Pergamon

Tetrahedron Vol. 50, No. 31, pp. 9365-9376, 1994

0040-4020/94 $7.00+0.00

0040-4020(94)00532-X

Allylation with Pummerer-generated Substituted Vinylthionium Ions

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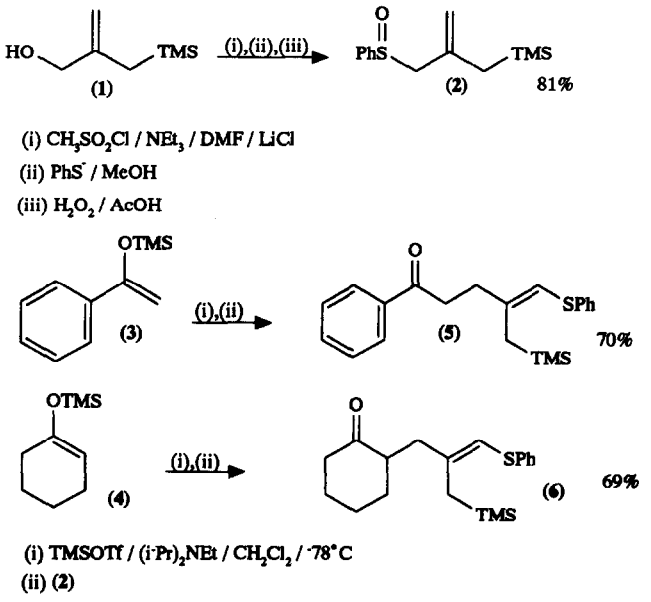
Abstract: Pummerer-derived substituted vinylthionium ions (allyl phenyl sulfoxide, TMSOTf, EtN(i-Pr)$_2$, CH_2Cl_2, -78°C) with a β-trimethylsilylmethyl (2), γ-phenyl (14), or γ-phenylthio (15) group allylate the enol silyl ethers of acetophenone (3) and cyclohexanone (4) in good yield. Allylation with (14) and (15) required slow addition of base in order to limit the rate of production of intermediate, and thus avoid unwanted sila-Pummerer type products. Hünigs's base conjugate addition was not observed in these cases. Both the (E)- and (Z)- forms of allyl sulfoxide (15) were shown to equilibrate to the (E)-transoid conformer prior to allylation resulting in exclusive (E)-vinyl sulfide formation. Blocking of the γ-position resulted in preferential α- attack.

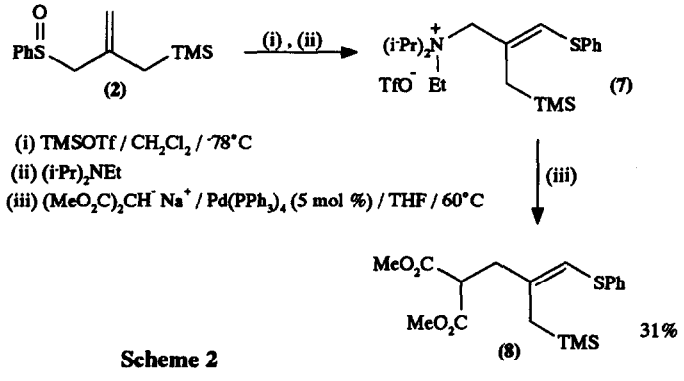
We have recently reported[1] that Pummerer-generated vinylthionium[2-9] ions from allylic sulfoxides using TMSOTf and Hunig's base readily alkylate enol silyl ethers in CH_2Cl_2 at -78°C. It was established that while masked Michael adducts were obtained in good yield from allyl phenyl sulfoxide and 2-methallyl phenyl sulphoxide, substitution by methyl at the α- or γ- positions of the vinylthionium intermediate resulted in competitive Hunig's base interception, and deprotonation to the diene, respectively, as side reactions.
In this paper we report on alternative β- and γ- substituted vinylthionium ions that may be generated using the Pummerer conditions and explore the chemistry of some of the products.

With the aim of developing its bifunctional chemistry, the reagent (2)[10] was prepared by thiophenoxide substitution and oxidation of Trost's 2-trimethylsilylmethylallyl alcohol (1)[11]. It was then reacted separately with the representative enol silyl ethers (3) and (4) used throughout this study of acetophenone and cyclohexanone respectively, under the Pummerer conditions described previously (TMSOTf, EtN(i-Pr)$_2$, CH_2Cl_2, -78°C). The masked Michael adducts (5) and (6) were obtained as (Z)-isomers exclusively in respectable yields of 70 and 69% respectively after column chromatography. Scheme 1.



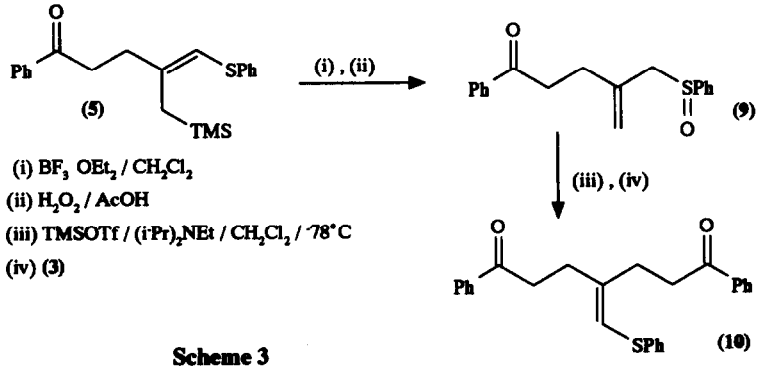
Scheme 1

Similarly, the bifunctional reagent (2) underwent masked Michael addition with dimethyl malonate using the Pd(0) catalysed allylic substitution variation described previously[1]. Accordingly, reaction of (2) with Hünig's base and TMSOTf in the absence of any enol silyl ether produced the Hünig's base salt (7) which could not be purified. Reaction of (7) with dimethyl sodiomalonate in the presence of a catalytic amount of $Pd(PPh_3)_4$ in THF at room temperature furnished the addition product (8) in 31% overall yield as its (Z) isomer exclusively. It is interesting to note in this instance with Hünig's base as the leaving group, that the (π-allyl) palladium complex does not desilylate to a zwitterionic intermediate similar to that derived from Trost's[12] annulating agent based on 2-trimethylsilylmethylallyl acetate. This may be accounted for by the poor nucleophilicity of the Hünig's base as well as the mild reaction conditions possible for generating the π-allyl complex owing to sulfur assistance in vinylthionium generation. Scheme 2.



