Pergamon

Tetrahedron 54 (1998) 2801–2808

TETRAHEDRON

Cobalt Catalysed Hydro-Sulfenylation of Michael Acceptors

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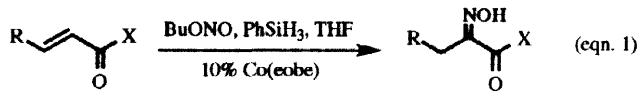
Received 27 November 1997; revised 22 December 1997; accepted 8 January 1998

Abstract: The reaction of certain types of Michael acceptors, limited to those having methylene groups, with a mixture of diphenyl disulfide and phenyl silane, under the influence of 10% of the cobalt catalyst, Co(eobe) **3**, results in the formation of hydro-sulfenylated products, such as α-phenylthio carbonyl compounds, in moderate to good yields. The process involves intermediates having radical character, judging by the 5-*exo-trig* cyclisation product **21** observed in the reaction of α,β-unsaturated ester **20** having a suitable unsaturated side-chain.

INTRODUCTION

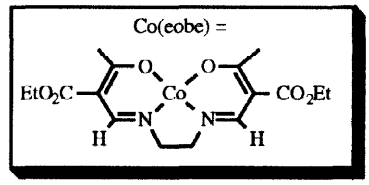
Recently, we became interested in a report by Kato and Mukaiyama, which described the preparation of α-hydroxyimino carbonyl compounds **2**, starting from the corresponding α,β-unsaturated carbonyl compounds **1**, (eqn. 1).[1]



(1) R = alkyl, X = R, OR, NR_2

(2)

Co(eobe) =



(3)

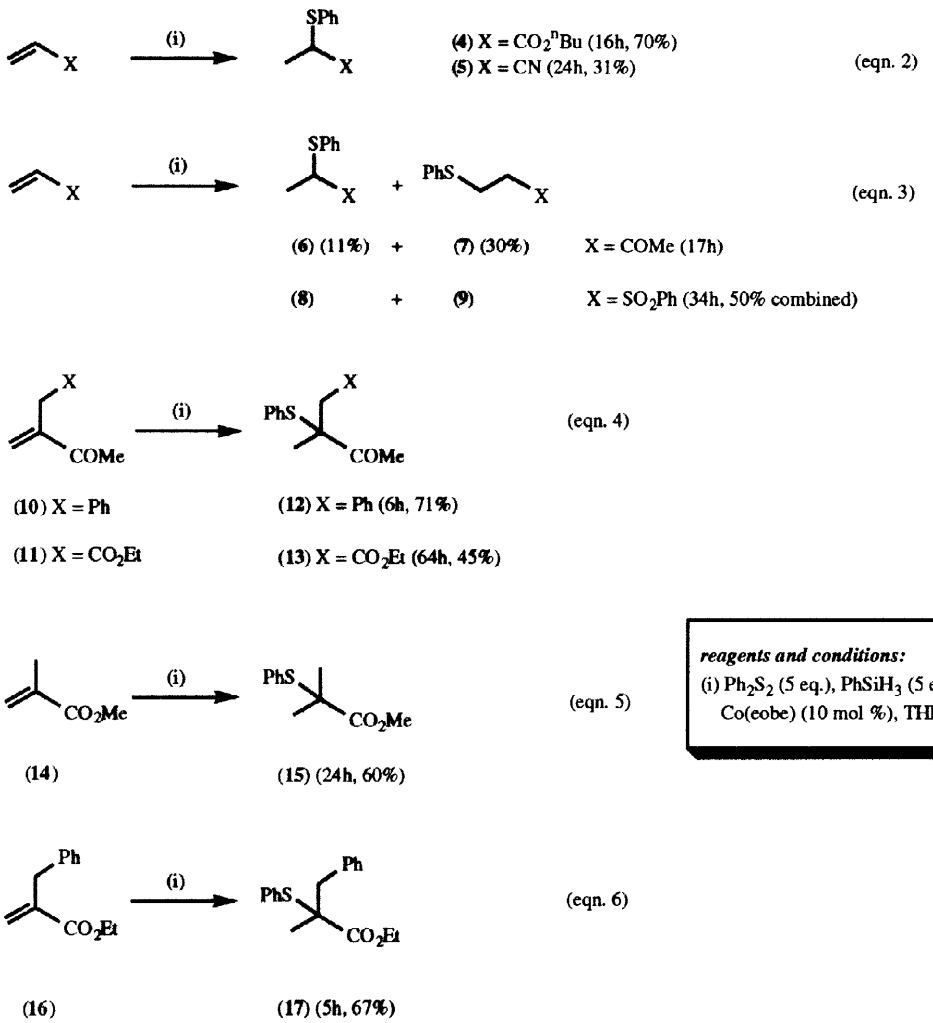
This transformation involves reaction of the Michael acceptor-type substrate with a mixture of butyl nitrite and phenyl silane, under the influence of a catalytic amount of the cobalt complex, Co(eobe) **3**. The reaction was proposed to proceed via an initial 1,4-hydrocobaltation process, generating a cobalt enolate intermediate, which then reacts with the electrophilic butyl nitrite to give an α-nitroso carbonyl compound which, on tautomerisation, gives the observed oxime product (see later).

