Tetrahedron Vol. 46, No. 6, pp. 2135-2148, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00

ACYL RADICAL CYCLIZATIONS IN SYNTHESIS. PART 2. FURTHER SUBSTITUENT EFFECTS ON THE MODE AND EFFICIENCY OF CYCLIZAION OF 6-HEPTENOYL RADICALS.

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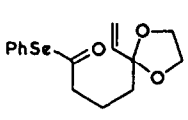
(*Received in UK 6 December* 1989)

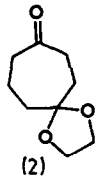
Abstract: In an attempt to determine the factors affecting exo-/endo- selectivity in the cyclization of 6-heptenoyl radicals various heteroatom substituted selenol esters were prepared and reacted with tributyltin hydride. The incorporation of a 7-phenylthio moiety results in clean, high yielding, cyclization in the exo- mode. Evidence is adduced for the reversibility of 6-heptenoyl radical cyclizations.

In part 1[1] of this series we recorded the effects of ether and cyclic ketal functions at the 3- and/or 5-positions of the 6-heptenoyl radical on the mode and efficiency of it's cyclization. We report here, in full,[2] the results of some further experiments involving heteroatom substituted 6-heptenoyl and related radicals undertaken with a view to the gaining of greater insight into this problem.

The 5,5-ethylenedioxy and 5-ethoxy substituted selenol esters (1) and (3) undergo preferential endo-mode cyclization to the cycloheptanones (2) and (5) on treatment with tributyltin hydride and a catalytic quantity of azoisobutyronitrite (AIBN) in benzene at reflux (Table, entries 1 and 2).[1]



(1)



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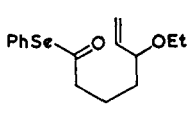

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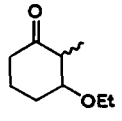

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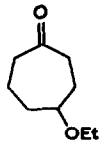
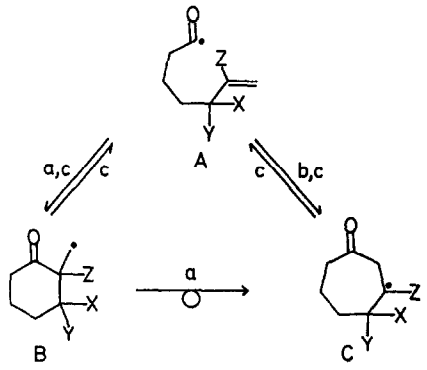
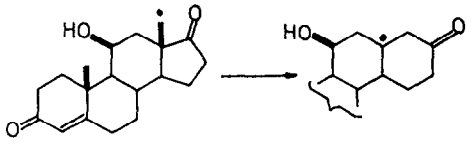


(5)

These unanticipated observations might be ascribed to any one of the three possibilities outlined in scheme 1: i) kinetic cyclization in the exo-mode followed by rapid ring expansion to the overall endo product (Scheme 1, path a) as is known[3] to happen with the closely related vinyl radical cyclizations; ii) direct endo-mode cyclization (scheme 1, path b); or iii) reversible cyclization in the exo-mode followed by eventual endo-cyclization (Scheme 1, path c).



Ring expansion of radicals of the type B (Scheme 1) to C has been reported[4] when the group Z is electron withdrawing (CO_2R, CN) and X = Y =H and also in the related example of the expansion of radical (6) to (7) (Scheme 2).[5]

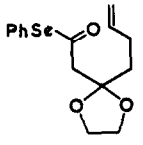


(6) (7)

Scheme 2

Direct endo-mode cyclization (Scheme 1, path b) might be favoured by the adoption of an appropriate conformation by the allylic ether moiety.[6] Both ring expansion and direct endo-mode cyclization might also be driven by the stabilisation which it has been suggested [7] is afforded to carbon centred radicals by a β *C-O* bond.

The removal of the ether and /or ketal groups from the 5-(allylic) position to the 3-position as in (8) and (11) results in a dramatic increase in yield coupled with a change in cyclization mode (Table, entries 3 and 4).[1]



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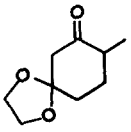
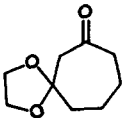
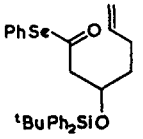


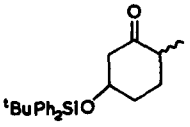
(9)



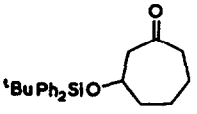
(10)



(11)



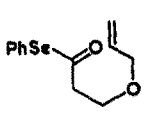
(12)



(13)

Clearly the increased yield is readily attributable to the 'Thorpe-Ingold' effect but the change in overall cyclization mode may be a consequence of the removal of steric hindrance at the internal alkene position; of the removal of conformational constraints imposed by allylic ethers; or of the lack of a stabilising β *C-O* bond for the endo-product.

