Synthesis and oxidative rearrangement of selenenylated dihydropyrans†

Sébastien Redon, Xavier Pannecoucke, Xavier Franck* and Francis Outurquin*

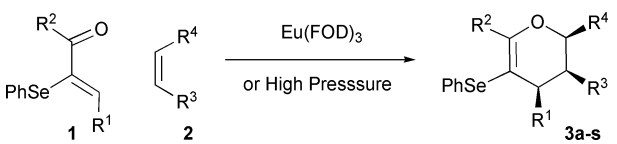
Received 6th December 2007, Accepted 1st February 2008
First published as an Advance Article on the web 27th February 2008
DOI: 10.1039/b718825k

Selenenylated dihydropyrans prepared by inverse demand hetero-Diels–Alder reactions undergo oxidative rearrangement when treated with H_2O_2, leading to tetrahydrofuran-2-ones by ring contraction.

Introduction

Oxidized organoselenium derivatives are sources of molecular diversity due to the richness of their chemistry.[1] Indeed, oxidation of aliphatic organoselenium derivatives is often used to introduce unsaturation by β-elimination (selenoxide) or to substitute the organoselenium residue by nucleophilic displacement (*e.g.*activation with NBS and substitution by an amine).[2] Allylic or propargylic phenylselanyl derivatives, when treated by an oxidant, undergo [2,3]-sigmatropic rearrangement leading to allylic alcohols (selenoxide), amines (selenylimine) or halides (halo-adduct).[3] On the other hand, vinylic or aromatic phenylselanyl derivatives can be oxidized to the selenoxide, which can be isolated in certain cases, or give rise to allenols by [2,3]-sigmatropic rearrangement in the case of 1,3-dienes.[4]

In continuation of our studies on the reactivity of selenenylated carbonyl derivatives of type **1**,[4] we became interested in their use as dienes in hetero-Diels–Alder reactions (Scheme 1) and studied the particular reactivity of these cycloadducts toward oxidants. Maybe owing to the sensitivity of selenenylated derivatives to Lewis acids or heat, only a few examples of Diels–Alder reactions with α-phenylselanyl-enals, -enones or dienes have been described.[5]



Scheme 1 Hetero-Diels–Alder reaction between 2-phenylselanyl-enals or -enones **1** and an alkene **2** leading to dihydropyrans **3a–s**.

Results and discussion

Inverse demand hetero-Diels–Alder reactions have been conducted mainly with electron-rich alkenes (vinyl ethers), leading to 2-alkoxy-5-phenylselanyl-3,4-dihydro-2*H*-pyrans **3a–l** in excellent yields (Table 1, entries 1–19).

In these cases, 2-phenylselenylated enals (Table 1, entries 1–11) proved to be more reactive than the corresponding enones (Table 1, entries 12–19) and the reaction worked well with 3–10 mol% of the commonly used $Eu(FOD)_3$ as the catalyst, at either room temperature or 50 °C.

When R^1 = aryl (Table 1, entries 6–11), the reaction is slower and high pressure can help, shortening the reaction time. In these cases, no catalyst was necessary. Cyclic vinyl-ethers such as dihydrofuran can also be used (Table 1, entries 3–5), leading to bicyclic compounds **3c–d** in good yields. Bulkier vinyl-ethers such as *n*-butyl- and even *t*-butyl- ethers can be used without loss of efficiency (Table 1, entries 9–10). With less reactive phenylselenylated enones (Table 1, entries 12–19), the reaction became slower and high pressure was needed to maintain efficiency, especially when R^1 or R^2 was an aryl group. When both R^1 and R^2 are aryl groups (Table 1, entries 18–19), no reaction occurred at all in the absence of high pressure. In order to have access to thio- or phenylselanyl- acetals, ethylvinylsulfide (Table 1, entries 20–23) and phenylvinylselenide (Table 1, entry 24) were engaged as dienophiles in the hetero-Diels–Alder reactions. The reactions were always high yielding, and high pressure was only needed in the case of the enone substituted by a phenyl group (Table 1, entry 23); thus 2-ethylsulfanyl-5-phenylselanyl-3,4-dihydro-2*H*-pyrans **3m–p** and the bis-selenenylated 2-ethylselanyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran **3q** could be obtained. With less electron rich dienophiles such as vinylacetate or styrene, the hetero-Diels–Alder reaction with a reactive enal never proceeded with vinylacetate, (Table 1, entry 25) and required high pressure and longer reaction times for styrene, leading to 2-phenyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran **3s** (Table 1, entries 26–27). It is noteworthy that in this case, no polymerisation of styrene was observed.

Once we had the cycloadducts in hand, we studied their oxidation. Using standard mild conditions (H_2O_2 35% in water, 4 eq., in CH_2Cl_2) the oxidation of acetals (R^4 = OR) ended up with an unprecedented ring contraction affording, when R^2 = H, 5-alkoxy-tetrahydrofuran-2-ones **5**. From acetal **3k** where R^2 = Me and R^4 = OR, a mixture of 5-alkoxy-tetrahydrofuran-2-one **5e** and acetylfuran **6** was observed (Scheme 2).

In order to elucidate the mechanism and characterize the intermediates, we performed the oxidation of **3a** in EtOAc or THF and, in these cases, only the selenoxide **4a** could be obtained, without rearrangement. When this selenoxide **4a** was reacted with H_2O_2 in CH_2Cl_2, rearrangement cleanly occurred, allowing us to propose that **4a** is the first intermediate in the rearrangement.

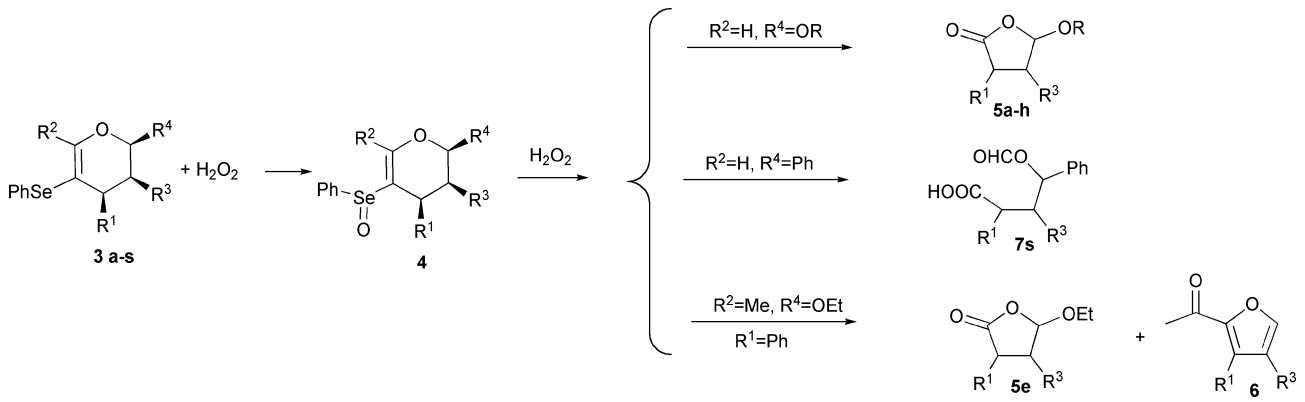
Université de Rouen, INSA de Rouen, CNRS UMR 6014, C.O.B.R.A. - I.R.C.O.F, 1 Rue Tesnière, 76131, Mont-Saint-Aignan cedex, France. Email: xavier.franck@insa-rouen.fr, francis.outurquin@univ-rouen.fr; Fax: +33 (0)235522959; Tel: +33 (0)235522402

† Electronic supplementary information (ESI) available: NOESY spectra of the *cis*- and *trans*- isomers of tetrahydrofuran-2-one **5e**. See DOI: 10.1039/b718825k