This mild and catalytic process appeared very attractive for synthesis, and we were intrigued by the possibility of trapping the putative cobalt enolate with alternative electrophiles. Herein we describe some of our explorations of this type of cobalt-catalysed process, which indicate that the intermediates in the reaction have radical rather than enolate type character, and which have resulted in the development of a method for the hydro-sulfenylation of certain types of unsaturated systems.

0040-4020/98/$19.00
PII: S0040-4020(98)00029-5

RESULTS AND DISCUSSION

Although we had no problem in reproducing the type of oxime synthesis indicated in eqn. 1, it did not prove possible to significantly broaden the scope of the reaction to generate alternative types of product. Thus, reactions of typical Michael acceptors with mixtures of the Co(eobe) catalyst, phenyl silane and various types of electrophile, including alkylating agents, aldehydes, acid chlorides or chlorotrimethylsilane, gave none of the anticipated products. Only in the case of reactions including diphenyldisulfide did we find that the expected products of apparent conjugate reduction and electrophilic quench were formed. After some initial experimentation we converted a range of substrates into hydro-sulfenylated products in this way (eqn. 2–6).

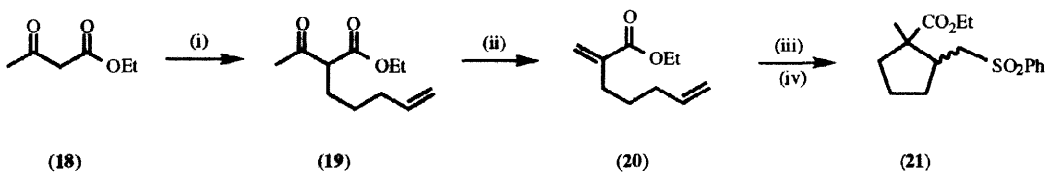


In most cases the α-sulfenyl carbonyl compound was obtained in good yield, although the reaction often took several days to reach completion. The formation of sulfenylated nitrile **5** and sulfone **8** also indicates that alkenes having non-carbonyl types of activating group may also participate in the reaction. In the latter case, and also in the reaction involving methyl vinyl ketone (eqn. 3) the yield of the α -sulfenyl product was reduced due to the competing formation of β-sulfenyl compounds **7** and **9**. This is presumably due to

uncatalysed Michael type addition of either thiol or PhS· radicals, which are produced from the starting disulfide as the reaction proceeds.[2] Blank experiments, in which the cobalt catalyst was omitted, gave only this type of β-sulfenylated product (other blank experiments also showed that the silane must be present for the hydro-sulfenylation reaction to occur). The principal limitation of the reaction is that β-substitution of the alkene acceptor completely halts the reaction and therefore only methylene compounds can be used. This is disappointing and a little surprising, since β-substitution seems to be tolerated in the originally reported process illustrated in eqn. 1.

At this stage we considered that, far from involving a cobalt enolate, these reactions might involve carbon-centred radicals, or at least intermediates having radical character. Firstly, formation of an intermediate alkyl cobalt species was most likely, and the literature reveals a plentiful chemistry of such species, involving carbon–cobalt bond homolysis to give carbon-centred radicals.[3] Secondly, although most electrophiles tried in the cobalt catalysed reaction did not work, the successful one, diphenyldisulfide, is a well known radical trap.[4]

To secure additional evidence of radical intermediates we synthesized the Michael acceptor system **20**, having an unsaturated side chain, starting with ethyl acetoacetate, Scheme 1.