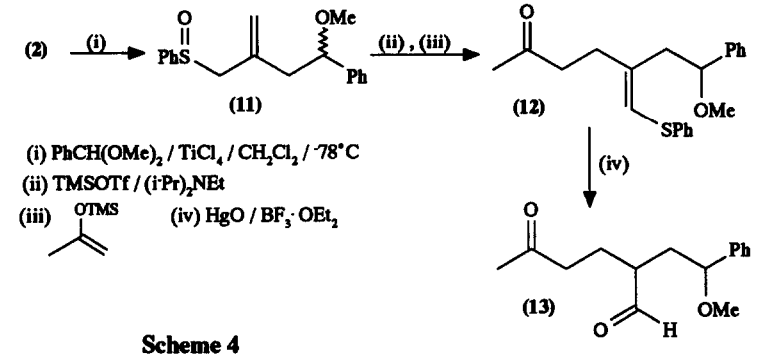
Scheme 2

Bifunctional reagent (2) could also be used to synthesise other β-substituted allyl phenyl sulfoxides for use in this study via protiodesilylation or dissociative electrophilic substitution. For instance, masked Michael adduct (5) underwent protiodesilylation followed by oxidation to the β-substituted sulfoxide (9) in 50% overall yield. Chemoselective masked Michael addition with (3) then furnished the 1,7-dione (10) in 65% yield. Unfortunately, the allylsilane of (5) and (6) (see Scheme 1) bearing a phenylthio substituent at the terminus of the double bond was deactivated towards dissociative electrophilic substitution with the normal partners, e.g acetals. Furthermore, it could not be cyclised onto the carbonyl group using $TiCl_4$, a reaction which has literature precedent[13] for the vinyl ether analogue. Scheme 3.



Scheme 3

Similarly, the allyl silane of the original bifunctional reagent (2), although generally disappointingly unreactive[14], did react with simple acetals such as those of propanal and benzaldehyde. Thus, reaction of (2) with benzaldehyde dimethyl acetal and $TiCl_4$ gave the β-substituted allyl phenyl sulfoxide (11) in 92% yield which underwent masked Michael addition with the enol silyl ether of acetone to give the vinyl sulfide (12) in 43% isolated yield as one geometrical isomer; δ_H = 6.00 ppm for the vinyl proton in the ^1H NMR and assigned as (Z). Compound (12) could be hydrolysed[15] ($HgO/BF_3{\cdot}OEt_2$) to the aldehyde (13) in 98% yield. Scheme 4.

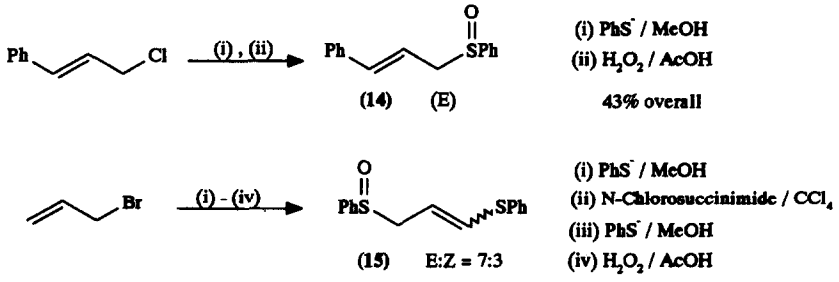


Scheme 4

Thus, these reactions establish the compatibility of various β-substituents with the Pummerer conditions for masked-Michael addition reactions proceeding via vinylthionium ions.

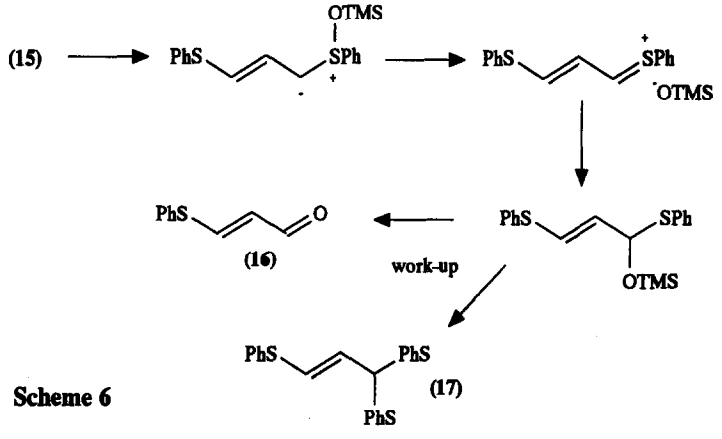
In order to extend the methodology to vinylthionium ions with γ-substituents other than methyl, the groups phenyl and phenylthio were chosen for the following reasons: they involved synthetically accessible

starting materials (preferred to the vinyl ether analogue of (15)), would introduce the question of regioselectivity and could not result in vinylthionium ion destruction by deprotonation. (E)-1-Phenyl-3-phenylsulfinylprop-1-ene (14) was prepared in two steps in 38% overall yield from (E)-cinnamyl chloride by thiophenoxide substitution followed by hydrogen peroxide (1 equivalent) oxidation in glacial acetic acid. The latter method proved to be the one of choice for sulfide to sulfoxide oxidations throughout this work. (14) was a stable crystalline solid at room temperature. 3-Phenylsulfinyl-1-phenylthiopropene (15) was readily prepared by thiophenoxide substitution and chemoselective oxidation of 3-chloro-1-phenylthiopropene, itself prepared as a 9:1 E:Z mixture by Pummerer-type chlorination[8] of allyl phenyl sulfide with N-chlorosuccinimide. (15) was obtained in 50% overall yield from allyl bromide as a 7:3 ratio of E:Z isomers as estimated by ^{1}H NMR. The change in E:Z ratio was attributed to acid-catalysed isomerisation during the oxidation. (15) was an oil, stable indefinitely at 0°C. Scheme 5.



