Tetrahedron Vol. 36, pp. 1399 to 1408
© Pergamon Press Ltd., 1980. Printed in Great Britain

0040-4020/80/0515-1399/$02.00/0

CYCLOFUNCTIONALISATION OF UNSATURATED ACIDS WITH BENZENESELENENYL CHLORIDE

KINETIC AND THERMODYNAMIC ASPECTS OF THE RULES FOR RING CLOSURE

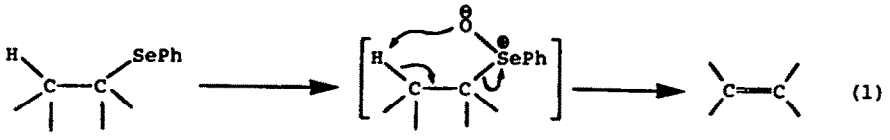
DERRICK L. J. CLIVE,* CHARLES G. RUSSELL,†
GIM CHITTATTU and ALOK SINGH
Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

(*Received in UK* 11 *July* 1979)

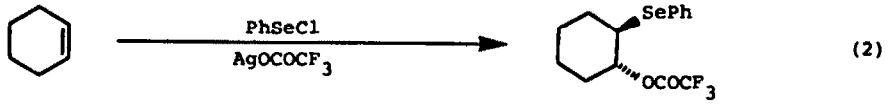
Abstract—Experimental procedures are described for the synthetically useful reaction by which olefinic acids are converted into lactones carrying a benzeneseleno-group. Data are presented to define some of the mechanistic details of this type of cyclofunctionalisation and kinetic and thermodynamic factors relevant to the Rules for Ring Closure are discussed. A nomenclature is introduced for a treatment of ring-fusion stereochemistry.

The recognition[1] of selenoxide fragmentation (eqn 1) as a mild and efficient route to olefins generated a requirement for synthetically attractive methods of introducing the benzeneseleno-group.[2] One of the first procedures to be studied in detail is the addition to olefins of reagents represented formally as PhSe–$OCOCF_3$[3] and PhSe–OAc[4] (eqn 2). The stereochemistry of reaction (2) is cleanly antarafacial but experiments with unsymmetrical olefins established[3] that the regioselectivity is poor. An improvement in this respect was likely to be a useful contribution to synthetic methodology because the selenoxide fragmentation (eqn 1) had been accepted rapidly as a standard method.[2a] In principle, a partially intramolecular process (eqn 3) might be sufficiently regioselective so that only one of the pathways shown (eqn 3) would, in general, be followed. Such a reaction involves not only stereo- and regiochemical control but also accomplishes a more substantial elaboration of the molecular framework than is possible with a totally intermolecular process. Reaction (3) conforms to a general pattern of intramolecular ring closure in which one terminus of the double bond involved in ring-formation becomes attached to a group (here PhSe—) that allows[2] further modifications at that site. The term *cyclofunctionalisation*[5] describes this type of synthetic operation.

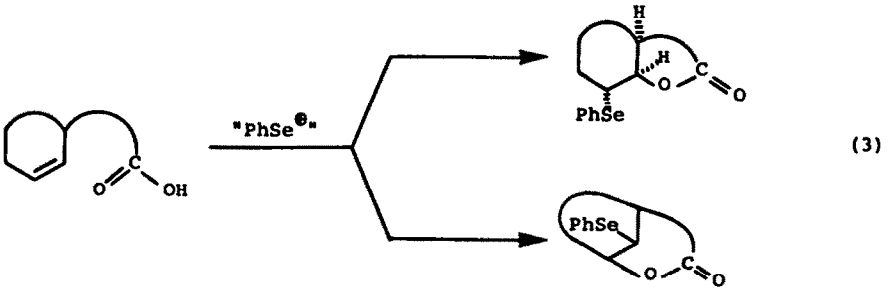
†National Research Council of Canada Postgraduate Scholar.



(1)



(2)



(3)

An example of cyclofunctionalisation in selenium chemistry was provided[6] by experiments in which the acid **1**, deliberately chosen for the presence of the α-substituents (whose rôle is to facilitate ring closure) was treated with the reagents **2** in boiling acetic acid. The lactones shown (eqn 4) were obtained in good yields but the potential utility of these experiments does not seem to have been appreciated for many years. Recently, the discovery represented by (eqn 4) was clearly recognised and was developed explicitly as a mild and routine synthetic method.[7,8]

In our initial experiments[7a] we converted the acids **3**, **4** and **5** (Table 1) into the corresponding lactones and we reported the fact that although the unsaturated acids react very quickly with benzeneselenenyl chloride (PhSeCl), formation of the γ-lactone product is comparatively slow. We report now experimental data for the preliminary work as well as for a number of additional examples. We also describe some mechanistic details of these cyclofunctionalisations and we discuss kinetic effects relevant to the Rules for Ring Closure.[9]

Cyclofunctionalisation

The general experimental procedure calls for dropwise addition of a solution of commercial (Aldrich) PhSeCl to a stirred solution of the acid. Usually, only 1 equivalent of the reagent is used and suitable solvents,‡ chosen arbitrarily, are EtOAc, Et_2O, $CHCl_3$, CH_2Cl_2, and CCl_4. It is often convenient to conduct these reactions at about 20° for an overnight period but, occasionally it is necessary to increase the rate of ring closure by using a higher temperature. For example, refluxing EtOAc was appropriate for acids **3** and **5**. The preparative results are summarised in the Table which shows the starting acids and the materials obtained by treatment with PhSeCl. γδ-Unsaturated acids are an accessible compound class[10] and all of the samples used are known compounds that were prepared by the literature methods.

The lactone nature of the reaction products (Table 1) is evident from IR measurements and the structures could usually be deduced from NMR data. For compounds **4a–6a** additional chemical evidence in support of the stereochemical assignments was obtained by heating the lactones with Ph_3SnH in boiling toluene. This treatment caused the replacement[11] of the benzeneseleno-group by hydrogen and the reduction products were identified by comparison with authentic samples. Similar reduction of **11a** and **12a** gave the expected lactones.

In the case of the products obtained from the stilbene acids, **12** and **13**, the NMR data do not allow the stereochemistry to be assigned in an unambiguous fashion; that shown is expected by analogy with our other examples.[12]

Lactones **10a** and **10b** are not clearly differentiated by NMR measurements and an examination of Dreiding models.[13] The assignments made are tentative.

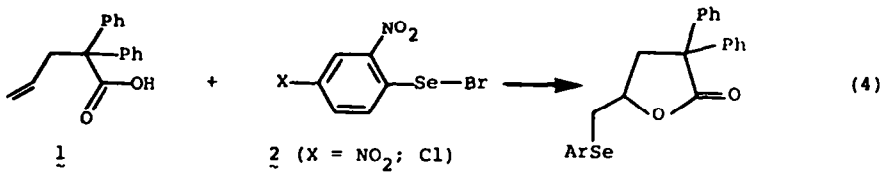
We have occasionally noticed that a reaction which is incomplete as judged by the presence of substantial carboxyl IR adsorption can still afford a good yield of the required lactone if work-up involves chromatography over silica gel. We have found that silica gel can play an important rôle in some cyclofunctionalisations. For example, yields in the cyclisation[8d] of urethanes (eqn 5) are raised 10–25% by running the reactions in the presence of dry silica gel.[14] However, we did not study the effect of this additive on the reactions of carboxylic acids because acceptable yields were usually obtained by control of reaction time and temperature.

