Synthesis and oxidative rearrangement of selenenylated dihydropyrans

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Selenenylated dihydropyrans prepared by inverse demand Hetero-Diels-Alder reactions undergo oxidative rearrangement when treated with H₂O₂, leading to tetrahydrofuran-2-ones by ring contraction.

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15

Introduction

Oxidized organoselenium derivatives are source of molecular diversity by the richness of their chemistry.¹ Indeed, oxidation of aliphatic organoselenium derivatives is often used to introduce an insaturation by β -elimination (selenoxide) or to substitute the organoselenium residue by nucleophilic displacement (eg. activation with NBS and substitution by an amine).² Allylic or propargylic phenylselenanyl 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 phenylselenanyl 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 the 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 and studied the particular reactivity of these cycloadducts toward oxidants. Maybe owing to the sensibility of selenenylated derivatives to Lewis acids or heat, only few examples of Diels-Alder reactions with α -phenylselenanyl-enals, -enones or dienes have been described.⁵

Results and discussion

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

In these cases, 2-phenylselenenylated 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 catalyst, at either room temperature or 50°C. When R¹=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-ether such as dihydrofuran can also be used (table 1, entries 3-5), leading to bicyclic compound **3c-d** in good yields. Bulkier vinyl ethers such as *n*-butyl- and even *t*-butyl- one can be used without loss of efficiency (table 1, entries 9-10). With less reactive phenylselenenylated enones (table 1, entries 12-19), the reaction became slower and high pressure was needed to maintain efficiency, especially when R¹ or R² was an aryl group. When both R¹ and R² 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 phenylselenanyl- acetals, ethylvinylsulfide (table 1, entries 20-23) and phenylvinylselenide (table 1, entry 24) were engaged as dienophile in hetero-Diels-Alder reactions. The reactions were always high yielding and high pressure was only needed in the case of enone substituted by a phenyl group (table 1, entry 23); thus 2-ethylsulfanyl-5-phenylselenanyl-3,4-dihydro-2H-pyrans **3m-p** and the bis-selenenylated 2-ethylselenanyl-5-phenylselenanyl-3,4-dihydro-2H-pyran **3q** could be obtained. With less electron rich dienophiles such as vinylacetate or styrene, Hetero-Diels-Alder reactions with reactive enal never proceeded with vinylacetate, (table 1, entry 25) and required high pressure and longer reaction time for styrene, leading to 2-phenyl-5-phenylselenanyl-3,4-dihydro-2H-pyrans **3s** (table 1, entries 26-27). It is noteworthy that in this case, no polymerisation of styrene was observed.

Scheme1 Hetero-Diels-Alder between 2-phenylselenanyl-enals or -enones **1** and an alkene **2** leading to dihydropyrans **3a-s**.

Once having 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 ($\text{R}^4=\text{OR}$) ended up with an unprecedented ring contraction affording, when $\text{R}^2=\text{H}$, 5-alkoxy-tetrahydrofuran-2-ones **5**. From acetal **3e** where $\text{R}^2=\text{Me}$ and $\text{R}^4=\text{OR}$, a mixture of 5-alkoxy-tetrahydro-furan-2-ones **5e** and acetylfuran **6** was observed (Scheme 2).

