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Homolytic Substitution at Selenium: Ring Closure of ω-(Benzylseleno)alkyl Radicals

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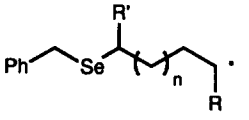
Abstract: *The ring closure of a series of ω-(benzylseleno)alkyl radicals (1) has been studied Thiohydroxamic esters derived from ω-(benzylseleno)alkanoic acids decompose smoothly, upon irradiation, with the loss of carbon dioxide to afford 5- and 6- membered selenium-containing rings in 78 - 95% yield The thiohydroxamic ester derived from 7-(benzylseleno)heptanoic acid affords the 7-membered heterocycle, selenopane in approximately 50% yield These reactions presumably involve intramolecular free radical homolytic substitution at selenium and appear to proceed readily for both primary and secondary carbon-centred radicals The 5-(benzylseleno)hex-2-yl radical (1f) appears to ring close without stereoselectivity, to give a 1 1 mixture of cis- and trans-2,4-dimethyltetrahydroselenophene, a finding in keeping with molecular mechanics (MM2) calculations*

In recent years there has been a rapid expansion in the use of free-radical techniques for the formation of carbon-carbon bonds. In particular, synthetic chemists have provided many elegant examples of the utility of intramolecular free-radical addition reactions as key steps in the overall strategy for the preparation of a wide range of complex molecules[2-10] In addition, intramolecular free-radical homolytic substitution reactions at the sulfur atom in alkyl sulfides and sulfoxides have been shown to be effective in the formation of carbon-sulfur bonds and have been employed in the synthesis of sulfur-containing ring systems[11-17].

Recently, work in our laboratories has been directed toward the development and understanding of free-radical methods of forming carbon-heteroatom bonds in synthesis In this context we reported that carbon-centred radicals undergo intramolecular homolytic substitution at the selenium atom in alkyl selenides to afford saturated and unsaturated selenium-containing rings in good yield[18,19]



1a n =1, R =R' =H
b n =2; R =R' =H
c n =3, R =R' =H
d n =1, R = Me, R' =H
e n =1, R = Et, R' =H
f n = 1, R = Me, R' = Me

Ab initio molecular orbital theory provides strong evidence that reactions at the selenium atom in alkyl selenides[20] and selenoxides[21] most probably involve transition structures in which the attacking and leaving groups adopt a co-linear arrangement, as opposed to hypervalent (9-Se-3) intermediates These data are to be compared with those for radical attack at the sulfur atom in sulfides and sulfoxides which suggest the involvement of a hypervalent intermediate when radical stabilizing groups are present on sulfur[22-24]; and for

radical attack at the tellurium atom in alkyl tellurides which predict the existence of a short-lived hypervalent intermediate[25]

In order to further establish the synthetic utility of free-radical homolytic substitution at selenium and to determine the factors controlling these reactions, we chose to examine the ring closure of substituted and unsubstituted ω-(benzylseleno)alkyl radicals (**1**) We report that primary and secondary alkyl radicals undergo rapid, efficient and non-stereoselective homolytic substitution at selenium to afford saturated selenium-containing heterocycles in good yield These data are consistent with molecular mechanics and *ab initio* calculations performed on these reactions

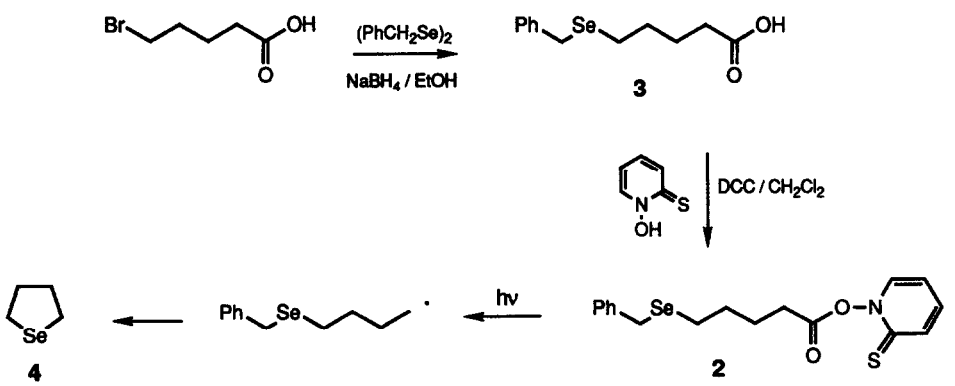
Results and Discussion

1 *Effect of ring size*

Prior to the commencement of this work, we were aware of only two examples in which carbon-centred radicals had been used to attack a selenium centre with the formation of a carbon-selenium bond Newcomb *et al* used diphenyldiselenide to trap alkyl radicals[26] while Byers and co-workers demonstrated that phenylselenides become involved in atom transfer reactions[27]

