A New and Effective Method for the Low Temperature Generation of Sulfonium Ylides from Allyl Sulfides

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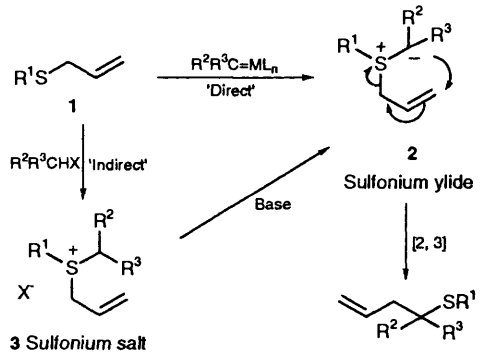
Allyl 4-methoxyphenyl sulfides can be converted into sulphonium ylides which undergo [2,3] sigmatropic rearrangement in high yield and with excellent stereoselectivity by repeated alternate additions of a diazonium salt and tetrafluoroboric acid at low temperature. Under these conditions, side reactions are suppressed and both cyclic and open-chain compounds, including one containing a tertiary amine, give homoallylic sulfides in good yield. Epoxides may be made from the products.

The [2,3] sigmatropic rearrangement of allyl sulfonium ylides is an extremely useful reaction and, as a result, both direct and indirect routes have been developed [1] for the preparation of the sulfonium ylides **2** from the allyl sulfides **1**. Reaction of the allyl sulfide **1** with a carbene,[2] a metal alkylidene complex (η^2-carbene complex)[2,3] or an aryne[4] (Scheme 1, direct pathway) gives the sulfonium ylide **2** directly. The carbene or metal alkylidene is generally generated from a diazo compound. Unfortunately, with carbenes and to a lesser extent with metal alkylidenes, cyclopropanation of the double bond competes with sulfonium ylide formation.[2,5] Furthermore, the homoallylic sulfide products are also substrates for sulfonium ylide formation so that a large excess of allyl sulfide to diazo compound is required for efficient conversion.[6] Therefore, metal-catalysed sulfonium ylide formation is generally restricted to intramolecular reactions.[7]

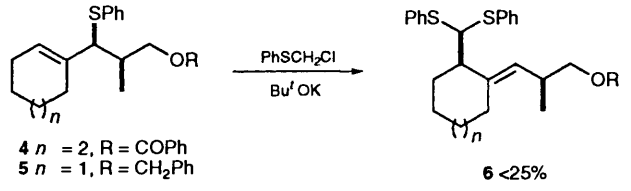
Alternatively, if the allyl sulfide **1** is alkylated to form a sulfonium salt **3**, it may then be deprotonated to the corresponding sulfionium ylide **2** (Scheme 1, indirect pathway).



Scheme 1 M = metal, L = ligand, X = Br, Cl, I, OSO_2CF_3

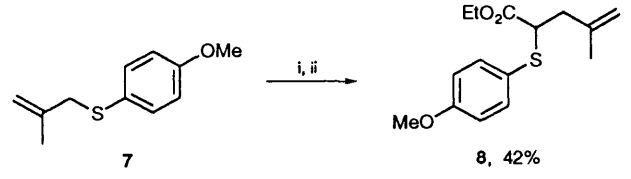
This indirect generation of the sulfonium ylide has been more successful.[8] It is best to use an alkyl halide in the presence of a silver salt with a non-nucleophilic counterion or an alkyl trifluoromethanesulfonate (triflate) as sulfonium salts are susceptible to nucleophilic attack.[9] These methods have been successful in a large number of cases and may be carried out at temperatures as low as −10 °C.

We had used stereoselective aldol reactions, PhS migration and the [2,3] sigmatropic sulfoxide rearrangement to prepare diols with 1,4 related chiral centres across an *E* double bond [10] and wished to extend this methodology to the formation of new carbon–carbon bonds using the [2,3] sigmatropic rearrangement of sulfonium ylides derived from the allyl sulfides **4** and **5**.



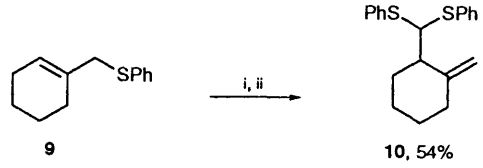
Scheme 2

Unfortunately, the allyl sulfide **4** failed to react with ethyl 2-trifluoromethylsulfonylacetate[8,11] at 0 °C and at room temperature, though the sulfonium salt was formed, it decomposed. A similar lack of reactivity was observed with the aryl allyl sulfide **7** between −10 and 0 °C. However, in this case, when the mixture was allowed to warm to room temperature alkylation proceeded smoothly. After 2.5 h the mixture was cooled to 0 °C and treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the [2,3] rearrangement product **8** in 42% yield (or 64% based on recovered starting material) (Scheme 3).



Scheme 3 *Reagents and conditions:* i, $CF_3SO_2OCH_2CO_2Et$, MeCN, room temp., 2.5 h; ii, DBU (1.9 equiv.), −10 °C, 20 min

When the allyl sulfide **9** was subjected to chloromethyl phenyl sulfide and potassium *tert*-butoxide in THF [12] the homoallylic sulfide **10** was obtained in 54% yield after HPLC (Scheme 4). However, when these conditions and various



Scheme 4 *Reagents and conditions:* i, $PhSCH_2Cl$ (1.5 equiv.); ii, Bu'OK (2 equiv.), THF, 15 °C, 2 h

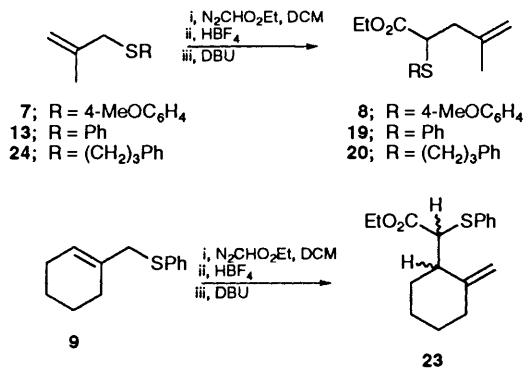
adaptations of them were applied to the more complicated allyl sulfides **4** and **5** the yields of homoallylic sulfides **6** were always less than 25% (Scheme 2).

From these results it seemed necessary to develop a low temperature method for the generation of the sulfonium salt. At this time, Kurth and co-workers described the intramolecular

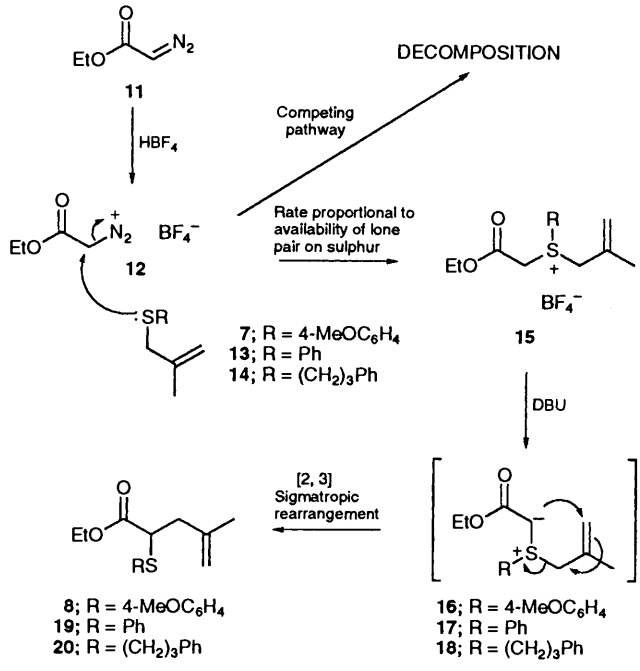
Table 1 [2,3] Sigmatropic rearrangements of simple allyl sulphides

Entry	Starting material	Temp. (°C)	Equivalents of reagents used: Diazo ester	HBF_4	DBU	Ratio of product: starting material	Product yield[a] (%)
1	**7**	−20	1.05	1.05	1.2	4:1	50
2	**13**	−20	1.05	1.05	1.2	2.1:1	42
3	**14**	−20	1.05	1.05	1.2	5.7:	63
4	**9**	−25	1.15	1.33	1.33	—	56[b]
5	**13**	−20	1.05	1.04	1.2	1.3:1	—[c]
6	**9**	−20	5.0	1.2	6.4	—	54[b]
7	**7**	−20	2.1	2.1	2.2	1:0	83[d]
8	**7**	−55	1.5	1.02	2.8	1:0	86[e]

[a] Isolated yield after chromatography. [b] No Stevens rearrangement product detected, product was a 3:2 mixture of diastereoisomers. [c] HBF_4 was added first, mixture of products was formed. [d] Sequential addition of the diazo ester and HBF_4. [e] Five alternate additions of the diazo ester and HBF_4.