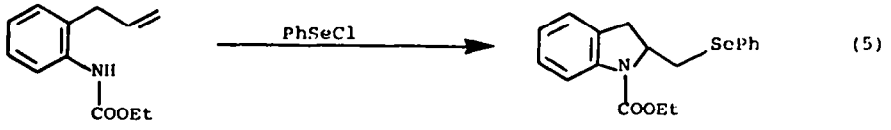
We investigated briefly several alternative procedures for cyclofunctionalisation of acids and their derivatives: The ester **16**[15] does not give a lactone under our usual conditions and the acid salt **17** failed to react appreciably on treatment with PhSeCl in THF or MeCN; it readily affords the lactone **4a** on reaction in AcOH. The free acid **3** (Table 1) was converted into the lactone **3a** by treatment with PhSe–NEt_2;[16] however, this reaction is not as clean as the normal process. Lactone formation was detected spectroscopically (IR) when acid **3** was treated with $PhSeCl_3$.[17]

Mechanistic considerations

All of the starting materials react rapidly with PhSeCl. The orange colour of the selenium reagent is quickly discharged, especially at the beginning of the addition and the solution assumes a lemon-yellow coloration which, particularly when Et_2O is the solvent, then fades slowly to a barely perceptible level.§

During early stages of the reaction, examination by TLC (silica gel) suggests that the starting material has disappeared but that little of the final γ-lactone has formed. Corresponding IR measurements confirm that lactonisation is incomplete because substantial carboxyl absorption is still present. The IR spectra taken¶ during the course of these reactions usually reveal the rapid development of absorption at about 1740 cm^{-1} which is





‡It is appreciated that details of the mechanism may depend on the nature of the solvent.

§The colour changes occur more slowly for the stilbene acids **12** and **13**.

¶Samples were removed from preparative runs or were generated directly in an IR cell by a simple stopped-flow apparatus.

Table 1.

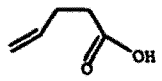
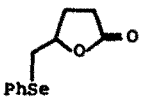
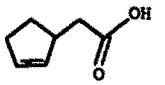
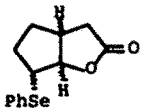
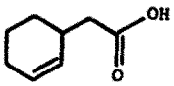
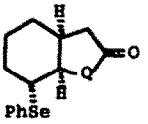
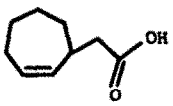
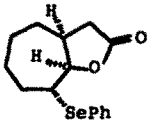
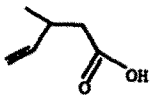
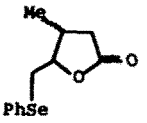
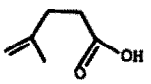
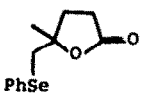
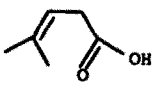
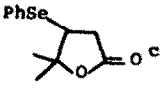
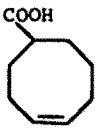
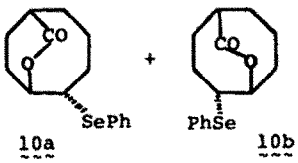
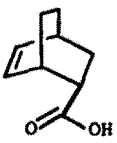
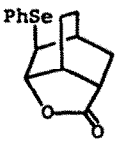
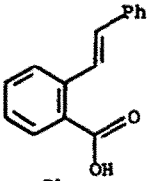
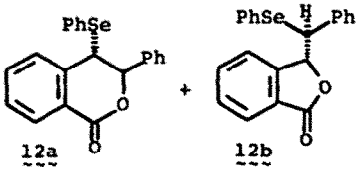
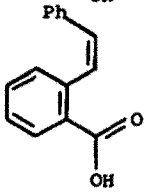
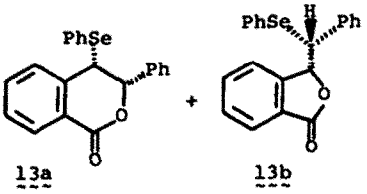
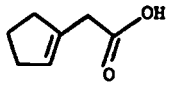
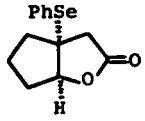
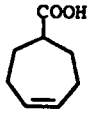
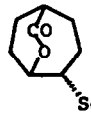
	Starting Acid		Product (%)	
3		3a		94%
4		4a		73%
5		5a		82%
6		6a		97%
7		7a		~69%[a]
8		8a		85%, 95%[b]
9		9a		[c]
10		10a + 10b		87%[d]
11		11a		[e] 76%
12		12a + 12b		89%[f]
13		13a + 13b		79%[g]

Table 1. (*Contd*)

Starting Acid		Product (%)		
14			14a	30%
15			15a	~76%

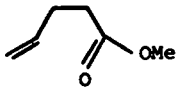
[a]A 1:1 mixture of isomers is formed. See Bartlett, P. A.; Myerson, J., *J. Am. Chem. Soc.* 1978, **100**, 3950.
[b]95%: corrected for impurity in **8**.
[c]The starting acid **9** was an impurity in **8** and compound **9a** was isolated in ~80% yield (based on the amount of **9** in **8** and assuming no isomerisation, **8**→**9**).
[d]Combined yield. Initially isolated proportions were: **10a**:**10b**:4:1.
[e]See Adams, T.; Moriarty, R. M., *J. Am. Chem. Soc.* 1973, **95**, 4071.
[f]Combined yield. Initially isolated proportions were: **12a**:**12b**:2:3.
[g]Combined yield. Initially isolated proportions were: **13a**:**13b**:3:1.

then replaced by the γ-lactone band of the final product. Evidently, several intermediates are being formed and the following observations serve to elucidate some important details of the reaction pathway:

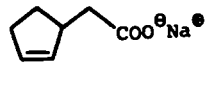
With the stilbene acid **12**, IR measurements showed fast production (in Et_2O) of a δ-lactone and slower formation of the γ-isomer. When the process was monitored by NMR (200 MHz) the methine signals of the δ-lactone were observed immediately. They then decreased (with respect to the total aromatic signals) and there was a corresponding increase in the signals characteristic of the γ-lactone **12b**. When the pure δ-lactone was treated with HCl (~1 equivalent) in dry Et_2O it was converted into the γ-isomer. Rearrangement was also observed by using $BF_3 \cdot Et_2O$.

Acid **10** gave two products, **10a** and **10b**. On storage in $CDCl_3$, the individual lactones were each converted into a mixture of both isomers, presumably under the influence of traces of acid.

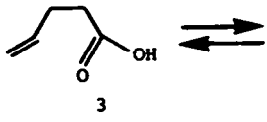
The initial event in several other examples (**3**–**6**), that we examined by NMR, is the immediate disappearance of the olefinic protons with retention of the carboxyl proton, and it is probable that a β-chloroselenide is formed in each case. For the acid **3** the spectra were the easiest to interpret and they suggest that a kinetically formed β-chloroselenide is produced. It then rearranges to the thermodynamic isomer (eqn 6).[18] The signals for the terminal $-CH_2-$ of **18** occur as a quartet centred at 3.89 δ (CCl_4; 200 MHz) and a triplet centred at 3.6 δ. The intensity of these multiplets gradually decreases and they are replaced by corresponding signals for **19**: a quartet centred at 3.20 δ and another at 3.12 δ.