 This journal is © The Royal Society of Chemistry 2008

Table 1 Synthesis of dihydropyrans **3**

Entry	R^1	R^2	R^3	R^4	Conditions	Compound (yield%)
1	Me	H	H	OEt	4% $Eu(FOD)_3$, r.t., 12 h	**3a** (93)
2	$CH_2OTBDMS$	H	H	OEt	3% $Eu(FOD)_3$, r.t., 12 h	**3b** (86)
3	Me	H	$-CH_2CH_2O-$		1.0 Gpa, 50 °C, 36 h	**3c** (84)
4	Me	H	$-CH_2CH_2O-$		5% $Eu(FOD)_3$, 40 °C, 12 h	**3c** (78)
5	H	H	$-CH_2CH_2O-$		3% $Eu(FOD)_3$, r.t., 12 h	**3d** (73)
6	Ph	H	H	OEt	10% $Eu(FOD)_3$, 40 °C, 48 h	**3e** (90)
7	Ph	H	H	OEt	1.0 Gpa, r.t., 15 h	**3e** (50)
8	Ph	H	H	OEt	1.0 Gpa, 50°C, 10 h	**3e** (99)
9	Ph	H	H	O*n*-Bu	5% $Eu(FOD)_3$, 80 °C, 12 h	**3f** (98)
10	Ph	H	H	O*t*-Bu	10% $Eu(FOD)_3$, 80 °C, 12 h	**3g** (97)
11	*p*-OMePh	H	H	OEt	5% $Eu(FOD)_3$, 40 °C, 12 h	**3h** (89)
12	Me	Me	H	OEt	10% $Eu(FOD)_3$, 40 °C, 48 h	**3i** (93)
13	Me	Me	H	OEt	1.0 Gpa, r.t., 20 h	**3i** (93)
14	Me	Ph	H	OEt	10% $Eu(FOD)_3$, 40 °C, 20 h	**3j** (35)
15	Me	Ph	H	OEt	1.2 Gpa, 50 °C, 20 h	**3j** (91)
16	Ph	Me	H	OEt	10% $Eu(FOD)_3$, 40 °C, 48 h	**3k** (46)
17	Ph	Me	H	OEt	1.2 Gpa, 50 °C, 20 h	**3k** (94)
18	Ph	Ph	H	OEt	10% $Eu(FOD)_3$, r.t., 48 h	**3l** (N.R.)
19	Ph	Ph	H	OEt	1.2 Gpa, 50 °C, 20 h	**3l** (93)
20	Me	H	H	SEt	4% $Eu(FOD)_3$, r.t., 12 h	**3m** (95)
21	Ph	H	H	SEt	10% $Eu(FOD)_3$, 40 °C, 12 h	**3n** (90)
22	Me	Me	H	SEt	10% $Eu(FOD)_3$, r.t., 12 h	**3o** (91)
23	Ph	Me	H	SEt	1.2 Gpa, 40 °C, 20 h	**3p** (90)
24	Me	H	H	SePh	10% $Eu(FOD)_3$, 80 °C, 24 h	**3q** (80)
25	Me	H	H	$OCOCH_3$	1.0 Gpa, 50 °C, 24 h	**3r** (N.R.)
26	Me	H	H	Ph	1.2 Gpa, 50 °C, 16 h	**3s** (24)
27	Me	H	H	Ph	1.2 Gpa, 50 °C, 48 h	**3s** (64)



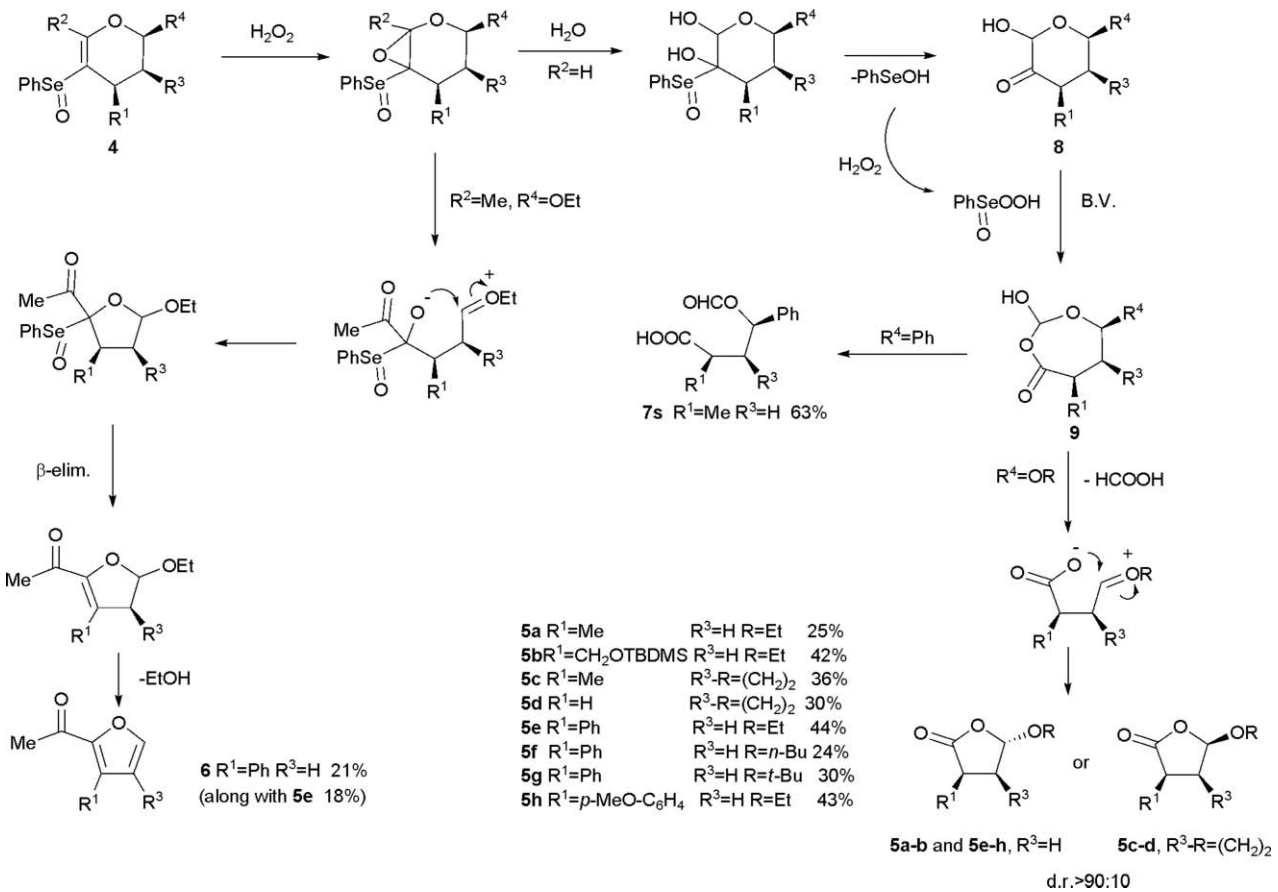
Scheme 2 Different products arising from oxidation of dihydropyrans **3**.

Dihydropyran **3s** (R^4 = Ph) was also subjected to H_2O_2 oxidation in CH_2Cl_2 and we only isolated acid **7s**, resulting from an oxidative cleavage of the double bond. In the case of dihydropyran **3l** (R^1 = R^2 = Ph), only the selenoxide **4l** could be obtained and no rearrangement occurred. When we used simple dihydropyran with no phenylselanyl residue, no oxidation occurred at all and the starting material was recovered unchanged (not shown). This surprising susceptibility of such 5-phenylselanyl-3,4-dihydro-2*H*-pyrans **3** to oxidation is due to the presence of the selenium residue and is reported for the first time.

Having identified intermediates and characterized the different reaction products according to the substitution of the dihydropyrans **3**, we can now propose a mechanism.

The presence of the selenium residue, first oxidized to the corresponding selenoxide **4**, is then responsible for the high polarization of the enolic double bond, which could easily be epoxidized by H_2O_2. Then, depending on the substitution at position 6 (R^2 = H or R^2 = Me), two different pathways can be observed (Scheme 3).

Firstly, when R^2 = H, water (solvent of H_2O_2) can attack at position 6 to give, after expulsion of "PhSeOH", the keto-hemiacetal **8**. PhSeOH can then be further oxidized by the excess of H_2O_2 to PhSe(O)OOH, phenylperseleninic acid, which is know as a strong but selective oxidant able to perform Baeyer–Villiger reactions.[6] Indeed, Baeyer–Villiger oxidation of the keto-hemiacetal **8** gives rise to the correponding lactone-hemiacetal **9**[7] which can rearrange with expulsion of formic acid and ring closure of the carboxylate onto the formed oxonium ion. This mechanism is supported by the isolation of carboxylic acid **7s**, from the reaction of dihydropyran **3s** where R^4 = Ph. Indeed, the same lactone-hemiacetal can be drawn but, in this case, R^4 is not electron donating enough to open the ring and fragmentation occurs, leading to carboxylic acid **7s** with a hydroxyl group functionalized as a formyl ester.

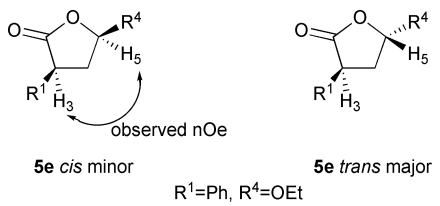


Scheme 3 Proposed mechanism.

Secondly, when R^2 = Me, the attack of water on the epoxide is slowed down (but still exists) by steric factors, thus the second pathway occurs thanks to the electron donating ability of R^4 = OEt, which can help open the 6-membered cycle and form an oxonium ion. The liberated hydroxyl in position 5 can then attack the oxonium, giving rise to a five-membered ring (5-*exo*-*trig*). This rearrangement is similar to the one observed by Armstrong and Chung in the synthesis of tetrahydrofuranones.[8] Then the selenoxide can β-eliminate to give a dihydrofuran which can further lose EtOH to yield the corresponding furan **6**.

Both pathways are competitive and depend on the substitution pattern (R^2). The presence of the selenium residue increases the reactivity of these dihydropyrans and makes it possible for the whole oxidation process to occur in very mild conditions. 5-alkoxy-tetrahydrofuran-2-ones **5** have been prepared in moderate yields, which can be explained by the relative instability of the intermediates and by the presence of water, which can trap oxonium ions. All attempts to remove water from the reaction were unsuccessful (use of urea–H_2O_2 complex).