In an attempt to distinguish between conformational effects due to the allylic oxygens in A(Scheme 1) and extra stabilization afforded by the β *C-O* bonds in C (Scheme 1) as the overriding regiodirecting factor in the cyclization of (1) and (3) we decided to prepare the selenol ester (14) and to study it's AIBN initiated reaction with tributyltin hydride. The removal of the allylic oxygen from an exo-cyclic position as in (1)→(2) and (3)→(5) to an endo-cyclic position as in (14)→(16) would not result in the loss of any stabilisation of the endo-mode ring closed radical by a β *C-O* bond. Thus if this stabilisation were the predominant factor then (16) should predominate over (15). On the other hand it seemed reasonable to assume that any conformational effect due to the allylic oxygen in (1) and (3) when translated to (12) would favour exo-mode cyclization. Furthermore it is known from the prototypical[8] 5-hexenyl radical rearrangement that the inclusion of an allylic oxygen within the chain increases that rate of exo-cyclization substantially more than that of endo-cyclization (Scheme 3).[9]



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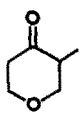

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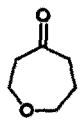

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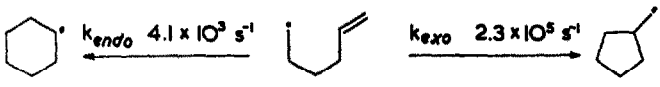
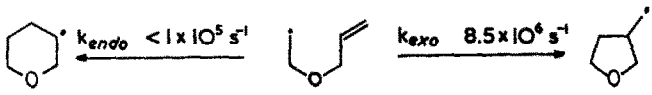


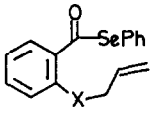
exo : *endo* 57 : 1 (25 °C)



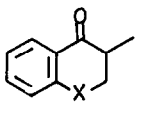
exo : *endo* > 85 : 1 (25 °C)

Scheme 3.

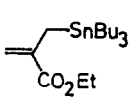
In the event treatment of selenol ester (14), prepared by the action of sodium phenylseleno(triethoxy)borate[10] (sodium phenylselenide) on the acyl chloride derived from 3-allyloxypropionic acid, with tributyltin hydride and AIBN in benzene at reflux resulted in the isolation of the oxacycloheptanone (16) and the oxacyclohexanone (15) in 25 and 12% yields respectively (Table, entry 5). In a similar vein the selenol esters (17)—(19) were prepared from *O*-allylsalicylic acid, *S*-allylsalicylic acid and *N*-acetyl-*N*-allylanthranilic acid in the first two cases by reaction of the derived acyl chlorides with sodium phenylselenide and in the latter case by the reaction of a mixed anhydride[11] prepared from the acid and isobutyl chloroformate with sodium phenyselenide. In each case the only product isolated on reaction with tributyltin hydride and AIBN at 80°C resulted from exo-mode cyclization (Table, entries 6-8). Reaction of (17) with the activated allylstannane (23)[12] in a tandem intra/intermolecular radical addition process also provided the exo-mode product (Table, entry 9). Analogous results have been observed by other workers with closely related systems.[13] Clearly the inclusion of two further sp^2 centres in the chain overrides any other effect and directs cyclization to the exo-mode.



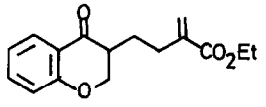
(17) X= O
(18) X= S
(19) X= NAc



(20) X= O
(21) X= S
(22) X= NAc

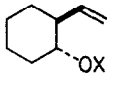


(23)

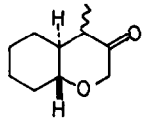


(24)

We next turned briefly to endo-cyclic homoallylic oxygen as a substituent. trans-2-Vinylcyclohexanol (25) was reacted in the form of it's sodium salt with ethyl bromoacetate to give the homoallylic ether (26) which was converted to the selenol ester (28) by saponification to (27) followed by treatment of the derived acyl chloride with sodium phenylselenide. Reaction of (28) with tributyltin hydride under medium pressure Hg photolysis at room temperature afforded two products (30) and (31) resulting from endo-mode cyclization of the acyl radical and decarbonylation followed by 5-exo-trig cyclization respectively (Table, entry 10). The exo-mode product of acyl radical cyclization (29) was not identified in the reaction mixture.



