 mol dm^{-3}; 5 × 200 mm^3) were added alternately over 9 min to a solution of the allylic sulfide **9** (93%, 166.5 mg, 0.481 mmol) under argon, with light excluded, at −54 to −50 °C. After 6 min DBU (96%; 190 mm^3, 1.22 mmol) was added to the mixture and the temperature allowed to rise from −52 to −29 °C over 22 min. After this the reaction was quenched by addition of glacial acetic acid (2 cm^3) to the mixture which was then poured into aqueous hydrochloric acid (1.0 mol dm^{-3}; 30 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure after which 94% of the mixture was separated by flash column chromatography on silica (24 g) eluting with hexane–ethyl acetate (12:1 to 6:1) to yield the *ester* **56** (109.1 mg, 61%; >91% pure) as an oil; HPLC hexane–ethyl acetate (6:1), t_R 21 min at 10 cm^3 min^{-1} did not allow complete purification; R_F(hexane–ethyl acetate 4:1) 0.35; ν_{max}(smear)/cm^{-1} 1729 (C=O), 1592 (Ar), 1570 (Ar) and 1494 (Ar); δ_H(250 MHz; $CDCl_3$) 7.36 (2 H, d, *J* 8.7, SC_6H_4OMe), 7.28–7.10 (5 H, m, Ph), 6.80 (2 H, d, *J* 8.7, SC_6H_4OMe), 5.15 (1 H, d, *J* 9.3, CH=), 3.96 (2 H, q, *J* 7.1, OCH_2Me), 3.77 (3 H, s, *Me*OAr), 3.56 (1 H, d, *J* 11.3, CHS), 3.35 (3 H, s, *Me*OCH_2), 3.24 (2 H, complex ABX secondary system, CH_2OMe), 2.80 (1 H, dsextet, *J* 9.1 and 6.8, C*H*Me), 2.64–2.33 (3 H, m, CH_2Ph), 1.74–1.50 (2 H, m, CH_2CH_2Ph), 1.65 (3 H, s, MeC=), 1.05 (3 H, t, *J* 7.1, *Me*CH_2O) and 1.04 (3 H, d, *J* 6.6, *Me*CH); δ_C(400 MHz; $CDCl_3$) 172.04b, 159.94b, 141.96b, 136.10a, 133.96a, 131.62b, 128.43a, 128.27a, 125.75a, 123.72b, 114.32a, 77.91b, 60.86b, 58.74a, 55.58a, 55.29a, 49.81a, 33.41b, 33.01a, 32.52b, 17.43a, 14.00a and 11.54a; *m/z* 456 (6%, M^+) and 135 (100) (Found: M^+, 456.2379. $C_{27}H_{36}O_4S$ requires *M*, 456.2334).

Epimerisation of the homoallylic sulfide 56: synthesis of (2*RS*,3*RS*,6*RS*,*E*)-ethyl 4,6-dimethyl-7-methoxy-2-(4-methoxyphenylsulfanyl)-3-phenethylhept-4-enoate 61

