A Regiospecific Route to Conjugated Enones *via* α-Phenylthio Ketones

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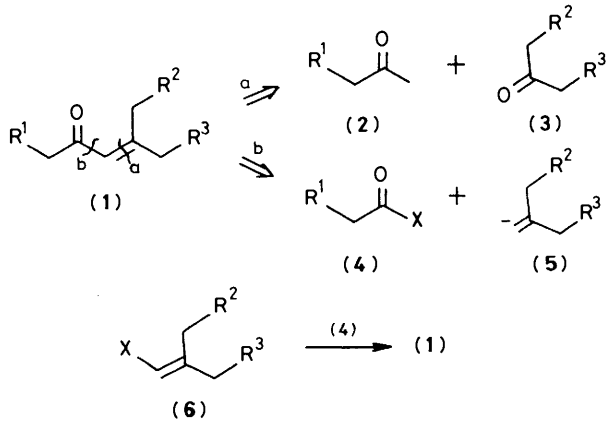
2,5-Dimethylhex-4-en-3-one, *E*-6-methylhept-2-en-4-one, *E*-7-methyloct-4-en-3-one, ar-turmerone, and *E*-7-oxo-oct-5-enoic acid were synthesized regiospecifically *via* α-phenylthio ketones from bisphenylthio carbanions and aldehydes.

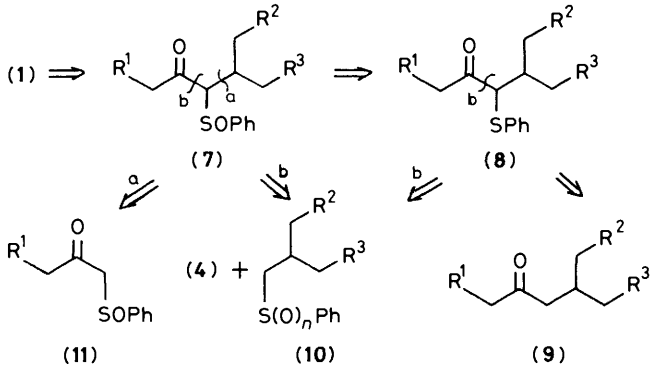
The enolisation of one carbonyl compound, and its condensation[1] with another aldehyde or ketone is the simplest route to conjugated enones (**1**). There remain problems of chemoselectivity as either partner (**2**) or (**3**) may enolise, and of regioselectivity as enolisation may occur on either side of the carbonyl group in the unsymmetrical ketone[2] (**2**). Specific enol equivalents[3] such as lithium enolates,[4] silyl enol ethers,[5] or enamines[6] have partly solved these problems but there is an obvious advantage in being able to plan enone syntheses using alternative disconnections, as in the syntheses of ar-turmerone described by Posner.[7] We report[8] an enone synthesis based on the strategy (**1b**): the acylation of a masked vinyl anion equivalent (**5**).



Direct acylation of vinyl-lithiums (**6**; X = Li) with lithium carboxylates is known[9] but acylation of vinyl anion equivalents (**6**), as in the aliphatic Friedel-Crafts reaction[10] (X = H) has been more popular. The vinylsilanes[11] (**6**; X = $SiMe_3$) give greater control as do some metal derivatives made from acetylenes including X = Cu,[12] Hg,[13] or Zr.[14]

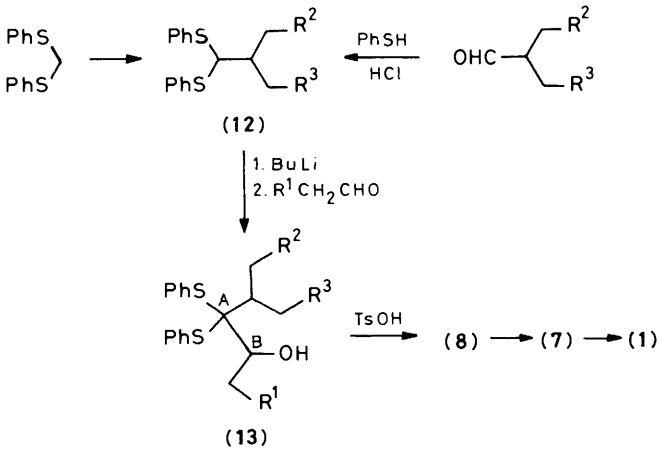
Thermal elimination of an α-phenylsulphinyl group is a well established route to enones[15] and the sulphoxides (**7**) are usually made by oxidation of the α-phenylthio ketones (**8**). Acylation of carbanions from sulphides or sulphoxides (**10**) would therefore be examples of strategy (**1b**) in which the carbanion (**10**) is a masked vinyl anion [*i.e.* synthon (**5**)]. The usual problems of proton transfer arise in these reactions but two equivalents of the dimethyl sulphoxide anion do react with simple esters[16] and the products can be alkylated,[17] though this strategy has not, in fact, been adapted to enone synthesis. Direct acylation of sulphoxides $PhS(O)CH_2R$ (R ≠ H) has occasionally been successful.[18] We attempted the acylation of $PhSCH_2Pr^i$ with the ester (**33**) but isolated only 3% of (**38**). Acylation of PhS(O)Me with the same ester gave 20% of the α-phenylthio ketone which we could not alkylate with Pr^iI to give (**37**).

Carbanions from sulphides $PhSCH_2R$ (R ≠ H) can be made



only with difficulty and acylation yields are low,[19] though successful acylation of one series of sulphides with aziridine amides has been reported.[20]

Changing the oxidation level at both functionalised carbon atoms (Scheme 1) avoids all these problems. Bisphenylthio



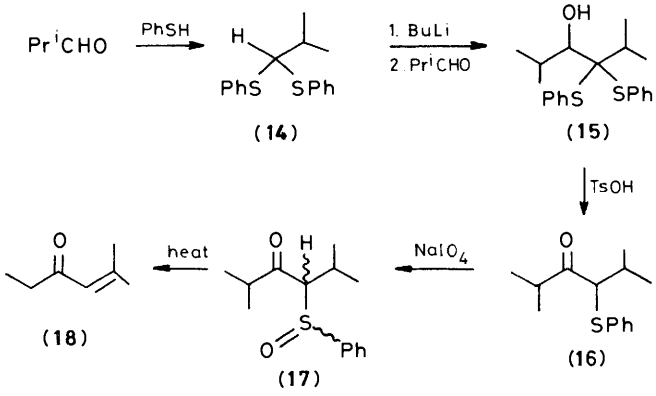
Scheme 1.

carbanions are easily made and react cleanly with aldehydes.[21] The intermediates (**13**) can be rearranged in acid to give the α-phenylthio ketones (**8**), thus automatically restoring the correct oxidation levels of carbon atoms A and B. The aldehyde R^1CH_2CHO is a masked acylating agent and the carbanion from (**12**) is a masked version of (**10**; *n* = 0). This approach to α-phenylthio ketones is connective and regioselective, unlike the sulphenylation[15,22] of the pre-formed ketone (**9**).

We present the synthesis of four enones (**18**), (**22**), (**30**), and (**39**) by this route[8] (Scheme 1) and of one enone (**47**) by a variation of this strategy. These examples were chosen to illustrate the problems of the aldol route.