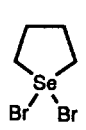
In order to establish the synthetic utility of intramolecular homolytic substitution at selenium, we chose initially to examine the reaction of the 5-(benzylseleno)pent-1-yl radical (**1a**) with the aim of preparing tetrahydroselenophene. To that end, the thiohydroxamic ester derivative[28] (**2**) of 5-(benzylseleno)pentanoic acid[29] (**3**) was prepared according to Scheme 1 Thus, 5-bromopentanoic acid was treated with dibenzyl diselenide-sodium borohydride in ethanol to give **3** which was converted to the bright yellow thiohydroxamic ester (**2**) by the action of N-hydroxypyridine-2-thione and dicyclohexylcarbodiimide (DCC) in dichloromethane in quantitative yield.

Scheme 1



We chose to use the thiohydroxamic ester radical precursor[28] developed by Barton, Crich and Motherwell in this study, as the radical (**1**) could be generated without the need for chain carriers such as tri-n-butyltin or tris(trimethylsilyl)silyl radicals, species known to attack both alkyl selenides and alkyl bromides[30,31] Indeed, it has been our experience that tri-n-butyltin hydride and tris(trimethylsilyl)silane reduce molecules containing both the phenylselenide and bromide moiety with little discrimination

When the thiohydroxamic ester (**2**) was dissolved in d_6-benzene in an NMR experiment[32] and the sample irradiated with a 150W tungsten lamp, the solution became colourless after 5 minutes 270 MHz ^{1}H NMR spectroscopy indicated the formation of tetrahydroselenophene (**4**) (^{1}H NMR δ 2.6 (m, 4H), 1 6 (m, 4H), ^{77}Se NMR δ 174) in 79% yield, demonstrating that intramolecular homolytic substitution at selenium is an efficient process Unfortunately, when this procedure was repeated on a preparative scale we were unable to isolate the selenophene (**4**) either by distillation or preparative GC, as **4** appeared to co-distil with the reaction solvent or decompose on the column Tetrahydroselenophene (**4**) is well known to azeotrope with solvents[33] We eventually chose to characterize **4** by conversion to the stable crystalline 1,1-dibromotetrahydroselenophene[33,34] (**5**) Thus, the crude reaction mixture was poured onto a flash chromatography column and the selenophene (**4**, R_f = 0 15) eluted with hexane Bromination was achieved by the dropwise addition of bromine in carbon tetrachloride Removal of the solvent gave **5** in 74% yield This represents the quickest and highest yielding procedure for the preparation of tetrahydroselenophene and demonstrates the versatility of homolytic substitution in synthesis



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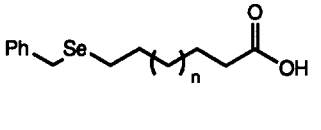
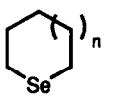


6 a n =1
b n =2



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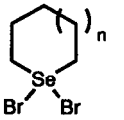

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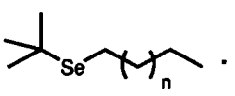
In similar fashion 6-(benzylseleno)hexanoic acid[29] (**6a**) was converted to selenane[35] (**7a**) in 78% yield and characterized (in the usual way) by conversion to 1,1-dibromoselenane[35] (**8a**) in 69% yield

In an attempt to prepare selenopane (**7b**), 7-(benzylseleno)heptanoic acid[29] (**6b**) was converted to the corresponding yellow thiohydroxamic ester in the usual way In an analogous NMR experiment to that previously described for **2**, the thiohydroxamic ester was irradiated and converted to selenopane[36,37] (**7b**) in approximately 50% yield. When the preparation of selenopane was repeated on a preparative scale, extensive formation of a white precipitate was observed. Attempted isolation of 1,1-dibromoselenopane (**8b**) in the usual way yielded no product. Selenopane is known to polymerize readily[36,37]

Clearly, primary carbon-centred radicals readily undergo homolytic substitution at selenium to produce selenium-containing heterocycles



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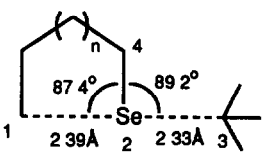