A mixture of the homoallylic sulfide **56** (21.8 mg, 47.6 μmol) and sodium ethoxide (from 4.9 mg of sodium, 0.214 mmol) in ethanol (2.4 cm^3) was stirred for 3 days at RT and then quenched with saturated aqueous ammonium chloride (10 cm^3) and extracted with diethyl ether (2 × 10 cm^3) and then dichloromethane (2 × 10 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a 1.05:1 ratio of **56**:**61** (19.5 mg, 89%), from which a sample of the pure *homoallylic sulfide* **61** was obtained by flash column chromatography on silica with hexane–ethyl acetate (12:1) as eluent; ν_{max}(smear)/cm^{-1} 3100–3040 (ArH and CH=), 1735 (C=O), 1595 (Ar), 1575 (Ar) and 1495 (Ar); δ_H(250 MHz; $CDCl_3$) 7.34 (2 H, d, *J* 8.8, ArH), 7.31–7.17 (5 H, m, PhH), 6.78 (2 H, d, *J* 8.7, ArH), 5.02 (1 H, d, *J* 9.3, CH=), 3.99 (1 H, dq, *J* 11.0 and 7.1, CH_ACH_BMe), 3.96 (1 H, dq, *J* 11.0 and 7.1, CH_ACH_BMe), 3.78 (3 H, s, *Me*OAr), 3.49 (1 H, d, *J* 11.3, CHS), 3.18 (1 H, dd, *J* 6.7 and 9.1, CH_DCH_EOMe), 3.15 (1 H, dd, *J* 6.9 and 9.2, CH_DCH_EOMe), 2.67 (1 H, dsextet, *J* 9.2 and 6.7, C*H*Me), 2.57 (1 H, m, C*H*CHS), 2.61–2.52 (1 H, m, CH_2Ph), 2.46–2.33 (2 H, m, one of each CH_2CH_2Ph), 1.75–1.60 (1 H, CH_2CH_2Ph), 1.59 (3 H, s, MeC=), 1.13 (3 H, t, *J* 7.1, *Me*CH_2) and 0.89 (3 H, d, *J* 6.7, *Me*CH); *m/z* 456 (27%, M^+), 226 (54, $MeOC_6H_4SCH_2CO_2Et$), 199 (51, M − $MeOC_6H_4SCHCO_2Et$ and MeOH), 110 (72, PhSH) and 91 (100, $PhCH_2$) (Found: M^+, 456.2370. $C_{27}H_{36}O_4S$ requires *M*, 456.2334).

(2*RS*,2′*SR*,2″*SR*,*E*)-Ethyl 2-[2′-(3″-methoxy-2″-methyl-1″-propylidenyl)cyclohexyl]-2-phenylsulfanylethanoate 57

Aliquots of ethyl diazoacetate (5 × 4 mm^3, 0.190 mmol) and then a pre-cooled solution of tetrafluoroboric acid–diethyl ether complex (1:1)† in dry dichloromethane (1.06 mol dm^{-3}; 3 × 30 mm^3, then 45 mm^3, then 42 mm^3) were added alternately over 9 min to a solution of the *syn* allylic sulfide **10** (32.6 mg, 92.3 μmol) in dichloromethane (0.2 cm^3), under argon, with light excluded, cooled in a solid CO_2–acetone bath. After 6 min DBU (96%, 40 mm^3, 0.257 mmol) was added to the mixture, the temperature of which was then allowed to rise to −34 °C over 45 min. After this, the reaction was quenched by the addition of glacial acetic acid (40 mm^3) to the mixture which was then poured into aqueous hydrochloric acid (1.0 mol dm^{-3}; 30 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the mixture was separated by flash column chromatography on silica (4 g) eluting with hexane–

diethyl ether (2:1) to give the *ester* **57** (26.2 mg, 65%, 90% purity) as an oil; R_F[hexane–diethyl ether (2:1)] 0.46; ν_{max}(smear)/cm^{-1} 1735 (C=O), 1575 (Ph) and 740 and 690 (monosubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.45–7.42 (2 H, m, Ph), 7.34–7.23 (8 H, m, Ph), 5.13 (1 H, d, *J* 9.0, =CH), 4.52 (2 H, s, CH_2Ph), 4.09 (1 H, d, *J* 11.6, CHS), 4.00 (2 H, q, *J* 7.2, OCH_2Me), 3.32 (1 H, dd, *J* 6.4 and 9.0, CH^AH^BOBn), 3.27 (1 H, dd, *J* 7.0 and 9.2, CH^ACH^BOBn), 2.79 (1 H, dsextet, *J* 8.9 and 6.8, CHMe), 2.64 (1 H, br d, *J* 11.5, $CH_{eq.}$CHS), 2.40 (1 H, dt, *J* 13.7 and *ca.* 4.3, $CH_{eq.}H_{ax.}$C=), 1.87 (1 H, dt, *J ca.* 8.5 and 13.0, $CH_{eq.}H_{ax.}$C=), 1.77–1.48 [5 H, m, $(CH_2)_3$], 1.36–1.19 [1 H, m, $(CH_2)_3$], 1.06 (3 H, t, *J* 7.0, OCH_2Me) and 1.03 (3 H, d, *J* 6.8, CH*Me*); δ_C(250 MHz; $CDCl_3$) 172.32b, 138.72b, 137.14b, 134.24b, 132.93a, 128.86a, 128.75, 128.29a, 127.59a, 127.49a, 127.40a, 75.56b, 72.88b, 60.87b, 52.26a, 46.38a, 32.43a, 31.29b, 27.74b, 25.60b, 22.01b, 18.03a and 13.99a.