The aldol route to enone (**18**) would require an unlikely condensation between acetone and 3-methylbutan-2-one: such a reaction has not been reported.[1] The enone (**18**) has been made by an aliphatic Friedel-Crafts reaction,[23] by alkylation of an unsaturated acyl anion equivalent,[24] and by a few special methods.[25] It has been used in the synthesis of chrysanthemic acid.[23]

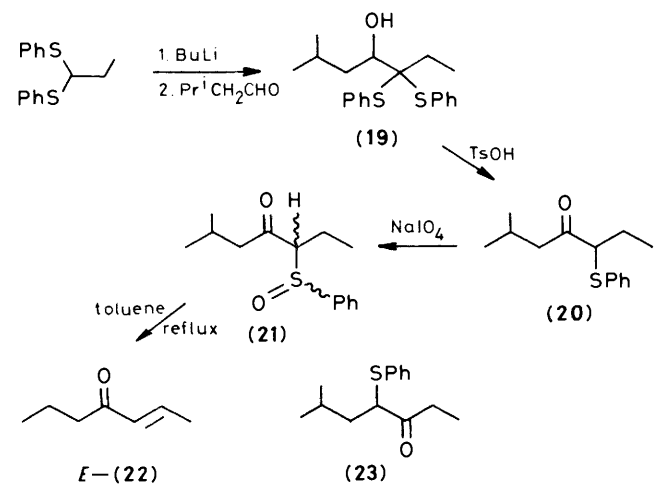
The bisphenylthio acetal[21] (**14**) from Pr^{i}CHO was combined with another molecule of the same aldehyde (Scheme 2) to give



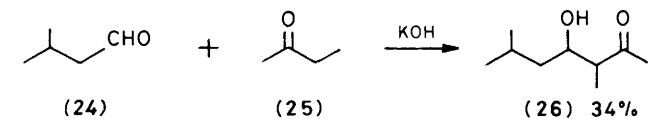
Scheme 2.

intermediate (**15**) which rearranged in acid to the α-phenylthio ketone (**16**). The occasional by-product from this rearrangement[21]—the transposed α-phenylthio ketone—is identical with (**16**) with this symmetrical carbon skeleton. Oxidation with $NaIO_4$ is slow but gives the mixture of sulphoxides (**17**) without any overoxidation to the sulphone. Distillation from a Kügelrohr apparatus gave enone (**18**) in good yield.

Enone (**22**) has been made in poor yield by an aldol reaction,[1,26] by acylation of an alkyl anion equivalent with a derivative of an unsaturated acid,[27] and by special methods,[28] and used in the synthesis of juvabione.[26] Our route (Scheme 3) gave a reasonable yield in the rearrangement step to give α-phenylthio ketone (**20**) with some transposed α-phenylthio

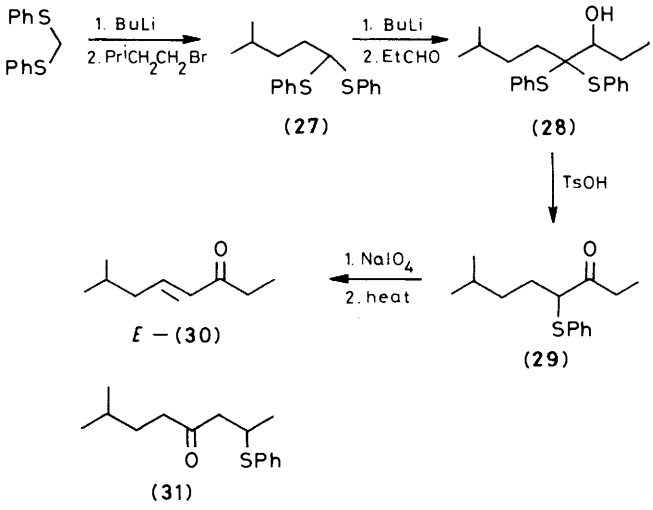


Scheme 3.



ketone (**23**): separation by chromatography and elimination in refluxing toluene (which we prefer for enones having di-substituted double bonds) gave only *E*-enone (**22**). The high *E* selectivity results from minimising steric interactions in the cyclic transition state for the sulphoxide elimination.[15]

Enone (**30**) is a natural perfume, being 2.8% of the dry weight of the sponge *Plakortis zygompha*.[29] The aldol route requires ketone (**25**) to condense with aldehyde (**24**): these give the enone precursor (**26**) with the correct chemoselectivity but the wrong regioselectivity.[1] The enone (**30**) has been synthesized by an interesting route using a cyclopropyl sulphide but unfortunately giving very low yields.[30] Our route (Scheme 4) uses the



Scheme 4.

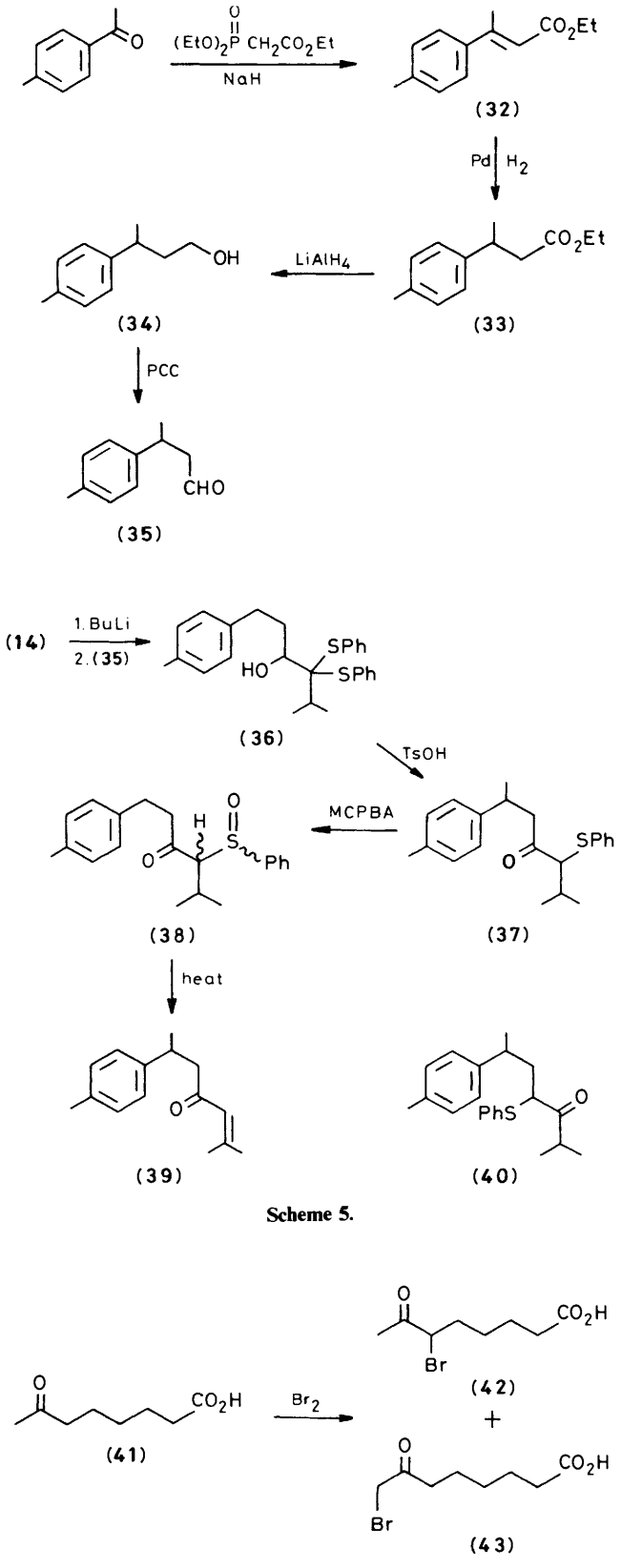
alkylation of bisphenylthiomethane to give the vinyl anion equivalent (**27**). Addition to EtCHO and rearrangement to α-phenylthio ketone (**29**) occurred in only moderate yields. The β-phenylthio ketone (**31**) was a by-product (16%) of this rearrangement: it could arise by PhSH addition to an enone or by elimination of water from alcohol (**28**), [1,3]-phenylthio shift,[31] and vinyl sulphide hydrolysis. Oxidation and elimination without isolation of the sulphoxides gave pure 'perfume' *E*-(**30**).

ar-Turmerone (**39**), a flavouring material in turmeric,[32] has been synthesized many times.[33] Posner[7] discusses syntheses based on the disconnection of each bond in the aliphatic part of the skeleton. The strategy of acylation of a vinyl anion equivalent has been applied in the aliphatic Friedel-Crafts reaction[34] and in the acylation of a Grignard reagent by a dithioester.[35]

We required the aldehyde (**35**) for our route. The unsaturated ester (**32**) is available[36] by the Wadsworth-Emmons reaction,[37] but we were not able to repeat the direct[36] reduction of unsaturated ester (**32**) to alcohol (**34**) by $LiAlH_4$ at 45 °C as reduction of the ester group alone occurred. Hydrogenation followed by $LiAlH_4$ reduction gave the alcohol (**34**) and PCC[38] oxidation gave the aldehyde[29] (**35**).