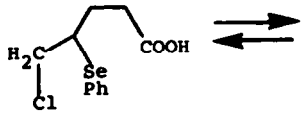
16



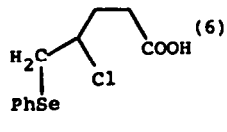
17



3

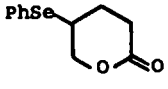


18

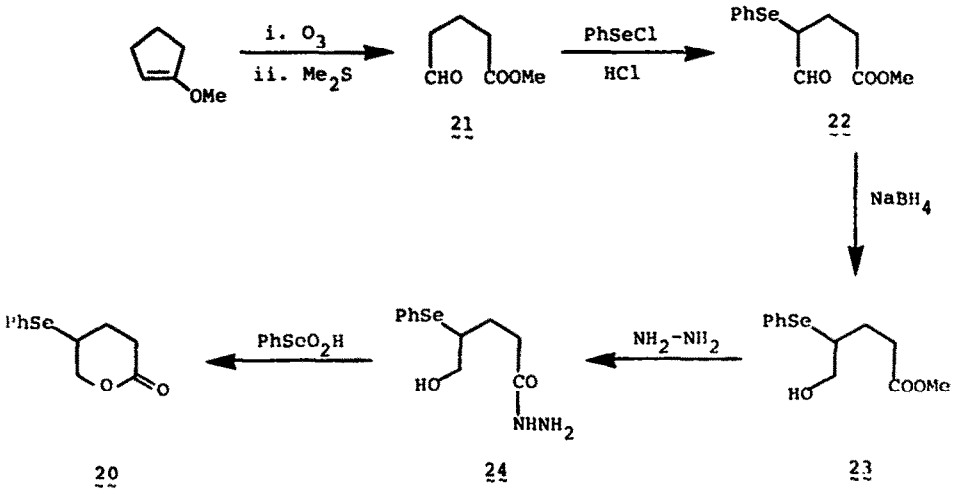


(6)

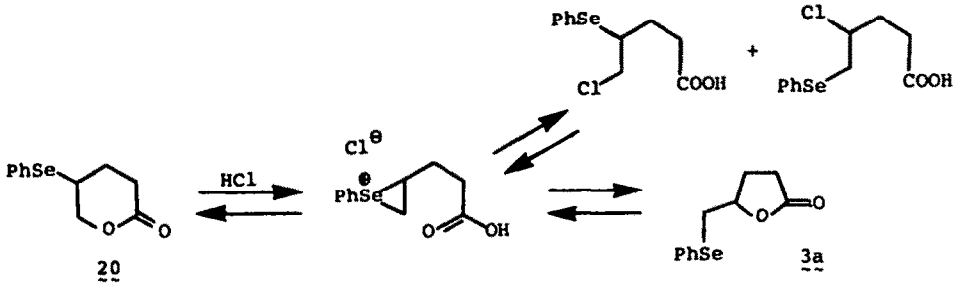
19



20



Scheme 1.



Scheme 2.**

None of our NMR spectra was amenable to more detailed interpretation and reactions run in chlorinated solvents in an NMR tube do not readily go to completion. Possibly the presence of HCl retards ring closure.

In contrast to the reactions of the stilbene acids, we could not isolate a δ-lactone from experiments with **3–6**. However, a specimen of compound **20** was prepared by the method shown in Scheme 1 and its properties were examined. Lactonisation of the hydroxyester **21** was not an easy process and had to be effected in the manner shown.[19] On treatment (under anhydrous conditions) with HCl in Et_2O the δ-lactone **20** underwent substantial rearrangement to the γ-lactone **3a**. As observed with the stilbene series (**12a**), $BF_3{\cdot}Et_2O$ also caused rearrangement.

The above observations can be summarised as follows:

(i) PhSeCl usually adds to the double bond faster than lactonisation occurs. A mixture of kinetic and thermodynamic β-chloroselenides can be formed.‖

(ii) In the case of the stilbene acid **10** a δ-lactone is produced and it is formed faster than the γ-isomer. The latter is the thermodynamic product.

(iii) Isolation or detection (NMR) of a δ-lactone from **3**, **4**, **5**, or **6** was not achieved but the δ-lactone **20** was shown to rearrange under the influence of acid.

One chemically reasonable mechanism for the rearrangement **20**→**3a** assuming *anhydrous* conditions is shown in Scheme 2.**

The observation of kinetic and thermodynamic products (e.g., from **12**) is the third instance of such a result in cyclofunctionalisations with selenium reagents.†† The first case[5] is shown in (eqn 7§§) and a more recent example[20] in (eqn 8).

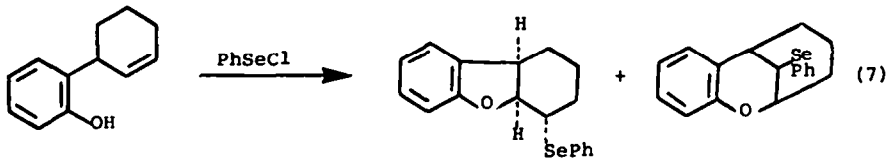
It is not yet clear whether cyclofunctionalisations, for any particular heterocyclic system, occur *via* an episeleniranium ion[21] (e.g. **27a** and **27b**) or by a concerted process[22] (e.g. **28a** and **28b**). It is likely that open ions are not involved because of the clean antarafacial addition of selenenyl reagents to disubstituted double bonds. In terms of the rules for ring closure[9] the 6-*endo* processes **27a** and **28a** and the 5-*exo* closures **27b** and **28b** are all allowed.

‖We did not detect β-chloroselenide formation with the stilbene acids.

**It is appreciated that adventitious traces of water, acting in a catalytic manner, may cause hydrolysis of the lactone to 5-hydroxy-4-phenylseleno-pentanoic acid which then becomes the precursor to the seleniranium ion shown.

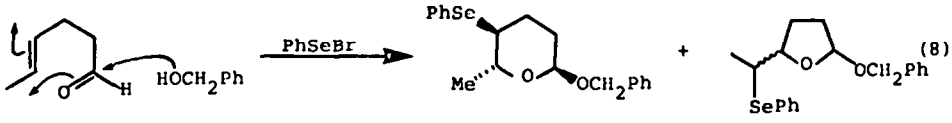
††We refer here to discrimination, by kinetic factors, between modes of cyclisation (see following discussion) that are *both* allowed by the rules for ring closure.

§§This is an example of regioselectivity where both termini of the double bond are equally substituted. The kinetic product is **25**. For eqn 8 the kinetic product is **26**.



(7)

25



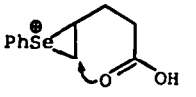
(8)

26

The examples of (eqns 7 and 8) and the stereospecific cyclisation of the stilbene acid **12** are reactions where the structures of the thermodynamic products disguise the kinetic preference between formal 5-*exo*- and 6-*endo*-pathways.[23,27]

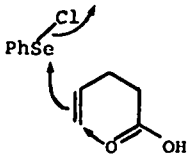
Ring-fusion stereochemistry

The bicyclic lactones **4a–6a** all have the *cis* ring-fusion shown. Presumably, the selenium reagent approaches from the face of the molecule *trans* to the carboxyalkyl side chain as this is likely to be favoured on steric grounds. However, attack from the other face can also lead to the observed products if formation of the β-chloroselenide is easily reversible and evidence for such reversibility is provided by the experiment summarised by (eqn 9). The step leading to the observed products can, therefore be pictured as in **29** or **30** (which arbitrarily show the process for 2-cyclopenten-1-acetic acid). Such reactions can be described (in the case of **29** and **30**) as 5-*exo*-5 processes. The first two symbols (i.e. "5-*exo*") have the usual meaning and indicate the formation of a 5-membered ring by an *exo*-trigonal closure. The numerical suffix (i.e. "5") specifies the size of the ring in which the double bond is initially located. An examination of Dreiding models and a consideration of the appropriate approach vectors for ring closure suggest that formation of *trans* fused products by a 5-*exo*-5 reaction is extremely unfavourable. This is not so for a 5-*exo*-7 reaction (see acid **6**). We did not however, detect any *trans*-fused lactone from **6**,[28] possibly as a result of the facile reversibility of some of the stages leading to the final product.