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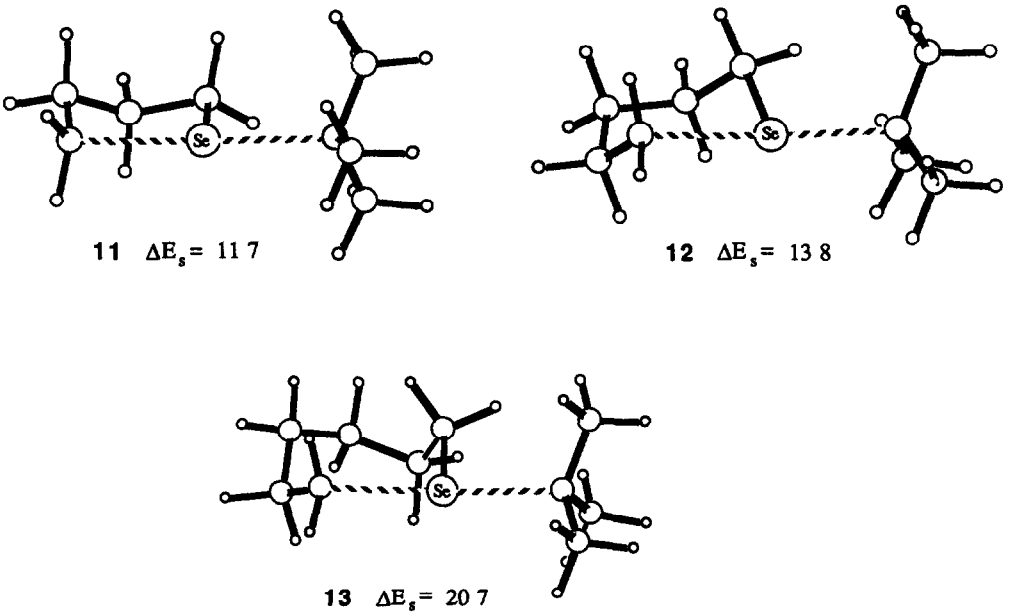
In order to gain further insight into the factors involved in these intramolecular homolytic substitution reactions, we chose to model the lowest energy conformers of the ground and transition states involved in the ring closure of the 4-(*tert*-butylseleno)but-1-yl, 5-(*tert*-butylseleno)pent-1-yl and 6-(*tert*-butylseleno)hex-1-yl radicals (**9**) in a similar manner to that published for intramolecular free-radical addition reactions (Beckwith-Schiesser model)[38] To that end the array of reacting centres was fixed at the geometry of the transition state determined by *ab initio* molecular orbital calculations for attack of methyl radical at *tert*-butylselenol[20] (*viz* r(1,2) = 2 39Å, r(2,3) = 2 33Å, θ(1,2,4) = 87.4°; θ(3,2,4) = 89.2°) The remaining structure (**10**) was optimized using molecular mechanics (MM2) in the usual way[38,39] The *tert*-butyl group was employed as the leaving

Figure 1. Calculated Transition Structures and Activation Energies[a] (ΔE_s) for the Ring Closure of ω-*Tert*-butylalkyl Radicals (**9**).



11 ΔE_s = 11 7 **12** ΔE_s = 13 8

13 ΔE_s = 20 7

[a]Energies in kcal mol^{-1} For definition of ΔE_s, see text.

group in this study as no data are available for transition states involving the benzyl radical, reactions involving the *tert*-butyl group are likely to proceed readily[16] and the benzyl group is resonance stabilized and not easily accommodated within the MM2 framework.

The strain energy component of the activation energy (ΔE_s) was determined by subtraction of the energy associated with the close approach of the attacking radical, the interaction of the leaving group (these are compensated for by favourable bonding interactions) and the strain energy associated with the ground state from the total strain energy of the transition state In this fashion, the strain energies (ΔE_s) involved in the formation of the transition structures (**10**) leading to tetrahydroselenophene (**4**), selenane (**7a**) and selenopane (**7b**) were calculated to be 11 7, 13 8 and 20.7 kcal mol^{-1} respectively Figure 1 displays the optimized structures and calculated values of ΔE_s for the transition states in this study

The calculated values of ΔE_s are somewhat higher than expected on the basis of the energies involved in intramolecular free radical addition reactions (6-10 kcal mol^{-1})[38], however, it should be remembered that these calculations make no allowance for the favourable bonding occuring in these transition states Nevertheless, these data provide a sound qualitative picture of the trends observed in these reactions

As observed for intramolecular addition[38], our calculations predict that, intramolecular homolytic substitution by carbon-centred radicals at selenium proceeds most efficiently in the formation of 5-membered rings Inspection of Figure 1 provides a rationale for this observation Clearly, structure **11** resembles the chair conformer of cyclohexane with a carbon-selenium separation of 2 39Å, similar to the transannular distance of