Scheme 5



Scheme 6

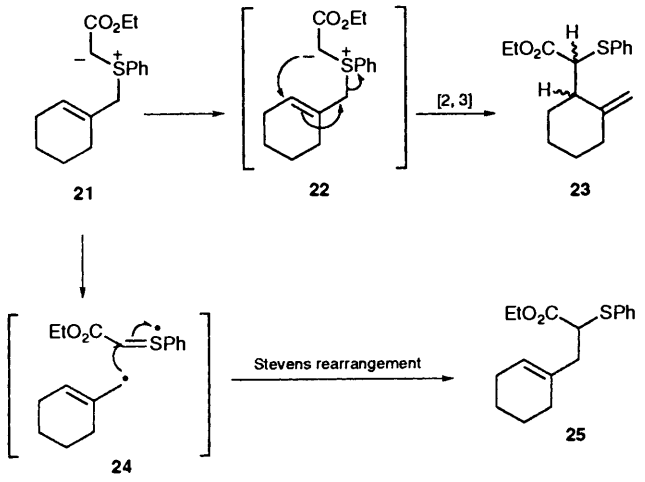
coupling of an allyl sulfide with a diazonium salt formed by the action of tetrafluoroboric acid on a diazo compound;[13] we decided to develop an intermolecular version of this reaction. The approach developed in this paper has now been successfully applied to the more complex allyl sulfides **4** and **5**: this work has been described in a preliminary communication.[14]

The role of the substituent on the sulfur atom was studied with the simple allyl sulfides **7**, **13** and **14**. Each of these was mixed with ethyl diazoacetate in dichloromethane, and then was treated with tetrafluoroboric acid at −20 °C. The yellow solutions effervesced and decolourised immediately. The sulfonium salts were not isolated, but DBU was added to form the sulfonium ylide which spontaneously rearranged to the corresponding homoallylic sulfides **8**, **19** and **20** (Scheme 5, Table 1 entries 1–3). Decomposition was avoided by this technique and it remained to maximise the degree of conversion. The yields of **8**, **19** and **20** follow the order of the nucleophilicity of the sulfur atom and we conclude that the differences in product yields and in the product-to-starting material ratios resulted from differences in the alkylation of the allyl sulfides **7**, **13** and **14**, not from differences in the [2,3] sigmatropic rearrangement of the ylides **16**, **17** and **18** (Scheme 6).

Another potential side reaction is the 1,2 Stevens rearrangement. This cannot be detected when **7**, **13**, or **14** rearrange, as the homoallylic sulfides **8**, **19**, **20** could arise either from the [2,3] sigmatropic rearrangement or from the 1,2 Stevens rearrangement.[15] However, the product **25** of the Stevens rearrangement of the sulfonium ylide **21** is different from that of the [2,3] sigmatropic rearrangement **23** and was not found (Scheme 7, Table 1, entry 4). The homoallylic sulfides **23** were isolated in 56% yield as a 3:2 mixture of the diastereoisomers. A decomposition product $PhSCH_2CO_2Et$ was also isolated in 18% yield. When this reaction was carried out in deuteriated dichloromethane the [2,3] sigmatropic rearrangement was found to be complete within 8 min of adding the base (−25 °C to room temperature) confirming that rearrangement is rapid. We deduce that the Stevens rearrangement is not a significant problem.

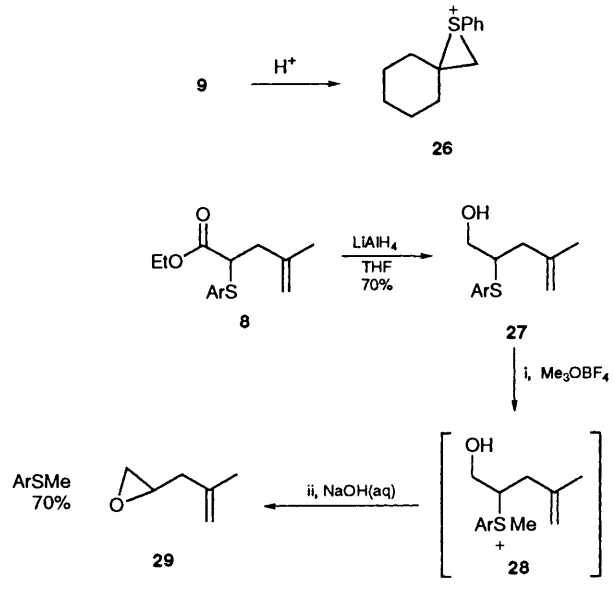
Attempts were made to improve the reaction conditions (Table 1, entries 5–8). When the tetrafluoroboric acid was added to allyl sulfide **13** first and then the ethyl diazoacetate was added slowly to the mixture (entry 5, Table 1), the product to starting material ratio was lower and the mixture contained other products. This is probably due to formation of the episulfonium ion **26** under the acidic conditions. When an excess of ethyl diazoacetate was used with the allyl sulfide **9**, the ethyl diazoacetate was consumed but there was no improvement in the yield of the homoallylic sulfide **23** (entry 6, Table 1). However, when repeated alternate additions of 1.05 equiv. of ethyl diazoacetate followed by 1.05 equiv. of tetrafluoroboric acid were made to the allyl sulfide **7** and the resulting mixture was treated with DBU, the homoallylic sulfide **8** was isolated in improved yield (entry 7, Table 1). The reaction was optimised by making five alternate additions of 0.3 equiv. of ethyl diazoacetate and 0.2 equiv. of a precooled solution of tetrafluoroboric acid in dichloromethane to the allyl sulfide **7** in dichloromethane at −55 °C. Deprotonation with DBU was carried out at the same temperature to give the homoallylic sulfide **8** in 86% yield (entry 8, Table 1).

The synthetic potential of the homoallylic sulfides was briefly examined: the arylthio group could be removed by reduction,[16] or the ester could be converted into the aldehyde to allow



Scheme 7 Stevens and [2,3] sigmatropic rearrangements

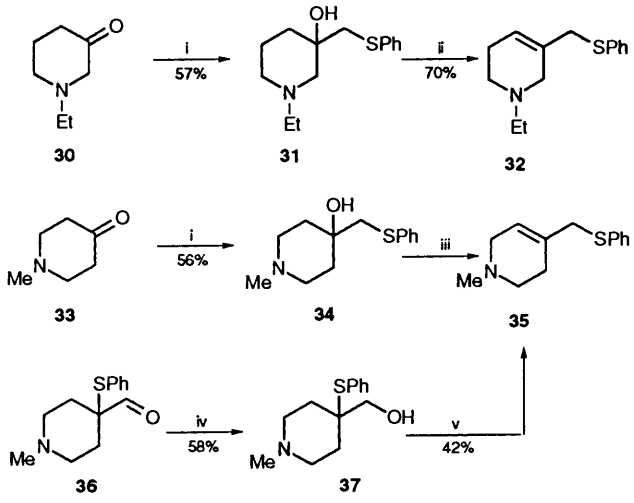
formation of a new allyl sulfide by the Wittig reaction and continued chain growth using iterative [2,3] sigmatropic sulfonium ylide rearrangements.[17] However, the course adopted was to convert the homoallylic sulfide into an epoxide. The homoallylic sulfide **8** was reduced to alcohol **27** in 70% yield (+24% recovered starting material) (Scheme 8). The alcohol



Scheme 8 Ar = 4-MeOC$_6$H$_4$

27 was treated with trimethyloxonium tetrafluoroborate to generate the sulfonium salt **28**.[18] This was not isolated but was subjected to aqueous sodium hydroxide and 4-methoxythioanisole was isolated in 70% yield. The epoxide **29** was too volatile to be isolated so the reaction was repeated in deuteriated dichloromethane and a ^{1}H NMR spectrum of the mixture after work-up revealed a 1:1.7 ratio of the epoxide **29** to 4-methoxythioanisole. This methodology allows the regiospecific synthesis of homoallylic epoxides.