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., 12h	3a (83)
2	CH_2OTBDMS	H	H	OEt	3% Eu(FOD) ₃ , r.t., 12h	3b (86)
3	Me	H	$-\text{CH}_2\text{CH}_2\text{O}-$		1.0 Gpa, 50°C, 36h	3c (84)
4	Me	H	$-\text{CH}_2\text{CH}_2\text{O}-$		5% Eu(FOD) ₃ , 40°C, 12h	3c (78)
5	H	H	$-\text{CH}_2\text{CH}_2\text{O}-$		3% Eu(FOD) ₃ , r.t., 12h	3d (73)
6	Ph	H	H	OEt	10% Eu(FOD) ₃ , 40°C, 48h	3e (90)
7	Ph	H	H	OEt	1.0 Gpa, r.t., 15h	3e (50)
8	Ph	H	H	OEt	1.0 Gpa, 50°C, 10h	3e (99)
9	Ph	H	H	<i>On</i> -Bu	5% Eu(FOD) ₃ , 80°C, 12h	3f (98)
10	Ph	H	H	<i>Or</i> -Bu	10% Eu(FOD) ₃ , 80°C, 12h	3g (97)
11	<i>p</i> -OMePh	H	H	OEt	5% Eu(FOD) ₃ , 40°C, 12h	3h (89)
12	Me	Me	H	OEt	10% Eu(FOD) ₃ , 40°C, 48h	3i (93)
13	Me	Me	H	OEt	1.0 Gpa, r.t., 20h	3i (93)
14	Me	Ph	H	OEt	10% Eu(FOD) ₃ , 40°C, 20h	3j (35)
15	Me	Ph	H	OEt	1.2 Gpa, 50°C, 20h	3j (91)
16	Ph	Me	H	OEt	10% Eu(FOD) ₃ , 40°C, 48h	3k (46)
17	Ph	Me	H	OEt	1.2 Gpa, 50°C, 20h	3k (94)
18	Ph	Ph	H	OEt	10% Eu(FOD) ₃ , r.t., 48h	3l (N.R.)
19	Ph	Ph	H	OEt	1.2 Gpa, 50°C, 20h	3l (88)
20	Me	H	H	SEt	4% Eu(FOD) ₃ , r.t., 12h	3m (95)
21	Ph	H	H	SEt	10% Eu(FOD) ₃ , 40°C, 12h	3n (90)
22	Me	Me	H	SEt	10% Eu(FOD) ₃ , r.t., 12h	3o (91)
23	Ph	Me	H	SEt	1.2 Gpa, 40°C, 20h	3p (90)
24	Me	H	H	SePh	10% Eu(FOD) ₃ , 80°C, 24h	3q (76)
25	Me	H	H	OCOCH_3	1.0 Gpa, 50°C, 24h	3r (N.R.)
26	Me	H	H	Ph	1.2 Gpa, 50°C, 16h	3s (24)
27	Me	H	H	Ph	1.2 Gpa, 50°C, 48h	3s (64)

In order to elucidate the mechanism and characterize 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.

Dihydropyran **3s** ($\text{R}^4=\text{Ph}$) was also submitted 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** ($\text{R}^1=\text{R}^2=\text{Ph}$), only the selenoxide **4l** could be obtained and no rearrangement occurred. When we used simple dihydropyran with no phenylselenanyl residue, no oxidation occurred at all and starting material was recovered unchanged (not shown). This surprising oxidation susceptibility of such 5-phenylselenanyl-3,4-dihydro-2*H*-pyrans **3** is due to the presence of the selenium residue and is reported for the first time.

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

Scheme 3 Proposed mechanism.

Having identified intermediates and characterized 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 polarisation of the enolic double bond, which can certainly be epoxidized by H₂O₂. Then, depending on the substitution on position 6 (R²=H or R²=Me), two different pathways can be observed (Scheme 3).

First, when R²=H, water (solvent of H₂O₂) can attack at the position 6 to give, after expulsion of “PhSeOH”, the keto-hemiacetal **8**. PhSeOH can then be further oxidized by the excess of H₂O₂ to PhSe(O)OOH, phenylperseleninic acid, which is known 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 corresponding lactone-hemiacetal **9** which can rearrange with expulsion of formic acid and ring closure of the carboxylate onto the formed oxonium. This mechanism is supported by the isolation of carboxylic acid **7s**, from the reaction of dihydropyran **3s** where R⁴=Ph. Indeed, the same lactone-hemiacetal can be drawn but, in this case, R⁴ is not electron donating enough to open the ring and fragmentation occurs, leading to carboxylic acid **7s** with an hydroxyl group functionalized as a formyl ester.

Second, when R²=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 R⁴=OEt which can help opening 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 *et al.* in the synthesis of tetrahydrofuranones.⁸ Then the selenoxide can β-eliminate to give a dihydro-furan which can further lose EtOH to yield the corresponding furan **6**.

Both pathways are competitive and depend on the substitution pattern (R²). The presence of the selenium residue increases the reactivity of these dihydropyrans and makes possible the whole oxidation process to occur in very mild conditions. 5-alkoxy-tetrahydrofuran-2-ones **5** have been prepared in moderate yields, what 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 out of the reaction were unsuccessful (use of urea-H₂O₂ complex).

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

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 as a main *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

Conclusion

To conclude, we have developed an efficient route toward selenenylated dihydropyrans through a high yielding inverse demand Hetero-Diels-Alder. This pathway allowed a general access to various dihydropyrans including thio- and seleno-acetals. Further oxidation of these selenenylated dihydropyrans ($R^4=OR$) with H_2O_2 proceeded with unprecedented rearrangement, affording 5-alkoxy-tetrahydro-furan-2-ones **5** through a contraction of the intermediate selenoxide **4**. A mechanism was postulated, passing through an epoxide which could then be transformed either in furan moiety or in 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. This probe is equipped with pulsedfield (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 have reliable information. Chemical shifts (δ) are expressed in ppm relative to TMS for 1H 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 analyser 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** (1mmol, 225mg) in ethyl vinyl ether (10 mmol, 0.96 ml) was introduced in a high-pressure vessel and compressed at the desired pressure and temperature. After decompression, the mixture was concentrated under vacuum. The residue was chromatographed on silicagel (eluent: Ethyl acetate /Cyclohexane: 3/97) to give 282 mg (95%) of 2-Ethoxy-4-methyl-5-phenylselenanyl-3,4-dihydro-2H-pyran **3a**.