(25) X=H
(26) X=CH_2CO_2Et
(27) X=CH_2CO_2H
(28) X=$CH_2COSePh$



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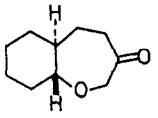
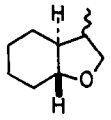
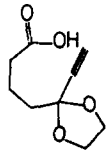


(30)

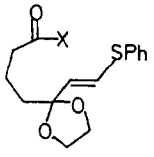


(31)

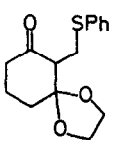
Finally we prepared the selenol ester (34) by AIBN initiated addition of thiophenol to the ynoic acid (32) giving the vinylsulphide (33) which was esterified by reaction with *N*-phenylselenophthalimide and tributylphosphine according to Grieco and Nicolaou.[14] Reaction of (34) with tributyltin hydride under the standard conditions resulted in the isolation, in 72% yield, of the cyclohexanone (36) (Table, entry 11). Unambiguous differentiateion of (36) from the alternative product (37) was not possible by ^{1}H-nmr spectroscopy. Therefore (36) was heated, in benzene, in a Dean-Stark apparatus with ethylene glycol and a catalytic quantity of p-toluenesulphonic acid leading to the formation of the symmetrical diketal (38) whose [13] C-nmr spectrum contained only seven aliphatic carbon signals and so rigorously identified the product from the cyclization reaction as (36).



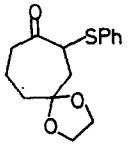
(32)



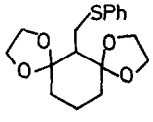
(33) X=OH
(34) X=SePh
(35) X=H



(36)



(37)



(38)

Clearly the introduction of a phenylthio residue at the terminal position of the alkene results in a significant improvement in cyclization yield and a reversal of cyclization mode (Table, compare entries 1 and 11). Unfortunately this effect does not allow differentiation between paths a,b, and c (Scheme 1) as it can be reasonably argued on the one hand that the extra bulk of the phenylthio group retards direct endo-mode cyclization or alternatively that the stabilisation afforded to the radical generated by exo-mode cyclization is sufficient to prevent ring expansion and /or opening.

Nevertheless the significant increase in yield of ring closed product (Table, entries 1 and 11) is meaningful and in our opinion is indicative of the α-phenylthio group stabilising the ring closed radical to such an extent that it does not undergo ring opening. The reason for the low yields of cyclization product from (1) and (3) would therefore be a consequence of the ready reversibility of the acyl radical ring closure reaction.[15] Unfortunately the lack of reactivity of (36) towards AIBN initiated reaction with tributyltin hydride has so far prevented the demonstration of this reversibility. The recent findings of Blanco and Mansouri are however strongly supportive of such ring opening reactions.[16]

We are led to the overall conclusion that the mode, exo-or endo-, of 6-heptenoyl radical cyclization and it's variation with substituents is dependant on a subtle interplay of conformation effects and the reversibility of the ring closure.

Table

Entry	Substrate	Products (% Yield)
1	(1)	(2)(32)
2	(3)	(4)(1), (5)(27)
3	(8)	(9)(72), (10)(12)
4	(11)	(12)(41), (13)(11)
5	(14)	(15)(12), (16)(25)
6	(17)	(20)(52)
7	(18)	(21)(66)
8	(19)	(22)(44)
9	(17)	(24)(23)
10	(28)	(30)(25), (31)(32)
11	(34)	(36)(72), (35)(6)

Acknowledgement:

We thank the SERC for financial support and for a studentship to S.M.F..

Experimental:

For general experimental see part 1.[1]

***Se*-Phenyl 4-Oxaselenohept-6-enoate (14)** 3-Allyloxypropionic acid[17] (0.18g, 1.37 mmol) was stirred in benzene (4ml) at room temperature with oxalyl chloride (1ml) and dimethyl formamide (1 drop). When effervescence had ceased (~ 1hr) the volatiles were removed in vacuo to give the crude acyl chloride which was dissolved in tetrahydrofuran (2ml) and added to a stirred solution of sodium phenylselenide in absolute ethanol at 0°C under a nitrogen atmosphere. The latter solution was prepared by reaction of diphenyl diselenide (0.213 g, 0.69 mmol) in absolute ethanol (10 ml) with sodium borohydride (53 mg, 1.4 mmol) at room temperature under nitrogen. After 45 min at 0°C the reaction was poured onto water (100 ml) and ether extracted. The extracts were dried on magnesium sulphate and concentrated in vacuo to give the crude product which was purified by chromatography on silica gel (eluant: dichloromethane) giving the title compound (14) as a pale yellow oil (0.218 g, 59%) with δ(60 MHz): 2.90(2H,t), 3.70(2H,t), 3.95(2H,m), 4.93-5.40(2H,m), 5.46-6.20(1H,m), 7.36(5H,m); $\bar{\nu}_{max}$ (film); 3065, 1718, 1641, 1105, cm^{-1}; m/z: 270(M^+), 198,183, 171, 157, 118, 113, 104, 91, 85, 78, 77. (Found:C, 53.41; H, 5.22 calc. for $C_{12}H_{14}O_2Se$: C, 53.54; H, 5.24%)