Concerning the diastereoselectivity of the rearrangement through the oxocarbenium ion, it appears that the resulting tetrahydrofuran-2-ones **5a–b** and **5e–h** are isolated mainly as the *trans* diastereomer (>90 : 10 in all cases), as the minor *cis* shows nOe correlations between H-3 and H-5 (Scheme 4). On the contrary, the stereochemistry of tetrahydrofuran-2-ones **5c-d** is all *cis*, the spectroscopic data being in accordance with previously published data.[9]



Scheme 4 Stereochemistry of tetrahydrofuran-2-one **5e**.

Conclusion

To conclude, we have developed an efficient route toward selenenylated dihydropyrans through a high yielding inverse demand hetero-Diels–Alder reaction. This pathway allowed general access to various dihydropyrans, including thio- and seleno-acetals. Further oxidation of these selenenylated dihydropyrans (R^4 = OR) with H_2O_2 proceeded to give an unprecedented rearrangement, affording 5-alkoxy-tetrahydrofuran-2-ones **5** through a contraction of the intermediate selenoxide **4**. A mechanism was postulated, passing through an epoxide that could then be transformed

 This journal is © The Royal Society of Chemistry 2008

into either a furan moiety or a 5-alkoxy-tetrahydrofuran-2-one, depending on the substitution pattern.

Experimental

General methods

NMR spectra were recorded on a Bruker DPX 300 spectrometer operating at 300 MHz for proton and 75.4 MHz for carbon spectra. This probe is equipped with pulsed-field (*z*) gradients. ^{77}Se NMR spectra were recorded at 21 °C on a Bruker DPX 400 spectrometer operating at 76.29 MHz for ^{77}Se, using a pulse length of 19 μs (90° pulse = 19 μs) and an optimized relaxation delay of 2 s. An average of 1500 scans for ^{77}Se NMR was necessary to obtain reliable information. Chemical shifts (δ) are expressed in ppm relative to TMS for ^{1}H and ^{13}C nuclei and to Me_2Se for ^{77}Se nuclei; coupling constants (J) are given in Hertz; coupling multiplicities are reported using conventional abbreviations. Elemental analyses were obtained on a Carlo-Erba 1106 analyzer and mass spectra on a HP5890 (electronic impact 70eV) using GC-MS coupling with a Jeol AX 500.

Typical procedure for the synthesis of dihydropyrans 3

Method under high pressure

The enal **1a** (1 mmol, 225 mg) in ethyl vinyl ether (10 mmol, 0.96 ml) was introduced to a high-pressure vessel and compressed to the desired pressure and temperature. After decompression, the mixture was concentrated under vacuum. The residue was chromatographed on silica gel (eluent: ethyl acetate–cyclohexane, 3 : 97) to give 282 mg (95%) of 2-ethoxy-4-methyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran **3a**.

Method with Eu(FOD)$_3$

To a mixture of enal **1a** (1 mmol, 225 mg) in ethyl vinyl ether (10 mmol, 0.96 ml), Eu(FOD)$_3$ (2%, 21 mg) was introduced under nitrogen, and the mixture stirred at the desired temperature. After the reaction was completed, monitored by TLC, the mixture was concentrated under vacuum. The residue was chromatographed on silica gel (eluent: ethyl acetate–cyclohexane, 3 : 97) to give 275 mg (93%) of 2-ethoxy-4-methyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran **3a**.

2-Ethoxy-4-methyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3a). Yield = 93%; yellow oil; R_f = 0.24 (AcOEt–cyclohexane, 5 : 95); ^{77}Se NMR δ (ppm) 331.7; ^{1}H NMR δ (ppm) 1.14 (d, J = 7.0 Hz, 3H), 1.25 (t, J = 7.0 Hz, 3H), 1.82 (ddd, 1H, J = 6.2, 6.4, 13.6 Hz, H-3), 2.13 (ddd, 1H, J = 2.5, 6.9, 15.1 Hz, H-3), 2.40 (ddd, 1H, J = 1.5, 6.9, 13.6 Hz, H-4), 3.58 (m, 1H), 3.91 (m, 1H), 5.10 (dd, J = 2.5, 6.2 Hz, 1H, H-2), 6.82 (d, J = 1.7 Hz, 1H, H-6), 7.17–7.25 (m, 3H), 7.40–7.44 (m, 2H). ^{13}C NMR δ (ppm) 15.4, 20.6, 30.3 (C-4), 36.3 (C-3), 64.6, 98.8 (C-2), 108.9 (C-5), 126.2, 129.1, 129.8, 132.6, 148.3 (C-6). IR (neat): 2975, 2928, 2873, 1622, 1578, 1476, 1438, 1373, 1130, 1070, 990, 840, 736, 691 cm^{-1}; MS (EI, 70 eV) m/z: 298 (48), 296 (25), 226 (100), 224 (53), 197 (15), 157 (50, PhSe$^+$), 117 (46), 115 (26), 91 (17), 78 (32), 77 (38, Ph$^+$), 51 (41), 41 (45). Anal. calcd for $C_{14}H_{18}O_2Se$ (297.25): C, 56.57; H, 6.10. Found: C, 56.63; H, 6.07.

2-Ethoxy-3,4-dihydro-4-[(*tert*-butyl)dimethylsilyl-methoxy]-5-phenylselanyl-2*H*-pyran (3b). Yield = 86%; yellow oil; R_f = 0.41 (AcOEt–cyclohexane, 3 : 97); ^{77}Se NMR δ (ppm) 339.2 ppm; ^{1}H NMR δ (ppm) −0.04 (s, 3H), −0.02 (s, 3H), 0.83 (s, 9H), 1.24 (t, J = 7.0 Hz, 3H), 1.97–2.05 (m, 1H, H-3), 2.16–2.25 (m, 1H, H-3), 2.43 (m, 1H, H-4), 3.52–3.67 (m, 2H), 3.81–3.91 (m, 2H), 5.12 (dd, J = 2.70, 4.1 Hz, 1H, H-2), 6.86 (d, J = 1.65 Hz, 1H, H-6), 7.19–7.26 (m, 3H), 7.38–7.40 (m, 2H). ^{13}C NMR δ (ppm) −5.2, 15.4, 18.4, 26.1, 30.1 (C-3), 37.7 (C-4), 64.5, 64.9, 98.4 (C-2), 103.7 (C-5), 126.3, 129.1, 129.8, 132.4, 149.8 (C-6); IR (neat): 2954, 2920, 2856, 1621, 1578, 1476, 1438, 1378, 1360, 1253, 1227, 1130, 1066, 1022, 995, 838, 776, 734, 690 cm^{-1}; MS (EI, 70 eV) m/z: 428 (M$^+$, 6), 371 (M$^+$ − C(Me)$_3$, 4), 297 (M$^+$ − OSiTBDM, 10), 237 (20), 219 (14), 157 (PhSe$^+$, 22), 73 (100); Anal. calcd for $C_{20}H_{32}O_3SeSi$ (427.50): C, 56.19; H, 7.54. Found: C, 56.43; H, 7.45.

4-Methyl-5-phenylselanyl-2,3,3a,7a-tetrahydro-4*H*-furo [2,3-*b*]pyran (3c). Yield = 84%; yellow oil; R_f = 0.28 (AcOEt–cyclohexane, 5 : 95); ^{1}H NMR δ (ppm) 1.06 (d, J = 7.1 Hz, 3H), 1.80–1.98 (m, 2H, H-3), 2.49 (m, 1H, H-9), 2.87 (m, 1H, H-4), 3.98 (m, 1H, H-2), 4.21 (m, 1H, H-2), 5.49 (d, J = 3.7 Hz, 1H, H-8), 6.84 (d, J = 2.0 Hz, 1H, H-6), 7.17–7.25 (m, 3H), 7.41–7.45 (m, 2H). ^{13}C NMR δ (ppm) 18.4, 23.6, 30.2 (C-4), 44.8 (C-9), 68.4, 100.5 (C-8), 104.9 (C-5), 126.3, 129.0, 130.0, 132.3, 148.6 (C-6). IR (neat): 2955, 2974, 2360, 1622, 1615, 1575, 1476, 1465, 1436, 1373, 1336, 1308, 1170, 1099, 1043, 1022, 995, 922, 891, 836, 736, 691 cm^{-1}; MS (EI, 70 eV) m/z: 296 (38), 294 (20), 226 (100), 224 (51), 157 (PhSe$^+$, 33), 117 (47), 77 (44, Ph$^+$), 51 (47), 41(80). Anal. calcd for $C_{14}H_{16}O_2Se$ (295.23): C, 56.95; H, 5.46. Found: C, 56.72; H, 5.40.