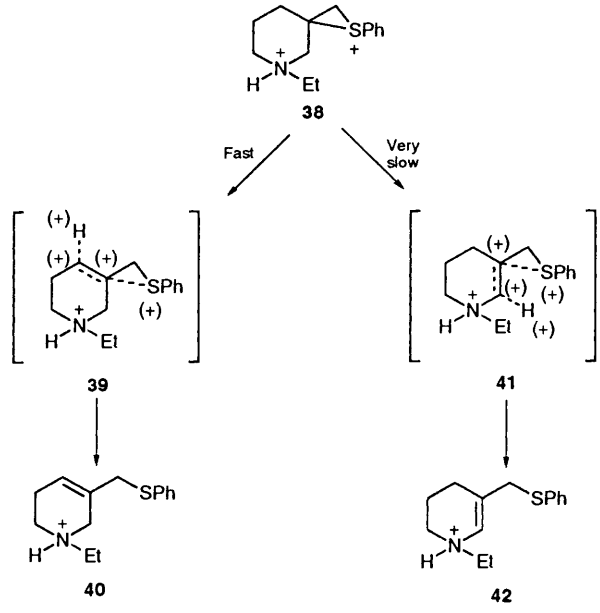
We decided to investigate the more challenging case of the [2,3] sigmatropic rearrangement of sulfonium ylides derived from the allyl sulfides **32** and **35** bearing an amino group. Here the nucleophilic nitrogen atom may compete with the sulfur atom for alkylation. The syntheses of these substrates parallel that previously published for the allyl sulfide **9**.[19] Phenylthiomethyllithium generated in the presence of diazabicyclo[2.2.2]octane (DABCO)[20] was added to each of the amines **30** and **33** to give the β-hydroxy sulfides **31** and **34** in 57% and 56%



Scheme 9 *Reagents and conditions:* i, PhSCH$_2$Li, DABCO; ii, TsOH (3 equiv.), PhMe, reflux, 16 h; iii, TsOH (4 equiv.), PhH, reflux 2.5 h; iv, NaBH$_4$, MeOH; v, TsOH (4 equiv.), 1.5 h

yield, respectively (Scheme 9). β-Hydroxy sulfides **34** and **37** (**37** was obtained in 58% yield by the reduction of the previously reported aldehyde **36**[21]) rearranged to the allyl sulfide **35** when heated under reflux in benzene with 4 equiv. of toluene-*p*-sulfonic acid for 1.5–2.5 h.[21] A small quantity of the vinyl sulfide was also formed in the reaction.

The β-hydroxy sulfide **31** required a 16 h reflux in toluene with 3 equiv. of toluene-*p*-sulfonic acid for conversion into the allyl sulfide **32** in 70% yield. The allyl sulfide **32** was the only amine product by TLC. This implies that the episulfonium ion **38** opens exclusively away from the protonated nitrogen atom so that the positive charges in the transition state move apart and no protonated enamine **42** is formed (Scheme 10). The β-

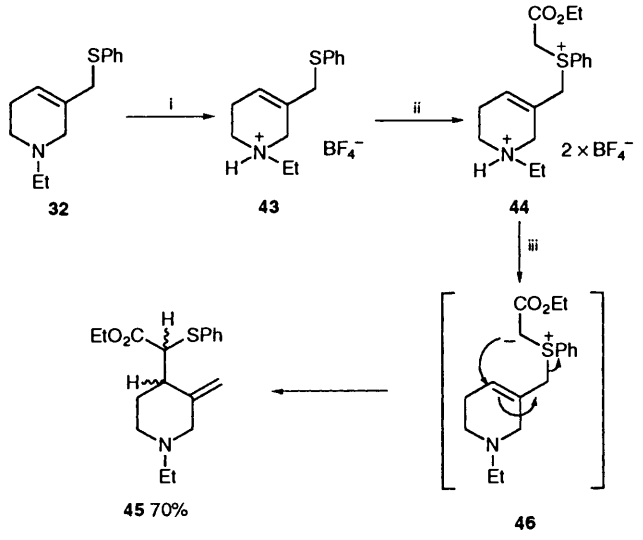


Scheme 10

hydroxy sulfides **34** and **31** when treated with trimethylsilyl trifluoromethanesulfonate in dichloromethane at −78 °C and then allowed to warm to room temperature gave only unchanged starting material.[21]

When the allyl sulfide **35** was treated with the standard Vedejs conditions, ethyl 2-trifluoromethylsulfonylacetate and then potassium *tert*-butoxide at −5 to 0 °C, a complex mixture was obtained. Applying our procedure, the allyl sulfide

32 was first treated with 1 equiv. of tetrafluoroboric acid at −56 °C to protect the amine, and then with five alternate additions of ethyl diazoacetate (1.7 equiv. in total) followed by tetrafluoroboric acid (1.7 equiv. in total) to generate the sulfonium salt **44** (Scheme 11). The sulfonium salt was not



Scheme 11 *Reagents and conditions:* i, HBF_4 (1 equiv.), DCM, −56 °C; ii, HBF_4 (1.7 equiv.) $CF_3SO_2OCH_2CO_2Et$ (1.7 equiv.); iii, Bu^{t}OK (4.6 equiv.), −56 °C to 0 °C, 2 h

isolated but was treated with 4.6 equiv. of potassium *tert*-butoxide and the mixture allowed to warm to 0 °C to give the homoallylic sulfides **45** in 70% yield as an inseparable 52:48 diastereoisomeric mixture after chromatography.

In summary, we have presented a new and effective method of making sulfonium salts and ylides at low temperature so as to carry out [2,3] sigmatropic rearrangements in high yield. The diazonium salt **12** formed *in situ* has several advantages as the alkylating agent for the allyl sulfides. Firstly, alkylation on the sulfur atom proceeds rapidly even at −55 °C. Secondly, the diazonium salt is short lived so that detection of unchanged starting material means that more reagent is required; if triflates are used, they are difficult to detect by TLC and the sulfonium salts tend to sit on the baseline so that it is difficult to discern whether reaction is proceeding smoothly, and whether more reagent is required. Thirdly, our methodology may be used on compounds containing an amino group without protection.

Experimental

Correct APTs (attached proton tests) were found for all compounds and were used to help assign the signals of the ^{13}C NMR spectra of diastereoisomeric mixtures.

3-(4-*Methoxyphenylthio*)-2-*methylpropene* **7**.—Sodium hydride (80% suspension in oil; 0.50 g, 16.7 mmol) was washed with light petroleum (b.p. 40–60 °C) and then covered with dry tetrahydrofuran (70 cm^3). 4-Methoxybenzenethiol 97%; 2.0 cm^3, 15.8 mmol) and 3-chloromethyl-2-methylpropene (98%; 2.0 cm^3, 19.8 mmol) were added to the mixture which was then stirred for 4 h 15 min, before being quenched with aqueous hydrochloric acid (2 mol dm^{-3}; 100 cm^3). The mixture was extracted with diethyl ether, and the extract washed with aqueous sodium hydroxide, dried ($MgSO_4$), and evaporated under reduced pressure. Flash column chromatography of the residue on silica (291 g), eluting with hexane–diethyl ether (40:1) gave the allyl sulfide **7** as an oil (1.91 g, 62%); R_F[hexane–diethyl ether (10:1)] 0.68; ν_{max}(smear)/cm^{-1} 3090 (C=CH_2), 1645 (C=C), 1595 (Ar), 1575 (Ar), 1495 (Ar), 900 (C=CH_2) and 825 (*para* disubstituted benzene); δ_H(300 MHz; $CDCl_3$) 7.35 (2 H, d, *J* 8.8, ArH), 6.84 (2 H, d, *J* 8.8, ArH), 4.67 (1 H, s, C=CH^{A}H^B), 4.76 (1 H, s, C=CH^{A}H^B), 3.80 (3 H, s, OMe), 3.32 (2 H, s, SCH_2) and 1.86 (3 H, s, =CMe); δ_C(75 MHz; $CDCl_3$) 159.06, 141.18, 133.93, 126.42, 114.39, 113.83, 55.32, 44.14 and 21.00; *m/z* 194 (56%, M$^+$) and 139 (100, $MeOC_6H_4S$) (Found: M$^+$, 194.0759. $C_{11}H_{14}OS$ requires 194.0765).