Reaction of Selenol Ester (14) with Tributyltin Hydride. Tributyltin hydride (250 mg, 0.86 mmol) and AIBN (10 mg) in benzene (2 ml) were added over 4 hr. to a solution of selenol ester (14) (171 mg, 0.65 mmol) in benzene (4 ml) at reflux under nitrogen. The reaction mixture was heated to reflux for a further hour then cooled to room temperature and concentrated in vacuo. Chromatography of the crude on silica gel (eluant: ether-40-60 petroleum ether 2:1) gave 3-methyltetrahydropyran-4-one (15) as a colourless oil (9 mg, 12%) with δ(400 MHz): 1.00(3H,d,J=6.8 Hz), 2.41(1H,m), 2.65(2H,m), 3.33(1H,t), 3.72(1H,m), 4.15(1H,m), 4.25(1H,m); $\bar{\nu}_{max}$(film): 2965, 1711, 1097 cm^{-1}; m/z: 114.0692 (M^+; calc. for $C_6H_{10}O_2$: 114.0681), 73, 56, 42,41,39. Further elution gave 4-oxepanone (16) as a colourless oil (19 mg, 25%) with δ(400 MHz): 3.89(4H,m), 2.70(4H,m), 1.88(2H,m), lit.[18] 1.76(2H), 2.53(4H), 3.73(4H); $\bar{\nu}_{max}$ (film): 1710 $cm,^{-1}$, lit.[18] 1710; m/z: 114.0686 (M^+; calc. for $C_6H_{10}O_2$: 114.0681), 87, 71, 56, 55, 43, 42, 41, 39.

***Se*-Phenyl *O*-Allylselenosalicylate** (17) O-Allylsalicylic acid [19] (5 g, 28 mmol) was heated to reflux with thionyl chloride (2.2 ml) for 1.5 hr. Kugelrohr distillation (175°C/water pump) of the crude reaction mixture gave the corresponding acid chloride (3.58 g, 65%) with $\bar{\nu}_{max}$: 1775 cm^{-1}. Sodium borohydride (0.22g, 6mmol) in absolute ethanol (10 ml) was added dropwise to a solution of diphenyl diselenide (0.93 g, 3 mmol) in absolute ethanol under a nitrogen atmosphere at room temperature. The above prepared acid chloride (1.00g, 5.08 mmol) in tetrahydrofuran (10 ml) was then added leading to the immediate formation of a white precipitate. The reaction mixture was stirred at room temperature for a further 1 hr., then diluted with

water and ether extracted (3 x 50 ml). The extracts were washed with water and brine, dried on sodium sulphate and concentrated in vacuo. Chromatography on silica gel (eluant: dichloromethane) gave the title compound (17) as a pale yellow crystalline solid (1.11 g, 69%) with mp. 48 °C (toluene); δ(60 MHz): 4.8(2H,d), 5.5(2H,m), 6.3(1H,m), 7.0-7.5(9H,m);$\bar{\nu}_{max}$($CHCl_3$): 3060, 1688, 1605 cm^{-1}. (Found: C, 60.13; H,4.37 calc. for $C_{16}H_{14}O_2Se$: C, 60.75; H, 4.43%)

Reaction of Selenol Ester (17) with Tributyltin Hydride *Tributyltin hydride* (0.4 ml, 1.65 mmol) and azoisobutyronitrite (15 mg) in benzene (2ml) were added to a solution of selenol ester (17) in benzene (5 ml) at reflux under nitrogen. After a further 1.5 hr at reflux the reaction mixture was allowed to cool to room temperature and the volatiles removed in vacuo. Chromatography (eluant: dichloromethane - 40 - 60 petroleum ether 1:1) of the residue on silica gave 3-methyl-4-chromanone[20] (20) as a colourless oil with δ(200 MHz): 1.25(3H,d), 2.85(1H,m), 4.2(1H,dd),4.5(1H,dd), 7.1(2H,m), 7.82(1H,dd), 7.95(1H,dd);$\bar{\nu}_{max}$ (film): 2998, 2990, 1684, 1604 cm^{-1}; m/z: 162(M^+), 120, 92, 76, 69, 64, 50, 39.