(18) (19) (20) (21)

reagents and conditions:
(i) NaH, DMF, $H_2C{=}CH(CH_2)_3Br$ (71%) (ii) LDA, $(CH_2O)_n$; Δ (63%) (iii) Ph_2S_2 (5 eq.), $PhSiH_3$ (5 eq.) Co(eobe) (10 mol %), THF, Δ (iv) Oxone®, THF, H_2O (14% two steps)

Scheme 1

Alkylation under typical conditions gave the unsaturated derivative **19**, which on further reaction under the conditions described by Ueno *et al*,[5] gave the desired methylene substrate **20**. Reaction of this compound under our standard sulfenylation conditions gave only low yields of products, which were difficult to isolate. However, by subjecting the crude reaction mixture to oxidation using Oxone® we were able to separate the cyclised products in the form of a diastereoisomeric mixture of sulfones **21**.

Despite the low yields of the sulfones **21** obtained, the observation of this type of product is good evidence for a *5-exo-trig* radical cyclisation, and hence for the intermediate cobalt species showing radical, rather than ionic, character.[6] The mechanism of the reaction probably involves reaction of the silane with the starting cobalt species, to generate a cobalt hydride, which then effects regioselective hydrocobaltation of the starting alkene. Homolysis of the intermediate alkyl-cobalt species and carbon-centred radical trapping by the disulfide then furnishes the product. This sequence is very similar to that proposed by Okamoto and co-workers for a cobalt-catalysed preparation of oximes from styrene (somewhat analogous to eqn. 1), which employs borohydride as the reducing agent.[7]

Acknowledgements

We are grateful to the DTI-LINK Asymmetric Synthesis Programme for support of this work.

EXPERIMENTAL

General Details

Melting points for solid products were determined using a Kofler hot-stage apparatus. IR spectra were recorded on either Perkin-Elmer 1720-X FTIR or Perkin-Elmer 1600 Series FTIR instruments as either KBr discs or solutions in CCl_4 or $CHCl_3$. NMR spectra were recorded on Bruker AM 250, Jeol FX270, Bruker AM 400, or Bruker DRX 500 machines, with either Me_4Si or residual protic solvent as internal standard. *J* values are recorded in Hz and abbreviations used are br. - broad, s - singlet, d - doublet, t - triplet, q - quartet, qu - quintet, m - multiplet, dd - double doublet (apparent multiplicity has been given in a few cases where multiplets have a simplified appearance due to identical couplings from non-equivalent protons). Multiplicities indicated for ^{13}C NMR were obtained using a DEPT sequence. Mass spectra were recorded on VG Micromass 70E or VG Autospec spectrometers.

Microanalyses were performed at the microanalytical laboratory at the University of Nottingham using a Perkin-Elmer 240B elemental analyser. Analytical tlc. was performed on Merck precoated silica gel F_{254} plates and visualised by one or more of the following; ultra-violet light, iodine, potassium permanganate, acidic ammonium molybdate (IV) or phosphomolybdic acid. Preparative chromatography was carried out on columns of Merck Kieselgel 60 (230-400 mesh).

Tetrahydrofuran and diethyl ether were distilled from sodium-benzophenone ketyl; light petroleum refers to petroleum ether b.p. 40-60 °C which was distilled prior to use.

Methyl vinyl ketone, acrylonitrile and methyl methacrylate were purchased from Aldrich and distilled before use. Phenyl vinyl sulfone was obtained through Oxone® oxidation of the corresponding sulfide. The unsaturated ketones **12** and **13** were prepared by the method of Ben Ayed and Amri,[8] and the unsaturated ester **16** by the method of Ueno *et al.*[5]