Ethyl 2-(4-*Methoxyphenylthio*)-4-*methylpent*-4-*enoate* **8** *by the Diazoacetate Method*.—Ethyl diazoacetate (5 × 0.140 cm^3, 6.66 mmol) and precooled tetrafluoroboric acid in dry dichloromethane (0.443 mol dm^{-3}; 5 × 2.0 cm^3) were added alternately over 9 min to a solution of the allyl sulfide **7** (840.7 mg, 4.33 mmol), under argon, with light excluded, at −60 to −45 °C. After 3 min, DBU (96%; 1.90 cm^3, 12.2 mmol) was added to the mixture the temperature of which was allowed to rise from −60 to −30 °C over 13 min. The reaction was quenched by pouring it into a mixture of aqueous hydrochloric acid (1.0 mol dm^{-3}; 150 cm^3) and dichloromethane (50 cm^3), after which further dichloromethane was added to make the volume up to 250 cm^3. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 100 cm^3). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The residual mixture was separated by flash column chromatography on silica (93 g) eluting with hexane–diethyl ether (10:1) to yield the *ester* **8** (1.04 g, 86%) as an oil; R_F[hexane–diethyl ether (10:1)] 0.28; ν_{max}(smear)/cm^{-1} 3080 (=CH_2), 1735 (C=O), 1650 (C=C), 1595 (Ar), 1570 (Ar), 1495 (Ar) and 830 (*para* disubstituted benzene); δ_H(300 MHz; $CDCl_3$) 7.45 (2 H, d, *J* 8.7, ArH), 6.86 (2 H, d, *J* 8.7, ArH), 4.83 (1 H, s, CH_ACH_B=), 4.76 (1 H, s, CH_ACH_B=), 4.11 (2 H, q, *J* 7.1, CH_2Me), 3.70 (1 H, dd, *J* 6.1 and 9.6, SCH), 3.64 (3 H, s, MeO), 2.61 (1 H, dd, *J* 9.5 and 14.7, $SCHCH_DH_E$), 2.24 (1 H, dd, *J* 6.1 and 14.7, $SCHCH_DH_E$), 1.76 (3 H, s, MeC=), and 1.20 (3 H, t, *J* 7.1, $MeCH_2$); δ_C(75 MHz; $CDCl_3$) 171.87, 160.22, 141.61, 136.45, 122.99, 114.43, 112.94, 60.94, 53.30, 49.76, 39.45d, 22.36 and 14.07; *m/z* 280 (80%, M$^+$), 225 [15, M − CH_2(Me)C=CH_2], 207 (12, M − CO_2Et), 179 [61, M − CH_2(Me)C=CH_2 and EtOH], 151 [57, M − CH_2(Me)C=CH_2, EtOH and CO], and 139 (100, $MeOC_6H_4S$) (Found: C, 64.65; H, 7.3; M$^+$, 280.1145. $C_{15}H_{20}O_3S$ requires C, 64.25; H, 7.2; *M*, 280.1133).

Ethyl 2-(4-*Methoxyphenylthio*)-4-*methylpent*-4-*enoate* **8** *by the Triflate Method*.—A solution of ethyl trifluoromethylsulfonylacetate (62.3 mg, 0.26 mmol) in dry acetonitrile (0.4 cm^3) was added to a stirred solution of the allyl sulfide **7** (41.6 mg, 0.21 mmol) in dry acetonitrile (0.4 cm^3), under argon, at − 10 °C. The mixture was allowed to warm to 0 °C over 1 h 20 min and then stirred for a further 2 h 30 min. DBU (65 mm^3, 0.42 mmol) was then added to the mixture at −10 °C. After 20 min the reaction was quenched by pouring the mixture into 1 mol dm^{-3} HCl (30 cm^3). Work-up, by extraction of aqueous mixture with dichloromethane (4 × 20 cm^3) followed by flash column chromatography of the residue on silica (5 g) eluting with hexane–diethyl ether (12:1) gave starting material **7** (13.9 mg, 33%) and the ester **8** (25.2 mg, 42%).

1-*Bis*(*phenylthio*)*methyl*-2-*methylenecyclohexane* **10**.—Following the procedure of Julia *et al*;[12] chloromethyl phenyl sulfide (130 mm^3, 0.97 mmol) was added to a stirred solution of the allyl sulfide **9** (131.7 mg, 0.645 mmol) and potassium tertiary butoxide (153.5 mg, 97%, 1.33 mmol) in dry THF (2.25 cm^3) at − 15 °C, under argon and the mixture was stirred for 2 h before being quenched with brine. After work-up, the mixture was separated by flash column chromatography on silica eluting with hexane–diethyl ether (50:3) and then by HPLC in hexane–diethyl ether (50:2) at 10 cm^3 min^{-1} to yield the *homoallylic*

sulfide **10** (123.7 mg, 59% 92% pure) as an oil; R_F[hexane–diethyl ether (15:1)] 0.47; ν_{max}(smear)/cm^{-1} 3080 (=CH_2), 3020 (PhH), 2990–2860 (C–H), 1645 (C=C), 1585 (Ph), 895 (C=CH_2), 745 and 695 (monosubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.46–7.43 (2 H, m, Ph), 7.39–7.34 (2 H, m, Ph), 7.31–7.21 (6 H, m, Ph), 4.85 (1 H, s, CH^AH^B=), 4.81 (1 H, s, CH^AH^B=), 4.70 [1 H, d, *J* 6.6, $CH(SPh)_2$], 2.55 [1 H, q, *J* 6.2, $CH_{eq}CH(SPh)_2$], 2.21 (1 H, d of unsymm.ts, averaged *J* 12.7 and 6.3, CH^DH^E), 2.05 (1 H, d of unsymm.ts, averaged *J* 13.0 and 6.5, CH^DH^E), 1.97 [2 H, q, *J* 5.9, $CH_2CH_{eq}CH(SPh)_2$], 1.71–1.62 (1 H, m, CH_2), 1.61–1.54 (2 H, m, CH_2) and 1.44 (1 H, dqn, *J* 12.2 and 6.1, CH_2); δ_C(400 MHz; $CDCl_3$) 148.68, 135.45, 134.56, 132.54, 128.84, 127.57, 127.41, 108.99, 61.54, 48.14, 34.65, 30.07, 28.16 and 23.86; *m/z* 326 (1.6%, M^+), 244 [25, $(PhS)_2C_2H_2$], 217 (92, M – PhS), 135 (66, $PhSC_2H_2$) and 110 (100, PhSH) (Found: M^+, 326.1156. $C_{20}H_{22}S_2$ requires M, 326.1156).

2-*Methyl*-3-(*phenylthio*)*propene* **13**.—By the method used for **7** above, thiophenol (97%; 1.0 cm^3, 9.45 mmol) and 3-chloromethyl-2-methylpropene (98%; 1.0 cm^3, 9.92 mmol) gave the allyl sulfide[19] **13** (1.05 g, 68%) as a yellow oil, which was further purified to give a colourless oil (320 mg, 21%); R_F[hexane–diethyl ether (15:1)] 0.72; ν_{max}(smear)/cm^{-1} 3080 (=CH_2), 1650 (C=C), 1590 (Ph), 900 (C=CH_2), 740 and 690 (monosubstituted benzene); δ_H(300 MHz; $CDCl_3$) 7.38–7.35 (2 H, m, Ph), 7.31–7.26 (2 H, m, Ph), 7.23–7.17 (1 H, m, Ph), 4.84 (2 H, s, =CH_2), 3.54 (2 H, s, SCH_2) and 1.87 (3 H, s, =CMe); δ_C(75 MHz; $CDCl_3$) 140.79, 136.5, 129.97, 128.71, 126.19, 113.96, 41.90 and 21.15; *m/z* 164 (24%, M^+), 149 (12, M – Me), 58 (100) and 55 [60, $CH_2(Me)C{=}CH_2$].