(2*RS*,2′*SR*,2″*RS*,*E*)-Ethyl 2-[2′-(3″-methoxycarbonyl-2″-methyl-1″-propylidenyl)cyclohexyl]-2-(4-methoxyphenylsulfanyl)ethanoate 58

Aliquots of ethyl diazoacetate (5 × 9 mm^3, 0.428 mmol) and then a pre-cooled solution of tetrafluoroboric acid–diethyl ether complex (1:1)† in dry dichloromethane (0.768 mol dm^{-3}; 4 × 100 mm^3, then 160 mm^3) were added alternately over 8 min to a solution of the *anti* allylic sulfide **19** (92.4 mg, 0.301 mmol) in dichloromethane (0.6 cm^3), under argon, with light excluded, at < −72 °C. After 3 min DBU (96%; 120 mm^3, 0.770 mmol) was added to the mixture which was then stirred for 30 min and finally treated with glacial acetic acid (75 mm^3, 1.31 mmol) to quench the reaction. The mixture was then poured into aqueous hydrochloric acid (1.0 mol dm^{-3}; 25 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the residue was separated by flash column chromatography on silica (11 g) eluting with hexane–ethyl acetate (8:1) to give the *diester* **58** (66.3 mg, 69%; >93% purity) as an oil; R_F[hexane–ethyl acetate (4:1)] 0.28; ν_{max}(smear)/cm^{-1} 1735 (C=O), 1595 (Ar), 1575 (Ar), 1495 (Ar) and 830 (*p*-disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.37 (2 H, d, *J* 8.8, ArH), 6.80 (2 H, d, *J* 8.8, ArH), 5.36 (1 H, d, *J* 9.2, CH=), 3.99 (2 H, q, *J* 7.1, CH_2Me), 3.89 (1 H, d, *J* 11.6, CHS), 3.78 (3 H, s, ArO*Me*), 3.66 (3 H, s, CO_2Me), 3.43 (1 H, dq, *J* 9.2 and 7.0, MeC*H*), 2.61 (1 H, br d, *J* 11.4, $CH_{eq.}$CHS), 2.37 (1 H, dt, *J* 13.9 and 4.2, $CH_{eq.}H_{ax.}$C=), 1.93 (1 H, dt, *J* 4.2 and 13.0, $CH_{eq.}H_{ax.}$C=), 1.79–1.70 [1 H, m, $(CH_2)_3$], 1.66–1.49 [4 H, m, $(CH_2)_3$], 1.37–1.25 [1 H, m, $(CH_2)_3$], 1.25 (3 H, d, *J* 7.0, CH*Me*) and 1.10 (3 H, t, *J* 7.1, CH_2Me); δ_C(400 MHz; $CDCl_3$) 175.39b, 172.09b, 159.94b, 139.45b, 136.30a, 124.56a, 124.05b, 114.30a, 60.80b, 55.28a, 53.38a, 51.72a, 46.07a, 38.08a, 31.45b, 27.72b, 25.90b, 22.08b, 18.26a and 14.04a; *m*/*z* 406 (21, M$^+$), 226 (26, $MeOC_6H_4S$-CH_2CO_2Et), 181 (41, M − $MeOC_6H_4SCHCO_2Et$), 149 (41, M − $MeOC_6H_4SCHCO_2Et$ and MeOH), 121 (37, M − $MeOC_6H_4SCHCO_2Et$, MeOH and CO) and 110 (100, PhSH) (Found: M$^+$, 406.1853. $C_{22}H_{30}O_5S$ requires *M*, 406.1813).

