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Alkenyl Nitrones Cyclizations Induced by Phenylselenenyl Bromide. A Convenient Synthetic Route to 1,2-Oxazines

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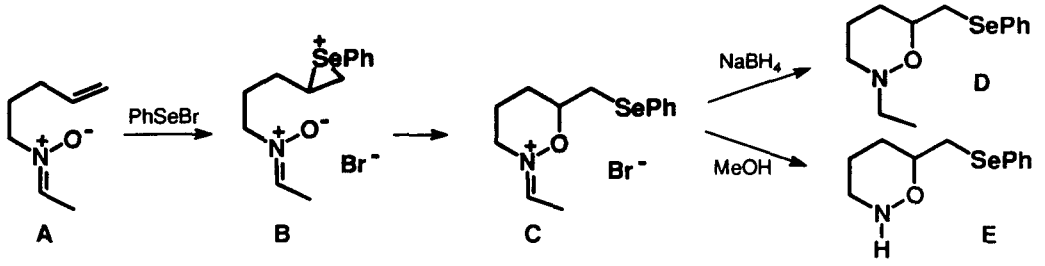
Abstract: Alkenyl nitrones reacted with phenyselenenyl bromide to afford ring closure reaction products deriving by the intramolecular capture of the seleniranium intermediates by the oxygen atom. Owing to the relative positions of the oxygen atom and of the carbon-carbon double bond in the nitrones employed, six-membered cyclic iminium salts were thus formed. These have ben directly treated with nucleophilic reagents and afforded 1,2-oxazine derivatives in good yield. It has been observed that, under the experimental conditions employed, the iminium salts in which the carbon-nitrogen double bond is exocyclic, depending on the nucleophile employed, gave the N-alkyl 1,2-oxazines and/or the N-unsubstituted 1,2-oxazines. On the contrary, with iminium salts in which the carbon-nitrogen double bond is endocyclic only N-alkyl 1,2-oxazines were obtained.

Phenylselenium-induced cyclization of alkenes containing internal nucleophiles is a very useful process to effect the synthesis of a variety of heterocyclic compounds.[1-3] Alkenols and alkenoic acids easily afford cyclic ethers or lactones by the formation of a carbon-oxygen bond. Nitrogen heterocycles can be similarly prepared by the formation of a carbon-nitrogen bond. In this case however some difficulties are encountered. Thus primary alkenyl amines do not give the desired ring closure reactions[4] which can instead be readily effected starting from primary N-protected alkenyl amines.[3-7] Alkenyl imines, on the contrary, cleanly undergo selenium-induced electrophilic cyclization to afford cyclic iminium compounds.[8-10] Several new cyclization reactions leading to nitrogen heterocycles have been recently reported.[11-16] An interesting example concerns the cyclization of terminal alkenyl oximes[17,18] which, in principle, shoud give rise to six-membered dihydro-1,2-oxazines, easily reducible to tetrahydro derivatives, and/or to five-membered cyclic nitrones depending on the geometry of the starting oximes. On the contrary, it was observed that the five-membered cyclic nitrones were the major, and sometimes the sole, reaction products because, under the experimental conditions employed, the starting oximes isomerize and the formation of the 1,2-oxazine is a reversible process.[18] Thus, tetrahydro-1,2-oxazines cannot be conveniently prepared from alkenyl oximes.