Typical procedure for catalytic hydro-sulfenylation of α-methylene compounds

Phenyl silane (0.63mg, 5mmol) and diphenyl disulfide (1.09g, 5mmol) were successively added to a solution of the methylene ketone **10** (160mg, 1mmol) and Co(eobe) (40mg, 0.1mmol) in THF (8cm^3). The mixture was then heated to reflux for 6h after which time the solvent was removed under reduced pressure. Purification of the crude oil by silica gel column chromatography (10:1 petrol:EtOAc) yielded the desired sulfide product **12**, as a clear oil (190mg, 71%), υ_{max} ($CHCl_3$)/cm^{-1} 1698 (C=O), 1602, 1583, 1457 (Ar); δ_H (250 MHz, $CDCl_3$) 1.32 (3H, s, CH_3), 2.41 (3H, s, $COCH_3$), 2.94 (1H, d, *J* 13.7, CH*H*Ar), 3.33 (1H, d, *J* 13.7, C*H*HAr), 7.16–7.43 (10H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 21.3 (CH_3), 25.5 ($COCH_3$), 42.6 (CH_2), 60.5 (C), 126.7 (CH, Ar), 128.1 (CH, Ar), 128.7 (CH, Ar), 129.3 (CH, Ar), 130.5 (CH, Ar), 130.7 (C, Ar), 136.1 (CH, Ar), 136.5 (C, Ar), 193.8 ($COCH_3$); *m/z* (EI) 270 (M^+, 5%), 227 (M–COMe, 100), 162 (M–SPh, 5), 149 (M–H–COMe–Ph, 63), 117 (M–H–COMe–SPh, 36) (Found 270.1083. $C_{17}H_{18}OS$ requires M, 270.1078).

Data for the other sulfide products

(4) Following the above general procedure with ^{n}butyl acrylate (0.07cm^3, 0.5mmol), phenylsilane (0.31cm^3, 2.5mmol), diphenyl disulfide (0.55g, 2.5mmol) and Co(eobe) (20mg, 0.05mmol). After reflux for 16h, evaporation of solvent and purification by silica gel column chromatography (20:1 petrol:EtOAc), the sulfide **4** was obtained as a clear oil (67mg, 70%), υ_{max} ($CHCl_3$)/cm^{-1} 1722 (C=O), 1583, 1456 (Ar); δ_H (250 MHz, $CDCl_3$) 0.82 (3H, t, *J* 4.6, CH_3), 1.20 (2H, sextuplet, *J* 4.6, CH_2), 1.41 (3H, d, *J* 4.4, $CHCH_3$), 1.52 (2H, m, CH_2), 3.72 (1H, q, *J* 4.4, $CHCH_3$), 3.99 (2H, t, *J* 4.6, CO_2CH_2), 7.15–7.27 (3H, m, ArH), 7.37–7.44 (2H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 13.6 (CH_3), 17.4 (CH_3), 18.9 (CH_2), 30.4 (CH_2), 45.2 (CH), 65.0 (CH_2), 127.8 (CH, Ar), 128.8 (CH, Ar), 132.8 (CH, Ar), 133.3 (C, Ar), 172.7 (CO_2CH_2); *m/z* (EI) 238 (M^+, 20%), 180 (M–Bu, 10), 137 (M–CO_2Bu, 100), 109 (PhS^+, 33) (Found 238.1021. $C_{13}H_{18}O_2S$ requires M, 238.1027).

(5)[9] Following the above general procedure with acrylonitrile (53mg, 1mmol), phenylsilane (0.63cm^3, 5mmol), diphenyl disulfide (1.09g, 5mmol) and Co(eobe) (40mg, 0.1mmol). After reflux for 36h, evaporation of solvent and purification by silica gel column chromatography (15:1 petrol:EtOAc), the sulfide **5** was obtained as a clear oil (50mg, 31%), υ_{max} ($CHCl_3$)/cm^{-1} 2239 (C≡N), 1584, 1453 (Ar); δ_H (250 MHz, $CDCl_3$) 1.61 (3H, d, *J* 7.3, CH_3CH), 3.81 (1H, q, *J* 7.3, CH_3CH), 7.40–7.44 (3H, m, ArH), 7.61–7.65 (2H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 18.7 (CH_3CH), 31.3 (CH_3CH), 119.8 (CN), 129.4 (CH, Ar), 129.5 (CH, Ar), 130.4 (C, Ar), 134.6 (CH, Ar); *m/z* (EI) 163 (M^+, 41%), 148 (M–Me, 3), 109 (PhS^+, 64), 83 (100) (Found 163.0457. C_9H_9NS requires M, 163.0456).