2 5Å, in cyclohexane Structure **12** resembles a distorted cyclohexane chair while **13** is calculated to have increased angle strain due to the requirements of the geometry of the reacting centres

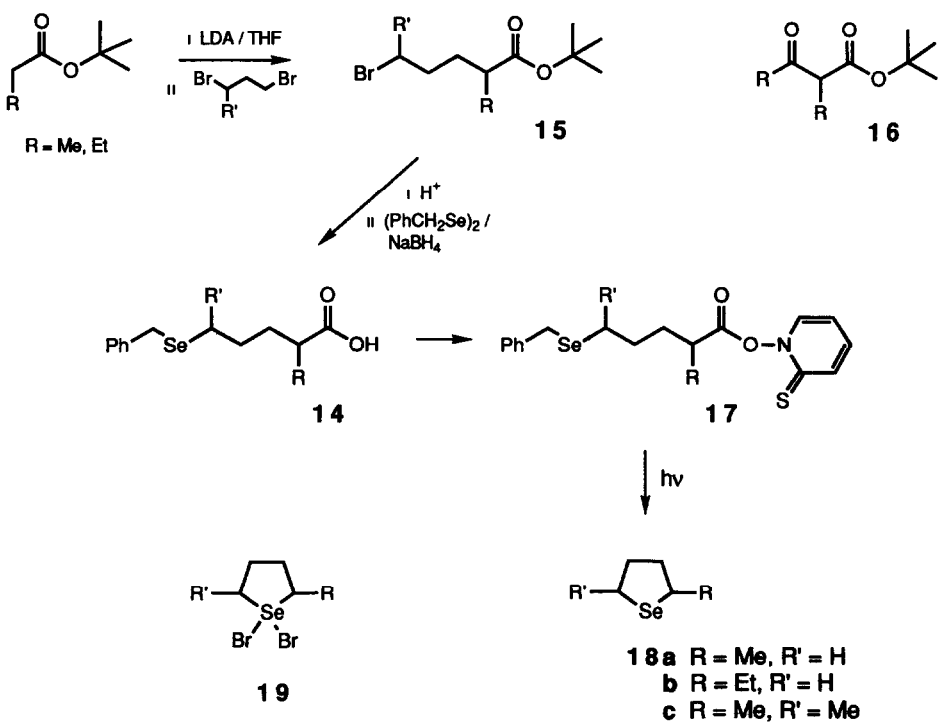
On the basis of our calculations, cyclization to afford the 7-membered ring (**7b**) is predicted to be about 9 kcal mol^{-1} less favourable than that leading to the 5-membered ring (**4**) and therefore, would be expected to proceed somewhat less efficiently than the other reactions studied

2 *Effect of Substitution*

In order to further explore factors operating in these intramolecular homolytic substitution reactions, a series of substituted (benzylseleno)pentanoic acids (**14**) were prepared by an extension of the method of Schlessinger and co-workers[40] (Scheme 2)

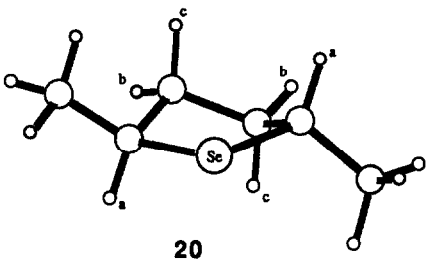
Tert-butyl propionate or *tert*-butyl butanoate was treated with lithium diisopropylamide (LDA) in THF at -78° followed by 1,3-dibromopropane or 1,3-dibromobutane to afford the bromo-ester (**15**) in yields of 20-56% This reaction was complicated by competitive self-condensation of the ester to produce the ketoester (**16**) in varying quantities. The ester (**15**) was then deprotected and further reacted with dibenzyl diselenide - sodium borohydride in ethanol to give the required (benzylseleno)pentanoic acid (**14**) in moderate yield The acid (**15**) was then converted to the thiohydroxamic ester and photolysed in the usual way to afford the substituted tetrahydroselenophene (**18**) in yields in excess of 90% in each case (NMR) In the usual manner, **18** was converted to the dibromide (**19**) and isolated as a yellow crystalline solid in all cases except 1,1-dibromo-2-ethyltetrahydroselenophene (**19b**) which was isolated as an orange oil which refused to crystallize

Scheme 2



These results clearly indicate that secondary alkyl radicals become involved in intramolecular homolytic substitution at selenium to afford substituted tetrahydroselenophenes with similar efficiency to the corresponding primary radical (**1a**) It is interesting to note that *ab initio* calculations suggest that the nature of the attacking carbon-centred radical has little importance in homolytic substitution at selenium[20].