(2*RS*,2′*SR*,2″*SR*,*E*)-2-[2′-(3″-Methoxy-2″-methyl-1″-propylidenyl)cyclohexyl]-2-(4-methoxyphenylsulfanyl)ethanol 66

Lithium aluminium hydride (95%; 4.4 mg, 0.109 mmol) was added to a stirred solution of the ester **54** (43.0 mg, 0.110 mmol) in dry diethyl ether (0.55 cm^3), with light excluded, at −7 °C. Stirring was continued for 4 h between −7 and 8 °C and then for 5.5 h at RT. The reaction was then quenched by the addition of aq. potassium sodium tartrate (1 mol dm^3; 20 cm^3) to the mixture which was then extracted with diethyl ether (2 × 20 cm^3). Aqueous sodium hydroxide (10%; 10 cm^3) was added to the aqueous mother-liquor and the mixture extracted with dichloromethane (2 × 25 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure and the mixture was separated by flash column chromatography on silica (4.5 g) with hexane–diethyl ether (1:1) as eluent to yield the *alcohol* **66** (26.0 mg, 68%) as an oil; diastereoisomeric ratio 89.8:5.8:4.4. The ^{1}H NMR and the IR spectra were taken on a 97.2:2.8 diastereoisomeric mixture and only the characterisation of the major diastereoisomer is given; R_F[dichloromethane–methanol (50:1)] 0.47; ν_{max}(smear) 3448 (OH), 1592 (Ar), 1570 (Ar), 1493 (Ar) and 828 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.37 (2 H, *J* 8.8, ArH), 6.82 (2 H, d, *J* 8.8, ArH), 4.99 (1 H, d, *J* 9.0, =CH), 3.79 (3 H, s, *Me*OAr), 3.57 (1 H, dd, *J* 3.6 and 11.9, CH_ACH_BOH), 3.55 (1 H, dd, *J* 4.3 and 11.9, CH_ACH_BOH), 3.36 (1 H, dt, *J* 10.3 and 4.0, CHS), 3.33 (3 H, s, *Me*OCH_2), 3.23 (1 H, dd, *J* 6.4 and 9.1, CH_ACH_BOMe), 3.16 (1 H, dd, *J* 7.4 and 9.1, CH_ACH_BOMe), 2.74 (1 H, dsextet, *J* 8.8 and 6.8, C*H*Me), 2.40–2.28 (2 H, m, $CH_{eq.}H_{ax.}$C=, C*H*CHS), 2.06 (1 H, br s, OH), 2.01 (1 H, unsymmetric dt, *J ca.* 3.6 and 12.3, $CH_{eq.}H_{ax.}$C=), 1.78–1.24 [6 H, m, $(CH_2)_3$] and 1.01 (3 H, d, *J* 6.7, *Me*CH); δ_C(400 MHz; $CDCl_3$) 159.57b, 139.47b, 135.71a, 126.90a, 124.35b, 114.58a, 78.19b, 60.04b, 58.75a, 55.31a, 54.33a, 44.73a, 32.13a, 30.21b, 28.02b, 26.31b, 22.44b and 17.98a; *m*/*z* 350 (6%, M$^+$), 183 (37, M − CO and $MeOC_6H_4S$) and 139 (100, $MeOC_6H_4S$) (Found: M$^+$, 350.1901. $C_{20}H_{30}O_3S$ requires *M*, 350.1916).