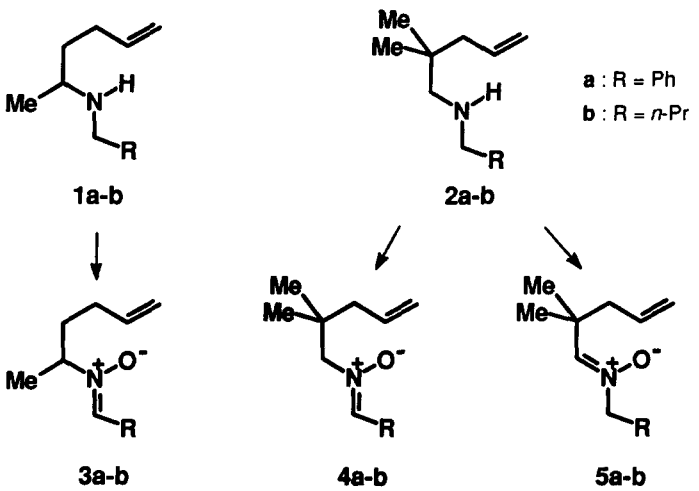
Scheme 1



We now report that tetrahydro-1,2-oxazine derivatives can be easily obtained using a new approach consisting in the use of alkenyl nitrones as the starting substrates. To our knowledge this is the first example of the use of alkenyl nitrones to effect ring closure reactions induced by electrophilic reagents. As indicated in Scheme 1, the reactions of the alkenyl nitrones, **A**, with phenyselenenyl bromide afforded the six-membered cyclic iminium salts, **C**, deriving by the intramolecular capture of the seleniranium intermediates, **B**, by the oxygen atom. These salts can be directly treated with nucleophilic reagents to afford N-alkyl, **D**, and/or N-unsubstituted 1,2-oxazine derivatives, **E**, in good yield.

The nitrones employed for the present investigation, **3a-b, 4a-b** and **5a-b** (Scheme 2), were obtained by oxidation[19] of the amines **1a-b** and **2a-b**. These were prepared by reduction of the corresponding keto imines and aldo imines with sodium cyanoborohydride. The oxidation of the amines **1a-b** gave the nitrones **3a-b** as the sole reaction products. The oxidation of the amines **2a-b** gave instead a mixture of the nitrones **4a-b** and **5a-b** (1:1.3 and 2.5:1 for **a** and **b**, respectively), which were separated by column chromatography. In every case only the more stable[20] *Z*-isomers were obtained. The configurations of these alkenyl nitrones were demonstrated by the results of differential NOE experiments.

Scheme 2



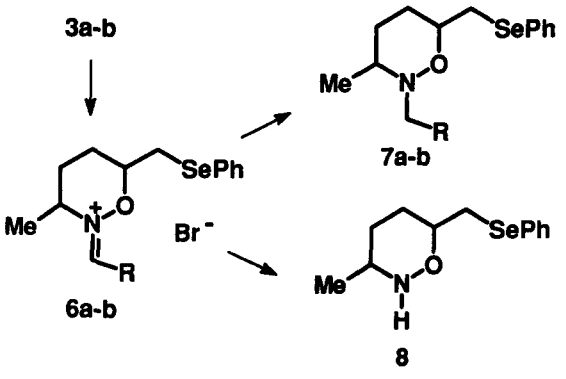
The cyclization reactions were carried out by adding phenylselenenyl bromide to the solution of the nitrones **3a-b, 4a-b** and **5a-b** in dichloromethane at room temperature. The progress of the reaction was monitored by TLC and GC-MS. After 1-1.5 h, the starting products were completely consumed and the appropriate reagents were added. In every case the first experiments were carried by diluting the solution with methanol and then adding sodium borohydride. The reaction mixtures deriving from **3a-b** and **4a-b** and PhSeBr were also left to react with methanol without adding the sodium borohydride. In the case of **5a-b** experiments were also carried out by adding water or sodium cyanide. In every case the resulting reaction mixtures were stirred at room temperature for 1- 2 h and then poured on water and worked up in the usual

way. The reaction products were obtained in a pure form by column chromatography on silica gel and were fully characterized by ^{1}H and ^{13}C NMR and GC-MS spectra.

Scheme 3 summarizes the results obtained from the nitrones **3a-b**. As indicated in Scheme 1, the reactions are proposed to proceed through the initial formation of the seleniranium ion intermediates which are trapped by the oxygen atom of the nitrones to afford the cyclic iminium bromides **6a-b**. The presence of these reaction intermediates was indicated by ^{1}H NMR spectra ($CDCl_3$) which were recorded when the reactions of the nitrones **3a-b** with PhSeBr were carried out in an NMR tube. The spectra could not be completely interpreted but they clearly indicated that two stereoisomeric cyclic iminium salts were present in solution. These reacted with the added nucleophiles to afford the final products.