5-Phenylselanyl-2,3,3a,7a-tetrahydro-4*H*-furo[2,3-*b*]pyran (3d). Yield = 73%; white crystals; m.p. = 48–50 °C; R_f = 0.29 (AcOEt–cyclohexane, 5 : 95); ^{1}H NMR δ (ppm) 1.84–2.05 (m, 2H, H-3), 2.27 (d, 1H, J = 17.7 Hz, H-4), 2.49 (m, 1H, H-9), 2.68 (dd, 1H, J = 1.9, 17.7 Hz, H-4), 3.95–4.01 (m, 1H, H-2), 4.18–4.25 (m, 1H, H-2), 5.40 (d, J = 3.8 Hz, 1H, H-8), 6.82 (s, 1H, H-6), 7.18–7.30 (m, 3H), 7.35–7.50 (m, 2H). ^{13}C NMR δ (ppm) 27.7, 28.3, 38.5 (C-9), 68.5 (C-2), 98.5, 98.7 (C-8), 126.6, 129.2, 130.4, 131.1, 147.5 (C-6). IR (neat): 2897, 1628, 1577, 1476, 1437, 1157, 1102, 1066, 1022, 933, 918, 857, 737, 691 cm^{-1}; MS (EI, 70 eV) m/z: 312 (32), 310 (17), 266 (8), 218 (85), 216 (44), 191 (50), 157 (51, PhSe$^+$), 129 (100), 115 (85), 105 (42), 77 (51, Ph$^+$), 53 (58), 51 (81), 44 (42). Anal. calcd for $C_{13}H_{14}O_2Se$ (281.20): C, 55.52; H, 5.02. Found: C, 55.14; H, 5.06.

2-Ethoxy-4-phenyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3e). Yield = 99%; yellow solid; m.p. = 73–74 °C; R_f = 0.26 (AcOEt–cyclohexane, 5 : 95); ^{77}Se NMR δ (ppm) 348.5; ^{1}H NMR δ (ppm) 1.21 (t, J = 7.0 Hz, 3H), 2.19 (ddd, 1H, J = 2.2, 8.1, 13.6 Hz, H-3), 2.38 (ddd, 1H, J = 2.2, 6.9, 13.6 Hz, H-3), 3.54–3.66 (m, 2H), 3.95 (m, 1H), 5.17 (dd, J = 7.4, 1.9 Hz, 1H, H-2), 7.03 (d, J = 1.7 Hz, 1H, H-6), 7.06–7.11 (m, 2H), 7.17–7.25 (m, 6H), 7.31–7.35 (m, 2H). ^{13}C NMR δ (ppm) 15.2, 38.0 (C-3), 42.6 (C-4), 64.6, 99.2 (C-2), 106.96 (C-5), 126.5, 126.7, 128.2, 128.4, 129.0, 130.7, 131.9, 142.8, 149.8 (C-6). IR (KBr): 2982, 2932, 2867, 1603, 1576, 1476, 1437, 1378, 1127, 1040, 906, 768, 730, 700 cm^{-1}; MS (EI, 70 eV) m/z: 360 (15), 358 (8), 314 (10), 288 (33), 286 (19), 237 (14), 179 (36), 178 (36), 158 (48), 157 (100, PhSe$^+$), 131 (78), 128 (56), 115

(44), 103 (31), 78 (64), 77 (73, Ph$^+$), 51 (69), 44 (40). Anal. calcd for $C_{19}H_{20}O_2Se$ (359.31): C, 63.51; H, 5.61. Found: C, 63.48; H, 5.53.

2-Butoxy-4-phenyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3f). Yield = 98%; yellow oil; R_f = 0.35 (cyclohexane–EtOAc, 97 : 3), ^{77}Se NMR δ (ppm) 350.0; ^{1}H NMR δ (ppm) 1.03 (t, J = 7.3 Hz, 3H), 1.47 (m, 2H), 1.68 (m, 2H), 2.33 (ddd, 1H, J = 1.8, 7.9, 13.7 Hz, H-3), 2.50 (ddd, 1H, J = 2.2, 6.9, 13.7 Hz, H-3), 3.64 (m, 1H), 3.75 (m, 1H, H-4), 4.02 (m, 1H), 5.28 (dd, J = 2.2, 7.3 Hz, 1H, H-2), 7.17 (d, J = 1.7 Hz, 1H, H-6), 7.20–7.24 (m, 2H), 7.30–7.35 (m, 6H), 7.44–7.50 (m, 2H). ^{13}C NMR δ (ppm) 13.9, 19.3, 31.7, 37.9 (C-3), 42.5 (C-4), 69.0, 99.3 (C-2), 106.8 (C-5), 126.4, 126.6, 128.1, 128.4, 129.0, 130.7, 131.9, 142.9, 149.9 (C-6). IR (neat): 3060, 2959, 2932, 2872, 1622, 1578, 1493, 1476, 1455, 1438, 1372, 1345, 1231, 1123, 1072, 1050, 1021, 911, 839, 823, 736, 699 cm^{-1}; MS (EI, 70 eV) m/z: 388 (20), 386 (10), 288 (80), 286 (42), 179 (28), 157 (PhSe$^+$, 42), 131 (92), 115 (43), 77 (38, Ph$^+$), 57 (34), 41(100). Anal. calcd for $C_{21}H_{24}O_2Se$ (387.36): C, 65.11; H, 6.24. Found: C, 64.99; H, 6.29.

2-*tert*-Butoxy-4-phenyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3g). Yield = 97%; yellow oil; R_f = 0.35 (cyclohexane–EtOAc, 97 : 3); ^{77}Se NMR δ (ppm) 347.3; ^{1}H NMR δ (ppm) 1.34 (s, 9H), 2.28 (m, 2H, H-3), 3.73 (m, 1H, H-4), 5.43 (dd, J = 2.6, 7.2 Hz, 1H, H-2), 7.08 (d, J = 1.8 Hz, 1H, H-6), 7.14–7.17 (m, 2H), 7.25–7.32 (m, 6H), 7.35–7.40 (m, 2H); ^{13}C NMR δ (ppm) 28.7, 39.5 (C-3), 43.2 (C-4), 75.8, 94.1 (C-2), 106.5 (C-5), 126.4, 126.6, 128.1, 128.4, 128.9, 129.3, 132.1, 143.0, 150.3 (C-6). IR (neat): 3045, 2958, 2831, 1622, 1614, 1580, 1494, 1477, 1455, 1436, 1393, 1367, 1267, 1240, 1179, 1118, 1057, 1021, 962, 916, 840, 735, 699 cm^{-1}; MS (EI, 70 eV) m/z: 388 (7), 386 (4), 332 (32), 288 (26), 286 (14), 179 (12), 157 (PhSe$^+$, 38), 131 (32), 115 (30), 77 (25, Ph$^+$), 57 (100). Anal. calcd for $C_{21}H_{24}O_2Se$ (387.36): C, 65.11; H, 6.24. Found: C, 65.21; H, 6.16.

2-Ethoxy-4-(4-methoxyphenyl)-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3h). Yield = 89%; yellow oil; R_f = 0.26 (AcOEt–cyclohexane, 3 : 97); ^{1}H NMR δ (ppm) 1.22 (t, J = 7.0 Hz, 3H), 2.14 (ddd, 1H, J = 2.2, 8.1, 13.7 Hz, H-3), 2.33 (ddd, 1H, J = 2.2, 6.9, 13.7 Hz, H-3), 3.53–3.65 (m, 2H), 3.77 (s, 3H), 3.93 (m, 1H), 5.13 (dd, J = 2.2, 7.3 Hz, 1H, H-2), 6.73–6.76 (m, 2H), 6.97–7.01 (m, 2H), 7.00 (d, J = 1.8 Hz, 1H, H-6), 7.17–7.21 (m, 3H), 7.31–7.35 (m, 2H). ^{13}C NMR δ (ppm) 15.2, 38.1 (C-3), 41.9 (C-4), 55.2, 64.6, 99.2 (C-2), 107.6 (C-5), 113.5, 126.4, 129.0, 129.4, 130.7, 131.9, 134.8, 149.5 (C-6), 158.3; IR (neat): 3056, 2975, 2930, 2834, 1614, 1579, 1514, 1476, 1455, 1439, 1378, 1360, 1344, 1303, 1281, 1251, 1177, 1122, 1057, 1033, 913, 876, 830, 780, 736, 691 cm^{-1}; MS (EI, 70 eV) m/z: 390 (30), 388 (16), 318 (100), 316 (52), 210 (57), 161 (80), 121 (63), 77 (50, Ph$^+$). Anal. calcd for $C_{20}H_{22}O_3Se$ (389.34): C, 61.69; H, 5.69. Found: C, 61.55; H, 5.88.

2-Ethoxy-3,4-dihydro-4,6-dimethyl-5-phenylselanyl-2*H*-pyran (3i). Yield = 93%; yellow oil; R_f = 0.30 (AcOEt–cyclohexane, 5 : 95); ^{77}Se NMR δ (ppm) 318.9; ^{1}H NMR δ (ppm) 1.18 (d, J = 7.1 Hz, 3H), 1.26 (t, J = 6.8 Hz, 3H), 1.80 (ddd, 1H, J = 6.0, 6.4, 13.6 Hz, H-3), 2.11 (ddd, 1H, J = 2.3, 6.8, 13.6 Hz, H-3), 2.12 (s, 3H), 2.41 (ddd, 1H, J = 1.2, 6.8, 13.9 Hz, H-4), 3.59 (m, 1H), 3.92 (m, 1H), 5.08 (dd, J = 2.3, 6.0 Hz, 1H, H-2), 7.13–7.25 (m, 3H), 7.30–7.34 (m, 2H). ^{13}C NMR δ (ppm) 15.4, 20.7, 21.5, 31.9 (C-4), 36.4 (C-3), 64.4, 98.7 (C-2), 104.1 (C-5), 125.6, 128.7, 129.1, 133.2, 154.9 (C-6). IR (neat): 2975, 2928, 2873, 1638, 1623, 1578, 1476, 1438, 1377, 1236, 1201, 1157, 1123, 1096, 1054, 1019, 957, 840, 734, 690 cm^{-1}; MS (EI, 70 eV) m/z: 312 (10), 310 (10), 251 (9), 240 (42), 238 (24), 197 (27), 171 (15), 157 (24, PhSe$^+$), 116 (28), 115 (33), 91 (21), 77 (38, Ph$^+$), 51 (39), 44 (54), 43 (100). Anal. calcd for $C_{15}H_{20}O_2Se$ (311.28): C, 57.87; H, 6.48. Found: C, 57.53; H, 6.37.