(6)[10] and **(7)**[11] Following the above general procedure with methyl vinyl ketone (0.1cm^3, 1mmol), phenylsilane (0.63cm^3, 5mmol), diphenyl disulfide (1.09g, 5mmol) and Co(eobe) (40mg, 0.1mmol). After reflux for 24h, evaporation of solvent and purification by silica gel column chromatography (15:1 petrol:EtOAc), gave firstly the sulfide **6** as a clear oil (20mg, 11%), υ_{max} ($CHCl_3$)/cm^{-1} 1714 (C=O), 1584 1483, 1455 (Ar), δ_H (250 MHz, $CDCl_3$) 1.41 (3H, d, *J* 7.0, CH_3CH), 2.29 (3H, s, CH_3CO), 3.77 (1H, q, *J* 7.0, CH_3CH), 7.23–7.51 (5H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 16.1 (CH_3CH), 26.3 (CH_3CO), 52.1 (CH_3CH), 127.1 (C, Ar), 128.0 (CH, Ar), 129.1 (CH, Ar), 132.6 (CH, Ar), 206.3 ($COCH_3$); *m/z* (EI) 180 (M^+, 11%), 137 (M–COMe, 47), 109 (PhS^+, 15), 83 (100) (Found 180.0613. $C_{10}H_{12}OS$ requires M, 180.0608), followed by sulfide **7** was as a clear oil (53mg, 30%), υ_{max} ($CHCl_3$)/cm^{-1} 1714 (C=O), 1584, 1483, 1463 (Ar), δ_H (250 MHz, $CDCl_3$) 2.15 (3H, s, CH_3CO), 2.78 (2H, t, *J* 7.3, $PhSCH_2$), 3.14 (2H, t, *J* 7.3, CH_2CO), 7.26–7.33 (5H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 27.3 ($PhSCH_2$), 30.0 ($COCH_3$), 43.0 (CH_2CO), 126.2 (CH, Ar), 128.9 (CH, Ar), 129.4 (CH, Ar), 135.6 (C, Ar), 206.5 ($COCH_3$); *m/z* (EI) 180 (M^+, 3%), 137 (M–COMe, 1), 109 (PhS^+, 1), 70 (M–SPh, 4).

(8) and **(9)** Following the above general procedure with phenyl vinyl sulfone (152mg, 1mmol), phenylsilane (0.63cm^3, 5mmol), diphenyl disulfide (1.09g, 5mmol) and Co(eobe) (400mg, 0.1mmol). After reflux for 24h, evaporation of solvent and purification by silica gel column chromatography (6:1 petrol:EtOAc), the sulfides **8** and **9** were obtained as a inseparable mixture (130mg, 50%), υ_{max} ($CHCl_3$)/cm^{-1} 1585, 1482, 1448 (Ar), 1320, 1143 (SO_2) δ_H (250 MHz, $CDCl_3$) 1.57 (3H, d, *J* 4.5,

CH_3CH), 3.08 (2H, m, $PhSCH_2$), 3.22 (2H, m, CH_2SO_2Ph), 4.20 (1H, q, *J* 4.5, CH_3CH), 7.08–7.85 (20H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 15.8 (CH_3CH), 26.3 (CH_2SPh), 55.5 (CH_2SO_2Ph), 67.3 (CH_3CH), 127.1 (CH, Ar), 127.3 (C, Ar) 128.0 (CH, Ar), 128.5 (CH, Ar), 128.8 (CH, Ar), 128.9 (CH, Ar), 129.2 (CH, Ar), 129.3 (CH, Ar), 129.5 (CH, Ar), 129.8 (C, Ar), 130.0 (CH, Ar), 133.2 (CH, Ar), 133.8 (CH, Ar), 133.9 (CH, Ar), 135.4 (C, Ar), 138.4 (C, Ar); *m/z* (EI) 278 (M^+, 46%), 136 (M–H–SO_2Ph, 100), 109 (PhS^+, 91) (Found 278.0430. $C_{14}H_{14}O_2S_2$ requires M, 278.0401).