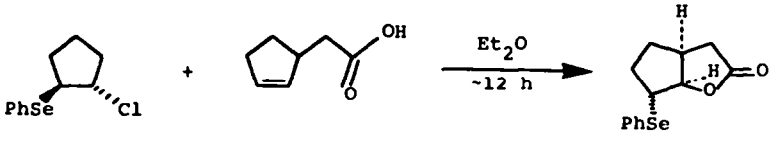
27a

27b



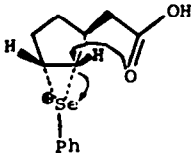
28a

28b

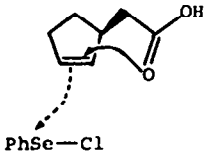


(9)

47% (NMR)



29



30

EXPERIMENTAL

Reactions were conducted under anhydrous conditions in a septum-closed flask whose contents were stirred magnetically and kept under a slight static pressure of N_2. All solvents were distilled before use: dry CH_2Cl_2 from CaH_2; dry $CHCl_3$ and EtOAc from P_2O_5 ($CHCl_3$ under N_2); dry Et_2O from metallic Na. During product isolation solns were evaporated under water pump vacuum at room temp. Where compounds were isolated simply by evaporation of their solns (without subsequent distillation or crystallisation) the residues were kept under oil pump vacuum and checked for constancy of weight. Unless indicated to the contrary isolated products were submitted directly for combustion analysis without need for additional purification. Plates for PLC were 60 × 20 × 0.1 cm and were heated at 110° for 1 h before use. Silica gel for PLC and TLC was Merck type 60-PF-254. Silica gel for column chromatography was Merck type 60 (70-230 mesh). Mass spectra were run at an ionizing voltage of 70 eV. B.Ps quoted for products distilled in a Kugelrohr apparatus refer to the oven temp. All chiral products were obtained as racemates.

Dihydro - 5 - [(*phenylseleno*)*methyl*] - 2(3H) - *furanone*, **3a**

Benzeneselenenyl chloride (955 mg, 5 mmol) in EtOAc (12 mL) was injected dropwise into a cold (*ca* −78°) soln of 4-pentenoic acid[29] (500 mg, 5 mmol) in EtOAc (10 mL). A further portion of EtOAc (3 mL) was used to rinse residual PhSeCl into the reaction vessel. The cold bath (and hence the mixture) was allowed to attain room temp. After an overnight period a sample still showed carboxyl absorption (IR). The soln was refluxed 3.5 hr to complete formation of **3a** (IR control). The solvent was evaporated and the product was isolated by chromatography over silica gel (60 × 2.5 cm) using 1:2-EtOAc: 2,2,4-trimethylpentane. Evaporation of the eluate gave **3a** (1.200 g, 94%) as a pale yellow, homogeneous (TLC, silica gel, 1:2-EtOAc: 2,2,4-trimethylpentane) oil: ^{1}H-NMR (400 MHz, $CDCl_3$) δ1.88–1.98 (m, centered at 1.93, 1H), 2.32–2.60 (m, 3H), 3.03 (dd, J = 15.2, 9.6 Hz, 1H), 3.26 (dd, J = 15.2, 7.2 Hz, 1H), 4.58–4.72 (m, centered at 4.63, 1H), 7.22–7.32 (m, 3H), 7.48–7.57 (m, 2H); IR (film) 1770 cm^{-1}; exact mass 256.0002 [calcd. for $C_{11}H_{12}O_2{}^{80}Se$, 256.0003]. For analysis a sample was distilled in a Kugelrohr: bp 120°C (0.005 mm). (Found: C, 51.88; H, 4.75; O, 12.79. Calcd. for $C_{11}H_{12}O_2Se$: C, 51.78; H, 4.74; O, 12.54).

(3aα, 6aα, 6aα) - *Hexahydro* - 6 - (*phenylseleno*) - 2H - *cyclopenta*[b]*furan* - 2 - *one*, **3a**

(a) *Use of the free acid.* With the exception noted below the procedure for **3a** was followed using 2-cyclopentene-1-acetic acid[30] (252 mg, 2 mmol) in EtOAc (5 mL) and PhSeCl (384 mg, 2.0 mmol) in EtOAc (5 mL + 5 mL rinse). After 24 hr at room temp (i.e. no reflux period) the reaction was complete (IR control). Chromatography over silica gel (60 × 1 cm) using 1:2-EtOAc: 2,2,4-trimethylpentane gave **4a** (412 mg, 73%) as a homogeneous (TLC, silica gel, 1:2-EtOAc: 2,2,4-trimethylpentane) pale yellow oil: ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.56 (m, 1H), 1.82 (m, 1H), 2.12–2.38 (m incorporating dd at 2.32, J = 19.3, 2.9 Hz, 3H), 2.80 (dd, J = 19.3, 10.4 Hz, 1H), 3.09 (m, 1H), 3.87 (m, 1H), 4.88 (d, J = 6.4 Hz, 1H), 7.20–7.32 (m, 3H), 7.44–7.56 (m, 2H); IR (film) 1773 cm^{-1}; exact mass 282.0148 [calcd. for $C_{13}H_{14}O_2{}^{80}Se$, 282.0159]. Material from another experiment was distilled in a Kugelrohr: b.p. 135° (0.001 mm). (Found: C, 55.61; H, 5.07, O, 11.39. Calcd. for $C_{13}H_{14}O_2Se$: C, 55.53; H, 5.02; O, 11.38).

(b) *Use of potassium salt.* Benzeneselenenyl chloride (382 mg, 1.9 mmol) in AcOH (5 mL) was injected dropwise into a soln of potassium 2-cyclopentene-1-acetate (265 mg, 1.61 mmol) in AcOH (5 mL). More AcOH was used to rinse all PhSeCl into the mixture. Formation of **4a** appeared to be complete after 15 min (TLC control). The solvent was evaporated and isolation as described for **3a** afforded pure (TLC) **4a** (340 mg, 75%).

(3aα, 7α, 7aα) - *Hexahydro* - 7 - (*phenylseleno*) - 2(3H) - *benzofuranone* **5a**

Benzeneselenenyl chloride (764 mg, 3.99 mmol) in EtOAc (10 mL) was injected into a soln of 2-cyclohexene-1-acetic acid[31] (500 mg, 3.99 mmol) in EtOAc (10 mL). More EtOAc (5 mL) was used to rinse all the PhSeCl into the reaction vessel. The mixture was refluxed for 7 hr, the solvent was evaporated and the residue was partitioned between ether and 5% w/v $NaHCO_3$aq. The ether soln was dried and evaporated. Chromatography of the residue over silica gel (60 × 2 cm) using 2:3-EtOAc: 2,2,4-trimethylpentane gave, after removal of solvent and Kugelrohr distillation, **5a** (975 mg, 82%) as a homogeneous (TLC, silica gel, 1:1-EtOAc: 2,2,4-trimethylpentane) oil: bp 125° (0.01 mm). (Found: C, 56.86, H, 5.47; O, 10.88. Calcd. for $C_{14}H_{16}O_2Se$: C, 56.96; H, 5.46; O, 10.84). Pure material from another experiment had: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.00–2.83 (m, 9H), 3.68 (q, J = 4 Hz, 1H), 4.40 (t, J = 4 Hz, 1H), 7.15–7.39 (m, 3H), 7.39–7.65 (m, 2H); IR (CCl_4) 1790 cm^{-1}; exact mass 296.0317 [calcd. for $C_{14}H_{16}O_2{}^{80}Se$, 296.0315].

(3aα, 8α, 8aα) - *Octahydro* - 8 - (*phenylseleno*) - 2H - *cyclohepta*[b]*furan* - 2 - *one*, **6a**

Benzeneselenenyl chloride (176.6 mg, 0.92 mmol) in ether (3 mL) was injected into a soln of 2-cycloheptene-1-acetic acid[28a] (142.0 mg, 0.92 mmol) in ether (3 mL). Additional ether (3 mL) was used to transfer residual PhSeCl. The mixture was stirred overnight at room temp. The solvent was evaporated and the residue was chromatographed over silica gel (60 × 2 cm) using 1:1-heptane: EtOAc. Evaporation of appropriate fractions afforded **6a** (277.0 mg, 97%) as a viscous, homogeneous (TLC, silica gel, 1:1-heptane: EtOAc) oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10–2.34 (m, 9H), 2.40–3.02 (m, incorporating dd at 2.84, J = 16.8, 9.5 Hz, 2H), 3.40 (t, J = 9.5, 8.8 Hz, 1H), 4.60 (dd, J = 10.0, 6.2 Hz, 1H), 7.15–7.36 (m, 3H), 7.42–7.68 (m, 2H); IR (film) 1785 cm^{-1}; exact mass 310.0473 [calcd. for $C_{15}H_{18}O_2{}^{80}Se$, 310.0473]. (Found: C, 58.16; H, 5.78; O, 10.51. Calcd. for $C_{15}H_{18}O_2Se$: C, 58.25; H, 5.87; O, 10.35).