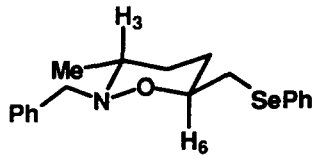
When sodium borohydride and methanol were employed, two kinds of compounds were isolated: the N-alkyl 1,2-oxazine, **7a-b**, and the N-unsubstituted 1,2-oxazine, **8**. Both types of compounds were obtained as a mixture of two stereoisomers which were formed in the ratios indicated in Scheme 3. These ratios were determined by NMR. **7a-b** were the expected products from the reactions of **6a-b** with sodium borohydride. The N-unsubstituted 1,2-oxazine, **8**, is instead the product deriving from the methanolysis of the iminium salts. As a matter of fact the $RCH(OMe)_2$ were also isolated from these reactions. Similar reactions of the iminium salts with alcohols or with water have already been reported.[14,21]

Scheme 3



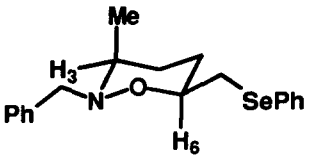
Nitrone	Reagent	Reaction Products (%)
3a	$NaBH_4$	**7a** (46%)[a] + **8** (35%)[b]
3b	$NaBH_4$	**7b** (36%)[c] + **8** (38%)[d]
3a	MeOH	**8** (70%)[b]
3b	MeOH	**8** (70%)[d]

a: 1:2 mixture (separated)
b: 1:4 mixture
c: 1:1.5 mixture
d: 1:2.5 mixture



$J_{3,4}$ = 2.8 Hz
$J_{3,4'}$ = 10.1 Hz
$J_{6,5}$ = 2.3 Hz
$J_{6,5'}$ = 10.4 Hz

7a (major isomer)



$J_{3,4}$ = 3.6 Hz
$J_{3,4'}$ = 4.1 Hz
$J_{6,5}$ = 4.0 Hz
$J_{6,5'}$ = 10.5 Hz

7a (minor isomer)

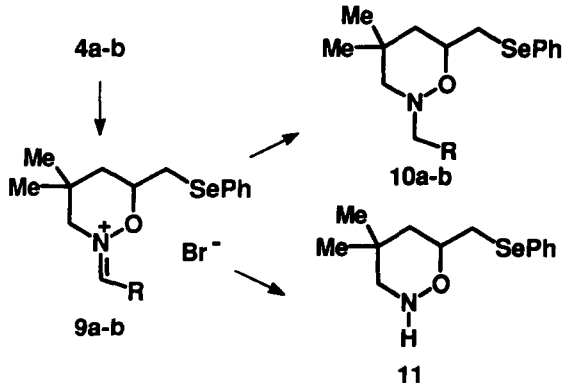
Thus, the present results indicate that, under the experimental conditions employed, the reactions of **6a-b** with sodium borohydride and with methanol proceed with comparable rates. This competition was rather unexpected since in the case of the corresponding five-membered cyclic iminium salts, under identical experimental conditions, the reaction with sodium borohydride in methanol afforded exclusively the N-alkyl isoxazolidines with no traces of the isoxazolidines deriving from the methanolysis of the iminium salts.[15]

When the solution containing **6a-b** was simply diluted with methanol, compound **8** was formed in good yield (Scheme 3).

As anticipated, compounds **7a-b** and **8** were mixtures of two stereoisomers. Only in the case of **7a** the two isomers could be separated by column chromatography. Their structures could be assigned by measuring the values of the vicinal coupling constants of the protons H_3 and H_6 with the protons in position 4 and 5, respectively. These coupling constants, which are reported in Scheme 3, indicate that the CH_2SePh group occupies an equatorial position in both isomers and that the methyl group is equatorial in the major isomer and axial in the minor isomer. Furthermore, differential NOE experiments indicate that the CH_2Ph is also equatorial in both cases. It seems reasonable to assume that the major and minor isomers of **7b** and **8** have structures similar to those of the two isomers of **7a**.

Similar results were obtained from the reactions of the nitrones **4a-b** with PhSeBr and then with sodium borohydride in methanol or with methanol. The results of these reactions are reported in Scheme 4. In this case the cyclic iminium salts **9a-b**, as well as the reaction products **10a-b** and **11** were obviously obtained as single stereoisomers. The intermediate cyclic iminium salts **9a-b** were fully characterized by ^1H and ^{13}C NMR spectra.