(13) Following the above general procedure with methylene ketone **11** (80mg, 0.5mmol), phenylsilane (0.31cm^3, 2.5mmol), diphenyl disulfide (0.55g, 2.5mmol) and Co(eobe) (20mg, 0.05mmol). After reflux for 64h, evaporation of solvent and purification by silica gel column chromatography (20:1 petrol:EtOAc), the sulfide **13** was obtained as a clear oil (60mg, 45%), υ_{max} ($CHCl_3$)/cm^{-1} 1729 (C=O), 1702 (C=O), 1460 (Ar); δ_H (250 MHz, $CDCl_3$) 1.22 (3H, t, *J* 7.1, CH_2CH_3), 1.61 (3H, s, CH_3), 2.39 (3H, s, $COCH_3$), 2.59 (1H, d, *J* 16.5, $CHHCO_2Et$), 2.94 (1H, d, *J* 16.5, $CHHCO_2Et$), 4.08 (2H, q, *J* 7.1, CH_2CH_3), 7.32–7.40 (5H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 14.1 (CH_3), 21.9 (CH_3), 24.5 ($COCH_3$), 41.9 (CH_2), 56.7 (C), 60.7 (CH_2), 129.0 (CH, Ar), 129.6 (C, Ar), 129.9 (CH, Ar), 137.0 (CH, Ar), 170.3 (CO_2CH_2), 203.3 ($COCH_3$); *m/z* (EI) 266 (M^+, 1%), 223 (M–COMe, 3), 138 (8), 109 (PhS^+, 5), 83 (100) (Found 266.0953. $C_{14}H_{18}O_3S$ requires M, 266.0977).

(15)[12] Following the above general procedure with methyl methacrylate **14** (0.05cm^3, 0.5mmol), phenylsilane (0.31cm^3, 2.5mmol), diphenyl disulfide (0.55g, 2.5mmol) and Co(eobe) (20mg, 0.05mmol). After reflux for 16h, evaporation of solvent and purification by silica gel column chromatography (20:1 petrol:EtOAc), the sulfide **15** was obtained as a clear oil (48mg, 60%), υ_{max} ($CHCl_3$)/cm^{-1} 1727 (C=O), 1580, 1462 (Ar); δ_H (250 MHz, $CDCl_3$) 1.50 (6H, s, CH_3), 3.87 (3H, s, CO_2CH_3), 7.30–7.40 (3H, m, ArH), 7.45–7.50 (2H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 25.9 (CH_3), 52.3 (CO_2CH_3), 128.7 (CH, Ar), 129.5 (CH, Ar), 136.8 (CH, Ar), 174.5 (CO_2Me); *m/z* (EI) 210 (M^+, 11%), 151 (M–CO_2Me, 52), 135 (M–CO_2Me–Me, 6), 121 (21), 109 (PhS^+, 91) (Found 210.0725. $C_{11}H_{14}O_2S$ requires M, 210.0715).

(17) Following the above general procedure with methylene ester **16** (95mg, 0.5mmol), phenylsilane (0.31cm^3, 2.5mmol), diphenyl disulfide (0.55g, 2.5mmol) and Co(eobe) (20mg, 0.05mmol). After reflux for 6h, evaporation of solvent and purification by silica gel column chromatography (40:1 petrol:EtOAc), the sulfide **17** was obtained as a clear oil (100mg, 67%), υ_{max} ($CHCl_3$)/cm^{-1} 1716(C=O), 1604, 1583, 1455 (Ar) δ_H (250 MHz, $CDCl_3$) 1.20 (3H, t, *J* 7.1, CH_3), 1.34 (3H, s, CH_3), 2.91 (1H, d, *J* 13.3, $CHHAr$), 3.45 (1H, d, *J* 13.3, $CHHAr$), 4.09 (2H, q, *J* 7.1, CO_2CH_2), 7.16–7.52 (10H, m, ArH); δ_C (67.5 MHz, $CDCl_3$) 14.0 (CH_3), 22.2 (CH_3), 44.3 (CH_2Ar), 55.3 (C), 61.1 ($CO_2CH_2CH_3$), 126.8 (CH, Ar), 128.1 (CH, Ar), 128.6 (CH, Ar), 129.4 (CH, Ar), 130.4 (CH, Ar), 130.9 (C, Ar), 136.5 (C, Ar), 137.0 (CH, Ar), 172.6 (CO_2Et); *m/z* (EI) 300 (M^+, 40%), 227 (M–CO_2Et, 14), 209 (M–CH_2Ph, 100), 163 (M–CH_2Ph–HOEt, 23), 137 (M–CH_2Ph–CO_2Et, 8), 135 (38), 117 (M–SPh–CO_2Et, 25), 109 (PhS^+, 17), 91($ArCH_2^+$, 53) (Found 300.1187. $C_{18}H_{20}O_2S$ requires M, 300.1184).