Our route to ar-turmerone (**39**) (Scheme 5) was uneventful except that the rearrangement to the α-phenylthio ketone (**37**) gave a poor yield (23%) and a similar amount (19%) of the transposed α-phenylthio ketone (**40**). Oxidation with one equivalent of MCPBA was fast and sulphoxide elimination in a Kügelrohr apparatus gave ar-turmerone. There are now some very short ar-turmerone syntheses[7,33,40] and ours is not as good as these.

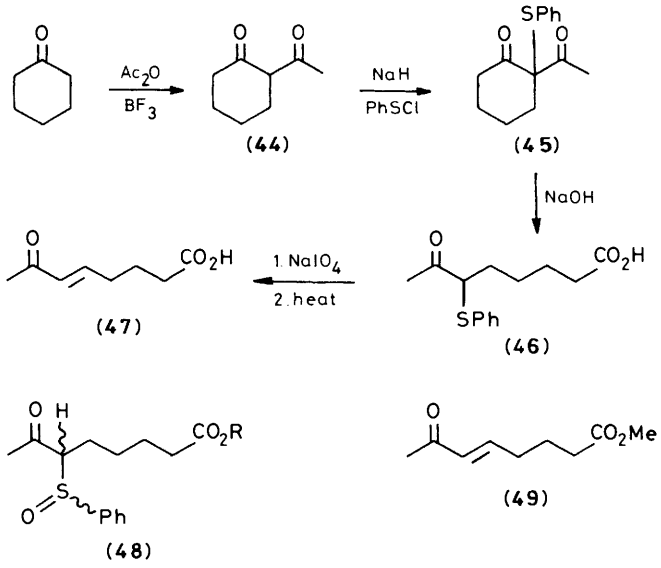
Finally, we made the unsaturated keto acid (**47**) by a different



Scheme 5.

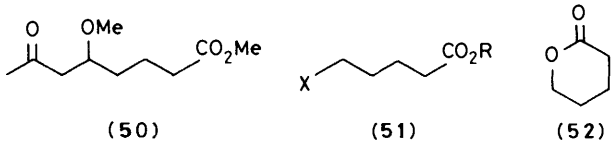
route using the same strategy with the α-phenylthio ketone (**46**) as an intermediate. The acid has been made[41] by a very inefficient bromination–dehydrobromination of the saturated keto acid (**41**). The 7:3 mixture of bromo ketones (**42**) and (**43**) could be separated only by crystallisation of the unwanted acetal derived from (**43**). It was used in the synthesis of natural pigments.[41]

Acetylation of cyclohexanone[42] gave the diketone (**44**) which was sulphenylated to give the tertiary sulphide (**45**). This can be isolated by column chromatography but cleavage of crude (**45**) with aqueous sodium hydroxide gave a good yield of α-phenylthio ketone (**46**). The phenylthio group helps cleavage by preventing the formation of the stable enolate of the starting material, *cf.* the cleavage[43] of (**44**) to (**41**), and by making the α-phenylthio enolate a better leaving group.[44]



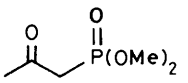
Scheme 6.

The acid (**46**) may be converted into the unsaturated acid (**47**) by a number of methods. Oxidation to the sulphoxide (**48**; R = H) and thermolysis (reflux in carbon tetrachloride) gives (**47**) directly in 78% yield contaminated by about 5% of a sulphur-containing impurity which is difficult to remove. Recrystallisation gave pure sulphoxide (**48**; R = H) in 55% yield and hence (**47**) in 98% yield after chromatography on a short column.



Alternatively, the acid (**46**) may be converted into its methyl ester (93%) whose oxidation and thermolysis without isolation of the sulphoxide (**48**; R = Me) gave the ester (**49**) in 66% yield from the acid (**46**). The ester (**49**) could be distilled directly from the reaction mixture. Attempted esterification of (**47**) with acidic methanol gave instead the β-methoxy ketone (**50**). Attempts to prepare acid (**47**) or ester (**49**) by alkylation of phenylthioacetone with δ-halogeno derivatives (**51**; X = Br, I) gave a maximum of 30% yield with lactone (**52**) as a major by-product.

The Wadsworth-Emmons reaction[37] between phosphonate (**53**) and available aldehyde ester[45] (**54**) provides an alternative route to the unsaturated keto ester (**49**) though in only moderate yield (58%). Both methods gave only *E*-stereochemistry and both methods are suitable for the synthesis of 5—10 g of acid or ester.



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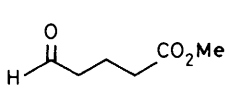

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Experimental

Melting points were measured on a Reichart Kofler hot-stage microscope and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 297 spectrophotometer, ^{1}H n.m.r. spectra on a Varian Associates EM390 (mainly) or a Bruker WM 250 spectrometer, and carbon n.m.r. spectra were recorded on a Bruker WM 250 spectrometer. Tetramethylsilane was used as internal standard for n.m.r. spectra. In the carbon spectra peaks marked * belong to *ortho*- or *meta*-carbons and are of double intensity. Mass spectra were obtained on an AEI MS 30 machine using a DS50S data system for high-resolution analysis.

Thin-layer chromatography (t.l.c.) was run on Merck silica gel $60F_{254}$ (0.25 mm) plates and preparative thick layer chromatography on silica gel GF_{254} (1 mm) plates, visualised with u.v. light, and material extracted with dichloromethane. Column chromatography was performed on Merck silica gel, 230—400 mesh.

All solvents used were distilled before use; tetrahydrofuran (THF) was dried by distillation from lithium aluminium hydride, stored over sodium wire, and redistilled from lithium aluminium hydride directly into the reaction flask. All aldehydes and ketones were distilled and stored over molecular sieves (4A). Alkyl halides were purified by passage through alumina.

Sodium hydride was obtained as a 50% dispersion in mineral oil and washed with hexane before use. Toluene-*p*-sulphonic acid was B.D.H. microanalytical grade, and all other reagents were of analytical grade. Brine refers to a saturated aqueous solution of sodium chloride, sodium hydrogen carbonate to a saturated aqueous solution, and sodium hydroxide to a 10% aqueous solution.

1,1-*Bisphenylthiopropane*.—Hydrogen chloride was bubbled through a stirred, ice-cooled solution of propanal (4.84 g, 5.76 ml, 80 mmol) in thiophenol (17.12 g, 20 ml, 192 mmol) for 30 min, and the mixture stirred for a further 2 h as it warmed up to room temperature. Ether (200 ml) was added, the solution washed with sodium hydroxide solution (3 × 50 ml) and water (2 × 50 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give the dithioacetal[21] (19.79 g, 95%), R_F (CH_2Cl_2) 0.77.