2-*Methyl*-3-(3-*phenylpropylthio*)*propene* **14**.—This compound was synthesised by the method used for **7** from phenylpropanethiol and methallyl chloride. The allyl sulfide **14** was obtained as an oil, b.p. 112 °C, 1 mmHg; R_F[hexane–diethyl ether (20:1)] 0.75; ν_{max}(smear)/cm^{-1} 3080 (=CH_2), 3030 (Ph), 2980–2860 (C–H), 1650 (C=C), 1610 (Ph), 1600 (Ph), 900 (C=CH_2), 745 and 700 (monosubstituted benzene); δ_H(300 MHz; $CDCl_3$) 7.34–7.28 (2 H, m, Ph), 7.23–7.20 (3 H, m, Ph), 4.84 (1 H, s, =CH^AH^B), 4.79 (1 H, s, =CH^AH^B), 3.13 (2 H, s, SCH_2C=), 2.73 (2 H, t, *J* 7.6, SCH_2CH_2), 2.46 (2 H, t, *J* 7.3, $PhCH_2$), 1.91 (2 H, qn, *J* 7.5, SCH_2CH_2), and 1.84 (3 H, s, =CMe); δ_C(75 MHz; $CDCl_3$) 141.64, 141.35, 128.45, 128.32, 125.84, 113.26, 39.27, 34.88, 30.79, 30.28 and 20.65; *m/z* 206 (27%, M^+), 150 (17, M – Me_2CCH_2), 117 (100, M – Me_2CCH_2 and HS) and 91 (76, $PhCH_2$).

Ethyl 4-Methyl 2-(*Phenylthio*)*pent*-4-*enoate* **19**.—Ethyl diazoacetate (53 mm^3, 0.504 mmol, 1.05 equiv.) was added to a stirred solution of the allyl sulfide **13** (78.8 mg, 0.48 mmol) in dry dichloromethane (0.96 cm^3) under nitrogen at −20 °C. After 6 min tetrafluoroboric acid (85% HBF_4·OEt_2 complex in ether; 95.3 mg, 0.5 mmol, 1.04 equiv.) in dichloromethane (0.6 cm^3) was added in two rapidly delivered aliquots to the mixture over 3 min. After 8 min, DBU (96%; 90 mm^3, 0.578 mmol, 1.05 equiv.) was added to the mixture and after a further 5 min the reaction was quenched with 2 mol dm^{-3} aqueous hydrochloric acid. The mixture was extracted with dichloromethane and the combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. About 20% of the crude mixture was removed for ^{1}H NMR analysis and the rest purified by flash column chromatography on silica (10 g), eluting with hexane–ether (10:1), to yield the *ester* **19** (50.5 mg, 42%) as a colourless oil, R_F[hexane–ether (5:1)] 0.63; ν_{max}(smear)/cm^{-1} 3080 (ArH), 2980–2860 (CH), 1735 (C=O), 1650 (C=C), and 1585 (Ar bend); δ_H(300 MHz; $CDCl_3$) 7.48 (2 H, m, ArH), 7.32 (3 H, m, ArH), 4.85 (1 H, s, CH_ACH_B=CMe), 4.79 (1 H, s, CH_ACH_B=CMe), 4.11 (2 H, q, *J* 7.2, CH_2Me), 3.67 (1 H, dd, J_{CE} 6.0 and J_{CD} 9.5, $PhSCH_CCH_DH_E$), 2.64 (1 H, dd, J_{DC} 9.5 and J_{DE} 14.6, $PhSCH_CCH_DH_E$), 2.47 (1 H, dd, J_{EC} 6.1 and J_{ED} 14.6, $PhSCH_CCH_DH_E$), 1.77 (3 H, s, $MeC{=}CH_2$) and 1.17 (3 H, t, *J* 7.2, $MeCH_2$); δ_C(100 MHz; $CDCl_3$) 14.02, 22.28, 39.69, 49.03, 61.07, 113.19, 127.98, 128.90, 133.00, 133.25, 141.41 and 171.83; *m/z* 250 (M^+, 32%), 195 [22, M – $Me(CH_2)C{=}CH_2$], 177 (35, M – CO_2Et), 149 [100, M – $Me(CH_2)C{=}CH_2$ and EtOH], 121 [83, M – $Me(CH_2)C{=}CH_2$, EtOH and CO] and 109 (58, PhS) (Found: C, 67.4; H, 7.1%; M^+, 250.1041. $C_{14}H_{18}O_2S$ requires C, 67.2; H, 7.25%; *M*, 250.1028).

Ethyl 4-*Methyl* 2-(3-*phenylpropyl*)*pent*-4-*enoate* **20**.—By the same procedure, tetrafluoroboric acid (diethyl ether complex, 85%; 80 mm^3, 0.5 mmol) was allowed to react with the allyl sulfide **14** (97.1 mg, 0.47 mmol) and ethyl diazoacetate (52 mm^3, 0.49 mmol) and then DBU (96%; 88 mm^3, 0.565 mmol). After work-up, 80% of the mixture was separated by flash column chromatography on silica (19 g) eluting with hexane–diethyl ether (20:1) to yield the *ester* **20** (69.3 mg, 63%) as an oil; R_F[hexane–diethyl ether (20:1)] 0.28; ν_{max}(smear) 3090 (=CH_2), 3070 (PhH), 1735 (C=O), 1650 (C=C), 1610 (Ph), 1500 (Ph), 750 and 700 (monosubstituted benzene); δ_H(300 MHz; $CDCl_3$) 7.33–7.28 (2 H, m, PhH), 7.23–7.18 (3 H, m, PhH), 4.83 (1 H, s, =CH_AH_B), 4.76 (1 H, s, =CH_AH_B), 4.18 (2 H, q, OCH_2Me), 3.47 (1 H, dd, *J* 6.2 and 9.6, CHS), 2.75–2.58 (5 H, m, CH_2S, CH_2Ph, CH_AH_BCHS), 2.37 (1 H, dd, *J* 6.1 and 14.7, CH_AH_BCHS), 2.01–1.86 (2 H, m, CH_2CH_2S), 1.76 (3 H, s, *Me*C=) and 1.26 (3 H, t, *J* 7.2, $MeCH_2$); δ_C(75 MHz; $CDCl_3$) 172.41, 141.81, 141.36, 128.50, 128.43, 126.00, 112.81, 61.08, 44.93, 39.53, 34.82, 30.88, 30.78, 22.42 and 14.23; *m/z* 292 (7.3%, M^+), 174 [24, $HSCH(CO_2Et)CH_2C(CH_2)Me$], 163 [43, M – CO_2Et and $CH_2C(CH_2)Me$], 142 [39, $EtO_2CCH_2CH_2C(CH_2)Me$], 118 (90, C_9H_{10}), 117 (100, C_9H_9) and 91 (90, $PhCH_2$) (Found: 292.1496. $C_{17}H_{24}O_2S$ requires 292.1497).