Reduction of **6a** *with* Ph_3SnH. Triphenyltin hydride[32] (344.4 mg, 0.98 mmol) was added from a syringe in three equal portions at 30 min intervals to a refluxing soln of **6a** (202.3 mg, 0.65 mmol) in toluene (3 mL). Refluxing was continued for 16 hr after the last addition. The mixture was applied to a column of silica gel (60 × 2 cm) and chromatography, using 1:1-heptane: EtOAc, gave (3aα, 8aα) - octahydro - 2H - cyclohepta[b]furan - 2 - one (82.8 mg, 82%) as a homogeneous (TLC, silica gel, 1:1-heptane: EtOAc) oil: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.00–3.04 (m, 13H), 4.65 (m, 1H); IR (film) 1780 cm^{-1}. No *trans* lactone[28a] was obtained.

cis- *and* trans - *Dihydro* - 4 - *methyl* - 5 - [(*phenylseleno*)*methyl*] - 2(3H) - *furanone*, **7a**

The method for **6a** was followed using 3-methyl-4-pentenoic acid[33] (500.0 mg, 4.38 mmol) in ether (6 mL) and PhSeCl (839.0 mg, 4.38 mmol) in ether (7 mL + 7 mL rinse). After a reaction period of 60 hr chromatography over silica gel (60 × 3 cm) using 1:1-heptane: EtOAc gave **7a** (821.0 mg, 69%) as a homogeneous (TLC, silica gel, 1:1-heptane: EtOAc) oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.01 (d, J = 8.4, 1.5H), 1.13 (d, J = 7.2 Hz, 1.5H), 2.12–2.58 (m, 1.5H), 2.62–2.84 (m, 1.5H), 2.90–3.32 (m, 2H), 4.24 (q, J = 6.0 Hz, 0.5H), 4.54–4.68 (m, 0.5H), 7.20–7.36 (m, 3H), 7.48–7.63 (m, 2H); IR (film) 1775 cm^{-1}; exact mass 270.0169 [calcd. for $C_{12}H_{14}O_2{}^{80}Se$, 270.0159]. Found: C, 53.57; H, 5.26; O, 11.93. Calcd. for $C_{12}H_{14}O_2Se$: C, 53.54; H, 5.24; O, 11.89.

Dihydro - 5 - *methyl* - 5 - [(*phenylseleno*)*methyl*] - 2(3H) - *furanone*, **8a** *and dihydro* - 5, 5 - *dimethyl* - 4 - (*phenylseleno*) - 2(3H) - *furanone*, **9a**

The method for **6a** was followed using 4-methyl-4-pentenoic acid[34,35] (150.0 mg, 1.32 mmol) in ether (3 mL) and PhSeCl (252.0 mg, 1.32 mmol) in ether (3 mL + 3 mL rinse). After a reaction period of 17 hr chromatography over silica gel (60 × 2 cm) using 1:1-heptane: EtOAc gave two lactones as homogeneous (TLC, silica gel, 1:1-heptane: EtOAc) oils: **8a** [301.0 mg, 85% (95% after correction for presence of **9** in the starting material)] and **9a** (38 mg, 10%). **8a**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.47 (s, 3H), 1.81–2.70 (m, 4H), 3.16 (s, 2H), 7.14–7.32 (m, 3H), 7.42–7.64 (m, 2H); IR (film) 1775 cm^{-1}; exact mass 270.0156 [calcd. for $C_{12}H_{14}O_2{}^{80}Se$, 270.0159]. (Found: C, 53.43; H, 5.21; O, 12.08. Calcd. for $C_{12}H_{14}O_2Se$: C, 53.34; H, 5.22; O, 11.84). **9a**: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.45 (s, 3H), 1.49 (s, 3H), 2.58–3.10 (m, centered at 2.85, 2H), 3.59–3.78 (m, centered at 3.68, 1H), 7.22–7.40 (m, 3H), 7.47–7.70 (m, 2H); IR (film) 1775 cm^{-1}; exact mass 270.0153 [calcd. for $C_{12}H_{14}O_2{}^{80}Se$, 270.0159].

1α,5β,6α) - 5 - (*Phenylseleno*) - 7 - *oxabicyclo*[4.2.2]*decan* - 8 - *one*, **10a** *and* 1α,4β,5α) - 4 - (*phenylseleno*) - 6 - *oxabicyclo*[3.3.2]*decan* - 7 - *one*, **10b**

The method for **6a** was followed using 4-cyclooctene-1-carboxylic acid[36] (127.0 mg, 0.82 mmol) in ether (3 mL) and PhSeCl (157.5 mg, 0.82 mmol) in ether (3 mL + 3 mL rinse). After a reaction period of 17 hr chromatography over silica gel (60 × 2 cm) using 1:1-heptane: EtOAc gave a mixture of **10a** and **10b** (223.4 mg, 88%) in a ratio of 80:20 (NMR) respectively. Enriched, crystalline samples of **10a** and **10b**, each containing not more than 15% of the other isomer, were obtained by PLC over silica gel using 1:1-heptane: EtOAc. **10a**: mp 51–56°; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.44–2.44 (m, 10H), 2.92–3.07 (m, 1H), 3.74 (dt, J = 11.1, 4.08 Hz, 1H), 4.72–4.86 (m, 1H), 7.24–7.34 (m, 3H), 7.46–7.60 (m, 2H); IR ($CHCl_3$) 1772 cm^{-1}; exact mass 310.0476 [calcd. for $C_{15}H_{18}O_2{}^{80}Se$, 310.0472]. **10b**: mp 35–48°; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.44–2.34 (m, 10H), 3.12–3.26 (m, 1H), 3.50–3.72 (m, 1H), 4.53 (dt, J = 7.5, 3.1, 2.5 Hz, 1H), 7.20–7.36 (m, 3H), 7.44–7.59 (m, 2H); IR ($CHCl_3$) 1715 cm^{-1}; exact mass 310.0476 [calcd. for $C_{15}H_{18}O_2{}^{80}Se$, 310.0472]. A mixture of **10a** and **10b** was used for combustion analysis: (Found: C, 58.28; H, 5.84; O, 10.27. Calcd. for $C_{15}H_{18}O_2Se$: C, 58.25; H, 5.87; O, 10.35).

3 - endo - *Hydroxy* - 2 - exo - (*phenylseleno*) - 5 - endo - *carboxybicyclo*[2.2.2]*octane lactone*, **11a**

The method for **6a** was followed using bicyclo[2.2.2]octa-5-ene - 2 - *endo* - carboxylic acid[37] (152.0 mg, 1.0 mmol) in ether (3 mL) and PhSeCl (211.0 mg, 1.1 mmol) in ether (3 mL + 3 mL rinse). After 18 hr the solvent was evaporated from the resulting suspension and the residue was crystallised twice from cyclohexane to obtain **11a** (234.1 mg, 76%) as a pure (TLC, silica gel, 3:2-heptane: EtOAc), crystalline compound: mp 114–115°; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.10–2.80 (m, 9H), 3.54–3.68 (m, 1H), 4.56–4.74 (m, 1H), 7.18–7.75 (m, 5H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 180.07, 133.03, 129.46, 128.66, 127.57, 83.19, 45.52, 36.46, 34.70, 29.29, 28.86, 22.01, 15.26 ppm; IR (CH_2Cl_2) 1775 cm^{-1}; exact mass 308.0316 [calcd. for $C_{15}H_{16}O_2{}^{80}Se$, 308.0316]. (Found: C, 58. 76; H, 5.27; O, 10.35. Calcd. for $C_{15}H_{16}O_2Se$: C, 58.64; H, 5.25; O, 10.41).