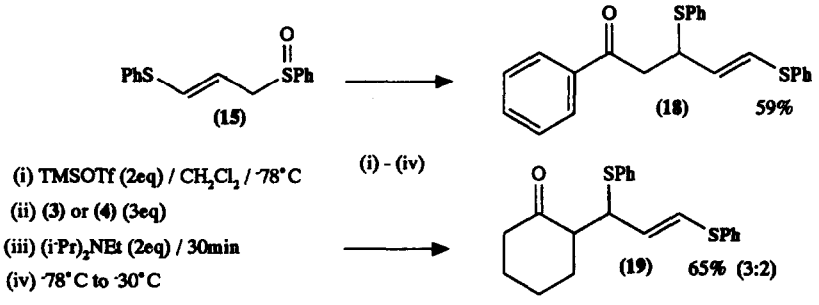
Scheme 5

Initially, reaction of (15) with the enol silyl ether (3) gave poor results. Use of the normal conditions; enol silyl ether (1.5 equivalents), TMSOTf (1 equivalent), Hünig's base (1 equivalent) and addition of the allyl sulfoxide (1 equivalent) last, gave the masked Michael adduct (18) in only 22% yield. The by-products were identified as (E)-3-phenylthioprop-2-enal (16) and (E)-1,3,3-tris(phenylthio)propene (17) and were obtained exclusively ((16) : (17) = 61:39) in the absence of enol silyl ether. Since none of the undesirable Hünig's base interception product was observed, one may conclude that steric congestion at the γ-position of the vinylthionium ion results in promotion of the by-products via a sila-Pummerer type mechanism[16] as depicted in Scheme 6.



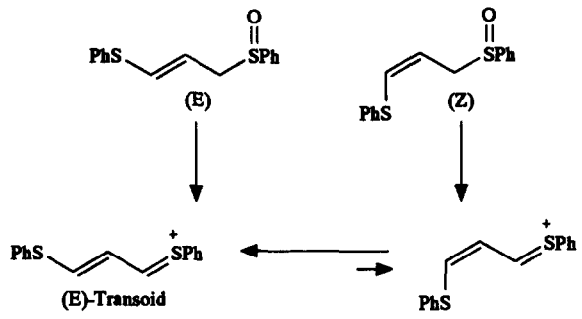
Scheme 6

Similarly, a low yield (17%) of the masked Michael adduct (19) was obtained with the enol silyl ether (4) along with the by-products (16) and (17). However, a systematic study of the stoichiometry, order and rate of addition of reagents succeeded in raising the yields of (18) and (19) to 59% and 65% respectively. The optimum reaction conditions were found to be addition of the allyl sulfoxide (15) (1eq.), TMSOTf (2eq.) and enol silyl ether (3 eq.) in that order at -78°C, followed by slow addition of the base (2eq.) over 30 minutes and warming the reaction to -30°C. These experimental conditions limit the rate of production of the vinylthionium ion intermediate and ensure that its concentration always remains low in comparison to the enol silyl ether, thus favouring addition over rearrangement. The γ-substituted vinylthionium ion from (15) constitutes an electrophilic equivalent to the carbanionic versions of Corey[17] and Cohen[18]. Scheme 7.



Scheme 7

Both masked Michael adducts (18) and (19) were obtained as pure (E)-isomers indicating configurational equilibration of the vinylthionium intermediate, derived from the 7:3 E:Z mixture of starting sulfoxide (15), to the more stable transoid (E)-form. Scheme 8. This thermodynamic equilibration, preceding Michael addition, operated with all of the γ-substituted vinylthionium ions studied to give (E)-vinyl sulfide products exclusively.



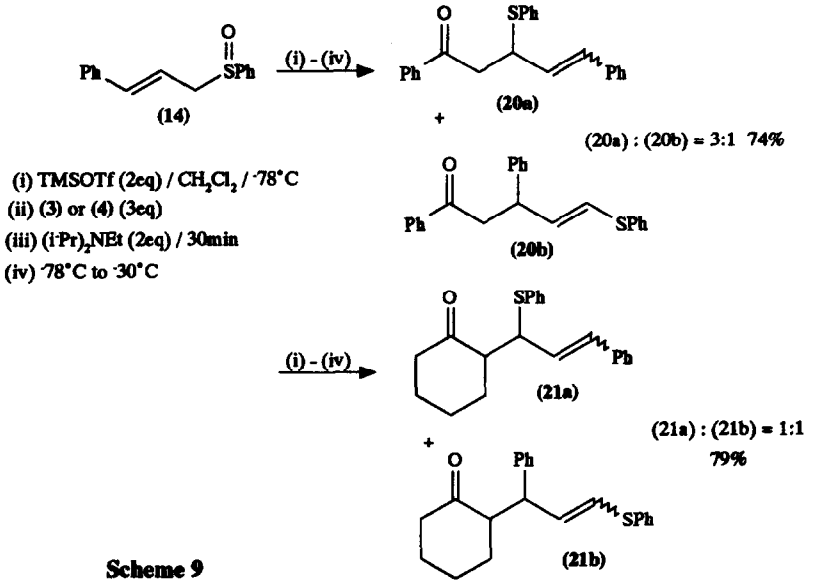
Scheme 8

A further consequence of the aforementioned equilibration was that the diastereoselectivity in formation of (19) as (3:2) was independent of the ratio of E/Z isomers present in sulfoxide (15). This was established by using a sample of (15) from medium pressure chromatography enriched in the (E)-isomer (8:1).

The low level of diastereoselection (3:2) is understandable when one considers the anti- and syn- extended transition state structures involving the (E)-transoid vinylthionium intermediate. It is clear that neither set of non-bonded interactions significantly favour either one of the transition states, and this is consistent with recent work on the diastereoselectivity aspects of additions to thionium ions reported by Heathcock[19].

Similarly, using the optimum conditions for addition described, the γ-phenyl sulfoxide (**14**) was reacted independently with enol silyl ethers (**3**) and (**4**) to give the addition products (**20**) and (**21**) in respectable yields of 74% and 79% respectively. (**20**) was obtained as a (3:1) mixture of chromatographically inseparable α:γ adducts (**20a,b**) reflecting the greater steric impedance by the phenyl substituent compared to the phenylthio group. Isomers (**20a,b**) could be readily distinguished by 200 MHz ^{1}H NMR. The masked Michael vinyl sulfide (**20b**) was obtained exclusively as an (E)-isomer (J = 15.8 Hz) as before. Similarly, (**21**) was obtained as a chromatographically inseparable (1:1) mixture of α:γ adducts (**21a,b**) both as a 1:1 mixture of diastereomers. However, in this case the geometry of the double bond of the vinyl sulfide (**21b**) could not be unequivocally assigned as (E)- owing to the complexity of the ^{1}H NMR spectrum of the mixture. Scheme 9. The preference for α-regioselectivity in the formation of (**20a,b**) is consistent with recent studies[3] of enol silyl ether addition to fluoroalkyl-substituted vinylthionium ions which utilised our methodology to give the corresponding α-adducts in good yields.