Finally cyclization of the 5-(benzylseleno)hex-2-yl radical (**1f**) gives rise to the question of stereoselectivity in homolytic substitution. When the required precursor (**17c**) was photolysed in the usual fashion and the crude reaction mixture subjected to ^{77}Se NMR spectroscopy, two signals of approximately equal intensity were observed at δ 407 6 and 395 2 (benzene) ppm The existence of approximately equal proportions of both isomers of **18c** was further established by ^{1}H NMR spectroscopy which revealed two doublets of approximately equal intensity at δ 1 35 (J=6 6 Hz) and 1 38 (J=6 6 Hz) ppm (d_6-benzene) corresponding to the equivalent pair of methyl groups in each isomer



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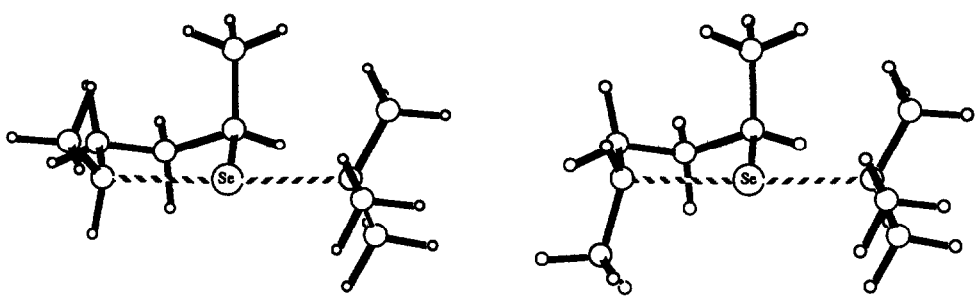
Chromatography, bromination and isolation in the usual manner gave rise to a 1.1 mixture of cis- and trans- 1,1-dibromo-2,5-dimethyltetrahydroselenophene (**19c**) as a crystalline solid, as evident by the appearance of two, approximately equal, signals in the ^{77}Se NMR spectrum at 716 3 and 750.5 ppm and two doublets in the ^{1}H NMR spectrum at 1 23 (J=7 0 Hz) and 1 37 (J=7 0 Hz) ppm

Figure 2. Calculated Transition Structures and Activation Energies[a] (ΔE_S) for the *Cis*- and *Trans*- Modes of Ring Closure of the 5-*Tert*-butylhex-2-yl Radical



21 ΔE_s= 11 4 **22** ΔE_s= 11 7

[a]Energies in kcal mol^{-1} For definition of ΔE_s, see text.

Fortunately, slow recrystallization of this mixure gave rise to predominately one isomer This isomer was assigned to be trans-1,1-dibromo-2,5-dimethyltetrahydroselenophene (trans- **19c**) on the basis of a ^{1}H NMR double irradiation experiment. Irradiation of the methyl doublet at δ 1 37 ppm resulted in the collapse of the multiplet at 4.4 ppm, corresponding to the proton on the carbon adjacent to selenium, to a doublet of doublets

with coupling constants of 4 0 and 12.1 Hz. These coupling data are consistent with the axial-equatorial and axial-axial couplings expected in trans-1,1-dibromo-2,4-dimethyltetrahydroselenophene (trans- **19c**) Indeed, application of the Karplus equation[41] to the MM2- optimized structure of trans-2,4-dimethyltetrahydroselenophene (**20**) gives rise to predicted coupling constants of 5.6 Hz (H_a-H_b) and 11.6 Hz (H_a-H_c), in good agreement with our observations

Further insight into the stereochemistry of this reaction was obtained by modelling the ground and transition states (**21, 22**) involved in the two modes of cyclization of the *tert*-butyl analogue of **1f**, namely the 5-(*tert*-butylseleno)hex-2-yl radical, as previously described. The calculated structural data and strain energies (ΔE_S) are displayed in Figure 2 The calculations predict little stereoselectivity in this reaction with the cis mode of cyclization preferred over that for the trans by only 0 3 kcal/mol with ΔE_S values of 11 4 and 11 7 kcal.mol^{-1} respectively. Clearly then, the calculated data are in agreement with the experimental observation that **1f** ring closes without stereoselectivity

Acknowledgement

We thank the Australian Research Council and Deakin University for Financial Support.

Experimental

5-Bromopentanoic acid and 6-bromohexanoic acid were purchased from Aldrich or Tokyo Kasei and were used without further purification 7-Bromoheptanoic acid[42], 5-bromo-2-ethylpentanoic acid[41], and dibenzyldiselenide[43] were prepared as previously described.