***Se*-Phenyl 2-(Prop-2-enylthio)selenobenzoate (18)** *S*-Allylthiosalicylic acid[21] (1.2g, 5.6 mmol) was allowed to react in benzene (5 ml) at room temperature with oxalyl chloride (2.5 ml) and dimethyl formamide (1 drop). After removal of the volatiles in vacuo the crude acid chloride was taken up in tetrahydrofuran (10 ml) and added at room temperature under nitrogen to a solution of sodium phenylselenide in ethanol prepared as described above from sodium borohydride (0.21 g) and diphenyl diselenide (0.87 g) in absolute ethanol (60 ml). After 1 hr at room temperature dilution with water and standard ether extraction gave the crude product which was purified by chromatography on silica gel (eluant: ether - 40-60 petroleum ether 5:1) giving the title compound (18) as a pale yellow solid (0.90 g, 48%) with mp. 54 °C (ether); δ(60 MHz): 3.7(2H,d), 5.0-6.4(3H,m), 7.0-8.0(9H,m);$\bar{\nu}_{max}$($CHCl_3$): 3072, 3025, 1678, 1638 cm^{-1} (Found: C, 57.74; H, 4.14 calc. for $C_{16}H_{14}OSSe$: C, 57.66; H, 4.23%).

Reaction of Selenol Ester (18) with Tributyltin Hydride. Tributyltin hydride (0.16 ml, 0.6 mmol) and AIBN (10 mg) in benzene (2 ml) were added to a solution of selenol ester (18) (200 mg, 0.6 mmol) in benzene (5 ml) at reflux under nitrogen. After 3 hr. at reflux the volatiles were removed in vacuo and the residue purified by chromatography on silica gel (eluant: ether-40-60 petroleum ether 7:1) giving 3-methyl-1-thiochroman-4-one[22] (21) as a colourless oil (70 mg, 66%) with δ(60 MHz): 1.5(3H,d), 3.1(3H,m) 7.0-8.1(4H,m);$\bar{\nu}_{max}$ (film): 3146, 3118, 1677, 1588 cm^{-1}; m/z: 178.0450(M^+, calc. for $C_{10}H_{10}OS$: 178.0452), 136, 108, 69, 28.

***Se*-Phenyl *N*-Acetyl-*N*-allylselenoanthranilate (19)** Sodium hydride (1.84 g of 80% dispersion, 61.4 mmol) was added portionwise to dry dimethylsulphoxide (50 ml) at room temperature. After 35 min. at room temperature a solution of N-acetylanthranilic acid [23](5.00 g), 27,9 mmol) in dimethylsulphoxide (8 ml) was added dropwise, followed after 1 hr. at room temperature by allyl bromide (2.67 ml, 30.7 mmol). The

reaction mixture was stirred overnight at room temperature than poured into water (100 ml) and extracted with ethyl acetate (3 x 25 ml). The combined extracts were washed sequentially with water and brine, dried over magnesium sulphate and concentrated in vacuo. Cystallization of the residue from ethyl acetate-40-60 petroleum ether afforded *N*-acetyl-*N*-allyl anthranilic acid as an off white solid (3.18 g, 52%) with mp. 147-148°C; δ(60 MHz): 1.8(3H,*s*), 3.6-4.0(1H,m), 4.5-5.2(3H,m), 5.5-6.2(1H,m), 7.05-7.60(3H,m), 8.0(1H,m), 11.1(1H,bs);$\tilde{\nu}_{max}$($CHCl_3$): 3479, 2952, 1715, 1655, 1616, 1595, 1488, 1392, 1220, 929 cm^{-1}. (Found: C, 66.11; H, 5.86; N, 6.26 calc. for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39%). A solution of this acid (0.826 g, 3.77 mmol) in tetrahydrofuran (5 ml) under nitrogen at -15°C was treated with *N*-methylmorpholine (0.44 ml, 3.95 mmol) and isobutyl chloroformate (0.513, 3.95 mmol). In a separate flask a solution of sodium phenylselenide in absolute ethanol (5 ml) was prepared from diphenyl diselenide (0.65 g, 2.07 mmol) and sodium borohydride (0.171 g, 4.52 mmol) under argon. This latter colourless solution was added dropwise, via a syringe, at -15°C to the mixed anhydride. The reaction mixture was then stirred for 2hr. at -15°C then poured into water (50 ml) and extracted with ether (2 x 20 ml). The combined extracts were washed with brine, dried and evaporated in vacuo to give a pale yellow solid. Chromatography on silica gel (eluant: ether - 40-60 petroleum ether 4:1) gave the title compound (19) as a white crystalline solid (1.142 g, 85%) with mp. 101-104°C (decomp.); δ(60 MHz): 1.8(3H,*s*), 3.6 - 3.9(1H,m), 4.5 - 5.2(3H,m), 5.5 - 6.3(1H,m), 7.1 - 7.6(8H,m), 7.9(1H,m);$\tilde{\nu}_{max}$($CHCl_3$): 3058, 1688, 1658, 1478, 1384, 1191, 893, 777, 677 cm^{-1}. (Found: C, 60.12; H, 4.74; N, 4.02 calc. for $C_{18}H_{17}NO_2Se$: C, 60.34; H, 4.78; N, 3.91%)