(2*RS*,2′*SR*,2″*SR*,*E*)-2-[2′-(3″-Methoxy-2″-methyl-1″-propylidenyl)cyclohexyl]-2-(4-methoxyphenylsulfanyl)ethyl 3,5-dinitrobenzoate 67

3,5-Dinitrobenzoyl chloride (freshly prepared, 18.6 mg, 80.7 μmol) was added to a stirred solution of the alcohol **66** (19.6 mg, 55.8 μmol) and DMAP (9.7 mg, 79.2 μmol) in dry dichloromethane (0.28 cm^3) under argon, at RT. After 15 min the reaction mixture was separated by flash column chromatography on silica (3.5 g) eluting with hexane–ethyl acetate (4:1) to give the *ester* **67** as a yellow crystalline solid (87%, 26.4 mg) of roughly the same diastereoisomeric ratio as the alcohol; recrystallisation of this from diethyl ether at −20 °C removed the unwanted minor diastereoisomer and further recrystallisation from hexane–diethyl ether gave the pure yellow needles; R_F[hexane–ethyl acetate (4:1)] 0.32 and (dichloromethane) 0.19; ν_{max}(Nujol mull) 3110 (=CH or ArH), 1745 (C=O), 1630 (C=C), 1590 (Ar), 1495 (Ar) and 830 (*p*-disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 9.19 [1 H, t, *J* 2.1, *para* proton of $C_6H_3(NO_2)_2$], 8.94 [2 H, d, *J* 2.1, *ortho* protons of $C_6H_3(NO_2)_2$], 7.35 (2 H, d, *J* 8.7, protons *ortho* to S of SC_6H_4OMe), 6.67 (2 H, d, *J* 8.7, protons *meta* to S of SC_6H_4OMe), 5.08 (1 H, d, *J* 8.9, C=CH), 4.69 (1 H, dd, *J* 3.9 and 11.6, CH_AH_BOCOAr), 4.56 (1 H, dd, *J* 6.4 and 11.6, CH_AH_BOCOAr), 3.72 (1 H, ddd, *J* 3.8, 6.3 and 9.1, CHS), 3.66 (3 H, s, *Me*OAr), 3.34 (3 H, s, CH_2OMe), 3.26 (1 H, dd, *J* 6.6 and 9.2, CH_DH_EOMe), 3.19 (1 H, dd, *J* 6.9 and 9.1, CH_DH_EOMe), 2.77 (1 H, dsextet, *J* 8.7 and 6.8, C*H*Me), 2.42–2.30 (2 H, m, $CH_{eq.}$CHS and $CH_{eq.}H_{ax.}$C=), 2.17 (1 H, unsymmetric dt, averaged *J* 3.7 and 12.2, $CH_{eq.}H_{ax.}$C=), 1.80–1.40 [6 H, m, $(CH_2)_3$] and 1.00 (3 H, d, *J* 6.7, CH*Me*).

(2*RS*,3*SR*,6*SR*,*E*) 7-Methoxy-2-(4-methoxyphenylsulfanyl)-4,6-dimethyl-3-phenethylhept-4-en-1-ol 68

Lithium aluminium hydride (95%; 6.1 mg, 0.152 mmol) was added to a stirred solution of the ester **56** (72.5 mg, 0.159 mmol) in dry diethyl ether (0.8 cm^3), with light excluded, at RT. Stirring was continued for 1 h 50 min after which the reaction was quenched by addition of brine (25 cm^3) to the mixture which was then extracted with diethyl ether (4 × 25 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and the mixture separated by flash column chromatography on silica (6 g) with hexane–ethyl acetate (4:1) as eluent to yield the *alcohol* **68** (53.3 mg, 81%) as an oil; R_F[hexane–ethyl acetate (4:1)] 0.17; ν_{max}(smear)/cm^{-1} 3449 (OH), 1592 (Ar), 1570 (Ar), 1493 (Ar) and 829 (*para* disubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.34 (2 H, d, *J* 8.7, C_6H_4OMe), 7.30–7.13 (5 H, m, Ph), 6.81 (2 H, d, *J* 8.7,