NMR spectra were recorded on a JEOL JNM-GX270 or PMX-60 spectrometer using deuteriochloroform ($CDCl_3$) as solvent, unless otherwise stated Mass spectra were recorded on a Hewlett Packard 5890 series II Gas Chromatograph/Mass Spectrometer Infrared spectra were recorded on a Biorad FTS-7 FT-IR Spectrophotometer Melting points were determined on a Reichert hot stage melting point apparatus and are uncorrected

5-Bromo-2,5-dimethylpentanoic acid Following the general procedure of Schlessinger[40], a solution of lithium diisopropylamide (LDA) in tetrahydrofuran was prepared by the addition of a 2 0M solution of *n*-butyllithium in cyclohexane (14 mL, 28 mmol) to a solution of diisopropylamine (3 8 mL, 27 mmol) in dry THF (40 mL) at 4° After 20 min the solution was cooled to -78° and *tert*-butyl propionate (3 0 g, 23 mmol) was added over a period of 5 min The solution was stirred for 30 min at -78° after which 1,3-dibromobutane (7 3g, 34 mmol) was added rapidly followed by dry hexamethylphosphoramide (HMPA) (1 2 mL, 7 4 mmol). The reaction was stirred at -78° for 30 min, after which it was stirred at 5° for 1h The reaction was acidified with 5% hydrochloric acid and extracted with hexane (3 x 30 mL), dried ($MgSO_4$) and the solvent removed *in vacuo* The resulting oil was separated by flash chromatography (1 1 dichloromethane/ether) to give ***tert*-butyl 5-bromo-2,5-dimethylpentanoate** as a colourless oil and a mixture of diastereoisomers (6 0g, 56%), bp ~ 75°/0 75mm (Kuegelrohr). ^{1}H NMR (CCl_4) δ 1 06 (d, 3H, J = 7Hz), 1 36 (s, 9H), 1 66 (d, 3H, J = 7Hz), 1 6 - 1 9 (m, 4H), 2 0 - 2 6 (m, 1H), 3 7 - 4.2 (m, 1H) IR ν_{max} 1730 cm^{-1} MS m/e 264/266 (10%, M$^+$), 247/249 (9%), 191/193 (100%), 163/165 (42%) $C_{11}H_{21}O_2Br$ requires C, 49 8, H, 7 9% Found C, 49 7, H, 8 1%

The ester was added to a solution of *p*-toluenesulfonic acid (1 4 g, 7 5 mmol) in dry benzene (150 mL) and the solution heated at reflux overnight After cooling, the solution was washed with water (150 mL) and the aqueous phase extracted with ether The combined organic phases were washed with water, dried ($MgSO_4$) and the solvent removed *in vacuo* to give the title acid (2 8 g, 60%) of sufficient purity for further use ^{1}H NMR δ 1 17 (d, 3H, J = 7Hz), 1.66 (d, 3H, J = 7Hz), 1 6 - 1 9 (m, 4H), 2 2 - 2 7 (m, 1H), 3 8 - 4 3 (m, 1H) ^{13}C

NMR δ 16.86, 26.26, 26 35, 31.30, 31.56, 38 17, 38.49, 38.60, 39.00, 50.80, 51 02, 74.52, 78 22, 182 73, 182.80.

5-Bromo-2-methylpentanoic acid. The title acid was prepared by the above procedure, using diisopropylamine (3 8 mL, 27 mmol), THF (40 mL), 2 34M n-butyllithium in hexane (14 mL, 27 mmol), *tert*-butyl propionate (3.45 mL, 23 mmol), 1,3-dibromobutane (4 1 mL, 34 mmol) and HMPA (1.3 mL, 7 3 mmol) ***Tert*-butyl 5-bromo-2-methylpentanoate** was isolated as a colourless oil (1 8g, 20%), bp ~ 65°/0 75mm (Kuegelrohr) ^{1}H NMR (CCl_4) δ 1 1 (d, 3H), 1 4 (s, 9H), 1 5-2.6 (m, 6H), 3 2-3 5 (m, 1H) IR ν_{max} 1727 cm^{-1} $C_{10}H_{19}O_2Br$ requires C, 47 8, H, 7 6% Found C, 48 2, H, 8 0%

The ester was dissolved in dichloromethane (15 mL) and 70% aqueous perchloric acid (15 mL) added The two-phase mixture was stirred at room temperature for 20 h and the phases separated. The organic phase was washed with water and the combined aqueous phases extracted with dichloromethane. The combined organic phases were dried ($MgSO_4$) and the solvent removed to give the title acid[44] as a colourless oil (1 2g, 84%) ^{1}H NMR δ 0 7-1 1 (m, 2H), 1 2 (d, 3H, J = 7 Hz), 1 4-2 9 (m, 4H), 3 2-3 6 (m, 1H), 12 0 (s(br), 1H)