Reaction of Selenol Ester (19) with Tributyltin Hydride. Tributyltin hydride (0.29 ml, 1mmol) and AIBN (20 mg) in benzene (2 ml) were added dropwise to a solution of the selenol ester (19) (350 mg, 0.9 mmol) in benzene (5 ml) at reflux under nitrogen. After 3 hr. the solvent was removed in vacuo and the residue purified by chromatography on silica gel (eluant: 40-60 petroleum ether-ether 2:1) to give *N*-acetyl-2,3-dihydro-3-methylquinolin-4-one (22) as a colourless oil (90 mg, 45%) with δ(60 MHz): 1.2(3H,d), 2.15(3H,*s*), 3.2 - 3.8(2H,m), 4.4(1H,m), 7.0 -8.0(4H,m); m/z: 203.0935 (M^+ calc. for $C_{12}H_{13}NO_2$: 203.0946), 161, 146, 142, 119, 104, 92, 77, 69, 56, 51, 43, 39, 28.

Reaction of Selenol Ester (17) with Allylstannane (23). Allylstannane (23) (476 mg, 1.65 mmol) and AIBN (20 mg) in benzene (1 ml) were added to a solution of selenol ester (17) (350 mg, 1.1 mmol) at reflux under nitrogen in benzene (5 ml). The reaction mixture was heated to reflux for 15 hr before the volatiles were removed in vacuo and the residue purified first by chromatography on silica gel (eluant: 40-60 petroleum ether-ether 3:1) and subsequently by preparative t.l.c. on silica gel (eluant: 40-60 petroleum ether-ether 3:1) to give ethyl 4-(chroman-4-on-3-yl)-2-methylenebutanoate (24) as an oil (70 mg, 23%) with δ(200 MHz): 1.2(3H,t), 1.7(1H,m), 2.05(1H,m) 2.5(2H,t), 2.75(1H,m), 4.2(3H,m), 4.6(1H,dd), 5.7(1H,d), 6.2(1H,d), 7.0(2H,m), 7.5(1H,dd), 7.9(1H,dd);$\tilde{\nu}_{max}$(film): 3100, 2900, 1696, 1620, 1580 cm^{-1} ; m/z: 274.1180(M^{+*}; calc. for $C_{16}H_{18}O_4$: 274.1205), 229, 205, 200, 179, 161, 160, 148, 147.

Se-Phenyl *trans*-2-Ethenylcyclohexyloxy)selenocrcetate (28) An approximately 1:2 *cis:trans* mixture of 2-vinylcyclohexanol[24] (3.0g, 23.7 mmol) and sodium hydride (0.749 g of 80%, 24.9 mmol) were heated to reflux with stirring under a nitrogen atomosphere in tetrahydrofuran (50 ml) for 2hr. After cooling to room temperature ethyl bromoacetate (3.97g, 23.7 mmol) was added over 5 min. resulting in a vigourous exothermic reaction. The reaction mixture was then brought to reflux for 3hr. before being cooled to room temperature and quenched with dilute hydrochloric acid. Ether extraction gave a brown oil (4.45 g) which was subjected to chromatography on silica gel (eluant: 40-60 petroleum ether-ether 8:1) giving the *trans*-ester (26) as a slight yellow oil (1.47 g) contaminated with a minor amount of a product tentatively identified as 2-ethenylcyclohexyl bromoacetate. Saponification of this mixture (1 g) with potassium hydroxide (0.71 g) in methanol (10 ml) and water (4 ml) at room temperature overnight was followed by dilution with dilute hydrochloric acid and extraction with ethyl acetate. The organic phase was extracted with 5% sodium hydrogen carbonate solution then dried and concentrated in vacuo to give alcohol (25) (128 mg). Acidification of the aqueous phase with dilute hydrochloric acid and reextraction with ethyl acetate gave, after drying on magnesium sulphate and concentration the pure acid (27) as a viscous oil (0.54 g, 20% from *cis/trans* (25)), with bp. 150°C (oven)/0.5 mm Hg; δ(200 MHz): 1.1(4H,m), 1.7(3H,m), 2.1(2H,m), 3.12(1H,ddd,J = 2 x 12, 4 Hz), 4.15(2H,AB quart, J = 17 Hz), 5.12(2H,m), 5.85(1H,m). Acid (27) (350 mg, 1.89 mmol) was allowed to react with oxalyl chloride (0.41 ml) and dimethyl formamide (1 drop) in benzene (5 ml) at room temperature for 1 hr. After removal of the volatiles the crude acid chloride in tetrahydrofuran (5 ml) was added, under nitrogen at room temperature, to a solution of sodium phenylselenide in absolute ethanol (6 ml) prepared from diphenyl diselenide (296 mg, 0.9 mmol) and sodium borohydride (72 mg, 1.89 mmol). After 1 hr. at room temperature the reaction was poured into water and extracted with ether. After concentration in vacuo the crude reaction mixture was purified by chromatography on silica gel (eluant: 40-60 petroleum ether-ether 8:1) giving the title compound (28) as a colourless oil (496 mg, 81%) with δ(200 MHz): 1.1 - 2.2(9H,m) 3.24(1H,ddd, J = 2 x 16, 4 Hz), 4.15(2H,AB quart, J = 16 Hz), 5.15(2H,m), 5.97(1H,m), 7.38(3H,m) 7.50(2H,m); $\tilde{\nu}_{max}$(film): 3065, 1718, 1638, 1017 cm^{-1}; m/z: 324 (M^+), 314, 296, 266, 243, 234, 217, 205, 158, 139, 109, 91, 83, 77, 67. (Found: C, 59.23; H, 6.21 calc. for $C_{16}H_{20}O_2Se$: C, 59.44; H, 6.24%).