4-*Methyl*-1,1-*bisphenylthiopentane* (**27**).—n-Butyl-lithium (1.4M-solution in hexane; 7.9 ml, 11 mmol) was added slowly to a solution of bisphenylthiomethane (2.32 g, 10 mmol) in dry THF (25 ml), under nitrogen at 0 °C. After 15 min 1-bromo-3-methylbutane (1.51 g, 1.20 ml, 10 mmol) was added dropwise, and the mixture stirred for 1 h. Ether (20 ml) was added, and the mixture washed with water (2 × 20 ml) and brine (2 × 10 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give the dithioacetal[21] (2.6 g, 86%), b.p. 110—118 °C/0.02 mmHg, R_F (CH_2Cl_2) 0.77.

6-*Methyl*-3,3-*bisphenylthioheptan*-4-*ol* (**19**).—n-Butyl-lithium (1.65M-solution in hexane; 1.2 ml, 2 mmol) was added to a stirred solution of 1,1-bisphenylthiopropane (0.48 g, 1.86 mmol) in dry THF (25 ml) and TMEDA (231 mg, 0.3 ml, 2.1 mmol) under nitrogen at 0 °C. After 15 min isovaleraldehyde (0.16 g, 0.2 mol, 1.87 mmol) was added dropwise to discharge the orange anion colour. Further n-butyl-lithium (0.3 ml) was then added and the orange colour again discharged with isovaleraldehyde (0.05 ml) after 15 min, and this addition procedure repeated. The ice-bath was removed and the solution stirred for 30 min, poured into water (25 ml), and extracted with ether (3 × 15 ml). The combined organic fractions were washed with water (3 × 15 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with 5% ether in light petroleum (b.p. 30—40 °C) to give the *alcohol* [450 mg, 70% (90% based on recovered starting material)] as an oil, R_F (CH_2Cl_2) 0.48, $\nu_{max.}$(CCl_4) 3 470 (OH) and 1 575 cm^{-1} (Ph); δ_H($CDCl_3$) 7.2—7.7 (10 H, m, 2 PhS), 3.79 (1 H, ddd, *J* 10, 7, 3 Hz, reduced to dd, *J* 10, 3 Hz by D_2O shake, C*H*OH), 2.43 (1 H, d, *J* 7 Hz, removed by D_2O shake, OH), 1.2—1.9 (5 H, m, MeCH_2 and Me_2CHCH_2), 0.95 (3 H, t, *J* 8 Hz, *Me*CH_2), and 0.93 and 0.81 (each 3 H, d, *J* 7 Hz, Me_2CH); *m/z* 259 [8%, EtC(SPh)$_2$], 237 (100, *M* − PhS), 180 [17, EtCH(SPh)CHO], 151 (23, EtCHSPh)$_2$, 123 (23, PhSCH_2), and 110 (50, PhSH). Also prepared by this method were the following.

7-*Methyl*-4,4-*bisphenylthio-octan*-3-*ol* (**28**).—Dithioacetal (**27**) and propanal gave the *alcohol* as an oil (47%), R_F (CH_2Cl_2) 0.46, $\nu_{max.}$(liquid film) 3 480 (OH) and 1 580 cm^{-1} (Ph); δ_H($CDCl_3$) 7.6—7.8 and 7.3—7.5 (10 H, m, 2 PhS), 3.58 (1 H, ddd, *J* 9, 6, 3 Hz, C*H*OH), 2.43 (1 H, d, *J* 6 Hz, OH), 1.2—1.9 (7 H, m, MeCH_2 and $Me_2CHCH_2CH_2$), 1.00 (3 H, t, *J* 7.5 Hz, *Me*CH_2), and 0.71 (6 H, d, *J* 7 Hz, Me_2CH), *m/z* 301 (6%, *M* − MeCH$_2$CHOH), 251 (100, *M* − PhS), 193 (16, *M* − PhS − MeCH$_2$CHO), 123 (40, PhSCH_2), 110 (68, PhSH), 109 (30, PhS), and 57 (45, Me_2CHCH_2).

2,5-*Dimethyl*-3,3-*bisphenylthiohexan*-4-*ol* (**15**).—Dithioacetal (**14**)[21] and isobutyraldehyde gave the *alcohol* as an oil (68%), R_F (CH_2Cl_2) 0.62, $\nu_{max.}$($CDCl_3$) 3 470 (OH) and 1 585 cm^{-1} (Ph); δ_H($CDCl_3$) 7.25—7.75 (10 H, m, 2 PhS), 3.74 (1 H, dd, *J* 5, 1.5 Hz, C*H*OH), 2.57 (1 H, d, *J* 5 Hz, OH), 2.0—2.5 (2 H, m, 2 Me_2C*H*), and 1.26, 1.10, 0.97, and 0.86 (each 3 H, d, *J* 7 Hz, *Me*CH); *m/z* 273 [10%, Me_2CHC(SPh)$_2$], 237 (100, *M* − PhS), 165 (75, Me_2CHCHSPh), 110 (35, PhSH), and 71 (80, Me_2CHCHO).

2-*Methyl*-6-(p-*tolyl*)-3,3-*bisphenylthioheptan*-4-*ol* (**36**).—Dithioacetal (**14**)[21] and aldehyde (**35**) gave the *alcohol* as an oil (58%; 89% based on recovered starting material) and a mixture of diastereoisomers, R_F (CH_2Cl_2) 0.64, $\nu_{max.}$(liquid film) 3 550, 3 470 (OH), 1 580, and 1 510 cm^{-1} (Ph); δ_H($CDCl_3$) 6.9—7.8 (14 H, m, 2 PhS and C_6H_4), 3.9—4.1 and 3.5—3.7 (1 H, m, C*H*OH, two diastereoisomers), 1.7—3.0 (5 H, m, MeC*H*CH_2, Me_2C*H* and OH), 2.30 (3 H, s, *Me*C_6H_4), and 1.0—1.3 (9 H, m, 3 Me); *m/z* 327 (100%, *M* − PhS), 273 [15, (PhS)$_2$CCHMe$_2$], 194 [40, Me_2CHC(SPh)CHOH], and 165 (60, Me_2CHCHSPh).

6-*Methyl*-3-*phenylthioheptan*-4-*one* (**20**).—The water of crystallisation of toluene-*p*-sulphonic acid monohydrate (80 mg, 0.42 mmol) was removed by azeotropic distillation with benzene and then a solution of the alcohol (**19**) (157 mg, 0.42 mmol) in benzene (1 ml) was added. After 1 min the mixture was cooled, poured into saturated sodium carbonate solution (20 ml), and extracted with ether (3 × 10 ml). The combined organic fractions were washed with water (3 × 10 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by t.l.c. on silica gel eluting with 5% ether in hexane to give the *ketone* (63.2 mg, 60%) as a pale yellow oil, R_F (CH_2Cl_2) 0.62, $\nu_{max.}$(CCl_4) 1 706 (CO) and 1 580 cm^{-1} (Ph); δ_H($CDCl_3$) 7.2—7.4 (5 H, m, PhS), 3.50 (1 H, t, *J* 7.5 Hz, PhSC*H*), 2.44 (2 H, d, distorted by diastereotopicity of the protons, CHCH_2CO), 2.1 (1 H, m, C*H*Me$_2$), 1.5—1.8 (2 H, m, MeCH_2), 0.99 (3 H, dd, *J* 7.5, 7.0 Hz, *Me*CH_2), and 0.87 and 0.84 (each 3 H, d *J* 5.5 Hz, *Me*CH) (Found: M^+, 236.1242. $C_{14}H_{20}OS$ requires *M*, 236.1235), *m/z* 236 (25%, M^+), 151 (100, PhSCHCH$_2$Me), 123