2-Ethoxy-3,4-dihydro-4-methyl-6-phenyl-5-phenylselanyl-2*H*-pyran (3j). Yield = 91%; white solid; m.p. = 66 °C; R_f = 0.31 (AcOEt–cyclohexane, 5 : 95); ^{77}Se NMR δ (ppm) 339.2; ^{1}H NMR δ (ppm) 1.27 (dd, J = 1.2, 6.9 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H), 1.93 (ddd, 1H, J = 5.9, 7.0, 13.7 Hz, H-3), 2.21 (ddd, 1H, J = 2.6, 7.2, 13.7 Hz, H-3), 2.49 (m, 1H), 3.67 (m, 1H), 4.03 (m, 1H), 5.24 (dd, J = 2.6, 5.9 Hz, 1H, H-2), 7.15–7.45 (m, 10H). ^{13}C NMR δ (ppm) 15.4, 21.7, 31.4 (C-4), 36.3 (C-3), 64.55, 99.4 (C-2), 106.7 (C-5), 126.0, 127.7, 128.8, 129.1, 129.3, 129.9, 132.8, 137.2, 155.2 (C-6). IR (KBr): 3055, 2960, 2926, 1620, 1596, 1578, 1476, 1438, 1372, 1264, 1134, 1093, 1063, 1023, 1008, 996, 884, 831, 765, 736, 696 cm^{-1}; MS (EI, 70 eV) m/z: 374 (14), 302 (40), 300 (20), 221 (10), 157 (28, PhSe$^+$), 145 (44), 105 (100), 77 (58, Ph$^+$), 51 (18). Anal. calcd for $C_{20}H_{22}O_2Se$ (373.34): C, 64.34; H, 5.94. Found: C, 64.49; H, 5.97.

2-Ethoxy-3,4-dihydro-6-methyl-4-phenyl-5-phenylselanyl-2*H*-pyran (3k). Yield = 94%; yellow oil; R_f = 0.33 (AcOEt–cyclohexane, 5 : 95); ^{77}Se NMR δ (ppm) 333.7; ^{1}H NMR δ (ppm) 1.25 (t, J = 7,2 Hz, 3H), 2.14 (ddd, 1H, J = 7.8, 9.0, 13.6 Hz, H-3), 2.24 (d, J = 1.8 Hz, 3H), 2.37 (ddd, 1H, J = 2.2, 7.2, 13.6 Hz, H-3), 3.57–3.73 (m, 2H), 3.98 (m, 1H), 5.14 (dd, J = 2.2, 7.8 Hz, 1H, H-2), 7.10–7.35 (m, 10H). ^{13}C NMR δ (ppm) 15.3, 20.8, 38.9 (C-3), 44.7 (C-4), 64.6, 99.3 (C-2), 102.1 (C-5), 125.9, 126.6, 128.3 (2C overlap), 129.1, 129.4, 132.8, 144.4, 156.8 (C-6). IR (neat): 3059, 2975, 2928, 1694, 1627, 1578, 1476, 1438, 1377, 1233, 1156, 1052, 1022, 871, 761, 691 cm^{-1}; MS (EI, 70 eV) m/z: 374 (8), 372 (4), 302 (24), 300 (13), 259 (11), 179 (22), 178 (26), 157 (14, PhSe$^+$), 145 (30), 128 (18), 115 (16), 77 (23, Ph$^+$), 51 (20), 44 (46), 43 (100). Anal. calcd for $C_{20}H_{22}O_2Se$ (373.34): C, 64.34; H, 5.94. Found: C, 64.05; H, 5.68.

2-Ethoxy-3,4-dihydro-4,6-diphenyl-5-phenylselanyl-2*H*-pyran (3l). Yield = 93%; yellow oil; R_f = 0.40 (AcOEt–cyclohexane, 5: 95); ^{77}Se NMR δ (ppm) 356.0; ^{1}H NMR δ (ppm) 1.25 (t, J = 7.2 Hz, 3H), 2.20 (ddd, 1H, J = 8.2, 9.2, 17.3 Hz, H-3), 2.42 (ddd, 1H, J = 2.0, 7.4, 13.6 Hz, H-3), 3.69 (m, 1H), 4.07 (m, 1H), 5.27 (dd, J = 2.0, 8.2 Hz, 1H, H-2), 7.10–7.35 (m, 13H), 7.50–7.53 (m, 2H). ^{13}C NMR δ (ppm) 15.3, 39.1 (C-3), 44.4 (C-4), 64.7, 100.3 (C-2), 105.1 (C-5), 126.5, 126.7, 127.7, 128.4, 128.5, 129.0, 129.1, 129.6, 131.3, 131.9, 136.6, 144.3, 156.8 (C-6). IR (neat) 2973, 2929, 2873, 1691, 1660, 1445, 1376, 1099, 770, 740, 697 cm^{-1}. MS (ESI, positive mode) m/z: 451 and 453 [M + H + O]$^+$. Anal. calcd for $C_{25}H_{24}O_2Se$ (435.40): C, 68.96; H, 5.56. Found: C, 68.76; H, 5.64.

2-Ethylsulfanyl-4-methyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3m). Yield = 95%; yellow oil; R_f = 0.25 (EtOAc–cyclohexane, 5: 95); ^{1}H NMR δ (ppm): 1.11 (d, J = 6.9 Hz, 3H), 1.33 (t, J = 7.6 Hz, 3H), 1.84 (ddd, J = 4.6, 9.4, 13.7 Hz, 1H, H-3), 2.33 (ddd, J = 2.6, 6.3, 13.7 Hz, 1H, H-3′), 2.49 (m, 1H, H-4), 2.77 (m, 2H), 5.24 (dd, J = 2.6, 9.4 Hz, H-2), 6.90 (d, J = 1.9 Hz, 1H, H-6),

This journal is © The Royal Society of Chemistry 2008

7.18–7.26 (m, 3H), 7.42–7.47 (m, 2H). ^{13}C NMR δ (ppm): 15.2, 20.8, 25.1, 31.8 (C-4), 37.65 (C-3), 80.75 (C-2), 108.9 (C-5), 126.3, 129.1, 130.0, 132.3, 150.1 (C-6). IR (neat): 2963, 2925, 2869, 1607, 1578, 1476, 1438, 1375, 1299, 1266, 1202, 1143, 1112, 1000, 844, 735, 690 cm^{-1}. MS (ESI, positive mode) m/z: 431 ([M + H + O]$^+$) (63), 429 (40), 243 (28), 193 (30), 191 (100), 166 (46), 143 (37), 122 (53). Anal. calcd for $C_{14}H_{18}OSSe$ (313.31): C, 53.66; H, 5.79; S, 10.23. Found: C, 53.34; H, 5.68; S, 10.36.

2-Ethylsulfanyl-4-phenyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3n). Yield = 90%; yellow oil; R_f=0.29 (EtOAc–cyclohexane, 5: 95); ^{1}H NMR δ (ppm): 1.33 (t, 3H, J = 7.6 Hz), 2.17–2.29 (m, 1H, H-3), 2.50 (ddd, 1H, J = 2.2, 6.8, 11.7 Hz, H-3), 2.70–2.85 (m, 2H), 3.67 (ddd, J = 1.5, 6.5, 10.2 Hz, 1H, H-4), 5.26 (dd, 1H, J = 1.9, 10.6 Hz, H-2), 7.07–7.10 (m, 2H), 7.09 (d, J = 1.5 Hz, 1H, H-6), 7.18–7.37 (m, 8H). ^{13}C NMR δ (ppm): 15.2, 24.8, 39.2 (C-3), 44.4 (C-4), 80.85 (C-2), 107.5 (C-5), 126.6, 127.0, 128.2, 128.4, 129.0, 130.9, 131.8, 142.5 (C-9), 151.6 (C-6). IR (neat): 3060, 2965, 2926, 1607, 1475, 1452, 1437, 1134, 1053, 1021, 758, 737, 700 cm^{-1}. MS (ESI) m/z: 393 (M + H + O)$^+$.