In conclusion, the present study on substituted vinylthionium ions confirms our earlier findings regarding the strength and limitations of the methodology. A β-trimethylsilylmethyl group stabilises the vinylthionium intermediate via inductive and hyperconjugative effects and survives the reaction conditions. Groups at the γ-position with no hydrogens at the δ-carbon, such as phenyl and phenylthio, eliminate the Hünig's base conjugate interception side reaction, although attention must be paid to the order and rate of addition of the reactants to avoid unwanted sila-Pummerer type side reactions. Moreover, blocking of the



Scheme 9

γ-position, results in preferential α-attack. γ-Substituted (E)- and (Z)-allyl sulfoxides have been shown to equilibrate to one (E)-transoid vinylthionium intermediate resulting in exclusive formation of (E)-vinyl sulfides from γ-addition products. This useful result shows promise for linking up with Ni(0) catalysed cross-coupling methodology for overall stereo-defined functionalised olefin synthesis. In the following paper, methodology involving $SnCl_4$ ionisation of substituted 3,3- and 1,3-bis(aryl- and alkylthio)propenes for efficient generation of substituted vinylthionium ions inaccessible using the Pummerer methodology, is described.

Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. I.r spectra were recorded on a Pye Unicam SP-300 spectrophotometer as 50 $mg.ml^{-1}$ solutions in $CHCl_3$ or CH_2Cl_2 and low resolution mass spectra on either a Finnegan-MAT 8200 or AEI MS9 spectrometer. High resolution mass spectra were obtained on a Varian MAT-212 spectrometer from the CSIR, Pretoria. ^1H and ^{13}C n.m.r. spectra were recorded on a Bruker AC-200 (200 MHz) spectrometer. Tetramethylsilane was used as standard and deuteriochloroform used as solvent in all cases. Elemental analyses were obtained from the CSIR, Pretoria.

All solvents were purified before use. In particular, tetrahydrofuran was distilled from sodium-benzophenone directly into the reaction flask. Column chromatography was performed using Merck Kieselgel 60 (70-230 mesh) with wet packed columns, while flash chromatography utilised dry-packed columns of Merck Kieselgel 60 (0.015-0.04 mm particle size). The enol silyl ether of acetone was prepared by Fleming's method[20] and those of acetophenone (**3**) and cyclohexanone (**4**) by the method of Dunogues[21] with chlorotrimethylsilane, triethylamine and sodium iodide in dry acetonitrile/hexane. 2-Trimethylsilylmethylallyl alcohol (**1**) was prepared by Trost's procedure[11]. (E)-1-Phenyl-3-phenylsulfinylprop-1-ene (**14**)[22] was made by thiophenoxide substitution and oxidation (H_2O_2/AcOH) of (E)-cinnamyl chloride. (E)-3-phenylthioprop-2-enal[23] (**16**) was prepared by α-chlorination/elimination of 3-phenylthiopropanal.

a) *2-Methylene-3-trimethylsilylpropyl phenyl sulfoxide* (**2**).

To a stirred solution of 2-trimethylsilylmethylallyl alcohol (**1**) (2.88g, 20 mmol) in dry DMF (10 ml) at 0°C were added dry triethylamine (3.1 ml, 22 mmol), methanesulfonyl chloride (1.7 ml, 22 mmol) and dry lithium chloride (1.06 g, 25 mmol), and the mixture left to warm to room temperature overnight. A solution of thiophenol (2.46 ml, 24 mmol) and potassium hydroxide (1.35 g, 24 mmol) in deoxygenated methanol (10 ml) was added slowly and the solution left stirring for a further 10 h. The mixture was poured into aqueous potassium hydroxide solution (100 ml of a 0.1 M solution) and extracted with hexane (3 x 50 ml). The combined extracts were dried ($MgSO_4$) and the solvent evaporated to furnish an oil which was chromatographed (hexane) to give 2-methylene-3-trimethylsilylpropyl phenyl sulfide (3.5g, 74%) as a clear oil; ν_{max} (CCl_4) 1620, 1580, 1475, 1435, 1270 and 855 cm^{-1}; δ_H 0.00 (9H, s), 1.68 (2H, s), 3.44 (2H, s), 4.60 (1H, s), 4.74 (1H, s), 7.13-7.33 (5H, m); δ_C -1.4, 25.1, 42.5, 111.3, 126.1, 128.7, 129.9, 136.6, 142.4; *m/z* 236 (M^+, 54), 221 (30), 168 (34), 131 (86), 130 (50), 73 (100), 45 (26).

To a solution of 2-methylene-3-trimethylsilylpropyl phenyl sulfide (1.01g, 4.3 mmol) in glacial acetic acid (15ml) at 10°C was added hydrogen peroxide (0.6 ml of an 8.8 M solution in water, 5.3 mmol). The solution was stirred at room temperature for 8 h and then poured into water (50 ml) and extracted with dichloromethane (3 x 50 ml). The combined organic layers were washed with a KOH solution (100 ml of 0.1 M solution, 10 mmol), dried ($MgSO_4$) and evaporated to give an oil which was chromatographed

(hexane:EtOAc 8:2) to furnish pure (**2**) (0.87g, 3.5 mmol, 81%) as a clear oil; ν_{max} ($CHCl_3$) 1625, 1585, 1475, 1440, 1245, 1030 and 840 cm^{-1}; δ_H -0.03 (9H, s), 1.54 (2H, dd, *J* 1.0 and 6.4 Hz), 3.25 (1H, dd, *J* 0.8 and 12.3 Hz), 3.47 (1H, dd, *J* 0.8 and 12.3 Hz), 4.71 (1H, q, *J* 0.8 and 1.0 Hz), 4.80 (1H, q, *J* 1.0 Hz), 7.42-7.48 (3H, m), 7.54-7.60 (2H, m); δ_C -1.5, 26.9, 67.6 115.6, 124.2, 129.0, 131.0, 136.5, 143.9; *m/z* 252 (M^+, 5), 237 (7), 198 (49), 131 (24), 99 (19) and 73 (100); HRMS *m/z* calcd. for $C_{12}H_{17}OSSi$ (M^+-CH_3) 237.0763, found 237.0763.

b) *(Z)-1-Phenyl-5-phenylthio-4-trimethylsilylmethylpent-4-en-1-one* (**5**).