(31, $PhSCH_2$), 109 (20, PhS), and 85 (38, Me_2CHCH_2CO), and also the regio-isomer 6-*methyl*-4-*phenylthioheptan*-3-*one* (**23**) as a pale yellow oil (33 mg, 31%), R_F (CH_2Cl_2) 0.53, $\nu_{max.}$(CCl_4) 1 710 (CO) and 1 585 cm^{-1} (Ph); δ_H($CDCl_3$) 7.3 (5 H, m, PhS), 3.10 (1 H, m, PhSC*H*), 2.65 (2 H, m, CH_2CO), 2.32 (2 H, distorted t, *J* 7 Hz, $PhSCHCH_2$), 1.4 (1 H, m, Me_2CH), and 0.8—1.1 (9 H, m, 3 Me); *m/z* 236 (83%, M^+), 193 (57, *M* − Me_2CH), 137 (25, $PhSC_2H_4$), 127 (20, *M* − PhS), 123 (31, $PhSCH_2$), 110 (44, PhSH), 83 (61, *M* − PhSH − Me_2CH), and 57 (100, EtCO). Also prepared by this method were the following.

7-*Methyl*-4-*phenylthio-octan*-3-*one* (**29**).—Alcohol (**28**) gave the *ketone* (49%) as an oil, R_F (CH_2Cl_2) 0.60, $\nu_{max.}$(liquid film) 1 710 (CO) and 1 585 cm^{-1} (Ph); δ_H($CDCl_3$) 7.2—7.5 (5 H, m, PhS), 3.61 (1 H, t, *J* 7 Hz, PhSC*H*), 2.58 (2 H, q, *J* 7.5 Hz, $COCH_2$), 1.2—1.9 (5 H, m, CH_2CH_2CH), 1.01 (3 H, t, *J* 7.5 Hz, $MeCH_2$), and 0.86 (6 H, d, *J* 6 Hz, Me_2CH) (Found: M^+, 250.1390. $C_{15}H_{22}OS$ requires *M*, 250.1391); *m/z* 250 (23%, M^+), 193 (72, *M* − EtCO), 137 (11, PhSCHMe), 123 (37, $PhSCH_2$), 110 (16, PhSH), 109 (15, PhS), 83 (100, *M* − PhSH − EtCO), and 57 (28, EtCO), and also 7-*methyl*-2-*phenylthio-octan*-4-*one* (**31**) as an oil (16%), R_F (CH_2Cl_2) 0.55, $\nu_{max.}$(liquid film) 1 710 (C=O) and 1 585 cm^{-1} (Ph); δ_H($CDCl_3$) 7.18—7.43 (5 H, m, PhS), 3.64—3.75 (1 H, m, PhSC*H*), 2.73 and 2.54 (2 H, ABX system, J_{AB} 17, J_{AX} 5.2, J_{BX} 8.5 Hz, $COCH_2CHSPh$), 2.36 (2 H, t, *J* 7.6 Hz, $COCH_2CH_2$), 1.37—1.61 (3 H, m, CH_2CHMe_2), 1.27 (3 H, d, *J* 6.7 Hz, *Me*CHSPh), and 0.86 (6 H, d, *J* 6.2 Hz, Me_2CH) (Found: M^+, 250.1388. $C_{15}H_{22}OS$ requires *M*, 250.1391), *m/z* 250 (89%, M^+), 179 [8, *M* − $Me_2CH(CH_2)_2$], 151 [25, $PhSCH(Me)CH_2$], 141 (8, *M* − PhS), 137 (60, PhSCHMe), 123 (15, $PhSCH_2$), 110 (66, PhSH), 109 (34, PhS), 99 [100, *M* − $PhSCH(Me)CH_2$], and 71 [95, $Me_2CH(CH_2)_2$].

2,5-*Dimethyl*-4-*phenylthiohexan*-3-*one* (**16**).—Alcohol (**15**) gave the *ketone* (63%) as an oil, R_F (CH_2Cl_2) 0.57, $\nu_{max.}$(CCl_4) 1 710 (CO) and 1 585 cm^{-1} (Ph); δ_H($CDCl_3$) 7.3 (5 H, m, PhS), 3.39 (1 H, d, *J* 9 Hz, PhSC*H*), 2.84 (1 H, septet, *J* 7 Hz, CHCO), 2.09 (1 H, d septet, *J* 9, 7 Hz, PhSCHC*H*), and 1.17, 1.06, 1.02, and 0.93 (each 3 H, d, *J* 7 Hz, Me); δ_C($CDCl_3$) 161.0 (s, CO), 133.4 (s, quaternary aromatic), 132.9 and 128.8 (d, *o*- and *m*-aromatic), 127.8 (d, *p*-aromatic), 63.6 (d, PhS*C*H), 39.0 and 28.4 (d, 2 Me_2CH), and 21.2, 20.5, 19.3, and 18.3 (q, 4 Me) (Found: M^+, 236.1227. $C_{14}H_{20}OS$ requires *M*, 236.1235), *m/z* 236 (20%, M^+), 165 (100, $PhSCHCHMe_2$), 151 (20, $PhSCHCH_2Me$), 123 (50, $PhSCH_2$), and 109 (20, PhS).

2-*Methyl*-6-(p-*tolyl*)-3-*phenylthioheptan*-4-*one* (**37**).—Alcohol (**36**) gave the *ketone* (23%) as an oil, R_F (CH_2Cl_2) 0.70, $\nu_{max.}$(liquid film) 1 710 (CO), 1 580 and 1 510 cm^{-1} (Ph); δ_H($CDCl_3$) 7.0—7.3 (9 H, m, PhS and C_6H_4), 3.29 and 3.18 (1 H, d, *J* 9 Hz, PhSC*H*, 1:1 mixture of diastereoisomers), 1.7—2.9 (4 H, m, CH_2CH and Me_2CH), 2.27 (3 H, s, MeC_6H_4), and 0.13—0.17 (9 H, m, 3 Me) (Found: M^+, 326.1696. $C_{21}H_{26}OS$ requires *M*, 326.1704), *m/z* 326 (15%, M^+), 165 (100, $PhSCHCHMe_2$), 151 (25, $PhSCHCH_2Me$), and 119 (50, MeC_6H_4CHMe); and also the regio-isomer 2-*methyl*-6-(p-*tolyl*)-4-*phenylthioheptan*-3-*one* (**40**) as an oil (19%), R_F (CH_2Cl_2) 0.63, δ_H($CDCl_3$), 7.0—7.3 (9 H, m, PhS and C_6H_4), 3.1—3.3 (1 H, m, PhSC*H*), 1.5—2.9 (4 H, m, CH_2CH and COCH), 2.29 (3 H, s, MeC_6H_4), and 0.9—1.3 (9 H, m, 3 Me) (Found: M^+, 326.1678. $C_{21}H_{26}OS$ requires *M*, 326.1704), *m/z* 326 (10%, M^+), 194 (20, $PhSCH_2COCHMe_2$), 175 (20, *M* − PhS − C_3H_6), 165 [30, $PhSCH(CH_2)_2Me$], and 119 (100, MeC_6H_4CHMe).