2-Ethylsulfanyl-4,6-dimethyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3o). Yield = 91%; yellow oil; R_f = 0.27 (EtOAc–cyclohexane, 5 : 95); ^{1}H NMR δ (ppm): 1.15 (d, 3H, J = 6.9 Hz), 1.34 (t, 3H, J = 7.4 Hz), 1.84 (ddd, J = 4.2, 9.4, 13.6 Hz, 1H, H-3), 2.15 (d, 3H, J = 1.8 Hz), 2.30 (ddd, J = 2.4, 6.5, 13.6 Hz, 1H, H-3′), 2.50 (m, 1H, H-4), 2.78 (m, 2H), 5.21 (dd, 1H, J = 2.4, 9.4 Hz, H-2), 7.15–7.25 (m, 3H), 7.35–7.38 (m, 2H). ^{13}C NMR δ (ppm): 15.3, 21.0, 21.8, 25.2, 33.3 (C-4), 38.1 (C-3), 80.5 (C-2), 104.4 (C-5), 125.7, 128.9, 129.2, 133.0, 157.2 (C-6). IR (neat): 2970, 2927, 2870, 1610, 1578, 1476, 1438, 1236, 1201, 1151, 1115, 1019, 957, 920, 734, 690 cm^{-1}; MS (EI, 70 eV) m/z: 330 (2), 328 (5), 240 (53), 238 (30), 197 (24), 171 (13), 157 (25, PhSe$^+$), 116 (28), 115 (34), 88 (30), 77 (24, Ph$^+$), 60 (56), 51 (24), 44 (41), 43 (100). Anal. calcd for $C_{15}H_{20}OSSe$ (327.34): C, 55.03; H, 6.16; S, 9.80. Found: C, 55.05; H, 5.81; S, 10.13.

2-Ethylsulfanyl-6-methyl-4-phenyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3p). Yield = 90%; yellow oil; R_f = 0.33 (EtOAc–Cyclohexane, 5 : 95); ^{1}H NMR δ (ppm): 1.34 (t, 3H, J = 7.4 Hz), 2.21 (d, J = 1.8 Hz, 3H), 2.15–2.25 (m, 1H, H-3), 2.46 (ddd, J = 1.9, 6.9, 15.6 Hz, 1H, H-3′), 2.80 (m, 2H), 3.73 (m, 1H, H-4), 5.23 (dd, 1H, J = 1.9, 10.8 Hz, H-2), 7.07–7.10 (m, 2H), 7.18–7.28 (m, 8H). ^{13}C NMR δ (ppm): 15.3, 20.95, 24.8, 40.2 (C-3), 46.35 (C-4), 80.7 (C-2), 102.8 (C-5), 126.0, 126.85, 128.0, 128.5, 129.1, 129.6, 132.6, 144.1, 158.85 (C-6). IR (neat): 3058, 3026, 2964, 2925, 2869, 1626, 1577, 1492, 1475, 1453, 1436, 1375, 1265, 1211, 1052, 1014, 972, 735, 701 cm^{-1}; MS (ESI, positive mode) m/z: 407 ([M + H+O]$^+$, 100), 405 (55), 319 (29); Anal. calcd for $C_{20}H_{22}OSSe$ (389.40): C, 61.68; H, 5.69; S, 8.23. Found: C, 61.35; H, 5.85; S, 8.57.

4-Methyl-2,5-bis-phenylselanyl-3,4-dihydro-2*H*-pyran (3q). Yield = 80%; yellow oil; R_f = 0.60 (EtOAc–cyclohexane, 5 : 95); ^{1}H NMR δ (ppm): 1.15 (d, 3H, J = 6.9 Hz), 1.98–2.07 (m, 1H, H-3), 2.45–2.59 (m, 2H, H-4, H-3), 5.76 (dd, 1H, J = 3.2, 8.2 Hz, H-2), 6.89 (d, 1H, J = 1.5 Hz, H-6), 7.15–7.67 (m, 10H). ^{13}C NMR δ (ppm): 21.1, 31.6 (C-4), 38.2 (C-3), 78.9 (C-2), 109.1 (C-5), 126.4, 128.2, 129.1, 129.2, 129.3, 130.1, 134.5, 135.3, 149.5 (C-6). IR (neat): 3056, 2961, 2922, 1686, 1579, 1476, 1436, 1301, 1229, 1190, 1140, 1107, 1022, 999, 847, 741, 690 cm^{-1}.

4-Methyl-2-phenyl-5-phenylselanyl-3,4-dihydro-2*H*-pyran (3s). Yield = 64%; yellow oil; R_f = 0.38 (AcOEt–cyclohexane, 3 : 97); ^{1}H NMR δ (ppm) 0.97 (d, J = 7.0 Hz, 3H), 1.69 (ddd, J = 2.4, 11.5, 13.7 Hz 1H, H-3), 2.16 (ddd, J = 1.8, 5.9, 13.7 Hz, 1H, H-3′), 2.48–2.59 (m, 1H, H-4), 4.91 (dd, J = 1.8, 11.5 Hz, 1H, H-2), 6.98 (d, J = 1.8 Hz, 1H, H-6), 7.10–7.40 (m, 10H). ^{13}C NMR δ (ppm) 20.7, 32.2 (C-4), 40.9 (C-3), 78.6 (C-2), 109.0 (C-5), 126.0, 126.2, 128.1, 128.6, 129.1, 129.9, 132.7, 140.9, 151.9 (C-6). IR (KBr): 3057, 1694, 1607, 1577, 1477, 1438, 1388, 1369, 1167, 1068, 1022, 737, 691 cm^{-1}; MS (EI, 70 eV) m/z: 330 (34), 328 (18), 226 (100), 224 (50), 207 (26), 157 (36, PhSe$^+$), 117 (44), 115 (40), 105 (42), 77 (52, Ph$^+$), 51 (46), 44 (38).

Typical procedure for the synthesis of selenoxides (4)

To a mixture of dihydropyran **3a** (1 mmol, 297 mg) in tetrahydrofuran (10 ml), was added slowly H_2O_2 35%$_w$ in water (0.4 ml, 4 eq.) at room temperature. After the reaction was completed, monitored by TLC (usually 2 hours), the layers were separated and the organic one dried and concentrated under vacuum. The residue was chromatographed on silica gel (eluent: MeOH–EtOAc, 1 : 99) to give 200 mg (64%) of 2-ethoxy-4-methyl-5-phenylseleninyl-3,4-dihydro-2*H*-pyran **4a**.

2-Ethoxy-4-methyl-5-phenylseleninyl-3,4-dihydro-2*H*-pyran (4a). Mixture of 2 diastereomers: 53 : 47. Yield = 64%; yellow oil; R_f = 0.31 (MeOH–AcOEt, 1 : 99); ^{1}H NMR δ (ppm) (0.90, 1.26) (d, J = 7.0 Hz, 3H), 1.21 (t, J = 7.0 Hz, 3H), 1.76 (m, 1H, H-3), 1.94 (m, 1H, H-3), (2.41, 2.55) (m, 1H, H-4), 3.55 (m, 1H), 3.87 (m, 1H), 5.05 (dd, J = 2.6, 5.1 Hz, 1H, H-2), (6.91, 7.04) (s, 1H, H-6), 7.48–7.55 (m, 3H), 7.70–7.74 (m, 2H). ^{13}C NMR δ (ppm) (15.1, 15.2), (19.8, 20.4), (24.4, 26.4, C-4), (35.4, 35.7, C-3), (64.7, 64.8), (99.0, 99.1, C-2), (121.0, 122.2, C-5), (126.1, 126.6), (129.2, 129.6), (131.2, 131.4), (138.2, 140,1), (146.1, 148.6, C-6). IR (neat): 3418, 3054, 2930, 1732, 1622, 1456, 1442, 1378, 1279, 1139, 1096, 1076, 1021, 990, 816, 744, 691 cm^{-1}; MS (EI, 70 eV) m/z: 314 (44), 312 (40), 234 (20), 232 (12), 157 (100, PhSe$^+$), 154 (60), 117 (15), 78 (16), 77 (75, Ph$^+$), 51 (68), 50 (38).

2-Ethoxy-3,4-dihydro-4,6-diphenyl-5-phenylseleninyl-2*H*-pyran (4l). Yield = 80%; yellow oil; R_f = 0.34 (AcOEt–cyclohexane, 80 : 20); ^{1}H NMR δ (ppm) 1.16 (t, J = 7.1 Hz, 3H), 2.07–2.26 (m, 2H, H-3), 3.54–3.65 (m, 2H), 3.96 (m, 1H), 5.14 (dd, J = 2.4, 7.1 Hz, 1H, H-2), 7.10–7.53 (m, 13H), 7.73–7.78 (m, 2H). ^{13}C NMR δ (ppm) 15.1, 39.3 (C-4), 39.7 (C-3), 64.8, 100.6 (C-2), 118.1 (C-5), 126.8, 126.9, 128.0, 128.4, 128.8, 129.0, 129.8, 130.6, 130.7, 134.1, 140.6, 141.3, 160.3 (C-6). IR (neat) 3418, 3061, 2976, 2931, 2360, 2340, 1652, 1615, 1574, 1494, 1455, 1445, 1379, 1275, 1134, 1058, 938, 808, 741, 699 cm^{-1}. MS (ESI, positive mode) m/z: 453 [M + H]$^+$ (100), 451 (80).

Typical procedure for the synthesis of tetrahydrofuranones (5)

To a mixture of dihydropyran **3a** (1 mmol, 297mg) in dichloromethane (10 ml), was added slowly H_2O_2 35%$_w$ in water (0.4 ml, 4 eq.) at room temperature. After the reaction was completed, monitored by TLC, the layers were separated and the organic one dried and then concentrated under vacuum. The residue was chromatographed on silica gel (eluent: ethyl Acetate–cyclohexane, 10 : 90) to give 36 mg (25%) of 5-ethoxy-3-methyl-tetrahydrofuran-2-one **5a**.