Reduction of **11a** *with* Ph_3SnH. Triphenyltin hydride (380 mg, 0.90 mmol) was added to a refluxing soln of **11a** (183 mg, 0.60 mmol) in toluene (2 mL). Refluxing was continued for 6 hr and the cooled mixture was applied to a column of silica gel (60 × 1 cm). Chromatography, using 3:2-hexane: EtOAc followed by sublimation (100°, 0.005 mm) gave 6 - *endo* - hydroxybicyclo[2.2.2]octan - 2 - *endo* - carboxylic acid lactone (64.8 mg, 70%): mp 203–204° [lit.[38] mp 205–206°]; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.38–2.12 (m, 9H), 2.38–2.78 (m, 2H), 4.56–4.76 (m, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 181.31, 78.49, 37.44, 34.41, 33.27, 27.67, 26.11, 23.57, 15.74 ppm; IR (CH_2Cl_2) 1770 cm^{-1}; exact mass 152.0833 [calcd. for $C_9H_{12}O_2$, 152.0835].

3,4 - *Dihydro* - 3 - *phenyl* - 4 - (*phenylseleno*) - 1H - 2 - *benzopyran* - 1 - *one*, **12a** *and* 1,3 - *dihydro* - 1 - [*phenyl*(*phenylseleno*)*methyl*]*isobenzofuran*, **12b**

The method for **6a** was followed using *trans*-stilbene-2-carboxylic acid[39] (200.0 mg, 0.84 mmol) in ether (3 mL) and PhSeCl (160.7 mg, 0.84 mmol) in ether (3 mL + 3 mL rinse). After a reaction period of 18 hr chromatography over silica gel (60 × 2 cm), using 5:1-heptane: EtOAc, gave a mixture of **12a** and **12b** (284.6 mg, 89%) in a 40:60 ratio (NMR). Enriched, crystalline samples of **12a** and **12b**, each containing not more than 5% (NMR) of the other isomer were obtained by PLC over silica gel using 5:1-heptane: EtOAc. **12a**: mp 121–126°; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.86 (d, J = 2.4 Hz, 1H), 5.85 (d, J = 2.4 Hz, 1H), 6.98–7.78 (m, 13H), 8.05 (m, 1H); IR (CCl_4) 1738 cm^{-1}; exact mass 380.0317 [calcd. for $C_{21}H_{16}O_2{}^{80}Se$, 380.0316]. **12b**: mp 120–127°; ^{1}H NMR (200 Hz, $CDCl_3$) 4.65 (d, J = 4.4 Hz, 1H), 5.87 (d, J = 4.4 Hz, 1H), 7.02–7.81 (m, 14H); IR (CCl_4) 1780 cm^{-1}; exact mass 380.0315 [calcd. for $C_{21}H_{16}O_2{}^{80}Se$, 380.0315].

Reduction of **12a** *with* Ph_3SnH. Triphenyltin hydride (265 mg, 0.75 mmol) was added to a refluxing soln of **12a** (189.5 mg, 0.5 mmol) in toluene (3 mL). After 45 min (TLC control) the solvent was evaporated and chromatography over silica gel (60 × 1 cm) using 7:3-heptane: EtOAc gave 3,4 - dihydro - 3 - phenyl - 1*H* - 2 - benzopyran - 1 - one (90 mg, 80%) as a white, crystalline compound: mp 89–90°; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.06–3.46 (m, 2H), 5.57 (dd, J = 12.4, 4.4 Hz, 1H), 7.24–7.64 (m, 13H), 8.16 (m, 1H); IR (CCl_4) 1735 cm^{-1}; exact mass 224.0837 [calcd. for $C_{15}H_{12}O_2$, 224.0837]. The material was identical to an authentic sample.[40]

3,4 - *Dihydro* - 3 - *phenyl* - 4 - (*phenylseleno*) - 1H - 2 - *benzopyran* - 1 - *one*, **13a** *and* 1,3 - *dihydro* - 1 - [*phenyl*(*phenylseleno*)*methyl*]*isobenzofuran*, **13b**

The method for **6a** was followed using *cis* - stilbene - 2 - carboxylic acid[41] (199.1 mg, 0.89 mmol) in ether (3 mL) and PhSeCl (170.0 mg, 0.89 mmol) in ether (3 mL + 3 mL rinse). After a reaction period of 48 hr chromatography over silica gel (60 × 2 cm) using 5:1-heptane: EtOAc gave a mixture of **13a** and **13b** (267.3 mg, 79%) in a 75:25 ratio (NMR): mp 99–116°; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.60 (d, J = 5.1 Hz, 0.25H), 4.68 (d, J = 2.7 Hz, 0.75H), 5.86 (m, 1H), 6.85–7.65 (m, 13H), 7.85 (m, 0.25H), 8.03 (m, 0.75H); IR (CCl_4) 1740 cm^{-1} (major), 1779 cm^{-1} (minor); exact mass 380.0319 (calcd. for $C_{21}H_{16}O_2{}^{80}Se$, 380.0316].

3aα,6aα) - *Hexahydro* - 3a - (*phenylseleno*) - 2H - *cyclopenta*[b]*furan* - 2 - *one*, **14a**

Benzeneselenenyl chloride (192 mg, 1.0 mmol) in CH_2Cl_2 (3 mL) was injected over 3 min into a stirred soln of 1-cyclopentene-1-acetic acid[42] (126 mg, 1.0 mmol) in CH_2Cl_2 (3 mL). More CH_2Cl_2 (1 mL) was used to rinse the residual contents of the syringe into the reaction vessel. After 16 hr the reaction was worked up although it was still incomplete (IR control). The solvent was evaporated and **14a** was isolated by chromatography over silica gel (60 × 1 cm) using $CHCl_3$. Removal of the solvent gave **14a** (94 mg, 33%) as a homogeneous (TLC, silica gel, $CHCl_3$) oil: ^{1}H NMR (100 Hz, $CDCl_3$) δ 1.45–2.22 (m, 6H), 2.57–3.02 (dd, J = 18.5, 2.8 Hz, 2H), 4.9 (t, J = 3.5 Hz, 1H), 7.18–7.48 (m, 3H), 7.48–7.79 (m, 2H); IR (film) 1770 cm^{-1}; exact mass 282.0151 [calcd. for $C_{13}H_{14}O_2{}^{80}Se$, 282.0159]. (Found: C, 55.64; H, 5.02; O, 11.26. Calcd. for $C_{13}H_{14}O_2Se$: C, 55.53; H, 5.02; O, 11.38).

(1α, 4β, 5α) - 4 - (*Phenylseleno*) - 6 - *oxabicyclo*[3.2.2]*non* - 7 - *one*, **15a**

The method for **6a** was followed using 4-cycloheptene-1-carboxylic acid[43] (250.0 mg, 1.78 mmol) in ether (3 mL) and PhSeCl (341.6 mg, 1.78 mmol) in ether (3 mL + 3 mL rinse). After a reaction period of 24 hr chromatography over silica gel (60 × 2 cm) using 1:1-heptane: EtOAc gave **15a** (400.0 mg, 76%) as a homogeneous (TLC, silica gel, 1:1-heptane: EtOAc) oil: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.56–2.40 (m, 8H), 2.66–2.88 (m, 1H), 3.42–3.70 (m, 1H), 4.56 (broad d, J = 4.6 Hz, 1H), 7.16–7.36 (m, 3H), 7.40–7.64 (m, 2H); IR (film) 1742 cm^{-1}; exact mass 296.0320 [calcd. for $C_{14}H_{16}O_2{}^{80}Se$, 296.0315].