(E)-6-*Methylhept*-2-*en*-4-*one* (**22**).—A saturated aqueous solution of sodium periodate (79 mg, 0.37 mmol) was added to a stirred solution of the sulphide (**20**) (87 mg, 0.37 mmol) in methanol (3 ml) under nitrogen at 0 °C. The mixture was allowed to warm to room temperature over 18 h, filtered, and the precipitate washed with methanol. The combined filtrate and washings were concentrated under reduced pressure, the residue dissolved in ether (20 ml), and the solution dried ($MgSO_4$) and evaporated under reduced pressure to give 6-*methyl*-3-*phenylsulphinylheptan*-4-*one* (**21**) (78 mg, 84%) as a yellow oil, R_F (CH_2Cl_2) 0.01—0.08, a 1:1 mixture *of* diastereoisomers, which were immediately refluxed in toluene (5 ml) for 1 h, cooled, and evaporated under reduced pressure. The residue was purified by t.l.c. on silica gel eluting with dichloromethane to give the enone (25 mg, 64%) as an oil, R_F (CH_2Cl_2) 0.24, whose spectra had been reported.[28a]

(E)-7-*Methyloct*-4-*en*-3-*one* (**30**).—Oxidation of sulphide (**29**) by sodium periodate as described above gave 7-*methyl*-4-*phenylsulphinyloctan*-3-*one* (100%) as an oil, R_F (CH_2Cl_2) 0.06 and 0.10, which was then heated in a Kügelrohr oven at 120 °C and 20 mmHg for 15 min. The distillate was purified by t.l.c. on silica gel eluting with dichloromethane to give the enone (56%) as an oil, R_F (CH_2Cl_2) 0.36, whose spectra have been reported.[29] Also prepared by this method was the following.

2,5-*Dimethylhex*-4-*en*-2-*one* (**18**).—Oxidation of sulphide (**16**) gave 2,5-*dimethyl*-4-*phenylsulphinylhexan*-3-*one* (**17**) (100%) as an oil, R_F (CH_2Cl_2) 0.05 and 0.09, which was immediately thermolysed to give the enone (72%) as an oil, R_F (CH_2Cl_2) 0.45, whose spectra have been reported.[25d]

Ethyl 3-(p-*Tolyl*)*but*-2-*enoate* (**32**).—Triethyl phosphonoacetate (55 g, 49 ml, 0.25 mol) was added dropwise to a stirred suspension of sodium hydride (15.8 g of a 50% dispersion in mineral oil, 0.33 mol) in dry dimethoxyethane (300 ml) under nitrogen at 0 °C. The mixture was stirred for 30 min at room temperature after which *p*-methylacetophenone (32.8 g, 33 ml, 0.25 mol) was added dropwise. The mixture was refluxed for 5 h, poured into water (200 ml), and extracted with ether (3 × 100 ml). The combined organic fractions were washed with brine (2 × 100 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was distilled to give the unsaturated ester[36] (33.9 g, 68%) as an oil, b.p. 87—92 °C/0.35 mmHg (lit.,[46] 158—164 °C/18 mmHg and[47] 147—153 °C/8 mmHg), R_F (CH_2Cl_2) 0.57.

Ethyl 3-(p-*Tolyl*)*butanoate* (**33**).—The unsaturated ester (**32**) (33.9 g, 0.166 mmol) in absolute ethanol (150 ml) was hydrogenated at 1 atm over 5% palladium on charcoal (25 g) for 6 h; the mixture was then filtered through Celite and the filtrate evaporated under reduced pressure to give the ester (32.8 g, 96%) as an oil R_F (CH_2Cl_2) 0.53, whose spectra have been reported.[48]

3-(p-*Tolyl*)*butan*-1-*ol* (**34**).—The ester (**33**) (32.8 g, 0.16 mmol) in dry THF (60 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (10 g, 0.26 mol) in dry THF (400 ml) under nitrogen. After 30 min a saturated aqueous solution of sodium potassium tartrate (Rochelle's salt) was added carefully, with cooling. The mixture was filtered, the filtrate concentrated under reduced pressure, and the residue extracted with ether (3 × 25 ml). The combined extracts were washed with brine (2 × 10 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give the alcohol[49] (22.3 g, 85%) as an oil, R_F (CH_2Cl_2) 0.18.

3-(p-*Tolyl*)*butanal* (**35**).—The alcohol (**34**) (1.77 g, 10.8 mmol) in dichloromethane (10 ml) was added quickly to a stirred suspension of pyridinium chlorochromate[38,50] (2.66 g, 12.4 mmol) in dichloromethane (30 ml) under nitrogen. After 1.5 h ether (50 ml) was added, the solution decanted, and the precipitate washed well with ether. The combined filtrate and

washings were evaporated under reduced pressure and the residue purified by column chromatography on silica gel (200 g) eluting with 5% ether in light petroleum (b.p. 30—40 °C) to give the aldehyde (1.0 g, 57%) as an oil, b.p. 84 °C/0.9 mmHg (lit.,[51] 110.5—111.5 °C/9 mmHg), R_F (CH_2Cl_2) 0.57.

Use of pyridinium dichromate[52] instead of pyridinium chlorochromate gave only 36% of the aldehyde.

4-(p-*Tolyl*)-1-*phenylthiopentan*-2-*one*.—n-Butyl-lithium (1.5M-solution in hexane, 0.71 ml, 1 mmol) was added to a stirred solution of thioanisole (124 mg, 0.12 ml, 1.0 mmol) and DABCO (112 mg, 1 mmol) in dry THF under nitrogen at 0 °C. After 45 min the ester (**33**) (206 mg, 1 mmol) in dry THF (1 ml) was added. The mixture was stirred at 0 °C for 1 h, then poured into water (20 ml) and extracted with ether (3 × 20 ml). The combined extracts were washed with brine (2 × 10 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (50 g) eluting with 5% ether in light petroleum (b.p. 30—40 °C) to give the *ketone* (58 mg, 20%; 40% based on recovered starting material) as an oil, R_F (CH_2Cl_2) 0.63, $\nu_{max.}$(liquid film) 1 710 (CO) and 1 585 cm^{-1} (Ph); δ_H($CDCl_3$) 7.30 (5 H, s, PhS), 7.15 (4 H, s, C_6H_4, C_6H_4), 3.54 (2 H, s, PhSCH_2CO), 3.31 (1 H, ddq, *J* 8, 7, 7 Hz, MeC*H*CH_2), 2.98 (1 H, dd, *J* 7, 16.5 Hz, CHC$H_A$$H_B$CO), 2.75 (1 H, dd, *J* 8, 16.5 Hz, CHC$H_A$$H_B$CO), 2.32 (3 H, s, *Me*$C_6H_4$), and 1.21 (3 H, d, *J* 7 Hz, *Me*CH) (Found: M^+, 284.1229. $C_{18}H_{20}OS$ requires *M*, 284.1235), *m/z* 284 (36%, M^+), 175 (*M* − PhS), 161 (9, *M* − $PhSCH_2$), 124 (21, PhSMe), 123 (18, $PhSCH_2$), 119 (100, *M* − $PhSCH_2COCH_2$), 105 (19, $MeC_6H_4CH_2$), and 91 (18, $PhCH_2$).

Alkylation of this α-phenylthio ketone using sodium hydride and isopropyl iodide failed to give any recognisable products.

2-*Methyl*-6-(p-*tolyl*)*hept*-2-*en*-4-*one* (**39**).—MCPBA (43 mg, 0.25 mmol) in ether (2 ml) was added slowly to a stirred solution of the sulphide (37) (81 mg, 0.25 mmol) in ether (5 ml) under nitrogen at 0 °C. After 30 min the mixture was washed with aqueous sodium thiosulphate (3 × 10 ml), sodium hydrogen carbonate (3 × 10 ml), and brine (2 × 10 ml), and then dried ($MgSO_4$), and evaporated under reduced pressure to give 2-*methyl*-6-(p-*tolyl*)-3-*phenylsulphinylheptan*-4-*one* (**38**) (64%) as an oil, R_F (CH_2Cl_2) 0.05—0.13. Thermolysis in a Kugelrohr oven as above gave the enone[48] (77%) as an oil, R_F (CH_2Cl_4) 0.58.