C_6H_4OMe), 5.08 (1 H, d, *J* 9.2, CH=), 3.78 (3 H, s, *Me*OAr), 3.58 (1 H, dd, *J* 4.4 and 12.0, CH_AH_BOH), 3.54 (1 H, dd, *J* 4.4 and 12.2, CH_AH_BOH), 3.33 (3 H, s, $MeOCH_2$), 3.23 (2 H, d, *J* 6.8, $MeOCH_2$), 3.08 (1 H, dt, *J* 8.4 and 4.4, CHS), 2.79 (1 H, dsextet, *J* 9.1 and 6.8), 2.60 (1 H, m, CH_2Ph or CHC=), 2.45–2.28 (2 H, m, CH_2Ph and/or CHC=), 1.89 (1 H, m, CH_2CH_2Ph), 1.68 (3 H, s, MeC=), 1.77–1.60 (1 H, m, CH_2CH_2Ph) and 1.02 (3 H, d, *J* 6.7, *Me*CH); δ_C(400 MHz; $CDCl_3$) 159.54b, 142.40b, 135.44a, 133.94b, 131.80a, 128.42a, 128.31a, 125.73a, 124.67b, 114.61a, 77.91b, 60.89b, 58.72a, 56.97a, 55.31a, 48.49a, 33.78b, 32.89a, 31.41b, 17.39a and 13.60a; *m/z* 414 (7%, M^+), 139 (47, $MeOC_6H_4S$), 135 (49) and 91 (100, $PhCH_2$) (Found: M^+, 414.2236. $C_{25}H_{34}O_3S$ requires *M*, 414.2228).

(1*RS*,2′*SR*,5′*RS*)-1-(7′-Methoxy-4′,6′-dimethyl-4′-phenylhept-4′-en-3′-yl)oxirane 69

Trimethyloxonium tetrafluoroborate (46.2 mg, 0.312 mmol) was added in a number of aliquots over 1 h 25 min to a stirred solution of the alcohol **68** (42.3 mg, 0.102 mmol) in dry dichloromethane (1.0 cm^3) at RT followed by aqueous sodium hydroxide (10%; 1.4 cm^3). Stirring was continued for 3 h after which the reaction mixture was neutralised with saturated aqueous ammonium chloride (50 cm^3) and extracted with dichloromethane (4 × 50 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure and flash column chromatography of the residue on silica eluting with hexane–ethyl acetate (8 : 1) yielded the *epoxide* **69** (18.3 mg, 65%) as a colourless oil, purity > 90%. Attempts to purify the product further by HPLC and preparative TLC failed to improve the quality of the sample; R_F[hexane–ethyl acetate (4 : 1)] 0.4, pale under UV, stains strongly yellow with $KMnO_4$; δ_H(250 MHz; $CDCl_3$) 7.30–7.16 (5 H, m, PhH), 5.02 (1 H, d, *J* 9.1, C=CH), 3.34 (3 H, s, OMe), 3.23 (1 H, dd, *J* 6.9 and 8.8, CH_ACH_BOMe), 3.19 (1 H, dd, *J* 6.9 and 9.2, CH_AH_BOMe), 2.88 (1 H, unsymmetric dt, averaged *J* 7.0 and 3.4, $CH(O)CH_{trans}$-H_{cis}), 2.72 (1 H, dsextet, partially obscured, *J* 9.0 and 6.7, *CH*Me), 2.70 (1 H, unsymmetric t, *J* 4.1 and 4.6, $CH(O)CH_{trans}$-H_{cis}), 2.60 [1 H, dd, *J* 5.6 and 9.8, distortion in ABX system leads to the smaller dd being too small to observe, CH_AH_BPh], 2.55 [1 H, dd, *J* 7.2 and 9.2, distortion in ABX system leads to the smaller dd being too small to observe, CH_AH_BPh], 2.47 [1 H, dd, *J* 2.7 and 5.0, $CH(O)CH_{trans}H_{cis}$], 2.01–1.70 (3 H, m, CHC= and CH_2CH_2Ph), 1.68 [3 H, d, *J* 0.9, MeC=] and 0.97 (3 H, d, *J* 6.7, CH*Me*).

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