The bifunctional reagent (**2**) (157 mg, 0.62 mmol) in dichloromethane (2 ml) was added slowly to a stirred solution of 1-phenyl-1-trimethylsilyloxyethene (**3**) (147 mg, 0.77 mmol), diisopropylethylamine (0.15 ml, 0.86 mmol) and TMSOTf (0.15 ml, 0.78 mmol) in dichloromethane (3 ml) at -78 °C. After 30 mins the reaction was poured into saturated sodium hydrogen carbonate solution (25 ml) and extracted with dichloromethane (3 x 25 ml). Drying ($MgSO_4$), evaporation of solvent and chromatography (hexane:EtOAc 9:1) of the residue gave (**5**) (155 mg, 0.44 mmol, 70%) as a colourless oil; ν_{max} (CCl_4)1675, 1595, 1570, 1465, 1435, 1240 and 845 cm^{-1}; δ_H 0.02 (9H, s), 1.80 (2H, s), 2.48 (2H, t, *J* 7.6 Hz), 3.05 (2H, t, *J* 7.6 Hz), 5.71 (1H, s), 6.96-7.15 (5H, m), 7.25-7.49 (3H, m), 7.76-7.91 (2H, m); δ_C -0.7, 24.1, 32.9, 36.9, 112.3, 125.3, 127.5, 127.9, 128.5, 128.7, 133.0, 136.7, 137.5, 144.5, 199.0; *m/z* 354 (M^+, 21), 264 (29), 244 (39), 155 (50), 73 (100); HRMS *m/z* calcd. for $C_{21}H_{26}OSSi$ 354.1474, found 354.1474.

c) *(Z)-2-(3-Phenylthio-2-trimethylsilylmethylallyl)cyclohexanone* (**6**).

To a stirred solution of 1-trimethylsilyloxycyclohexene (173 mg, 1.02 mmol) in dichloromethane (3 ml) at -78 °C were added diisopropylethylamine (0.17 ml, 1 mmol), TMSOTf (0.19 ml, 1 mmol) and (**2**) (194 mg, 0.77 mmol) in dichloromethane (1 ml). After 30 mins at -78 °C the mixture was poured into aqueous sodium hydrogen carbonate (25 ml) and extracted with dichloromethane (3 x 25 ml). After drying ($MgSO_4$) of the combined extracts and evaporation of solvent, column chromatography (hexane:EtOAc 95:5) of the residue gave (**6**) as a clear oil (181 mg, 0.54 mmol, 69%); ν_{max} ($CHCl_3$) 1715, 1585, 1480, 1440, 1250 and 855 cm^{-1}; δ_H 0.03 (9H, s), 1.29 (1H, m), 1.60 (2H, m), 1.61 (2H, s), 1.73-2.20 (4H, m), 2.27-2.49 (3H, m), 2.67 (1H, dd, *J* 4.3 and 14.4 Hz), 5.72 (1H, s), 7.05-7.22 (5H, m); δ_C -0.4, 21.9, 23.2, 25.3, 27.2, 33.7, 38.8, 40.5, 112.7, 125.2, 127.4, 128.8, 138.2, 145.3, 212.0; *m/z* 332 (M^+, 8), 223 (19), 133 (25), 73 (100); HRMS *m/z* calcd. for $C_{19}H_{28}OSSi$ 332.1630, found 332.1632.

d) *Dimethyl (Z)-2-(3-phenylthio-2-trimethylsilylmethylallyl)propanedioate* (**8**).

To the bifunctional reagent (**2**) (112 mg, 0.44 mmol) in dichloromethane (3 ml) at 0 °C were added diisopropylethylamine (0.1 ml, 0.57 mmol) and TMSOTf (0.1 ml, 0.52 mmol) dropwise. After 10 mins the solvent was removed *in vacuo* to give an orange solid which was dissolved in dry THF (5 ml). To this solution was added tetrakis(triphenylphosphine)palladium(0) (20 mg, 0.02 mmol) resulting in a deep red colour. Dimethyl sodiomalonate, prepared as a solution in THF (2 ml) from dimethyl malonate (270 mg, 2 mmol) and sodium hydride (70 mg of a 60% dispersion in mineral oil, 1.8 mmol), was then added. The solution was refluxed for 1 hour, quenched with water (30 ml) and extracted with dichloromethane (3 x 30 ml). Drying ($MgSO_4$), evaporation of solvent and chromatography (hexane:EtOAc 9:1) gave (**8**) (50 mg, 0.14 mmol, 31% based on bifunctional reagent) as a colourless oil; ν_{max} ($CHCl_3$) 1730, 1580, 1480, 1435 and 855 cm^{-1}; δ_H 0.00 (9H, s), 1.76 (2H, s), 2.65 (2H, dd, *J* 1.0 and 7.8 Hz), 3.60 (1H, t, *J* 7.8 Hz), 3.64 (6H, s), 5.76 (1H, d, *J* 1.0 Hz), 6.98-7.21 (5H, m); δ_C -0.7, 23.8, 37.4, 50.2, 52.6, 114.9, 125.6, 127.8, 128.8, 137.2, 140.7, 169.2; *m/z* 366 (M^+, 14), 334 (14), 276 (19), 161 (23), and 73 (100); HRMS *m/z* calcd. for $C_{18}H_{26}O_4SSi$

366.1321, found 366.1320.

e) *1-Phenyl-4-phenylsulfinylmethylpent-4-en-1-one* (**9**).