2-*Methyl*-1-*phenylthiopropane*.—Isobutyl bromide (32.8 g, 0.24 mmol) in ethanol (50 ml) was added slowly to a stirred solution of thiophenol (26.4 g, 24.6 ml, 0.24 mol) and sodium hydroxide (9.6 g, 0.24 mol) in ethanol (150 ml) under nitrogen. After 18 h the solution was concentrated under reduced pressure, diluted with water (200 ml), and extracted with ether (3 × 100 ml). The combined extracts were washed with sodium hydroxide solution (2 × 50 ml), water (2 × 20 ml), and brine (2 × 20 ml), and then dried ($MgSO_4$) and evaporated under reduced pressure. The residue was distilled to give the sulphide[53] (35.5 g, 89%) as an oil, b.p. 47—48 °C/0.3 mmHg (lit.,[54] 103—104.5 °C/11 mmHg), R_F (CH_2Cl_2) 0.78.

2-*Methyl*-1-*phenylsulphinylpropane*.—Sodium periodate (80.4 g, 0.38 mol) in water (700 ml) was added to a stirred solution of the above sulphide (31.2 g, 0.19 mol) in methanol (700 ml) under nitrogen at 0 °C. The mixture was allowed to warm up to room temperature over 24 h and then filtered and the precipitate washed with methanol. The combined filtrate and washings were concentrated under reduced pressure and extracted with ether (4 × 100 ml). The combined extracts were washed with brine (2 × 100 ml), dried ($MgSO_4$), and evaporated under reduced pressure to give the sulphoxide[55] (34.0 g, 99%) as an oil, R_F (CH_2Cl_2) 0.05, (Et_2O) 0.38.

2-*Methyl*-6-(p-*tolyl*)-3-*phenylsulphinylheptan*-4-*one* (**38**).—n-Butyl-lithium (1.6M-solution in hexane; 0.9 ml, 1.45 mmol) was added dropwise to a stirred solution of the above sulphoxide (290 mg, 1.59 mmol) in dry THF under nitrogen at 0 °C. After 5 min the ester (**33**) (299 mg, 1.45 mmol) in dry THF (1 ml) was added. The mixture was stirred at room temperature for 30 min and at 50 °C for 1 h, and then poured into water (20 ml) and extracted with ether (3 × 20 ml). The combined extracts were washed with brine (2 × 20 ml), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (50 g) using gradient elution from 5% ether in light petroleum (b.p. 30—40 °C) to 100% ether to give the *ketone* (16 mg, 3%; 6% based on recovered starting materials) as an oil, R_F (CH_2Cl_2) 0.05—0.14, (Et_2O) 0.61; δ_H($CDCl_3$) 7.0—7.6 (9 H, m, PhSO and C_6H_4), 2.9—3.2 (1 H, m, PhSOC*H*), 2.4—2.6 (2 H, m, $COCH_2$), 2.32 (3 H, s, Ar*Me*), 2.0—2.1 (1 H, m, MeC*H*CH_2), 1.68 (1 H, br s, Me_2CH), and 0.8—1.4 (9 H, m, 3 Me) (Found: M^+, 342.1651. $C_{21}H_{26}O_2S$ requires *M*, 342.1653), *m/z* 342 (0.6%, M^+), 217 (50, *M* − PhSO), 173 (11, *M* − PhSO − C_3H_8), 161 (15, *M* − $PhSOCHCHMe_2$), 132 [50, *M* − $Me_2CHSO(Ph)CHO$], 119 (100, MeC_6H_4CHMe), and 105 (22, $MeC_6H_4CH_2$).

7-*Oxo*-6-*phenylthio-octanoic Acid* (**46**).—Sodium hydride (2.35 g of a 50% dispersion in mineral oil) was washed with hexane (3 × 30 ml) and dry ether (2 × 20 ml) under nitrogen and then dried *in vacuo* to give pure sodium hydride (1.06 g, 44 mmol) which was suspended in THF (100 ml). 2-Acetylcyclohexanone (**44**) (6.16 g, 44 mmol), in THF (30 ml) was added dropwise with stirring at room temperature and the resulting white suspension stirred for 30 min. Benzenesulphenyl chloride (6.34 g, 44 mmol) in THF (30 ml) was then added dropwise to give a clear green solution containing 2-acetyl-2-phenylthiocyclohexanone (**45**). Sodium hydroxide (1.8 g, 45 mmol) in water (150 ml) was added and the resulting mixture shaken for 20 min at room temperature. The THF was evaporated under reduced pressure and dilute HCl added dropwise until a precipitate had just formed (pH 9) and the solution was then extracted with dichloromethane (4 × 50 ml). The aqueous layer was then acidified to pH 2 by addition of dilute HCl and re-extracted with dichloromethane (3 × 50 ml). The combined organic fractions from this second extraction were dried (Na_2SO_4) and evaporated under reduced pressure to give the *acid* (10.4 g, 88%) as an oil, R_F (EtOAc) 0.43, $\nu_{max.}$(liquid film) 3 600—2 300br (CO_2H), 1 705 (CO and CO_2H), and 1 585 cm^{-1} (PhS); δ_H($CDCl_3$) 1.3—2.0 [6 H, m, $(CH_2)_3$], 2.23 (3 H, s, MeCO), 2.33 (2 H, t, *J* 7 Hz, CH_2CO), 3.60 (1 H, t, *J* 7 Hz, CHS), 7.2 − 7.5 (5 H, m, PhS), and 10.47 (1 H, br s, CO_2H) (Found: M^+ 266.0990. $C_{14}H_{18}O_3S$ requires *M*, 266.0977), *m/z* 266 (100%, M^+) and 223 (70, *M* − C_2H_3O).

In a separate experiment the clear green solution described above was quenched with 1M-HCl (50 ml), water (100 ml) was added, the layers were separated and the aqueous layer was extracted with ether (4 × 50 ml). The combined organic fractions were dried ($MgSO_4$), evaporated under reduced pressure, and the resulting oil purified by flash chromatography[56] on silica gel eluting with dichloromethane—15% hexane to give 2-*acetyl*-2-*phenylthiocyclohexanone* (**45**) (7.8 g, 72%) as a colourless oil, R_F (EtOAc) 0.64, $\nu_{max.}$(liquid film) 1 700 cm^{-1} (CO); δ_H($CDCl_3$) 1.4—2.9 [8 H, m, $(CH_2)_4$], 2.30 (3 H, s, CH_3CO), and 7.21 (5 H, s, PhS) (Found: M^+, 248.0868. $C_{14}H_{16}O_2S$ requires *M*, 248.0871), *m/z* 248 (9%, M^+) and 206 (100, *M* − CH_2CO).

(E)-7-*Oxo*-*oct*-5-*enoic Acid* (**47**).—Sodium periodate (7.7 g, 35 mmol) in water (100 ml) was added to a solution of (**46**) (7.98 g, 30 mmol) in methanol (150 ml) at 0 °C and the solution allowed to warm to room temperature over 6 h and then stirred for a

further 40 h. The resulting precipitate was removed by filtration through Celite and the filtrate extracted with chloroform (4 × 40 ml). The combined organic fractions were dried (Na_2SO_4) and evaporated under reduced pressure to give a 1:1 diastereoisomeric mixture of (**48**; R = H) (98%) as a white solid. Recrystallisation from ethyl acetate–hexane gave the pure sulphoxides (**48**; R = H) (55%). A solution of (**48**; R = H) (2 g) in carbon tetrachloride (120 ml) was heated under reflux for 6 h, cooled, and evaporated under reduced pressure to give an oil. The sulphur-containing products were separated on a short, fat column of silica gel, eluting with dichloromethane and subsequent elution with ethyl acetate gave the enone (1.09 g, 98%) as a colourless liquid which decomposed on attempted reduced pressure distillation; R_F (EtOAc) 0.32; n.m.r., i.r. and u.v. spectra agree with those previously reported.[41] When the intermediate sulphoxides (**48**; R = H) were not recrystallised the enone was obtained in 88% yield from (**46**) but contained *ca.* 5% of a sulphur-containing impurity which could not be removed satisfactorily by column chromatography.