Reaction of Selenol Ester (28) with Tributyltin Hydride. Tributyltin hydride (170 mg, 0.58 mmol) and AIBN (10 mg) in benzene (1 ml) were added dropwise over 20 min. at room temperature to a stirred solution of (28) (168 mg, 0.55 mmol) under irradiation from a 100 W medium pressure Hg lamp in benzene (5 ml) under a nitrogen atmosphere. After irradiation for 2hr. at room temperature the solvent was removed in vacuo and the crude reaction mixture subject to chromatography on silica gel (eluant: 40-60 petroleum ether-ether 8:1) yielding first the perhydrobenzofuran (31) a colourless oil (28 mg, 32%) as a single, unassigned diastereoisomer with δ(400 Mhz): 1.02(3H,d,J = 6.5 Hz), 0.85 - 2.15(10H,m), 3.14(1H,m), 3.39(1H,t,J = 8.4 Hz), 4.03(1H,t,J = 8.4 Hz); δ^{13}C(100 MHz): 15.66, 24.19, 25.60, 27.45, 31.59, 38.41, 52.55, 74.27, 83.90; $\tilde{\nu}_{max}$(film): 2925, 1040 cm^{-1}; m/z: 140.1185(M^+, calc. for $C_9H_{16}O$: 140.1201), 125, 110, 97, 95, 81,

69, 68, 67, 55, 41. Further elution with the same solvent gave the perhydrobenoxepinone (30) as a colourless oil(26 mg, 25%) with δ(400 MHz): 0.95-2.00(11H,m), 2.40(1H,m), 2.85(1H,m), 2.94(1H,m), 3.93(1H,d,J=18Hz), 4.23(1H,d,J = 18Hz); δ^{13}C(100 MHz); 25.09, 25.27, 30.81, 32.48, 33.83, 41.96, 46.65, 77.59, 88.30, 215.79; m/z: 168.1165(M^+,calc.for $C_{10}H_{16}O_2$: 168.1150), 136, 110, 96, 94, 82, 81, 68, 67, 65, 53, 52.

Se-Phenyl 5,5-Ethylenedioxy-7-phenylthioselenohept-6-enoate (34). To a stirred solution of acid (32)[1] (500 mg, 2.7 mmol) in benzene (5 ml) at reflux under nitrogen was added thiophenol (300 mg, 2.7 mmol) and AIBN (10 mg) in benzene (2 ml). After 2hr at reflux further thiophenol (300 mg) was added. After a total of 4 hr. at reflux the reaction mixture was cooled to room temperature and the volatiles removed in vacuo. Filtration on silica gel (eluant: 40-60 petroleum ether-ether 1:1) gave 5,5-ethylenedioxy-7-phenylthiohept-6-enoic acid (33) as a colourless viscous oil (780 mg, 88%) with δ(60 MHz): 1.53 - 2.63(6H,m), 3.93(4H,m), 5.5(1H,d,J = 15 Hz), 6.5(1H,d,J = 15 Hz), 7.3(5H,m), 11.27(1H,bs). Tributylphosphine (0.33 ml, 1.32 mmol) and after 15 min, acid (33) (195 mg, 0.66 mmol) were added to a solution of *N*-phenylselenophthalimide (400 mg, 1.32 mmol) in tetrahydrofuran (10 ml) under nitrogen at room temperature. After stirring for 1.5 hr. at room temperature the reaction was poured onto water and ether extracted. The extracts were washed with 2M sodium hydroxide solution and water, dried on magnesium sulphate and concentrated in vacuo. Chromatography on silica gel (eluant: 40-60 petroleum ether-ether 3:1) gave the title compound (34) as a colourless oil (154 mg, 54%) with δ(60 Mhz): 1.60 - 2.85(6H,m), 3.90(4H,m), 5.5(1H,d,J = 15 Hz), 6.5(1H,d,J = 15 Jz), 7.3(10H, m);$\bar{\nu}_{max}$(film): 3058, 1718, 1605 cm^{-1}; m/z: 434(M^+), 279, 208, 177, 168, 157, 135, 109, 95, 91, 85, 77, 65, 55. (Found: C, 58.55; H, 5.14 calc. for $C_{21}H_{22}O_3SSe$: C, 58.19; H, 5.12%).