Compound (**5**) (235 mg, 0.66 mmol) in dichloromethane (2 ml) was added dropwise into a stirred solution of boron trifluoride etherate (0.2 ml, 1.6 mmol) in dry dichloromethane (5 ml) at room temperature. The deep red solution was stirred for half an hour and then quenched with water (30 ml). The aqueous solution was extracted with dichloromethane (3 x 50 ml), the combined extracts dried ($MgSO_4$) and evaporated. Chromatography (hexane:EtOAc 9:1) of the residue gave the allyl sulfide product (121 mg, 0.43 mmol, 65%) as an oil; ν_{max} ($CHCl_3$) 1660, 1635, 1590, 1575, 1470 and 1430 cm^{-1}; δ_H 2.63 (2H, t, *J* 7.5 Hz), 3.15 (2H, t, *J* 7.5 Hz), 3.60 (2H, s), 4.86 (1H, d, *J* 1.2 Hz), 4.93 (1H, d, *J* 0.9 Hz), 7.17-7.37 (5H, m), 7.41-7.56 (3H, m), 7.93-7.98 (2H, m); δ_C 28.7, 36.8, 40.8, 113.6, 126.3, 128.0, 128.5, 128.7, 130.1, 133.0, 136.1, 136.8, 143.4, 199.2; *m/z* 282 (M^+, 52), 173 (53), 105 (100), 91 (21), and 77 (53). This was then oxidised with hydrogen peroxide (0.06 ml of an 8.8 M solution in water, 0.53 mmol) in glacial acetic acid (5 ml) at 0°C. After stirring for 90 minutes at room temperature, the reaction was diluted with water (30 ml) and extracted with dichloromethane (3 x 30 ml). The combined organic extracts were washed with saturated sodium hydrogen carbonate solution (30 ml), dried and the solvent evaporated. Chromatography of the residue (hexane:EtOAc 7:3) gave (**9**) (98 mg, 0.33 mmol, 77%) as a colourless solid; ν_{max} ($CHCl_3$) 1680, 1640, 1600, 1580, 1445 and 1040 cm^{-1}; δ_H 2.53 (2H, t, *J* 7.3 Hz), 3.16 (2H, t, *J* 7.3 Hz), 3.49 (1H, d, *J* 12.7 Hz), 3.60 (1H, d, *J* 12.7 Hz), 4.95 (1H, d, *J* 0.6 Hz), 5.07 (1H, d, *J* 0.7 Hz), 7.42-7.57 (5H, m), 7.61-7.67 (3H, m), 7.93-7.98 (2H, m); δ_C 30.0, 36.3, 65.6, 117.9, 124.1, 127.8, 128.5, 128.9, 131.0, 133.0, 136.5, 137.7, 143.6, 198.6; *m/z* 298 (M^+, 7), 207 (22), 110 (48), 105 (100), 91 (42) and 77 (57).

f) *1,7-Diphenyl-4-phenylthiomethyleneheptane-1,7-dione* (**10**).

To a stirred solution of diisopropylethylamine (0.1 ml, 0.57 mmol), TMSOTf (0.1 ml, 0.52 mmol) and 1-phenyl-1-trimethylsilyloxyethene (**3**) (90 mg, 0.47 mmol) in dichloromethane (3 ml) at -78 °C was added the allyl sulfoxide (**9**) (92 mg, 0.31 mmol) in dichloromethane (2 ml). After 40 minutes the reaction was poured into saturated sodium hydrogen carbonate solution (30 ml) and extracted with dichloromethane (3 x 30 ml). Drying ($MgSO_4$), evaporation of solvent and chromatography (hexane:CH_2Cl_2 8:2) gave (**10**) (80 mg, 0.2 mmol, 65%) as a clear oil. Found: C, 77.18; H, 6.40. $C_{26}H_{24}O_2S$ requires C, 77.97; H, 6.04%; ν_{max} ($CHCl_3$) 1675, 1600, 1585, 1480 and 1450 cm^{-1}; δ_H 2.62 (4H, m), 3.09 (4H, m), 5.99 (1H, s), 7.07-7.19 (5H, m), 7.31-7.50 (6H, m), 7.84-7.91 (4H, m); δ_C 26.9, 31.1, 36.7, 36.7, 118.6, 126.0, 128.0, 128.1, 128.3, 128.5, 128.6, 128.9, 133.0, 133.1, 136.5, 136.6, 136.7, 142.9, 199.0, 199.3; *m/z* 400 (M^+, 8), 382 (25), 105 (100), 77 (29).

g) *4-Methoxy-4-phenyl-2-phenylsulfinylmethyl-1-butene* (**11**).

Titanium tetrachloride (1.0 ml of a 1.3 M solution, 1.3 mmol) was added to a solution of benzaldehyde dimethyl acetal (186 mg, 1.22 mmol) in dichloromethane (3 ml) at -78 °C under N_2 positive pressure. After 5 minutes, (**2**) (205 mg, 0.81 mmol) in dichloromethane (2 ml) was added dropwise. The solution was stirred at -78°C for 15 minutes and then quenched at -78°C with a saturated solution of aqueous sodium hydrogen carbonate (10 ml). The aqueous layer was extracted with dichloromethane (3 x 50 ml), the combined extracts dried ($MgSO_4$) and the solvent evaporated off. Chromatography (hexane:EtOAc 8:2) yielded (**11**) (225 mg, 0.75 mmol, 92%) as a clear oil consisting of two diastereomers in a 1:1 ratio; ν_{max} ($CHCl_3$) 1635, 1440, 1090, 1030 and 915 cm^{-1}; δ_H 2.38 (2H, m), 2.56 (2H, m), 3.18 (3H, s), 3.19 (3H, s), 3.39 (1H, dd, *J* 0.7, 12.5 Hz), 3.57 (1H, dd, *J* 0.7, 12.5 Hz), 3.52 (2H, s), 4.30 (1H, m), 4.30 1H, m), 4.89 (1H, d, *J* 0.8 Hz), 4.95 (1H, d, *J* 0.8 Hz), 5.05 (1H, d, *J* 1.2 Hz), 5.08 (1H, d, *J* 1.2 Hz), 7.25-7.36 (5H, m), 7.46-7.52 (3H, m),

7.56-7.64 (2H, m); δ_C 44.4, 44.7, 56.3, 56.4, 65.3, 65.6, 82.8, 82.9, 120.3, 120.7, 124.1, 124.1, 126.4, 126.4, 127.6, 127.6, 128.3, 128.3, 128.8, 128.9, 130.8, 130.9, 135.6, 135.9, 141.1, 141.1, 143.6, 143.7; *m/z* 268 (M^+-32, 3), 175 (15), 143 (100), 128 (37), 121 (40), 91 (14), 77 (15); HRMS *m/z* calcd. for $C_{17}H_{16}OS$ (M^+-CH_3OH) 268.0922, found 268.0922.

h) *(Z)-5-(2-Methoxy-2-phenethyl)-6-phenylthiohex-5-en-2-one* (12).