Unsaturated ketoester 19

Ethyl acetoacetate (1cm^3, 8mmol) was added dropwise to a stirred solution of NaH (200mg, 8.1mmol) in DMF (30cm^3) under N_2. The reaction mixture was stirred for 15 min and then 1-bromo-5-pentene (1.1cm^3, 8.1mmol) added. The solution was heated to reflux for 24h before cooling and quenching with H_2O (20cm^3). The crude material was extracted with CH_2Cl_2 (3 × 20cm^3), washed once with H_2O (20cm^3), dried over $MgSO_4$, filtered and evaporated. Purification by silica gel column chromatography (15:1/petrol:EtOAc) gave the desired alkylated product **19** (1.13g, 71%) as a clear oil, υ_{max} ($CHCl_3$)/cm^{-1} 1732, 1694 (C=O), 1643 (C=C); δ_H (250 MHz, $CDCl_3$), 1.28 (3H, t, *J* 7.1, CH_3), 1.38 (2H, m, CH_2), 1.85 (2H, m, CH_2), 2.08 (2H, q, *J* 7.2, $CH_2CH=CH_2$), 3.41 (1H, t, *J* 7.2, COC*H*CO), 4.20 (2H, q, *J* 7.1, $CO_2CH_2CH_3$), 4.99 (2H, m, CH_2=CH), 5.78 (1H, m, CH_2=C*H*;); δ_C (67.5 MHz, $CDCl_3$) 13.8 ($CO_2CH_2CH_3$), 26.2 (CH_2), 27.3 (CH_2), 28.4 (CH_3CO), 33.1 (CH_2), 59.4 (CO*C*HCO), 60.9 ($CO_2CH_2CH_3$), 114.7 ($CH=CH_2$) 137.6 ($CH=CH_2$), 168.5 (CO_2Et), 202.7 (CH_3CO); *m/z* (EI) 198 (M^+, 3%), 169 (M–Et, 17), 156 (M–MeCO, 100), 153 (M–HOEt, 11), 143 (59), 130 (M–$(CH_2)_3CH=CH_2$, 66), 110 (M–MeCO–OEt, 23), 101 (67) (Found 198.1259. $C_{11}H_{18}O_3$ requires M, 198.1256).

Exo-methylene ester 20

The dicarbonyl compound **19** (1.75g, 8.8mmol) was added to a stirred solution of LDA (8.8 mmol - made from 1.6M BuLi and $^iPr_2NH$) in THF (35cm^3) at -78°C under N_2. After 10 min the solution was allowed to warm to room temperature and excess paraformaldehyde (1.2g) added. The solution was heated to reflux overnight, and then cooled and quenched with aq $NaHCO_3$ solution (20cm^3). The crude material was then extracted with CH_2Cl_2 (3 × 20cm^3), dried over $MgSO_4$, filtered and evaporated. Purification by silica gel column chromatography (10:1/petrol:EtOAc) gave the desired unsaturated ester **20** as a clear oil (0.93g, 63%), υ_{max} ($CHCl_3$)/cm^{-1} 1713 (C=O), 1626 (C=C); δ_H (250 MHz, $CDCl_3$), 1.30 (3H, t, *J* 7.1, CH_3), 1.57 (2H, qu, *J* 7.0, CH_2), 2.08 (2H, q, *J* 7.0, $CH_2CH_2CH=CH_2$), 2.31 (2H, t, *J* 7.0, CH_2), 4.21 (2H, q, *J* 7.1, $CO_2CH_2CH_3$), 4.99 (2H, m, CH=CH_2), 5.51 (1H, s, CH*H*=C), 5.78 (1H, m, C*H*=CH_2), 6.14 (1H, s, C*H*H=C); δ_C (67.5 MHz, $CDCl_3$) 14.2 ($CO_2CH_2CH_3$), 27.6 (CH_2), 31.3 (CH_2), 33.2 (CH_2), 60.5 ($CO_2CH_2CH_3$), 114.7 ($CH=CH_2$), 124.4 (CH_2=C), 138.3 (CH_2=*CH*), 140.8 (CH_2=*C*), 167.2 (CO_2Et); *m/z* (EI) 168 (M^+, 2%), 153 (M–Me, 6), 139 (M–Et, 6), 123 (M–OEt, 7), 99 (M–$(CH_2)_3CH=CH_2$, 8), 95 (33), 69 (100) (Found 168.11567. $C_{10}H_{16}O_2$ requires M, 168.11504).