Scheme 4

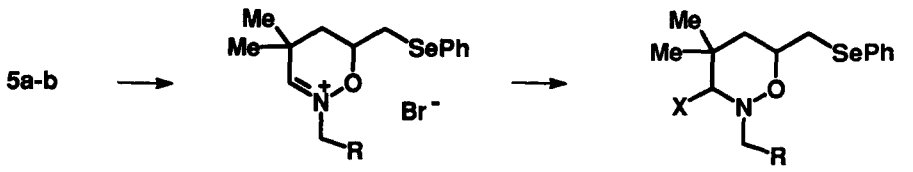


Nitrone	Reagent	Reaction Products (%)	
4a	$NaBH_4$	**10a** (62%)	+ **11** (12%)
4b	$NaBH_4$	**10b** (45%)	+ **11** (28%)
4a	MeOH		**11** (68%)
4b	MeOH		**11** (64%)

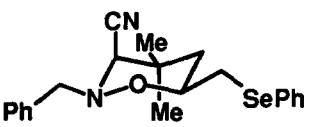
Under the same conditions the nitrones **5a-b** gave different results. These are reported in Scheme 5. In this case also the rections with PhSeBr afforded the iminium salts **12a-b** as single stereoisomers, which could be fully characterized by ^1H and ^{13}C NMR spectra. The reactions with sodium borohydride and methanol proceeded smoothly to afford the reduction products **10a-b** in excellent yield. Methanolysis of the

iminium salts **12a-b**, which would give rise to ring opening, was not observed. From the reactions with water or with sodium cyanide the only products observed were those deriving from the addition of the hydroxy, **13a-b**, or the cyano groups, **14a-b**, respectively, at the partially positive carbon atom in position 3. Interestingly, compounds **13a-b** and **14a-b** were formed as single stereoisomers. In all the compounds **10**, **13** and **14** the values of the coupling constants of H_6 with the two protons in position 5 indicated that the $PhSeCH_2$ group occupies an equatorial position. In the case of compound **14a**, differential NOE and NOESY experiments showed that the $PhCH_2$ group also occupies an equatorial position and that the CN group is axial (Scheme 5). Molecular models indicate that, owing to the presence of the two methyl groups in the 4 position, the attack of the nucleophile at the carbon 3 of the iminium salt from the direction leading to the observed product is largely preferred. From a comparison of the ^1H and ^{13}C NMR spectra it can be suggested that compounds **13a**, **13b** and **14b** have similar configurations.

Scheme 5



Nitrone	Reagent	Reaction Products (%)
5a	$NaBH_4$	**10a** (95%)
5b	$NaBH_4$	**10b** (95%)
5a	H_2O	**13a** (68%)
5b	H_2O	**13b** (65%)
5a	NaCN	**14a** (78%)
5b	NaCN	**14b** (95%)



14a

The results described above demonstrate that the reactions of alkenyl nitrones with PhSeBr give rise to cyclic iminium salts and that these intermediates suffer attack by nucleophilic reagents at the positive carbon atom. The structures of the final products depend on the nucleophile employed and on the structure of the starting nitrone. The iminium salts in which the carbon-nitrogen double bond is exocyclic react with sodium borohydride to afford N-alkyl 1,2-oxazines. On the contrary, when methanol is employed, the reactions evolve towards the N-unsubstituted 1,2-oxazines resulting from the methanolysis of the iminium salts. This behaviour is in agreement with the results reported in the literature for the reactions of iminium salts having similar structures with sodium borohydride,[10,14] water[15] or ethanol.[21] On the other hand, with iminium salts in which the carbon-nitrogen double bond is endocyclic the reactions stop at the stage of the addition of the nucleophile at the positive carbon atom in every case.

The selenium induced cyclization of alkenyl nitrones described in this paper represents a new process which has been used to develop a convenient synthesis of 1,2-oxazine derivatives. Very likely other electrophilic reagents can be employed to promote this cyclization. It can be also anticipated that the structures of the starting nitrones can be modified so that other types of heterocycles can be obtained.

EXPERIMENTAL

GLC analyses and MS spectra were carried out with an HP 5890 gaschromatograph (dimethyl silicone column, 12.5 m) equipped with an HP 5971 Mass Selective Detector. ^1H and ^{13}C NMR spectra were recorded at 200 and 50.32 MHz, respectively, on a Bruker AC 200 instrument; $CDCl_3$ was used as solvent and TMS as standard. Elemental analyses were carried out on a Carlo Erba 1106 Elemental Analyzer and were in good agreement with the calculated values. All new compounds were fully characterized by MS, ^1H, and ^{13}C NMR spectroscopy.

Synthesis of the Alkenyl Nitrones. Using standard procedures, 5-hexen-2-one and 2,2-dimethyl-4-pentenal were allowed to react with benzylamine and with *n*-butylamine. The resulting imines were reduced to the amines **1a-b** and **2a-b** by treatment with sodium cyanoborohydride and hydrochloric acid in methanol.[22] The crude reaction products were directly oxidized with hydrogen peroxide and sodium tungstate.[19] The reaction mixtures were worked up in the usual way and the products were purified by column chromatography on silica gel using a mixture of dichloromethane and methanol (99:1) as eluant. Physical and spectral properties are reported below. Reaction yields are indicated in parentheses.