Method with Eu(FOD)₃.

To a mixture of enal **1a** (1mmol, 225mg) 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, controlled by TLC, the mixture was concentrated under vacuum. The residue was chromatographed on silicagel (eluent: Ethyl Acetate/Cyclohexane: 3/97) to give 275 mg (93%) of 2-Ethoxy-4-methyl-5-phenylselenanyl-3,4-dihydro-2H-pyran **3a**.

2-Ethoxy-4-methyl-5-phenylselenanyl-3,4-dihydro-2H-pyran (3a). yield=93%; yellow oil; $R_f=0.24$ (AcOEt/Cyclohexane: 5/95); ^{77}Se NMR δ (ppm) 331.7; 1H 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-phenylselenanyl-2H-pyran (3b). yield = 86%; yellow oil; $R_f=0.41$ (AcOEt/cyclohexane: 3/97); ^{77}Se NMR δ (ppm) 339.2 ppm; 1H 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-phenylselenanyl-2,3,3a,7a-tetrahydro-4H-furo

[2,3-b]pyran (3c). yield=84%; yellow oil; $R_f=0.28$ (AcOEt/Cyclohexane: 5/95); 1H NMR δ (ppm) 1.06 (d, $J=7.1$ Hz, 3H), 1.80-1.98 (m, 2H), 2.49 (m, 1H, H-3), 2.87 (m, 1H, H-4), 3.98 (m, 1H), 4.21 (m, 1H), 5.49 (d, $J=3.7$ Hz, 1H, H-2), 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-3), 68.4, 100.5 (C-2), 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-Phenylselenanyl-2,3,3a,7a-tetrahydro-4H-furo[2,3-b]pyran (3d). yield=73%; white cristal; m.p.=48-50°C; $R_f=0.29$ (AcOEt/Cyclohexane: 5/95); 1H 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 $\text{C}_{13}\text{H}_{14}\text{O}_2\text{Se}$ (281.20): C, 55.52; H, 5.02. Found: C, 55.14; H, 5.06.

2-Ethoxy-4-phenyl-5-phenylselanyl-3,4-dihydro-2H-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; ^1H 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 $\text{C}_{19}\text{H}_{20}\text{O}_2\text{Se}$ (359.31): C, 63.51; H, 5.61. Found: C, 63.48; H, 5.53.

2-Butoxy-4-phenyl-5-phenylselanyl-3,4-dihydro-2H-pyran (3f). yield=98%; yellow oil; R_f =0.35 (cyclohexane/EtOAc: 97/3); ^{77}Se NMR δ (ppm) 350.0; ^1H 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 $\text{C}_{21}\text{H}_{24}\text{O}_2\text{Se}$ (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-2H-pyran (3g). yield=97%; yellow oil; R_f =0.35 (cyclohexane/EtOAc: 97/3); ^{77}Se NMR δ (ppm) 347.3; ^1H 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 $\text{C}_{21}\text{H}_{24}\text{O}_2\text{Se}$ (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-2H-pyran (3h). yield=89%; yellow oil; R_f =0.26 (AcOEt/cyclohexane: 3/97); ^1H 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 $\text{C}_{20}\text{H}_{22}\text{O}_3\text{Se}$ (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-2H-pyran (3i). yield=93%; yellow oil; R_f =0.30 (AcOEt/Cyclohexane: 5/95); ^{77}Se NMR δ (ppm) 318.9; ^1H 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 $\text{C}_{15}\text{H}_{20}\text{O}_2\text{Se}$ (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-2H-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; ^1H 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). Calcd for $\text{C}_{20}\text{H}_{22}\text{O}_2\text{Se}$ (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-2H-pyran (3k). yield=94%; yellow oil; R_f =0.33 (AcOEt/cyclohexane: 5/95); ^{77}Se NMR δ (ppm) 333.7; ^1H 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 $\text{C}_{20}\text{H}_{22}\text{O}_2\text{Se}$ (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-2H-pyran (3l). yield=93%; yellow oil; R_f =0.40 (AcOEt/cyclohexane: 5/95); ^{77}Se NMR δ (ppm) 356.0; ^1H 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 $[\text{M}+\text{H}+\text{O}]^+$. Anal. Calcd for $\text{C}_{25}\text{H}_{24}\text{O}_2\text{Se}$ (435.40): C, 68.96; H, 5.56. Found: C, 68.76; H, 5.64.