Reaction of Selenol Ester (34) with Tributyltin Hydride. Tributyltin hydride (200mg, 0.69 mmol) and AIBN (10 mg) in benzene (1 ml) were added to a solution of (34) (300 mg, 0.69 mmol) in benzene (5 ml) at reflux under nitrogen. After 1 hr the solvent was removed in vacuo and the residue subject to silica gel chromatography (eluant: 40-60 petroleum ether-ether 1:1) giving the aldehyde (35) as a colourless oil (12 mg, 6%) with δ(60 MHz): 1.20 - 2.80(6H,m), 3.95(4H,m), 5.5(1H,d,J = 15 Hz), 6.5(1H,d,J = 15 Hz), 9.7(1H,bs);$\bar{\nu}_{max}$(film): 3050, 1718, 1671 cm^{-1}; m/z: 278.1009 (M^+; calc.for $C_{15}H_{18}O_3S$: (M^+): 278.0976), 207, 163, 135, 109, 99,91,65,55. Further elution gave 3,3-ethylenedioxy-2-(phenylthiomethyl)cyclohexanone (36) (139 mg, 72%) as a white crystalline solid with mp. 79°C (petroleum ether-ether); δ(400 Mhz): 1.5-2.1(4H,m), 2.30(1H,dt,J = 12.9, 6.2 Hz, H-6eq.), 2.45(1H,m,H-6ax.), 3.03(1H,dd,J = 8.8, 3.2 Hz, H--2), 3.11(1H,dd,J = 13.6, 3.2 Hz, 1 x CH,SPh), 3.28(1H,dd,J = 13.6, 8.8 Hz, 1 x CH_2 SPh), 3.9-4.1(4H,m), 7.1 - 4.0(5H,m); δ^{13}C(100 MHz): 20.12, 25.49, 33.93, 40.42, 59.95, 65.27, 111.91, 125.32, 127.66, 128.87, 137.36, 206.06; m/z: 278(M^+), 207, 170, 169, 163, 123, 109, 100, 99, 65, 55, 45. (Found: C, 64.65: H, 6.48 calc. for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52%)

1,1;3,3-Bis(ethylenedioxy)-2-(phenylthiomethyl)cyclohexane (38). Ketone(36) (100 mg, 0.36 mmol), ethylene glycol (62 mg, 0.36 mmol) and p-toluenesulphonic acid (5 mg) were heated to reflux in benzene (5 ml) under

a Dean-Stark water separator for 3 hr. After cooling to room temperature the reaction mixture was diluted with ether (30 ml) and washed with water (2x 30 ml) and brine (30 ml). The extracts were dried on magnesium sulphate, concentrated in vacuo and purified by chromatography on silica gel (eluant: 40-60 petroleum ether-ether 2:3) to give the title compound (38) as a white crystalline solid (85 mg, 73%) with mp. 89°C (petroleum ether-ether); δ(400 MHz): 1.38 - 1.48(2H,m), 1.58 - 1.64(2H,m), 1.86(2H,dt, J = 13.7, 3.5 Hz), 2.46(1H,t,J = 6Hz), 3.10(2H,d,J = 6Hz), 3.96(8H,m), 7.1 - 7.35(5H,m); δ^{13}C(100 MHz); 19.08, 27.00, 33.98, 52.14, 64.17, 65.47, 110.60, 125.01, 127.72, 128.68, 139.64; m/z: 322(M^+), 215, 214, 115, 114, 113, 109, 0, 99, 86, 69, 55, 49. (Found: C, 63.23; H, 6.73 calc. for $C_{17}H_{22}SO_4$: C, 63.33; H, 6.87%)

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