Ethyl 2-(2-*methylenecyclohexyl*)-2-(4-*methoxyphenylthio*)-*acetate* **23**.—By the same procedure but at −25 °C, tetrafluoroboric acid (diethyl ether complex, 85%; 142.3 mg, 0.75 mmol) was allowed to react with the allyl sulfide **9** (114.3 mg, 0.5.6 mmol) and ethyl diazoacetate (68 mm^3, 0.65 mmol) and then DBU (111 mm^3, 0.7.4 mmol). After 13 min the reaction was quenched with glacial acetic acid–dichloromethane (1:9; 3 cm^3). Work-up and flash column chromatography of the residue on silica (19 g) eluting with hexane–diethyl ether (15:1) gave starting material **9** (20.9 mg, 18%) and a mixture of diastereoisomers (A:B, 64:36) of the *ester* **23** (91.0 mg, 56%) as an oil; R_F[hexane–diethyl ether (15:1)] 0.17; ν_{max}(smear)/cm^{-1} 3080 (=CH_2), 1735 (C=O), 1650 (C=C) and 1585 (Ph); δ_H(250 MHz; $CDCl_3$) 7.50–7.42 (2H$^{A\&B}$, m, PhH), 7.33–7.21 (3 H$^{A\&B}$, m, PhH), 4.86 (1 H^B, s, =CH_AH_B), 4.85 (1 H^B, s, =CH_AH_B), 4.66 (1 H^A, s, =CH_AH_B), 4.63 (1 H^A, s, =CH_AH_B), 4.11–3.96 (2H^A and 3H^B, m, CO_2CH_2 and CH^BS), 3.90 (1 H^A, d, *J* 11.5, CHS), 2.72 (1 H^A, dt, *J* 11.1 and 4.3, *CH*CHS), 2.65 (1 H^B, dt, *J* 10.7 and 5.0, *CH*CHS), 2.25–2.00 [2 H$^{A\&B}$, m, $(CH_2)_5$], 2.00–1.40 [6 H$^{A\&B}$, m, $(CH_2)_5$], 1.12 (3 H^B, t, *J* 7.1, Me) and 1.09 (3 H^A, t, *J* 7.1, Me); δ_C(100 MHz; $CDCl_3$) 172.07^A, 171.88^B, 149.03^B, 147.46^A, 133.96$^{A\&B}$, 132.96^A, 132.78^B, 128.94^B, 128.82^A, 127.73$^{A\&B}$, 110.50^A, 109.11^B, 60.96^A, 60.80^B, 53.55^B, 52.18^A, 44.97^A, 44.74^B, 33.42^B, 32.74^A, 31.45^A, 29.88^B, 28.30 and 28.27$^{A\&B}$, 22.54^B, 22.23^A and 14.00$^{A\&B}$; *m/z* 290 (2.7%, M^+), 196 (5.8, $PhSCH_2CO_2Et$), 99 (60, $CHCHCO_2Et$), 83 (75, C_6H_{11}) and 55 (100, C_4H_7) (Found: M^+, 290.1341. $C_{17}H_{22}O_2S$ requires *M*, 290.1367).

2-(4-*Methoxyphenylthio*)-4-*methylpent*-4-*en*-1-*ol* **27**.—The ester **8** (815.7 mg, 2.91 mmol) in dry THF (14.5 cm^3) was reduced with lithium aluminium hydride (95%; 117.2 mg, 2.93 mmol) over 7 h at 0 to 12 °C. The reaction was quenched

with aqueous potassium sodium tartrate (0.5 mol dm^{-3}; 200 cm^3) and aqueous sodium hydroxide (10% solution; 30 cm^3) and extracted with diethyl ether (4 × 100 cm^3) and then dichloromethane (1 × 100 cm^3). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. Flash column chromatography on silica (80 g) with dichloromethane–methanol (150:1) as eluent gave recovered starting material (191.6 mg, 24%) and the *alcohol* **27** (485.0 mg, 70%) as an oil; R_F(dichloromethane) 0.15; ν_{max}(smear)/cm^{-1} 3420 (OH), 3080 (=CH_2), 1650 (C=C), 1595 (ArH), 1575 (ArH), 1495 (ArH), 830 (*para* disubstituted benzene) and 895 (C=CH_2); δ_H(250 MHz; $CDCl_3$) 7.41 (2 H, d, *J* 8.7, ArH), 6.84 (2 H, d, *J* 8.9, ArH), 4.85 (1 H, d, *J* 1.6, =CH_AH_B), 4.78 (1 H, dd, *J* 0.8 and 1.8, =CH_ACH_B), 3.80 (3 H, s, MeO), 3.58 (1 H, dd, *J* 4.5 and 11.5, CH_DCH_EOH), 3.43 (1 H, dd, 6.2 and 11.5, CH_DCH_EOH), 3.16 (1 H, qn broad irregular, CHS), 2.29 (1 H, dd, secondary ABX system, *J* 6.4 and 15.5, CH_ACH_BC=), 2.27 (1 H, dd, secondary ABX system, *J* 8.6 and 15.5, CH_ACH_BC=), 2.12* (1 H, s b, OH) and 1.74 (3 H, s, MeC=); δ_C(100 MHz; $CDCl_3$) 159.90d, 142.25d, 136.36u, 122.50d, 114.57u, 113.26d, 62.93d, 55.32u, 50.63u, 39.81d and 22.13u; *m/z* 238 (49, M^+), 183 [20, M^+ – MeC(CH_2)CH_2], 165 [11, M^+ – MeC(CH_2)CH_2 and H_2O], 140 (46, $MeOC_6H_4SH$) and 139 (100, $MeOC_6H_4S$) (Found: M^+, 238.1035. $C_{13}H_{18}O_2S$ requires *M*, 238.1028).

1-(2-*Methylallyl*)*oxirane* **29**.—Following the published procedure,[18] trimethyloxonium tetrafluoroborate (60.4 mg, 0.41 mmol) was added in three aliquots over 33 min to a stirred solution of the alcohol **27** (55.2 mg, 0.23 mmol) in deuteriated dichloromethane (1.5 cm^3), with light excluded, after which the mixture stirred for a further 37 min. Aqueous sodium hydroxide (10%; 1.5 cm^3) was added to the mixture which was then stirred for a further 21 h before it was quenched with aqueous hydrochloric acid (3 mol dm^{-3}; 1.5 cm^3). The layers were separated and the aqueous mixture was extracted with deuteriated dichloromethane (1.5 cm^3). The combined organic layers were dried ($MgSO_4$) and filtered and the $MgSO_4$ was washed with further deuteriated dichloromethane (1 cm^3). ^1H NMR spectra of the combined filtrates revealed the composition of the mixture to be the *epoxide* **29**, 4-methoxythioanisole, dimethyl ether and water in a ratio of 1:1.7:0.5:1; *epoxide* **29**: R_F(CH_2Cl_2) 0.36 (blue with anisaldehyde); δ_H(250 MHz; CD_2Cl_2) 4.82 (2 H, s, CH_2=), 2.99 (1 H, ddt, J_{AC} 2.7, J_{AB} 3.9 and *J* 5.7, CH^AOCH^{B}H^C), 2.74 (1 H, unsymmetric t, J_{BA} 4.1 and J_{BC} 4.9, CH^{A}OCH^BH^C), 2.45 (1 H, dd, one peak obscured, J_{CA} 2.6 and J_{CB} 5.2, CH^{A}OCH^BH^C), 2.21 (2 H, d, *J* 5.6, CH_2) and 1.79 (3 H, s, Me). 4-Methoxythioanisole: R_F(CH_2Cl_2) 0.62; δ_H(250 MHz; CD_2Cl_2) 7.25 (2 H, d, *J* 8.9, ArH), 6.85 (2 H, d, *J* 8.8, ArH), 3.77 (3 H, s, MeO) and 2.43 (3 H, s, Me), identical with material isolated in 74% yield from the same reaction in nondeuteriated dichloromethane. Dimethyl ether: δ_H(250 MHz; CD_2Cl_2) 3.27 (6 H, s, MeO).

1-*Methyl*-4-[(*phenylthio*)*methyl*]-1,2,5,6-*tetrahydropyridine* **35**.—(*a*) Toluene-*p*-sulfonic acid monohydrate (712.7 mg, 3.75 mmol) was added to a stirred solution of the alcohol **34** (228.3 mg, 0.96 mmol) in dry benzene (15 cm^3), under argon, with light excluded, after which the mixture was heated under reflux for 2.5 h. After acid/base work-up, the combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure and the mixture separated by flash column chromatography on silica, eluting with ethyl acetate–ethanol–conc.aqueous ammonia (25:10:1) to give the *allyl sulfide* **35** (109.7 mg, 52%, 92% pure) as a yellow oil. A pure sample was obtained by chromatography in dichloromethane–methanol; R_F[ethyl acetate–ethanol–conc.aqueous ammonia (25:10:1)] 0.57; ν_{max}(smear)/cm^{-1} 3060 (=CH_2), 2960–2860 (CH), 2790 (NCH_2 and NMe), 1585 (Ph), 740 and 695 (monosubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.35–7,12 (5 H, m, Ph), 5.49 (1 H, br s, =CH_2), 3.48 (2 H, s, CH_2S), 2.85 (2 H, br s, NCH_2C=), 2.51 (2 H, t, *J* 5.7, CH_2CH_2N), 2.31 (3 H, s, NMe) and 2.35–2.23 (2 H, br peak obscured by Me signal, CH_2CH_2N); δ_C(100 MHz; $CDCl_3$) 136.53, 131.52, 130.05, 128.67, 126.15, 122.98, 56.93, 52.37, 45.61, 40.92 and 28.05; *m/z* 219 (6.3%, M^+) and 110 (100, PhSH) (Found: M^+, 219.1084. $C_{13}H_{17}NS$ requires *M*, 219.1082).