2-Ethylsulfanyl-4-methyl-5-phenylselanyl-3,4-dihydro-2H-pyran (3m). yield=95%; yellow oil; R_f =0.25 (EtOAc/Cyclohexane: 5/95); ^1H 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), 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 $[\text{M}+\text{H}+\text{O}]^+$, (63), 429 (40), 243 (28), 193 (30), 191 (100), 166 (46), 143 (37), 122 (53). Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{OSSe}$ (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-phenylselenanyl-3,4-dihydro-2H-pyran (3n). yield=90%; yellow oil; R_f =0.29 (EtOAc/Cyclohexane: 5/95); ^1H 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): 393 (M+H+O).

2-Ethylsulfanyl-4,6-dimethyl-5-phenylselenanyl-3,4-dihydro-2H-pyran (3o). yield=91%; yellow oil; R_f =0.27 (EtOAc/Cyclohexane: 5/95); ^1H 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 $\text{C}_{15}\text{H}_{20}\text{OSe}$ (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-phenylselenanyl-3,4-dihydro-2H-pyran (3p). yield=88%; yellow oil; R_f =0.33 (EtOAc/Cyclohexane: 5/95); ^1H 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 ($[\text{M}+\text{H}+\text{O}]^+$, 100), 405 (55), 319 (29); Anal. Calcd for $\text{C}_{20}\text{H}_{22}\text{OSe}$ (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-phenylselenanyl-3,4-dihydro-2H-pyran (3q). yield=80%; yellow oil; R_f =0.60 (EtOAc/Cyclohexane: 5/95); ^1H 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-phenylselenanyl-3,4-dihydro-2H-pyran (3s). yield=64%; yellow oil; R_f =0.38 (AcOEt/Cyclohexane: 3/97); ^1H 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, controlled by TLC (usually 2 hours), the layers were separated and the organic one dried and concentrated under vacuum. The residue was chromatographed on silicagel (eluent: MeOH/ EtOAc: 1/99) to give 200 mg (64 %) of 2-Ethoxy-4-methyl-5-phenylseleninyl-3,4-dihydro-2H-pyran **4a**.

2-Ethoxy-4-methyl-5-phenylseleninyl-3,4-dihydro-2H-pyran (4a). mixture of 2 diastereomers: 53/47. yield=64%; yellow oil; R_f =0.31 (MeOH/AcOEt: 1/99); ^1H 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-2H-pyran (4l). yield=80%; yellow oil; R_f =0.34 (AcOEt /cyclohexane: 80/20); ^1H 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 $[\text{M}+\text{O}+\text{H}]^+$ (100), 451 (80).

Typical procedure for the synthesis of tetrahydrofuranones (5).

To a mixture of dihydropyran **3a** (1mmol, 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, controlled by TLC, the layers were separated and the organic one dried and then concentrated under vacuum. The residue was chromatographed on silicagel (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), ^1H 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 $\text{C}_7\text{H}_{12}\text{O}_3$ (144.166): C, 58.31; H, 8.39. Found: C, 57.96; H, 8.43.

5-Ethoxy-3-((tert-butyl)dimethylsilyl-methoxy)-tetrahydrofuran-2-one (5b). yield=42 %; yellow oil; R_f =0.35 (Cyclohexane/EtOAc: 90/10), **major trans isomer**: ^1H 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 $\text{C}_{13}\text{H}_{26}\text{O}_4\text{Si}$ (274.43): C, 56.90; H, 9.55. Found: C, 57.18; H, 9.63.

Minor cis isomer: ^1H 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), ^1H 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 $\text{C}_7\text{H}_{10}\text{O}_3$ (142.15): C, 59.14; H, 7.09. Found: C, 59.08; H, 7.34.
- 5-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), ^1H 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 $\text{C}_6\text{H}_8\text{O}_3$ (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), ^1H 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 $\text{C}_{12}\text{H}_{14}\text{O}_3$ (206.23): C, 69.88; H, 6.84. Found: C, 69.84; H, 6.85.
- Minor cis isomer: ^1H 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), ^1H 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 $\text{C}_{14}\text{H}_{18}\text{O}_3$ (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); ^1H 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 $\text{C}_{14}\text{H}_{18}\text{O}_3$ (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), ^1H 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 $\text{C}_{13}\text{H}_{16}\text{O}_4$ (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); ^1H 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, 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 $\text{C}_{12}\text{H}_{10}\text{O}_2$ (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); ^1H 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). Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_4$ (222.23): C, 64.85; H, 6.35.

50

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