Attempted Esterification of (**47**) *in Acidic Methanol.*—The acid (**47**) (0.5 g, 2.4 mmol) and concentrated H_2SO_4 (1 ml) in methanol (25 ml) were heated at reflux under nitrogen for 2 h. After the mixture had cooled, water (50 ml) was added and the solution extracted with dichloromethane (3 × 20 ml). The combined extracts were washed with sodium hydrogen carbonate (2 × 20 ml) and water (20 ml), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by flash chromatography[57] on silica gel, eluting with ethyl acetate—15% hexane to give *methyl 7-oxo-5-methoxyoctanoate* (**50**) (0.44 g, 68%) as a colourless liquid, R_F (EtOAc) 0.55, $\nu_{max.}$(liquid film) 1 734 (CO_2Me) and 1 714 cm^{-1} (MeCO); $\delta_H(CDCl_3)$ 1.3—1.9 [4 H, m, $(CH_2)_2$], 2.13 (3 H, s, MeCO), 2.2—2.8 (4 H, m, 2 × CH_2CO), 3.29 (3 H, s, MeOCH), 3.63 (3 H, s, CO_2Me), and 3.55—3.8 (1 H, m, C*H*OMe) (Found: M − Me, 187.0969. $C_9H_{15}O_4$ requires M, 187.0969), m/z 187 (4%, M − Me), 155 (5, M − Me − MeOH), 113 (30), and 101 [100, $(CH_2)_3CO_2Me^+$].

Methyl 7-Oxo-6-phenylthio-octanoate.—The acid (**46**) (10.6 g, 40 mmol) and concentrated H_2SO_4 (3 ml) in methanol (100 ml) were heated at reflux for 2 h under nitrogen and then cooled to room temperature, diluted with water (100 ml), and extracted with dichloromethane (3 × 50 ml). The combined organic fractions were washed with sodium hydrogen carbonate (50 ml) and water (50 ml), dried, and evaporated under reduced pressure to give a crude oil which was purified on a short, fat column of silica gel, eluting with ethyl acetate to give the *ester* (10.4 g, 93%) as a light yellow oil, R_F (EtOAc) 0.70, $\nu_{max.}$(liquid film) 1 736 (CO_2Me) and 1 708 cm^{-1} (MeCO); $\delta_H(CDCl_3)$ 1.2—2.1 [6 H, m, $(CH_2)_3$], 2.24 (3 H, s, MeCO), 2.30 (2 H, t, J 7 Hz, CH_2CO), 3.61 (1 H, t, J 7 Hz, SCH), 3.67 (3 H, s, OMe), and 7.3—7.5 (5 H, m, SPh) (Found: M^+, 280.1124. $C_{15}H_{20}O_3S$ requires M, 280.1133), m/z 280 (52%, M^+), 249 (6, M − OMe), 237 (35, M − C_2H_3O), 205 (100, M − $C_3H_7O_2$), 109 (50, PhS^+), and 110 (47, PhS^+H).

(E)-*Methyl 7-Oxo-oct-5-enoate* (**49**).—(*a*) Sodium periodate (10.7 g, 50 mmol) in water (100 ml) was added to a stirred solution of methyl 7-oxo-6-phenylthio-octanoate (10.4 g, 37.4 mmol) in methanol (200 ml) at room temperature and stirring was continued for 24 h before filtration through Celite and removal of most of the methanol under reduced pressure. Water (100 ml) was added and the resulting suspension extracted with dichloromethane (4 × 50 ml). The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the sulphoxides (**48**; R = Me) which were not purified but dissolved in carbon tetrachloride (200 ml) and heated at reflux for 16 h under nitrogen. After the solution had cooled it was evaporated under reduced pressure to give a yellow liquid. Some decomposition occurred on distillation of this crude product at reduced pressure (88—90 °C, 0.5 mmHg) but the *enone* (4.2 g, 66%) was obtained as a light green liquid, R_F (EtOAc) 0.56, $\nu_{max.}$(liquid film) 1 732 (CO_2Me), 1 668, and 1 628 cm^{-1}) (C=C–CO); $\delta_H(CDCl_3)$ 1.76 (2 H, quint, J 7 Hz, $CH_2CH_2CH_2$), 2.20 (3 H, s, MeCO), 2.1—2.4 (4 H, m, $CH_2CH_2CH_2$), 3.65 (3 H, s, MeO), 6.05 (1 H, dt, J 16, < 1 Hz, CHCO), and 6.78 (1 H, dt, J 16, 6 Hz, CH_2CH) (Found: M^+, 170.0934. $C_9H_{14}O_3$ requires 170.0943), m/z 170 (29%, M^+), 97 (100, M − $C_3H_5O_2$), and 96 (70, M − $C_3H_6O_2$); $\lambda_{max.}$(EtOH) 221.5 nm (14 000).

(*b*) Dimethyl acetylmethylphosphonate (10.0 g, 0.06 mol; Lancaster) in dry THF (100 ml) was added over 5 min to a mechanically stirred suspension of sodium hydride (50% dispersion in mineral oil; 2.89 g, 0.06 mol) in dry THF (400 ml) and stirring was continued for 4 h under nitrogen (the suspension becomes white and viscous). Methyl 5-oxopentanoate[57] (7.83 g, 0.06 mol) in dry THF (100 ml) was then added, and stirring continued for a further 3 h before addition of glacial acetic acid (3.6 ml) and evaporation under reduced pressure. The residue was mixed with water (150 ml), extracted with ether (4 × 100 ml), and the combined extracts evaporated under reduced pressure to give a brown liquid which was purified on a short, fat column of silica gel, eluting with ethyl acetate followed by distillation at reduced pressure (b.p. 78—80 °C/0.2 mmHg) to give the *enone* (5.90 g, 58%) as a colourless liquid.

Attempted Synthesis of (**46**) *by Alkylation of* (*Phenylthio*)*acetone.*—Potassium t-butoxide (3.4 g, 33 mmol) in dry THF (30 ml) was added to a stirred solution of (**51**; X = Br, I, R = H)[58] (32 mmol) in THF (50 ml) under nitrogen at room temperature to give a suspension of the potassium salt. (Phenylthio)acetone (5.0 g, 30 mmol) in THF (30 ml) was added to a stirred solution of potassium t-butoxide (3.4 g, 33 mmol) in THF (50 ml) under nitrogen at 0 °C to give a red solution. The suspension of the potassium salt of (**51**) was added dropwise with stirring to this solution and the resulting suspension allowed to warm to room temperature over 2 h and then refluxed for a further 2 h. The cooled solution was evaporated under reduced pressure, diluted with water (100 ml), and extracted with dichloromethane (4 × 50 ml). The combined organic fractions were washed with brine (2 × 30 ml), dried (Na_2SO_4), and concentrated under reduced pressure to give an oil. N.m.r. analysis showed that only *ca.* 40% of the (phenylthio)acetone had reacted. Distillation at reduced pressure gave a mixture of recovered (phenylthio)acetone (54%), the lactone (**52**) (0.5 g, 16%) and a residue (3 g).

The above procedure was repeated using the methyl ester of (**51**).[59] N.m.r. analysis of the crude reaction product showed that only 33% of the (phenylthio)acetone had reacted.

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