(*b*) In the same way, the alcohol **37** (85 mg, 0.36 mmol) and toluene-*p*-sulfonic acid (298.5 mg, 1.57 mmol) were heated under reflux in benzene for 1.5 h. After work-up and flash column chromatography with ethyl acetate–ethanol–conc.-aqueous ammonia (50:8:1) the *allyl sulfide* **35** (33.4 mg, 43%, 98% purity) was obtained as a yellow oil.

1-*Ethyl*-3-[(*phenylthio*)*methyl*]-1,2,5,6-*tetrahydropyridine* **32**.—In a similar way, toluene-*p*-sulfonic acid monohydrate (897.7 mg, 4.72 mmol) and the alcohol **30** (394.7 mg, 1.57 mmol) were heated under reflux for 16 h in dry toluene (7.85 cm^3). After work-up, flash column chromatography on silica (40 g) eluting with dichloromethane–methanol–triethylamine (300:10:1) yielded the *allyl sulfide* (256 mg, 70%) as a yellow oil; R_F[dichloromethane–methanol–conc. aqueous ammonia (10:1:1 drop)] 0.43; ν_{max}(smear)/cm^{-1} 3090–3060 (C=CH), 3010 (PhH), 2990–2910 (CH), 2830–2750 (NCH_2), 1585 (Ph), 1480 (Ph), 740 and 690 (monosubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.35–7.13 (5 H, m, Ph), 5.59 (1 H, s, C=CH), 3.49 (2 H, s, CH_2S), 3.02 (2 H, d, *J* 1.8, NCH_2C=), 2.50 (2 H, q, *J* 7.2, NCH_2Me), 2.47 (2 H, unsymmetric t, *J* 5.7 and 7.1, two peaks coincident with those of the q at 2.50, CH_2CH_2N), 2.16–2.06 (2 H, m, CH_2CH_2N) and 1.12 (3 H, t, NCH_2*Me*); δ_C(100 MHz; $CDCl_3$) 136.48, 131.57, 130.00, 128.70, 126.19, 123.61, 54.17, 52.05, 49.37, 39.75, 25.93 and 12.22; *m/z* 233 (0.5%, M^+), 232 (1.3%, M – H), 218 (2.1, M – CH_4) and 123 (100, $PhSCH_2$) (Found: M^+, 233.1222. $C_{14}H_{19}NS$ requires *M*, 233.1238).

1-*Methyl*-4-[(*phenylthio*)*methyl*]*piperidin*-4-*ol* **34**.—Following the procedure of Hannaby *et al.*,[19] phenylthiomethyllithium was generated from thioanisole (99%; 2.1 cm^3, 17.7 mmol) and allowed to react with 1-methyl-4-piperidone (1 cm^3, 15.4 mmol). Work-up and flash column chromatography of the residue on silica with ethyl acetate–ethanol–conc. aqueous ammonia (100:20:1 then 25:10:1) as eluent gave the *alcohol* **34** (1.18 g, 56%) as peach coloured crystals, m.p. 96–97 °C; R_F[ethyl acetate–ethanol–conc. aqueous ammonia (25:10:1)] 0.30; ν_{max}(Nujol mull of HCl salt)/cm^{-1} 3370 (OH), 2740–2300 (NH^+, NCH_2, NMe) and 1580 (Ph); δ_H(250 MHz; $CDCl_3$) 7.40 (2 H, d, *J* 7.2, PhH), 7.32–7.14 (3 H, m, PhH), 3.10 (2 H, CH_2SPh), 2.60 (2 H, dt, *J* 11.6 and 3.8, 2 × $CH_{eq}N$), 2.33 (2 H, dt, *J* 11.6 and 7.2), 2.29 (3 H, s, MeN) and 1.68 (4 H, dd, *J* 7.2 and 4.2, 2 × CH_2CH_2N); δ_C(100 MHz; $CDCl_3$) 136.71, 129.55, 129.01, 128.32, 68.74, 51.32, 47.92, 46.02 and 36.49; *m/z* 237 (16%, M^+), 124 (8, PhSMe) and 114 (100, M^+ – $PhSCH_2$); (Found: M^+, 237.1202. $C_{13}H_{19}NOS$ requires *M*, 237.1187).

1-*Ethyl*-3-[(*phenylthio*)*methyl*]*piperidin*-3-*ol* **31**.—By the same method, phenylthiomethyllithium was generated from thioanisole (99%; 4.9 cm^3, 41.3 mmol) and allowed to react with 1-ethyl-3-piperidone (1.81 g, 14.2 mmol). Work-up and flash column chromatography of the residue on silica with dichloromethane–methanol–conc. aqueous ammonia (150:10:1) as eluent, gave the *alcohol* **31** (2.04 g, 57%) as a golden oil; R_F[dichloromethane–methanol–conc. aqueous ammonia (150:10:1)] 0.43; ν_{max}(smear)/cm^{-1} 3470 (OH), 3060 (PhH), 2980–2860 (CH), 2780–2810 (NCH_2), 1585 (Ph), 740 and 690 (monosubstituted benzene); δ_H(300 MHz; $CDCl_3$) 7.41–7.37 (2 H, m, Ph), 7.28–7.22 (2 H, m, Ph), 7.17–7.12 (1 H, t, *J* 7.3, Ph), 3.45 (1 H, br s, OH), 3.12 (1 H, d, *J* 13.2, CH_AH_BS), 3.08 (1 H,

d, J 13.2, CH_AH_BS), 2.75–2.68 (2 H, m, $NCH_{ax}H_{eq}COH$ and $NCH_{ax}H_{eq}CH_2$), 2.43 (2 H, q, J 7.3, CH_2Me), 2.09 (1 H, d, J 11.1, $NCH_{ax}H_{eq}COH$), 2.02 (1 H, dt, J 2.8 and 11.1, $NCH_{ax}H_{eq}CH_2$), 1.88–1.73 (1 H, m, $NCH_{ax}H_{eq}CH_2COH$), 1.69 (1 H, br d, J 12.9, $CH_2CH_{ax}H_{eq}COH$), 1.57 (1 H, dqn, 13.4 and 4.0, $CH_{ax}CH_{eq}CH_2COH$), 1.40 (1 H, dt, J 4.6 and 12.3, $CH_2CH_{ax}H_{eq}COH$) and 1.03 (3 H, t, J 7.2, Me); δ_C(75 MHz; $CDCl_3$) 137.46, 129.12, 128.79, 125.81, 69.95, 62.25, 52.89, 51.96, 44.01, 34.80, 21.78 and 11.96; m/z 251 (5.0%, M^+), 142 (100, M − PhS), 124 (21, M − PhS and H_2O), 72 (37, $C_4H_{10}N$) and 58 (27, C_3H_8N) (Found: C, 67.1; H, 8.25; N, 5.6. $C_{14}H_{21}NOS$ requires C, 66.9; H, 8.4; N, 5.6).

[1-*Methyl*-4-(*phenylthio*)*piperidin*-4-*yl*]*methanol* **37**.—Sodium borohydride (49.7 mg, 1.31 mmol) was added slowly to a stirred solution of the aldehyde **32** (354.5 mg, 1.51 mmol) in methanol and the mixture was stirred for 0.5 h before acid/base work-up and extraction into dichloromethane. The combined organic layers were dried (Na_2SO_4) and the solvent removed under reduced pressure to yield the alcohol **37** as off-white plates (205.8 mg, 58%), m.p. 113–115 °C; ν_{max}(Nujol mull)/cm^{-1} 3110 (OH), 3080 (PhH), 3000–2850 (CH), 2800–2700 (NCH_2, NMe), 1585 (Ph), 1575 (Ph), 700 and 740 (monosubstituted benzene); δ_H(250 MHz; $CDCl_3$) 7.49–7.28 (5 H, m, Ph), 3.30 (2 H, s, CH_2OH), 2.72–2.50 [5 H, m, $N(CH_2)_2$ and OH], 2.33 (3 H, s, NMe) and 1.66 [4 H, unsymmetric t, $(CH_2)_2CS$]; δ_C(100 MHz, $CDCl_3$) 137.42, 129.42, 129.24, 128.94, 67.27, 54.12, 51.16, 46.22 and 32.13; m/z 237 (2%, M^+) and 128 (100, M − PhS) (Found: M^+, 237.1183; $C_{13}H_{19}NOS$ requires 237.1187).