Cyclisation–oxidation of 20 to give sulfone 21

Phenyl silane (1.6cm^3, 12.5mmol) and diphenyl disulfide (1.0g, 5mmol) were added successively to a solution of the methylene ester **20** (420mg, 2.5mmol) and Co(eobe) (100mg, 0.25mmol) in benzene (25cm^3). The mixture was then heated to reflux overnight after which time the solvent was evaporated under reduced pressure. Purification of the resulting oil by silica gel column chromatography (40:1 petrol:EtOAc) gave the desired 5-*exo*-trig cyclised product (146mg, 21%) which was found to be contaminated with inseparable by-products.

For conversion to the sulfone, oxone® (464mg, 0.76mmol) in water (6cm^3) was added to a stirred solution of the cyclised sulfide obtained as described above (123mg, 0.52mmol) in THF (7cm^3) at 0°C. After stirring the reaction mixture overnight the products were extracted into CH_2Cl_2 (3 × 5cm^3), dried over $NaSO_4$, filtered and evaporated. The resulting oil was then purified by silica gel column chromatography to

give a 1:1 mix of cis/trans isomers of the cyclised product **21** as colourless crystals (140mg, 65%), Mp 92–93°C, (Found. C, 61.68; H, 7.18. $C_{16}H_{22}O_4S$ requires C, 61.91; H, 7.14%); υ_{max} ($CHCl_3$)/cm^{-1} 1713 (C=O), 1587, 1482, 1462 (Ar), 1320, 1124 (SO_2).

Less polar isomer δ_H (500 MHz, $CDCl_3$) 1.20 (3H, s, CCH_3), 1.22 (3H, t, *J* 7.2, CH_3), 1.48 (1H, m), 1.54–1.60 (2H, m), 1.67 (1H, m), 1.75 (1H, m), 2.07–2.19 (3H, m), 3.17 (1H, dd, *J* 10.2, 14.1, $CHHSO_2Ph$), 3.30 (1H, dd, *J* 1.7, 14.1, $CHHSO_2Ph$), 4.05–4.10 (2H, m, $CO_2CH_2CH_3$), 7.58 (2H, t, *J* 7.8, ArH), 7.66 (1H, t, *J* 7.8, ArH), 7.92 (2H, d, *J* 7.8, ArH); δ_C (67.5 MHz, $CDCl_3$) 14.1 (CH_3), 22.4 (CH_3), 22.9 (CH_2), 31.0 (CH_2), 37.3 (CH_2), 44.5 (CH), 52.8 (C), 58.0 (CH_2SO_2Ph), 58.9 ($CO_2CH_2CH_3$), 127.0 (CH, Ar), 129.2 (CH, Ar), 133.6 (CH, Ar), 139.7 (C, Ar), 175.7 (CO_2Et).

More polar isomer δ_H (400 MHz, $CDCl_3$) 1.04 (3H, s, CCH_3), 1.17 (3H, t, *J* 7.2, $CO_2CH_2CH_3$), 1.46-1.76 (4H, m), 2.04 (1H, m), 2.23 (1H, m), 2.57 (1H, m), 2.98 (1H, dd, *J* 11.1, 13.8, $CHHSO_2Ph$), 3.43 (1H, dd, *J* 2.6, 13.8, $CHHSO_2Ph$), 4.01-4.06 (2H, t, *J* 7.2, $CO_2CH_2CH_3$), 7.58 (2H, t, *J* 8.0, ArH), 7.65 (1H, t, *J* 8.0, ArH), 7.92 (2H, d, *J* 8.0, ArH); δ_C (67.5 MHz, $CDCl_3$) 14.5 (CCH_3), 18.3 ($CO_2CH_2CH_3$), 22.4 (CH_2), 30.2 (CH_2), 37.4 (CH_2), 41.0 (CH), 51.9 (C), 58.5 (CH_2SO_2Ph), 61.0 ($CO_2CH_2CH_3$), 128.3 (CH, Ar), 129.6 (CH, Ar), 134.0 (CH, Ar), 140.0 (C, Ar), 176.8 (CO_2Et); *m/z* (EI) 310 (M^+, 4%), 265 (M–OEt, 24). 169 (M–SO_2Ph, 80), 95 (M–SO_2Ph–CO_2Et, 95) (Found 310.1223. $C_{16}H_{22}O_4S$ requires M, 310.1239).

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