5 - (*Phenylseleno*) - *tetrahydropyran* - 2 - *one*, **20**

Ozone was passed through a cold (*ca* −78°) soln of 1-methoxycyclopentene[44] (12.78 g, 130.2 mmol) in MeOH (190 mL) until the soln became blue. The excess of O_3 was removed by a stream of N_2 and Me_2S (16.15 g, 260 mmol) was added dropwise to the cold soln. The cooling bath was removed and the mixture was left overnight. Evaporation of the solvent gave a residue which was dissolved in CH_2Cl_2 (150 mL). The soln was washed with water (3 × 50 mL), dried (Na_2SO_4), and evaporated. Distillation using a spinning band apparatus gave **21** (4.79 g, 34%) as a pure (vpc) liquid: ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.58–2.72 (m, 6H), 3.63 (s, 3H), 9.75 (t, J = 1.4 Hz, 1H); IR (film) 2820, 2720, 1735 and 1720 cm^{-1}.

To a soln of **21** (3.25 g, 25 mmol) in EtOAc (100 mL) was added PhSeCl (5.79 g, 30 mmol) in EtOAc (120 mL).[45] Conc HCl (2 drops) was added and the mixture was stirred for 17 hr. The solvent was evaporated and the yellow residue was chromatographed over silica gel (60 × 2.5 cm) using 1:1-heptane: EtOAc to give **22** (1.93 g, 22%) as a homogeneous (TLC, silica gel, 1:1-heptane: EtOAc) liquid: IR (film) 3060, 2820, 2720, 1730 and 1700 cm^{-1}.

$NaBH_4$ (600 mg, 15.9 mmol) was added in portions to a stirred soln of **22** (1.1 g, 13.85 mmol) in MeOH (15 mL). 15 Min after the

last addition the mixture was poured into sat $NaHCO_3$aq (15 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The organic layer was dried (Na_2SO_4) and evaporated. Chromatography of the residue over silica gel (60 × 1 cm) using 1:1–heptane: EtOAc gave **23** (580 mg, 52%) as a pure (TLC, silica gel, 1:1–heptane: EtOAc) liquid: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.62–3.82 [m (including a sharp singlet at 3.67), 11H], 7.15–7.40 (m, 3H), 7.42–7.72 (m, 2H); IR (film) 3450, 1732 cm^{-1}; exact mass 288.0264 [calcd. for $C_{12}H_{16}O_3{}^{80}Se$, 288.0265].

The ester **23** (213 mg, 0.74 mmol) was converted into the hydrazide **24** by the addition of 85% w/w $NH_2NH_2{\cdot}H_2O$ (180 mg) in MeOH (2 mL). After stirring the mixture for 40 hr (TLC control) the solvent was evaporated to afford **24** (178 mg, 83%) as a pale yellow oil: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.64–2.52 (m, 4H), 2.92–4.06 (m, 7H), 7.16–7.65 (m, 5H); IR (film) 3400, 1640 cm^{-1} (broad); exact mass 288.0386 [calcd. for $C_{11}H_{16}N_2O_2{}^{80}Se$, 288.0377].

A soln of **24** (70 mg, 0.24 mmol) in CH_2Cl_2 (2 mL) was added slowly from a syringe to a stirred suspension of $PhSeO_2H$[46] (94 mg, 0.50 mmol) in CH_2Cl_2 (1 mL). The rate of addition was controlled so as to maintain a steady rate of N_2 evolution. When N_2 evolution had ceased the mixture was stirred for an additional 30 min. The solvent was evaporated and the residual yellow oil was chromatographed over silica gel (30 × 1 cm) using 1:1–heptane: EtOAc to give **20** (33 mg, 54%) as a yellow, homogeneous (TLC, silica gel, 1:1–heptane: EtOAc) oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.80–2.08 (m, 1H), 2.20–2.42 (m, 1H), 2.46–2.80 (2H), 3.50 (heptet, J = 4.9 Hz, 1H), 4.25 (dd, J = 11.6, 9.6 Hz, 1H), 4.47 (qd, J = 11.6, 4.8, 1.8 Hz, 1H), 7.22–7.48 (m, 3H), 7.52–7.72 (m, 2H); IR ($CHCl_3$) 1735 cm^{-1}; exact mass 255.9994 [calcd. for $C_{11}H_{12}O_2{}^{80}Se$, 256.0002].

Exchange reaction between trans - 1 - *chloro* - 2 - (*phenylseleno*)*cyclopentane and* 2 - *cyclopentene* - 1 - *acetic acid*

Benzeneselenenyl chloride (150 mg, 0.78 mmol) in ether (5 mL) was added dropwise from a syringe to a soln of cyclopentene (106.7 mg, 1.57 mmol) in ether (5 mL). The resulting faintly colored mixture was stirred for 30 min at room temp and then 2-cyclopentene - 1 - acetic acid (98.8 mg, 0.78 mmol) in ether (5 mL) was added. After a further period of 17 hr the solvent was evaporated and the residue was chromatographed over silica gel (60 × 2 cm) using 5:1–heptane: EtOAc to afford a mixture (146.2 mg) of *trans* - 1 - hydroxy - 2 - (phenylseleno)cyclopentane [formed by hydrolysis of *trans* - 1 - chloro - 2 - (phenylseleno)cyclopentane] and **4a** in a 60:40 ratio (NMR). The mixture had: ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.20–2.40 (m, 5.8H), 2.60–3.24 (m, including a q centered at 2.81, J = 18.3, 10.6 Hz, 1.2H), 3.38 (m, 0.4H), 3.87 (m, 0.6H), 4.12 (m, 0.4H), 4.88 (d, J = 6.3, 0.6H); IR (film) 3460, 1772 cm^{-1}.

Acknowledgements—Acknowledgement is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society for partial[7a] support of this work and to the Research Corporation, the National Research Council of Canada and the University of Alberta. We thank Professor H.B. Dunford for loan of stopped-flow equipment.

REFERENCES

[1a]D. L. J. Clive, *J. Chem. Soc.* Chem. Comm. 695 (1973); [b]K. B. Sharpless, M. W. Young and R. F. Lauer, *Tetrahedron Letters* 1979 (1973); [c]H. J. Reich, J. M. Renga and I. L. Reich, *J. Am. Chem. Soc.* **97**, 5434 (1975).

[2a]D. L. J. Clive, *Tetrahedron* **34**, 1049 (1978); [b]D. L. J. Clive, *Aldrichimica Acta* **11**, 43 (1978); [c]K. B. Sharpless, K. M. Gordon, R. F. Lauer, D. W. Patrick, S. P. Singer and M. W. Young, *Chemica Scripta* **8A**, 9 (1975); [d]H. J. Reich, *Acc. Chem. Res.* **12**, 22 (1979).

[3a]D. L. J. Clive, *J. Chem. Soc.* Chem. Comm. 100 (1974); [b]H. J. Reich, *J. Org. Chem.* **39**, 428 (1974).

[4]K. B. Sharpless and R. F. Lauer, *J. Org. Chem.* **39**, 429 (1974).

[5]D. L. J. Clive, G. Chittattu, N. J. Curtis, W. A. Kiel and C. K. Wong, *J. Chem. Soc.* Chem. Comm. 725 (1977).

[6]M. de Moura Campos and N. Petragnani, *Chem. Ber.* **93**, 317 (1960).

[7a]D. L. J. Clive and G. Chittattu, *J. Chem. Soc.* Chem. Comm. 484 (1977); [b]K. C. Nicolaou and Z. Lysenko, *J. Am. Chem. Soc.* **99**, 3185 (1977).