5-Ethoxy-3-methyl-tetrahydrofuran-2-one (5a). Yield = 25%; yellow oil; R_f = 0.20 (cyclohexane–EtOAc, 80 : 20); ^{1}H NMR δ (ppm) 1.18–1.27 (m, 6H), 1.97 (m, 1H, H-4), 2.35 (m, 1H, H-4), 2.83 (m, 1H, H-3), 3.58 (m, 1H), 3.83 (m, 1H), 5.44 (d, 1H, J = 5.6 Hz); ^{13}C NMR δ (ppm) 14.95, 15.25, 32.7 (C-3), 37.3 (C-4), 64.94, 101.8 (C-5), 180.0 (C-2). IR (neat): 2978, 2936, 1778, 1738, 1446, 1378, 1349, 1213, 1169, 1112, 1040, 981, 951, 917 cm^{-1}; MS (EI, 70 eV) m/z: 143 (2), 100 (42), 99 (32), 85 (43), 72 (19), 57 (96), 43 (95), 42 (95), 41 (100). Anal. calcd for $C_7H_{12}O_3$ (144.166): C, 58.31; H, 8.39. Found: C, 57.96; H, 8.43.

5-Ethoxy-3-((*tert*-butyl)dimethylsilyl-methoxy)-tetrahydro-furan-2-one (5b). Yield = 42%; yellow oil; R_f = 0.35 (cyclohexane–EtOAc, 90 : 10); major *trans* isomer: ^{1}H NMR δ (ppm) 0.05 (s, 6H), 0.87 (s, 9H), 1.22 (t, 3H, J = 7.1 Hz), 2.19 (ddd, 1H, J = 1.6, 9.4, 13.4 Hz, H-4), 2.46 (ddd, 1H, J = 5.9, 8.6, 13.4 Hz, H-4′), 2.88 (m, 1H, H-3), 3.59 (dq, J = 7.1, 9.5 Hz, 1H), 3.75 (dd, J = 3.1, 9.9 Hz, 1H), 3.86 (dq, J = 7.0, 9.5 Hz, 1H), 3.99 (dd, J = 3.7, 10.0 Hz, 1H), 5.48 (dd, 1H, J = 1.6, 5.9 Hz, H-5); ^{13}C NMR δ (ppm) -5.5, 15.0, 18.2, 25.8, 31.6 (C-4), 41.6 (C-3), 61.3, 65.1, 102.8 (C-5), 177.3 (C-2); IR (neat): 2956, 2931, 2858, 1782, 1472, 1446, 1377, 1349, 1259, 1116, 1004, 955, 901, 837, 779, 736 cm^{-1}; MS (EI, 70 eV) m/z: 230 (2), 229 (8), 218 (20), 217 (100), 171 (70), 143 (94), 129 (16), 99 (24), 75 (84). Anal. calcd for $C_{13}H_{26}O_4Si$ (274.43): C, 56.90; H, 9.55. Found: C, 57.18; H, 9.63.

Minor *cis* isomer: ^{1}H NMR δ (ppm) 0.06 (s, 6H), 0.89 (s, 9H), 1.23 (t, 3H, J = 7.1 Hz), 2.18 (ddd, 1H, J = 4.6, 7.5, 13.5 Hz, H-4), 2.51 (ddd, 1H, J = 6.0, 9.7, 13.5 Hz, H-4), 2.78 (m, 1H, H-3), 3.63 (dq, 1H, J = 7.1, 9.3 Hz), 3.83–3.94 (m, 3H), 5.50 (dd, J = 4.6, 6.0 Hz, 1H, H-5); ^{13}C NMR δ (ppm) -5.4, 15.1, 18.4, 25.9, 31.6 (C-4), 43.2 (C-3), 62.0, 65.9, 103.6 (C-5), 176.2 (C-2).

3-Methyl-tetrahydro-furo[2,3-*b*]furan-2-one (5c). Yield = 36%; yellow oil; R_f = 0.39 (cyclohexane–EtOAc, 50 : 50); ^{1}H NMR δ (ppm) 1.27 (d, 3H, J = 7.3 Hz), 1.82–2.08 (m, 2H), 2.93 (m, 1H, H-4), 3.12 (m, 1H, H-3), 3.96–4.10 (m, 2H), 6.00 (d, 1H, J = 4.8 Hz); ^{13}C NMR δ (ppm) 11.7, 25.1, 38.2 (C-4), 44.2 (C-3), 68.9, 106.6 (C-5), 177.1 (C-2). IR (neat): 2981, 2898, 1777, 1716, 1454, 1379, 1359, 1295, 1251, 1176, 1109, 953, 907, 868, 736 cm^{-1}; Anal. calcd for $C_7H_{10}O_3$ (142.15): C, 59.14; H, 7.09. Found: C, 59.08; H, 7.34.

Tetrahydro-furo[2,3-*b*]furan-2-one (5d). Yield = 30%; white solid; m.p. 48–50 °C; R_f = 0.37 (cyclohexane–EtOAc, 50 : 50); ^{1}H NMR δ (ppm) 1.74–1.82 (m, 1H, H-4), 2.17–2.27 (m, 1H, H-4′), 2.44 (dd, J = 3.4, 18.4 Hz, 1H, H-3), 2.88 (dd, J = 10.2, 18.4 Hz, 1H, H-3′), 3.12–3.20 (m, 1H, H-8), 3.90–3.99 (m, 1H, H-5), 4.06–4.13 (m, 1H, H-5′), 6.08 (d, J = 5.6 Hz, 1H, H-7); ^{13}C NMR δ (ppm) 32.3 (C-4), 35.0 (C-3), 38.4 (C-8), 67.4 (C-5), 108.5 (C-7), 175.5 (C-2). IR (neat): 2986, 1770, 1636, 1455, 1418, 1360, 1300, 1252, 1186, 1109, 1004, 968, 871, 834 cm^{-1}; Anal. calcd for $C_6H_8O_3$ (128.12): C, 56.24; H, 6.29. Found: C, 56.16; H, 6.43.

5-Ethoxy-3-phenyl-tetrahydrofuran-2-one (5e). Yield = 44%; yellow oil; major *trans* isomer: R_f = 0.28 (cyclohexane–EtOAc, 90 : 10); ^{1}H NMR δ (ppm) 1.26 (t, 3H, J = 7.1 Hz), 2.48 (ddd, 1H, J = 5.5, 11.2, 13.3 Hz, H-4), 2.63 (dd, 1H, J = 8.8, 13.3 Hz, H-4), 3.64 (m, 1H), 3.90 (m, 1H), 4.05 (dd, J = 8.8, 11.2 Hz, 1H, H-3), 5.58 (d, 1H, J = 5.5 Hz), 7.22–7.38 (m, 5H); ^{13}C NMR δ (ppm) 15.1, 38.4 (C-4), 44.3 (C-3), 65.2, 101.8 (C-5), 127.8, 128.1, 129.1, 136.6, 177.2 (C-2). IR (neat): 2978, 2931, 1775, 1734, 1498, 1456, 1378, 1342, 1206, 1140, 1108, 1040, 996, 935, 899, 752, 695, 642 cm^{-1}; MS (EI, 70 eV) m/z: 207 (24), 162 (66), 133 (56), 105 (100), 104 (31), 103 (30), 92 (10), 77 (35), 51 (22), 44 (48). Anal. calcd for $C_{12}H_{14}O_3$ (206.23): C, 69.88; H, 6.84. Found: C, 69.84; H, 6.85.

Minor *cis* isomer: ^{1}H NMR δ (ppm) 1.29 (t, 3H, J = 7.0 Hz), 2.33 (ddd, 1H, J = 4.8, 8.2, 13.8 Hz, H-4), 2.92 (ddd, 1H, J = 5.9, 10.3, 13.8 Hz, H-4′), 3.71 (dt, J = 7.1, 9.5 Hz, 1H), 3.84 (dd, J = 8.2, 10.3 Hz, 1H, H-3), 3.98 (dt, J = 7.1, 9.5 Hz, 1H), 5.62 (dd, 1H, J = 4.8, 5.9 Hz, H-5), 7.25–7.38 (m, 5H); ^{13}C NMR δ (ppm) 15.1, 37.1 (C-4), 46.0 (C-3), 66.1, 102.9 (C-5), 127.7, 128.2, 129.0, 137.0, 176.0 (C-2). IR (neat): 2978, 2929, 1773, 1719, 1498, 1456, 1378, 1353, 1146, 1120, 1043, 996, 927, 753, 698 cm^{-1}.