(11) (218 mg, 0.72 mmol) in dry dichloromethane (2 ml) was added slowly to a solution of 2-trimethylsilyloxypropene (274 mg, 2.1 mmol), diisopropylethylamine (0.4 ml, 2.3 mmol) and TMSOTf (0.4 ml, 2.2 mmol) in dry dichloromethane (3 ml) at -78°C under nitrogen. The solution was stirred at -78°C for 45 minutes and then quenched by the addition of water. Extraction with dichloromethane (3 x 25 ml) followed by washing with ice-cold aqueous HCl and $NaHCO_3$ solutions respectively, drying ($MgSO_4$) and evaporation of solvent gave a residue which was purified by column chromatography (hexane:EtOAc 9:1) to yield (12) (105 mg, 0.31 mmol, 43%) as a clear oil; ν_{max} ($CHCl_3$) 1705, 1580, 1455, 1435 amd 1095 cm^{-1}; δ_H 2.12 (3H, s), 2.38 (2H, m), 2.57 (2H, m), 2.61 (1H, dd, *J* 5.9, 13.6 Hz), 2.76 (1H, dd, *J* 8.0, 13.6 Hz), 3.20 (3H, s), 4.34 (1H, dd, *J* 5.9, 8.0 Hz), 6.0 (1H, s), 7.12-7.32 (5H, m), 7.32-7.35 (5H, m); δ_C 29.8, 31.6, 41.0, 41.6, 56.7, 82.7, 119.4, 125.9, 126.5, 127.6, 128.3, 128.3, 128.8, 136.7, 141.1, 141.5, 207.8; *m/z* 340 (M^+, 2), 308 (M^+-32, 1), 121 (100), 91 (8), 77 (11) and 43 (11); HRMS *m/z* calcd. for $C_{21}H_{24}O_2S$ 340.1497, found 340.1497.

i) *2-(2-Methoxy-2-phenethyl)-5-oxohexanal* (13).

The vinyl sulfide (12) (86 mg, 0.25 mmol) in THF (3 ml) was added to a solution of HgO (390 mg, 1.8 mmol) and BF_3-OEt_2 (0.25 ml, 2 mmol) in 15% aqueous THF (5 ml). The resulting mixture was stirred at room temperature for 1 h, then poured into a mixture of water (25 ml) and dichloromethane (25 ml). The layers were separated and the aqueous phase extracted with dichloromethane (2 x 25 ml). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure to leave a residue which was purified by column chromatography (hexane:EtOAc 7:3) to give the aldehyde (13) (62 mg, 0.25 mmol, 100%) as a clear oil consisting of 2 diastereomers in a 1:1 ratio; ν_{max} ($CHCl_3$) 1710, 1450, 1380 and 1100 cm^{-1}; δ_H 1.57-2.66 (7H, m), 2.12 (3H, s), 2.13 (3H, s), 3.02 (3H, s), 3.16 (3H, s), 4.28 (1H, m), 7.23-7.37 (5H, m), 9.48 (1H, d, *J* 1.1 Hz), 9.67 (1H, s); δ_C 29.7, 30.0, 30.2, 36.7, 44.7, 46.9, 56.0, 56.3, 78.7, 81.2, 126.2, 126.3, 127.8, 128.3, 128.6, 128.7, 140.5, 140.9, 201.3, 205.3, 208.0; *m/z* 247 (M^+-1, 0.2), 236 (8), 203 (30) 146 (15), 121 (78), 104 (14), 99 (100) and 77 (14); HRMS *m/z* calcd. for $C_{13}H_{15}O_2$ (M^+-C_2H_5O) 203.1070, found 203.1070.

j) *3-Phenylsulfinyl-1-phenylthiopropene* (15).

1,3-Bis(phenylthio)propene[24] (22) (11.46 g, 44.35 mmol) was dissolved in glacial acetic acid (50 ml) and hydrogen peroxide (5.08 ml, 48.8 mmol) added. After stirring for 1.5 h the reaction mixture was poured into water (50 ml) and extracted with dichloromethane (3 x 50 ml). The combined extracts were washed with a saturated sodium hydrogen carbonate solution and then dried over magnesium sulfate. The solvent was evaporated *in vacuo* to yield an oil which, on purification by column chromatography (hexane:CH_2Cl_2 1:1) gave a mixture of the (E)- and (Z)-isomers of 3-phenylsulfinyl-1-phenylthiopropene (15) (9.17 g, 33.42 mmol, 75%) as a pale yellow oil. ^1H NMR showed the ratio of E:Z isomers to be 7:3; ν_{max} 3060, 1607, 1582, 1479, 1370 and 1043 cm^{-1}; δ_H (E-isomer) 3.56 (2H, m,), 5.46 (1H, dt, *J* 7.8, 15.1 Hz), 6.24 (1H, d, *J* 15.1 Hz), 7.1-7.7 (10H, m,); δ_H (Z-isomer) 3.79 (2H, m,), 5.71 (1H, dt, *J* 7.8, 9.2 Hz), 6.53 (1H, d, *J* 9.3 Hz), 7.1-7.7 (10H, m,); δ_C both isomers 56.1 (Z), 59.6 (E), 116.8 (E), 118.0 (Z), 124.0, 124.1, 126.7, 127.1, 128.7, 128.8, 128.9, 129.2, 130.7, 130.7, 130.8, 130.9, 132.6 (Z), 132.8 (E), 133.3, 134.4 (E & Z), 142.4 (E), 142.8 (Z); (*m/z*) 218.1 (12), 150.1 (11), 149.1 (M^+-SOPh, 100), 147.0 (16), 134.1 (12), 116.1 (32), 115.1 (16), 109.0 (13); HRMS *m/z* calcd. for C_9H_9S (M^+-SOPh) 149.0425, found 149.0425.

k) *(E)-1,3,3-Tris(phenylthio)propene* **(17).**
(E)-3-Phenylthioprop-2-enal (0.1 g, 0.61 mmol), thiophenol (0.14 ml, 1.36 mmol) and phosphorus pentoxide (0.26 g, 1.83 mmol) were stirred together in dichloromethane (20 ml) at 0°C for 1 hour. The reaction was quenched with a KOH solution (1M) and then extracted with CH_2Cl_2. After drying ($MgSO_4$) and evaporation of solvent the residue was purified by column chromatography (hexane:CH_2Cl_2 9:1) to yield **(17)** (0.14 g, 0.37 mmol, 61%) as a white crystalline solid. Found: C, 68.22; H, 4.93. $C_{21}H_{18}S_3$ requires C, 68.81; H, 4.95%; m.p. 84°C (CCl_4); ν_{max} 3010, 1578 and 1370 cm^{-1}; δ_H 4.95 (1H, d, *J* 8.6 Hz), 5.78 (1H, dd, *J* 8.6, 14.8 Hz), 6.12 (1H, d, *J* 14.8 Hz), 6.96-7.50 (15H, m); δ_C 57.9, 126.6, 126.8, 128.1, 128.9, 129.1, 129.7, 133.1, 133.3, 133.4, 134.3; (*m/z*) 259 (10), 258 (19), 257 (M^+-SPh, 100.0), 148 (18), 147 (59), 110 (15); HRMS *m/z* calcd. for $C_{15}H_{13}S_2$ (M^+-SPh) 257.0459, found 257.0459.