[8a]D. L. J. Clive, G. Chittattu and C. K. Wong, *Can. J. Chem.* **55**, 3894 (1977); [b]K. C. Nicolaou and Z. Lysenko, *Tetrahedron Letters* 1257 (1977); [c]see ref. 5; [d]D. L. J. Clive, C. K. Wong, W. A. Kiel and S. M. Menchen, *J. Chem. Soc.* Chem. Comm. 379 (1978), [e]D. L. J. Clive, G. Chittattu and C. K. Wong, *J. Chem. Soc.* Chem. Comm. 441 (1978); [f]K. C. Nicolaou, W. E. Barnette and R. L. Magolda, *J. Am. Chem. Soc.* **100**, 2567 (1978).

[9]J. E. Baldwin, *J. Chem. Soc.* Chem. Comm. 734 (1976).

[10]See M. Petrzilka, *Helv. Chim. Acta* **61**, 2286 (1978).

[11a]D. L. J. Clive, G. Chittattu and C. K. Wong, *J. Chem. Soc.* Chem. Comm. 41 (1978); [b]D. L. J. Clive, G. Chittattu, V. Farina and C. K. Wong, manuscript in preparation.

[12a]G. Berti, *Tetrahedron* **4**, 393 (1958); [b]B. Capon, J. Farquarson and D. J. McNeillie, *J. Chem. Soc.* Perkin Trans. 2, 914 (1977); [c]For halolactonisation of 5-phenyl-4-pentenoic acid see M. Julia and A. Guy-Rouault, *C.R. Acad. Sci., Paris* **258**, 3728 (1964).

[13]M. Doyle, R. Hafter and W. Parker, *J. Chem. Soc.* Perkin Trans. 1, 364 (1977).

[14]D. L. J. Clive, V. Farina and A. Singh, manuscript in preparation.

[15]H. Singer and J. D. Unpleby, *Tetrahedron* **28**, 5769 (1972).

[16]H. J. Reich and J. M. Renga, *J. Org. Chem.* **40**, 3313 (1975).

[17]O. Behaghel and H. Seibert, *Ber. Dtsch. Chem. Ges.* **66**, 708 (1933).

[18a]See D. R. Hogg and G. M. Beverly, *J. Chem. Soc.* Chem. Comm. 138 (1966); [b]S. Raucher, *J. Org. Chem.* **42**, 2950 (1977).

[19]For oxidation of simple hydrazides with $PhSeO_2H$ see: T. G. Back, *J. Chem. Soc.* Chem. Comm. 278 (1978).

[20]K. B. Sharpless and S. Current, *Tetrahedron Letters* 5075 (1978).

[21a]G. H. Schmid and D. G. Garratt, *Ibid.* 3991 (1975); [b]H.J. Reich and J. E. Trend, *Can. J. Chem.* **53**, 1922 (1975); [c]G. H. Schmid and D. G. Garratt, *The Chemistry of Functional Groups.* Supplement A. *The Chemistry of Double-Bonded Functional Groups.* (Edited by S. Patai) pp. 855–866, Wiley, London (1977).

[22]L. Do Amaral and S. C. Melo, *J. Org. Chem.* **38**, 800 (1973).

[23a]See M. Eigen, *Angew. Chem.* Int. Ed. **3**, 1 (1964), (see particularly, p. 16); [b]C. K. Ingold, *Structure and Mechanism in Organic Chemistry* (2nd Edition) p. 826. Ithaca, Cornell University Press, (1969); [c]Among simple compounds the thermodynamically preferred ring sizes are as follows: lactones[24]: 5 > 6; cyclic hemiacetals[25]: 6 > 5; cyclic thioethers[26]: 5 > 6; [d]For the preferences between 6-*endo* and 5-*exo*-trigonal closure in medium ring dienes see: E. G. Scovell and J. K. Sutherland, *J. Chem. Soc.* Chem. Comm. 275 (1977).

[24a]J. Stoddart, *Stereochemistry of Carbohydrates* p. 177. New York, Wiley-Interscience (1971); [b]γ-Lactones are usually formed faster than δ-lactones: C. Galli, G. Illuminati, L. Mandolini and P. Tamborra, *J. Am. Chem. Soc.* **99**, 2591 (1977).

[25]See ref. 24*a* p. 158.

[26a]J. F. Messerly, H. L. Finke and S. S. Todd, *J. Chem. Thermodynamics* **6**, 635 (1974); [b]D. R. Stull, E. F. Westrum, Jr. and G. C. Sinke, *The Chemical Thermodynamics of Organic Compounds.* Wiley, New York (1969); [c]S. Ikegami and J. Ohishi, Y. Shimizu, *Tetrahedron Letters* 3923 (1975); [d]J. E. Baldwin and M. A. Christie, *J. Am. Chem. Soc.* **100**, 4597 (1978); [d]S. Kukolja and S. R. Lammert, *Ibid.* **94**, 7169 (1972).

[27]For recent interest in modes of cyclisation see: [a]S. Danishefsky, *Accts. Chem. Res.* **12**, 66 (1979); [b]B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.* **101**, 1595 (1979).

[28a]See W. Herz and L. A. Glick, *J. Org. Chem.* **28**, 2970 (1963); [b]H. O. House, R. G. Carlson and H. Babad, *Ibid.* **28**, 3359 (1963); [c]M. Julia and F. Le Goffic, *Bull. Soc. Chim. Fr.* 1555 (1965); the relative sizes for which *trans* ring fusion might be expected to be observed (in irreversible reactions) has not been established.

[29]R. P. Linstead and H. N. Rydon, *J. Chem. Soc.* 580 (1933).

[30]Commercially available; Aldrich.

[31]M. Fetizon, M. Golfier, M. T. Montaufier and J. Rens, *Tetrahedron* **31**, 987 (1975).
[32]H. G. Kuivila and O. F. Beumel, Jr., *J. Am. Chem. Soc.* **83**, 1246 (1961).
[33]V. Jager and H. J. Günther, *Tetrahedron Letters* 2543 (1977).
[34]L. Crombie, A. J. B. Edgar, S. H. Harper, M. W. Lowe and D. Thompson, *J. Chem. Soc.* 3552 (1950).
[35]NMR indicated the presence of approximately 10% of 4-methyl-3-pentenoic acid as an impurity in the starting material.
[36a]G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, R. Ferrell, *J. Am. Chem. Soc.* **85**, 207 (1963); [b]R. S. Monson, *Advanced Organic Synthesis, Methods and Techniques* p. 84. Academic Press, New York (1971).
[37]W. R. Boehme, E. Schipper, W. G. Scharpf and J. Nichols, *J. Am. Chem. Soc.* **80**, 5488 (1958).
[38]H. W. Whitlock, Jr., *J. Am. Chem. Soc.* **84**, 3412 (1962).
[39]D. F. De Tar and L. A. Carpino, *Ibid.* **78**, 475 (1956).
[40]E. Leupold, *Ber. Dtsch. Chem. Ges.* **34**, 2829 (1901).
[41]G. Berti, *Gazz. Chim. Ital.* **86**, 883 (1956).
[42]J. D. Fissekis and B. A. Markert, *J. Org. Chem.* **31**, 2945 (1966).
[43]H. Marschall, F. Vogel and P. Weyerstahl, *Liebigs Ann.* **9**, 1557 (1977).
[44]R. A. Wohl, *Synthesis* 38 (1974).
[45]K. B. Sharpless, R. F. Lauer and A. Y. Teranishi, *J. Am. Chem. Soc.* **95**, 6137 (1973).
[46]J. D. McCullough, E. S. Gould, *J. Am. Chem. Soc.* **71**, 674 (1949).
[47]This work was reported at the Canadian Institute of Chemistry Annual Conference, Vancouver, June 4th, 1979.