5-Butoxy-3-phenyl-tetrahydrofuran-2-one (5f). Yield = 24%; yellow oil; R_f = 0.26 (cyclohexane–EtOAc, 90 : 10); ^{1}H NMR δ (ppm) 0.94 (t, 3H, J = 7.3 Hz), 1.40 (m, 2H), 1.60 (m, 2H), 2.49 (ddd, 1H, J = 5.5, 11.2, 13.3 Hz, H-4), 2.64 (ddd, 1H, J = 0.9, 8.8, 13.3 Hz, H-4), 3.58 (dt, 1H, J = 6.6, 9.5 Hz), 3.86 (dt, 1H, J = 6.6, 9.3 Hz), 4.05 (ddd, J = 0.9, 8.8, 11.2 Hz, 1H, H-3), 5.59 (d, 1H, J = 5.5 Hz, H-5), 7.25–7.40 (m, 5H); ^{13}C NMR δ (ppm) 13.9, 19.3, 31.5, 38.4 (C-4), 44.3 (C-3), 69.5, 102.0 (C-5), 127.8, 128.1, 129.0, 136.6, 177.2 (C-2), IR (neat): 3031, 2958, 2873, 1778, 1770, 1728, 1715, 1605, 1497, 1456, 1345, 1264, 1204, 1137, 1107, 1060, 998, 933, 800, 751, 696, 643 cm^{-1}; MS (EI, 70 eV) m/z: 191 (10), 190 (52), 161 (12), 134 (28), 133 (40), 105 (100), 92 (61), 78 (28), 77 (29), 57 (21). Anal. calcd for $C_{14}H_{18}O_3$ (234.29): C, 71.77; H, 7.74. Found: C, 72.10; H, 7.69.

5-*tert*-Butoxy-3-phenyl-tetrahydrofuran-2-one (5g). Yield = 30%; yellow oil; R_f = 0.20 (cyclohexane–EtOAc, 90 : 10); ^{1}H NMR δ (ppm) 1.32 (s, 9H), 2.53 (m, 2H, H-4), 4.08 (t, 1H, J = 9.8 Hz), 5.87 (dd, 1H, J = 2.8, 3.9 Hz), 7.24–7.38 (m, 5H); ^{13}C NMR δ (ppm) 28.8, 29.8, 39.5 (C-4), 44.7 (C-3), 97.2 (C-5), 127.7, 128.1, 129.1, 136.9, 177.3 (C-2). IR (neat): 2979, 2930, 2854, 1778, 1770, 1738, 1732, 1606, 1498, 1455, 1395, 1368, 1338, 1266, 1180, 1138, 1102, 995, 933, 900, 858, 798, 750, 694, 641 cm^{-1}; MS (EI, 70 eV) m/z: 191 (2), 190 (8), 161 (12), 134 (61), 133 (25), 105 (40), 104 (18), 103 (18), 92 (22), 77 (16), 57(100). Anal. calcd for $C_{14}H_{18}O_3$ (234.284): C, 71.77; H, 7.74. Found: C, 71.74; H, 7.81.

5-Ethoxy-3-(4-methoxyphenyl)-tetrahydrofuran-2-one (5h). Yield = 43%; yellow oil; R_f = 0.18 (cyclohexane–EtOAc, 90 : 10); ^{1}H NMR δ (ppm) 1.26 (t, 3H, J = 7.1 Hz), 2.46 (ddd, 1H, J = 5.7, 11.1, 13.2 Hz, H-4), 2.62 (ddd, 1H, J = 0.8, 8.8, 13.2 Hz, H-4), 3.64 (m, 1H), 3.80 (s, 3H), 3.90 (m, 1H), 4.01 (dd, J = 8.8, 11.1 Hz, 1H, H-3), 5.58 (d, 1H, J = 5.5 Hz), 6.87–6.92 (m, 2H), 7.16–7.20 (m, 2H); ^{13}C NMR δ (ppm) 15.0, 38.4 (C-4), 43.4 (C-3), 55.4, 65.1, 101.7 (C-5), 114.4, 128.5, 129.2, 159.1, 177.5 (C-2); IR (neat): 2978, 2933, 1771, 1615, 1515, 1445, 1342, 1249, 1206, 1181, 1142, 1104, 1035, 936, 905, 831, 804, 781, 760, 736, 689 cm^{-1}; MS (EI, 70 eV) m/z: 236 (13), 192 (46), 163 (92), 147 (50), 135 (100), 119 (20), 105 (16), 91 (40), 77 (20), 66 (19). Anal. calcd for $C_{13}H_{16}O_4$ (236.26): C, 66.08; H, 6.83. Found: C, 66.28; H, 6.62.

1-(3-Phenylfuran-2-yl)ethanone (6). Yield = 21%; yellow oil; R_f = 0.4 (AcOEt–cyclohexane, 15 : 85); ^{1}H NMR δ (ppm) 2.46 (s, 3H), 6.66 (d, 1H, J = 1.6 Hz, H-4), 7.36–7.44 (m, 3H), 7.55 (d, 1H, J = 1.6 Hz, H-5), 7.61–7.64 (m, 2H); ^{13}C NMR δ (ppm) 27.8, 115.0 (C-4), 128.2, 128.6, 129.3, 132.0, 133.5, 144.7 (C-5), 147.3, 188.0. IR (neat) 1676, 1565, 1503, 1474, 1448, 1394, 1356,

This journal is © The Royal Society of Chemistry 2008

1284, 1241, 1162, 1130, 1096, 1065, 1019, 978, 932, 886, 761, 694, 639 cm^{-1}; MS (EI, 70 eV) m/z: 186 (92), 185 (75), 143 (4), 128 (4), 115 (100), 89 (30), 63 (18), 43 (20). Anal. calcd for $C_{12}H_{10}O_2$ (186.20): C, 77.40; H, 5.41. Found: C,77.04; H, 5.80.

4-Formyloxy-2-methyl-4-phenylbutanoic acid (7s). Yield = 63%; yellow oil; R_f=0.66 (AcOEt–cyclohexane, 100 : 0); ^{1}H NMR δ (ppm) 1.15 (d, J = 6.8 Hz, 3H), 1.74–1.82 (m, 1H, H-3), 2.34–2.44 (m, 2H), 5.85 (dd, J = 5.3, 6.4 Hz, 1H, H-4), 7.16–7.28 (m, 5H), 7.98 (s, 1H). ^{13}C NMR δ (ppm) 17.1, 36.3, 39.7, 73.8, 126.7, 128.6, 128.8, 139.4, 160.4, 182.3. IR (neat): 2977, 2936, 2360, 2341, 1732, 1715, 1456, 1170, 758, 700 cm^{-1}. MS (ESI, negative mode) m/z: 443 ([2M − H]$^-$, 100), 221 ([M − H]$^-$, 37).

Acknowledgements

We gratefully acknowledge Dr Isabelle Chataigner for her help in performing the high pressure hetero-Diels–Alder reactions. The Conseil Régional Haute-Normandie is also acknowledged for financial support to S. R. through a doctoral fellowship.

Notes and references

1 (*a*) T. Wirth, *Organoselenium Chemistry: Modern developments in Organic Synthesis*, Springer, Berlin, 2000; (*b*) T. G. Back, *Organoselenium Chemistry: A Practical Approach*, Oxford University Press, New York, NY, 1999; (*c*) A. Krief and L. Hevesi, *Organoselenium Chemistry I*, Springer, Berlin, 1988; (*d*) D. C. Liotta, *Organoselenium Chemistry*, Wiley, New York, 1987; (*e*) S. Patai, *The Chemistry of Organic Selenium and Tellurium Compounds*, Wiley, New York, 1987, vol. 1 and 2; (*f*) C. Paulmier, *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon, Oxford, 1986.
2 (*a*) C. Paulmier, *Phosphorus, Sulfur and Silicon*, 2001, **172**, 25; (*b*) C. Miniejew, F. Outurquin and X. Pannecoucke, *Tetrahedron*, 2006, **62**, 2657; (*c*) C. Miniejew, F. Outurquin and X. Pannecoucke, *Org. Biomol. Chem.*, 2004, **2**, 1575; (*d*) X. Franck, E. Langlois and F. Outurquin, *Synthesis*, 2007, 719.
3 (*a*) H. J. Reich and J. M. Renga, *J. Org. Chem.*, 1975, **40**, 3313; (*b*) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, 1972, **94**, 7154.
4 S. Redon, A.-L. Berthe-Berkaoui, X. Pannecoucke and F. Outurquin, *Tetrahedron*, 2007, **63**, 3707.
5 (*a*) H. J. Reich, M. J. Kelly, R. E. Alson and R. C. Holton, *Tetrahedron*, 1983, **39**, 949; (*b*) K. Uneyama, K. Takano and S. Torii, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 2867; (*c*) S.-S. P. Chou and C.-C. Hung, *Synth. Commun.*, 2001, **31**, 1097; (*d*) S.-S. P. Chou and C.-C. Hung, *Synth. Commun.*, 2002, **32**, 3119.
6 (*a*) J. Młochowski, M. Brzszcz, M. Giurg, J. Palus and H. Wójtowicz, *Eur. J. Org. Chem.*, 2003, 4329; (*b*) G.-J. ten Brink, J.-M. Vis, I. W. C. E. Arends and R. A. Sheldon, *J. Org. Chem.*, 2001, **66**, 2429.
7 Such an intermediate has been observed during the oxidation of cyclohexene to adipic acid, see: S.-O. Lee, R. Raja, K. D. M. Harris, J. M. Thomas, B. F. G. Johnson and G. Sankar, *Angew. Chem., Int. Ed.*, 2003, **42**, 1520.
8 A. Armstrong and H. Chung, *Tetrahedron Lett.*, 2006, **47**, 1617.
9 D. Enders, J. Vazquez and G. Raabe, *Eur. J. Org. Chem.*, 2000, 893–901.