Standard procedure for the preparation of ω-benzylselenoalkanoic acids (3, 6, 14)

6-Benzylselenohexanoic acid (6a). Sodium borohydride (900 mg, 24 mol) was added, in portions, to a solution of dibenzyldiselenide (3 4 g, 10 mmol) in dry ethanol (50 mL) After the evolution of hydrogen had ceased (ca. 1 h), 6-bromohexanoic acid (4.0 g, 20 mmol) in ethanol (10 mL) was added with the immediate precipitation of a white solid The mixture was stirred at room temperature, under nitrogen, for 15 h after which satd sodium bicarbonate (10 mL) was added The product mixture was poured into water (30 mL), washed with 2 1 ether/hexane (2 x 30 mL) and acidified with 6N hydrochloric acid The resulting solution was extracted with 2 1 ether/hexane (3 x 30 mL), the combined organic phases dried (Na_2SO_4) and the solvent removed *in vacuo* to give the title acid as a pale solid of sufficient purity for further use (5 9 g, 94%), mp = 45-48° (lit[29] mp = 40-41°) ^{1}H NMR (d_6-acetone) δ 1 2 - 2 6 (m, 10H), 3 80 (s, 2H), 7 27 (m, 5H), 8 20 (s(br), 1H) ^{77}Se NMR (C_6H_6) δ 256 0

5-Benzylselenopentanoic acid (3) was prepared from 5-bromopentanoic acid following the standard procedure as a yellow solid in 85% yield, mp = 40-41° (lit[29] mp = 45-46 5°). ^{1}H NMR (d_6-acetone) δ 1 5 - 2 8 (m, 8H), 3 80 (s, 2H), 7 23 (m, 5H), 8 17 (s(br), 1H) ^{77}Se NMR (C6H6) δ 255 6

7-Benzylselenoheptanoic acid (6b) was prepared from 7-bromoheptanoic acid following the standard procedure as a pale solid in 46% yield, mp = 44 - 46° (lit[29] mp = 49 5 - 50 5°) ^{1}H NMR (d_6-acetone) δ 1 2 - 1 9 (m, 8H), 2 1 - 2.6 (m, 4H), 3 73 (s, 2H), 7 13 (m, 5H), 8 73 (s(br), 1H) MS m/e 300 (6%, M^+), 91 (100%)

5-Benzylseleno-2-methylpentanoic acid (14a) was prepared from 5-bromo-2-methylpentanoic acid following the standard procedure in 50% yield as a pale oil ^{1}H NMR δ 1 15 (d, 2H, J = 7 Hz), 1 4-1 8 (m, 4H), 2 4-2 6 (m, 3H), 3 77 (s, 2H), 7 21-7 35 (m, 5H) ^{13}C NMR δ 16 84, 23 47, 26 96, 27 71, 33 55, 38 91, 126 61, 128 43, 128 75, 183.04 ^{77}Se NMR δ 253

5-Benzylseleno-2-ethylpentanoic acid (14b) was prepared from 5-bromo-2-ethylpentanoic acid following the standard procedure in 47% yield as a pale oil ^{1}H NMR (CCl_4) δ 0 87 (t, 3H, J = 7 Hz), 1 1 - 1 8 (m, 6H) 2 0 - 2 5 (m, 4H), 3 65 (s, 2H), 7 13 (m, 5H), 11 9 (s(br), 1H) ^{13}C NMR δ 11 6, 23 4, 25 0, 26 8, 27 9, 31 6, 46 6, 126 5, 128 3, 128 7, 139 3, 182 6 MS m/e 300 (8%, M^+), 129 (10%), 91 (100%)

5-Benzylseleno-2-methylhexanoic acid (14c) was prepared from 5-bromo-2-methylhexanoic acid following the standard procedure in 52% yield as a mixture of diastereoisomers ^{1}H NMR (CCl_4) δ 1 0 - 2 5 (m, 11H), 3 71 (s, 2H), 4.0 - 4.5 (m, 1H), 7 06 (m, 5H), 10 8 (s(br), 1H) ^{13}C NMR δ 16 6, 16 7, 21 9, 22 0, 22 1, 22.3, 26.0, 28.0, 30 6, 31.2, 31 3, 31 5, 34 6, 34 8, 35 0, 38 8, 38 9, 126 3, 128 2, 128 5, 139 2, 182 4, 182 5 ^{77}Se NMR δ 350 3, 350 9

Standard procedure for the preparation of the cyclic selenides (5, 8, 19)