l) **General Procedure for reactions of enol silyl ethers (3) and (4) with Allylic Sulfoxides (14) and (15).**
The allylic sulfoxide (0.50 mmol, 1.0 eq.) was dissolved in dichloromethane (3 ml) and cooled to -78°C under a nitrogen atmosphere. TMSOTf (0.18 ml of a 5.5 M solution 1.00 mmol, 2.0 eq.) and enol silyl ether (1.50 mmol, 3.0 eq.) were then added by syringe in that order. Diisopropylethylamine (0.19 ml, 1.00 mmol, 2.0 eq.) in dichloromethane (2 ml) was then added dropwise using a syringe pump over a period of 30 minutes. The reaction mixture was stirred for an additional 10 minutes at -78°C and then for a further 20 minutes at -30°C. At this stage the reaction was quenched with 0.1 M HCl (2 ml) and then added to 25 ml of 0.1 M HCl in a separating funnel. After extraction with dichloromethane (3 x 20 ml), the combined organic extracts were washed with aq. $NaHCO_3$, dried over $MgSO_4$ and evaporated *in vacuo* to give the crude product material. This was subjected to column chromatography (hexane:CH_2Cl_2 1:1) to give the pure alkylation product. The following products were obtained:

m) *(E)-1-Phenyl-3,5-bis(phenylthio)pent-4-en-1-one* **(18)**; 59% ; Found: C, 72.71; H, 5.90. $C_{23}H_{20}OS_2$ requires C, 73.37; H, 5.35%; m.p. 88-89°C (hexane/CCl_4); ν_{max} ($CHCl_3$) 3024, 1686, 1601, 1584 and 1270 cm^{-1}; δ_H 3.30 (2H, dd, *J* 1.3, 2.6, 6.9 Hz), 4.45 (1H, dt, *J* 6.7, 8.1 Hz), 5.81 (1H, dd, *J* 8.7, 14.9 Hz), 6.08 (1H, d, *J* 14.8 Hz), 6.97-7.94 (15H, m); d_C 42.3, 46.6, 124.5, 126.1, 127.5, 127.8, 127.9, 128.2, 128.3, 128.4, 132.6, 133.0, 133.0, 133.4, 134.9, 136.3, 196.2; (*m/z*) 267 (M^+-SPh, 8), 157 (52), 105 (100), 77 (51).

n) *(E)-2-(1,3-Bis(phenylthio)allyl)cyclohexanone* **(19)**; 65% as a 60:40 mixture of diastereomers; ν_{max} ($CHCl_3$) 2939, 1708, 1584, 1371 and 1088 cm^{-1}; δ_H (Minor diastereomer) 1.58-2.55 (8H, m), 2.67 (1H, m), 4.31 (1H, dd, *J* 5.5, 9.1 Hz), 5.80 (1H, dd, *J* 9.2, 14.9 Hz), 6.10 (1H, d, *J* 14.8 Hz), 6.97-7.51 (10H, m); δ_H (Major diastereomer, characteristic signals) 4.09 (1H, m), 5.93 (2H, m); δ_C (Mixture of diastereomers) 24.5, 24.5, 27.2, 27.4, 30.2, 30.7, 41.9, 42.0, 51.5, 52.6, 54.0, 54.2, 123.9, 125.1, 126.2, 126.2, 127.4, 127.5, 128.6, 128.7, 128.8, 128.8, 129.7, 129.8, 131.3, 132.7, 133.0, 133.6, 134.3, 134.5, 135.5, 135.4, 209.3, 209.6; (*m/z*) 245 (M^+-SPh, 61), 136 (10), 135 (100), 110 (29), 109 (12); HRMS *m/z* calcd. for $C_{15}H_{17}OS$ (M^+-SPh) 354.1112, found 354.1113.

o) *1,5-Diphenyl-3-phenylthiopent-4-en-1-one* **(20a)** and *(E)-1,3-diphenyl-5-phenylthiopent-4-en-1-one.* **(20b)**, 74% as a 3:1 regioisomeric mixture. Found (mixture): C, 80.39; H, 5.85. $C_{23}H_{20}OS$ requires C, 80.20; H, 5.85%; ν_{max} (mixture, $CHCl_3$) 3095, 1665, 1581, 1565, 1252 and 665 cm^{-1}; δ_H (α-adduct (**20a**)) 3.40 (2H, m), 4.26 (1H, dt, *J* 5.4, 6.2 Hz), 6.16 (2H, m), 7.08-7.95 (15H, m); δ_H (γ-adduct (**20b**)) 3.40 (2H, m), 4.49 (1H, dt, *J* 6.5, 7.5 Hz), 6.16 (1H, dd, *J* 7.8, 15.7 Hz), 6.30 (1H, d, *J* 15.8 Hz), 7.08-7.95 (15H, m); δ_C (**20a**) carbonyl 196.7; (**20b**) carbonyl 197.6; (*m/z*) 235 (M^+-SPh, 52), 115 (54), 105 (100), 77 (45).

p) *2-(3-Phenyl-1-phenylthioallyl)cyclohexanone* (**21a**) and *2-(1-phenyl-3-phenylthioallyl)cyclohexanone.* (**21b**), 79% as a 1:1 regioisomeric mixture, each isomer as a 1:1 diastereomeric mixture; ν_{max} (mixture, $CHCl_3$) 3024, 1711, 1481, 1450 and 1220 cm^{-1}; δ_H 1.21-2.46 (8H, m), 2.76 (1H, m), 3.83 (1H, dd, *J* 5.8, 9.5Hz, 1 diastereomer of α-adduct (**21a**)), 4.01 (1H, m, 1 diastereomer of α-(**21a**) and γ-(**21b**) adducts each), 4.27 (1H, dd, *J* 5.7, 8.7 Hz, 1 diastereomer of γ-adduct (**21b**)), 6.16 (2H, m), 7.08-7.48 (10H, m); δ_C (**21a**) carbonyl 209.6 and 209.9; δ_C (**21b**) carbonyl 210.9 and 211.9; (*m/z*) 225 (10), 213 (54), 117 (39), 115 (100), 91 (37); HRMS (*m/z*) calcd. for $C_{21}H_{22}OS$ 322.1391, found 322.1391.

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(*Received in UK* 18 *April* 1994; *revised* 10 *June* 1994; *accepted* 17 *June* 1994)