Ethyl 1-*Ethyl*-3-*methylenepiperidin*-4-*yl*(*phenylthio*)*acetate* **45**.—A precooled solution of tetrafluoroboric acid (0.98 mol dm^{-3} solution in dichloromethane; 300 mm^3, 0.295 mmol) was added to a stirred solution of the allyl sulfide **32** (73.3 mg, 0.31 mmol) in dry dichloromethane (0.63 cm^3), under argon, with light excluded, at −56 °C; ethyl diazoacetate (5 × 11 mm^3, 0.52 mmol) and further precooled tetraflouroboric acid (0.98 mol dm^{-3} solution in dichloromethane; 4 × 100 mm^3, then 130 mm^3, 0.52 mmol) were then added alternately to the mixture over 9 min. After 2.5 min, potassium tertiary butoxide (161.6 mg, 1.44 mmol) was also added to the mixture which was then allowed to warm to 0 °C over 2 h. The reaction was quenched with saturated aqueous sodium hydrogencarbonate (30 cm^3) and extracted with dichloromethane (4 × 20 cm^3). Acid/base work-up is inappropriate as the hydrochloride salt is soluble in dichloromethane. The combined organic layers were dried (Na_2SO_4) and evaporated removed under reduced pressure. Flash column chromatography of the residue on silica eluting with dichloromethane–methanol (20:1) gave a (52:48) diastereoisomeric mixture of the *esters* **45** (70.5 mg, 70%) as a brown oil, R_F[dichloromethane–methanol (20:1)] 0.25; ν_{max}(smear)/cm $^{-1}$ 3074 (C=CH_2), 2972–2930 (CH), 2796 (NCH_2), 2747 (NCH_2), 1733 (C=O), 1652 (C=C), 1583 (Ph), 904 (C=CH_2), 748 and 692 (Ph); δ_H(250 MHz; $CDCl_3$) 7.49–7.41 (2 $H^{A\&B}$, m, Ph), 7.34–7.25 (3 $H^{A\&B}$, m, Ph), 5.09 (1 H^B, s, CH_AH_B=), 5.05 (1 H^B, s, CH_AH_B=), 4.91 (1 H^A, s, CH_AH_B=), 4.78 (1 H^A, s, CH_AH_B=), 4.08–3.97 (2 $H^{A\&B}$, m, $MeCH_2O$), 3.97 (1 H^B, d, J 10.5, CHS), 3.86 (1 H^A, d, J 11.4, CHS), 2.99 (1 H^A, d, J 12.0, =CCH_AH_BN), 2.98 (1 H^B, d, J 12.0, =CCH_AH_BN), 2.89 (1 $H^{A\&B}$, d, J 12.0, =CCH_AH_BN), 2.75–2.51 (3 $H^{A\&B}$, m, CHC= and CH_2CH_2N), 2.44 (2 $H^{A\&B}$, q, J 7.2, $MeCH_2N$), 2.15 (1 H^A, ddt, 7.3, 13.9 and 4.6, $CH_{ax}H_{eq}CH_2N$), 2.02–1.86 (1 $H^{A\&B}$, m, B: $CH_{ax}H_{eq}CH_2N$ and A: $CH_{ax}H_{eq}CH_2N$), 1.60 (1 H^B, ddd, J 5.0, 10.4 and 13.7, $CH_{ax}H_{eq}CH_2N$), 1.12 (3 H^A, t, J 7.1, OCH_2Me) and 1.09 (3 H^A and 6 H^B, t, J 7.0, NCH_2Me and B: OCH_2Me); δ_C(100 MHz; $CDCl_3$) 171.61$^{A\&B}$, 144.31^A, 142.43^B, 133.63^B, 133.48^A, 133.01$^{A\&B}$, 128.99^A, 128.88^B, 128.00^A, 127.89^B, 113.06^B, 111.55^A, 61.10^B, 60.93^A, 58.72^A, 58.38^B, 53.13^A, 52.10$^{A\&B}$, 51.87^B, 50.38^A, 50.09^B, 42.84^B, 42.44^A, 30.03^B, 28.69^A, 13.97^B and 12.17^A; m/z 319 (1.1%, M^+), 210 (6.1, M − PhS) and 124 (100, M −$PhSCHCO_2Et$) (Found: M^+, 319.1618. $C_{18}H_{25}NO_2S$ requires M, 319.1618).

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References

1 B. M. Trost and L. S. Melvin Jr., *Sulfur Ylides, Emerging Synthetic Intermediates*, Academic Press, New York, 1975; R. W. Hoffmann, *Angew, Chem., Int. Ed. Engl.*, 1979, **18**, 563.
2 W. Ando, *Acc. Chem. Res.*, 1977, **10**, 179; W. Ando in S. Patai, ed. *The Chemistry of Diazonium and Diazo groups*, J. Wiley and Sons, Chichester, 1978, p. 445.
3 M. P. Doyle, *Acc. Chem. Res.*, 1986, **19**, 348 and references therein.
4 G. M. Blackburn and W. D. Ollis, *J. Chem. Soc., Chem. Commun.*, 1968, 1261.
5 W. H. Tamblyn, S. R. Hoffman and M. P. Doyle, *J. Organomet. Chem.*, 1981, **216**, C64.
6 Z. Kosarych and T. Cohen, *Tetrahedron Lett.*, 1982, **23**, 3019.
7 C. J. Moody and R. J. Taylor, *Tetrahedron Lett.*, 1988, **29**, 6005; F. Kido, S. C. Sinha, T. Abiko, M. Watanabe and A. Yoshikoshi, *Tetrahedron*, 1990, **46**, 4887; F. Kido, T. Abiko and M. Kato, *J. Chem. Soc., Perkin Trans. 1*, 1992, 229.
8 E. Vedejs, *Acc. Chem. Res.*, 1984, **17**, 358.
9 D. Darwish and G. Tourigny, *J. Am. Chem. Soc.*, 1966, **88**, 4303; E. Vedejs, J. P. Hagen, B. L. Roach and K. L. Spear, *J. Org. Chem.*, 1978, **43**, 1185.
10 V. K. Aggarwal and S. Warren, *Tetrahedron Lett.*, 1986, **27**, 101; 1987, **28**, 1925; V. K. Aggarwal, I. Coldham, S. McIntyre and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1991, 451.
11 E. Vedejs, D. A. Engler and M. J. Mullins, *J. Org. Chem.*, 1977, **42**, 3109.
12 C. Huynh, V. Ratovelomanana and S. Julia, *Bull. Soc. Chim. Fr.*, 1977, 710.
13 M. J. Kurth, S. H. Tahir and M. M. Olmstead, *J. Org. Chem.*, 1990, **55**, 2286.
14 R. C. Hartley, I. C. Richards and S. Warren, *Tetrahedron Lett.*, 1992, **33**, 8155.
15 R. K. Olsen and J. O. Currie, in S. Patai, ed. *The Chemistry of the Thiol Group*, part 2, Wiley, London, 1974, pp. 561–566.
16 For review see T.-Y. Luh and Z.-J. Ni, *Synthesis*, 1990, 89.
17 R. Oehrlein, R. Jeschke, B. Ernst and D. Bellus, *Tetrahedron Lett.*, 1989, **30**, 3517.
18 C. H. Behrens, S. Y. Ko, K. B. Sharpless and F. J. Walker, *J. Org. Chem.*, 1985, **50**, 5687.
19 M. Hannaby and S. Warren, *Tetrahedron Lett.*, 1985, **26**, 3133; *J. Chem. Soc., Perkin Trans. 1*, 1989, 303; 1992, 3007; M. Hannaby, P. Judson and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2609.
20 E. J. Corey and D. Seebach, *J. Org. Chem.*, 1966, **31**, 4097.
21 I. Coldham and S. Warren, *Tetrahedron Lett.*, 1989, **30**, 5937; *J. Chem. Soc., Perkin Trans. 1*, 1992, 2303; 1993, 1637.

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