1,1-Dibromotetrahydroselenophene (5) 5-Benzylselenopentanoic acid (3) (1 0 g, 3 7 mmol), N-hydroxypyridine-2-thione (0 48 g, 3 8 mmol) and dicyclohexylcarbodiimide (DCC) (0 80 g, 3 8 mmol) were stirred in dichloromethane (10 mL) under nitrogen at 5°, shielded from background light, for 1 5 h The precipitate was filtered off and the solvent removed *in vacuo*, at room temperature, shielded from background light The yellow residue was dissolved in dry benzene (25 mL) and the solution irradiated, under reflux, with a 125W tungsten lamp at a distance of 50 mm until the yellow colour had disappeared and the evolution of carbon dioxide had ceased (ca. 45 min) The solution was poured onto a flash chromatography column and eluted with hexane The fractions containing tetrahydroselenophene (R_f ~ 0 15) were combined and a solution of bromine in carbon tetrachloride added until the bromine colour persisted The solvent was removed *in vacuo* to give the title compound as solid which was recrystallized from ethanol as yellow needles (0 8 g, 71%), mp = 91-91 5° (lit[33] mp = 92°) ^{1}H NMR δ 2 82 (m, 4H), 4 12 (m, 4H) ^{13}C NMR δ 32 7, 63 3

1,1-Dibromoselenane (8a) was prepared from 6-benzylselenohexanoic acid (**6a**) following the standard procedure as orange prisms in 69% yield, mp = 119-120° (lit[35] mp = 117-118°) ^{1}H NMR δ 1 80 (m, 2H), 2 28 (m, 4H), 3 94 (m, 4H) ^{13}C NMR δ 20 3, 21 6, 50 7

1,1-Dibromo-2-methyltetrahydroselenophene (19a) was prepared from 5-benzylseleno-2-methylpentanoic acid (**14a**) following the standard procedure as yellow needles in 87% yield, mp = 73-75° (lit[45] mp = 73-75° ^{1}H NMR δ 1 82 (d, 3H, J = 4Hz), 2 2-2 8 (m, 4H), 4 05 (m, 1H), 4 39 (m, 1H), 4.64 (m, 1H) ^{77}Se NMR δ 643 0 MS m/e 148 (65%, M-Br_2^+), 135 (82%), 69 (100%) HRMS Calcd for $C_5H_{10}SeBr_2$ M-Br_2^+ = 147 9956 Found 148 0098

1,1-Dibromo-2-ethyltetrahydroselenophene (19b) was prepared from 5-benzylseleno-2-ethylpentanoic acid (**14b**) following the standard procedure as a yellow oil (which refused to crystallize) in quantitative yield ^{1}H NMR δ 1 17 (t, 3H, J = 7 3 Hz), 2 1-2 9 (m, 6H), 4 0-4 6 (m, 2H) ^{13}C NMR δ 14 77, 25 41, 30 96, 37 81, 63 11, 86 40 ^{77}Se NMR δ 627 1 MS m/e 243 (8%, M-Br^+), 135 (97%), 91 (100%) HRMS Calcd for $C_6H_{12}SeBr_2$ M-Br^+ = 242 9289 Found 242 9333

1,1-Dibromo-2,5-dimethyltetrahydroselenophene (19c) was prepared from 5-benzylseleno-2-methylhexanoic acid (**14c**) following the standard procedure in 91% yield as a 1 1 mixture of diastereoisomers ^{1}H NMR δ 1 23 (d, 1 5H, J = 6Hz), 1 87 (d, 1 5H, J = 6Hz), 1 5 - 1 7 (m, 2H), 1 8 - 2 0 (m, 2H), 4 3 - 4 4 (m, 2H) ^{13}C NMR δ 18 43, 20 27, 39 11, 39 75, 79 24, 79 66 ^{77}Se (C_6H_6) NMR δ 716 3, 750 5 MS m/e 243 (20%, M-Br^+), 164 (100%) HRMS Calcd for $C_6H_{12}SeBr_2$ M-Br_2^+ = 164 0104 Found 164 0083

A sample was slowly recrystallized from ethanol to give predominantly one diastereoisomer assigned to be **trans-1,1-dibromo-2,5-dimethyltetrahydroselenophene** (trans/cis ~ 10 1, see text) mp = 89-94° ^{1}H NMR (C_6D_6) δ 1 87 (d, 3H, J = 6Hz), 1 5 - 1 7 (m, 2H), 1 8 - 2 0 (m, 2H), 4 3 - 4 4 (m, 2H) ^{13}C NMR δ 18 43, 39 75, 79 66

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