N-(Benzylidene)-1-methyl-4-pentenamine N-oxide (3a): oil (63%); ^1H NMR δ 8.3-8.18 (m, 2 H), 7.47-7.33 (m, 4 H), 5.79 (ddt, 1 H, J = 7.0, 10.3, 17.2 Hz), 5.1-4.98 (m, 2 H), 4.1-3.9 (m, 1 H), 2.32-1.95 (m, 3 H), 1.7-1.51 (m, 1 H), 1.47 (d, 3 H, J = 6.5 Hz); ^{13}C NMR δ 137.2, 132.9, 130.2, 130.0, 128.4, 128.3, 115.5, 71.3, 32.9, 30.1, 19.4. MS *m/z* (relative intensity) 203 (25), 158 (16), 132 (100), 117 (55), 104 (27), 82 (15), 77 (18), 67 (17), 55 (25), 41 (24). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.89; H, 8.34; N, 6.75.

N-(Butylidene)-1-methyl-4-pentenamine N-oxide (3b): oil (67%); ^1H NMR δ 6.66 (t, 1 H, J = 5.8 Hz), 5.7 (dddd, 1 H, J = 5.8, 7.1, 10.2, 17.2 Hz), 5.0-4.9 (m, 2 H), 3.75 (ddq, 1 H, J = 4.4, 6.5, 9.0 Hz), 2.5-2.33 (m, 2 H), 2.21-1.9 (m, 3 H), 1.61-1.45 (m, 1 H), 1.5 (sext, 2 H, J = 7.4 Hz), 1.41 (d, 3 H, J = 6.5 Hz), 0.92 (t, 3 H, J = 7.4 Hz); ^{13}C NMR δ 137.5, 137.2, 115.3, 69.6, 32.4, 30.1, 28.1, 19.2, 19.0, 13.8. MS *m/z* (relative intensity) 169 (25), 154 (14), 126 (100), 113 (14), 98 (55), 96 (19), 82 (28), 70 (18), 69 (18), 67 (34), 56 (23), 55 (96), 54 (17), 43 (20), 42 (32), 41 (70). Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.27. Found: C, 71.03; H, 11.26; N, 8.38.

N-(Benzylidene)-2,2-dimethyl-4-pentenamine N-oxide (4a): oil (30%); ^{1}H NMR δ 8.30-8.18 (m, 2 H), 7.40-7.23 (m, 4 H), 6.0-5.77 (m, 1 H), 5.12-4.98 (m, 2 H), 3.72 (s, 2 H), 2.19 (d, 2 H, J = 7.3 Hz), 1.1 (s, 6 H); ^{13}C NMR δ 148.7, 135.4, 133.9, 129.9, 128.1, 118.0, 75.9, 44.6, 34.7, 25.2. MS *m/z* (relative intensity) 217 (6), 172 (19), 118 (100), 104 (10), 91 (44), 81 (17), 77 (10), 55 (29), 41 (20). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.30; H, 8.75; N, 6.49.

N-(Butylidene)-2,2-dimethyl-4-pentenamine N-oxide (4b): oil (50%); ^{1}H NMR δ 6.59 (t, 1 H, J = 5.8 Hz), 5.71 (ddt, 1 H, J = 7.5, 10.7, 16.3 Hz), 5.12-4.99 (m, 2 H), 3.58 (s, 2 H), 2.45 (q, 2 H, J = 6.9 Hz), 2.14 (d, 2 H, J = 7.4 Hz), 1.53 (sext, 2 H, J = 7.3 Hz), 1.04 (s, 6 H), 0.99 (t, 3 H, J = 7.3 Hz); ^{13}C NMR δ 140.0, 134.0, 118.0, 74.1, 44.8, 34.1, 28.4, 25.4, 25.3, 18.8, 13.9. MS *m/z* (relative intensity) 183 (20), 168 (33), 140 (40), 138 (31), 126 (16), 110 (75), 99 (38), 84 (64), 83 (50), 69 (19), 68 (19), 56 (26), 55 (100), 41 (61). Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55; N, 7.64. Found: C, 72.16; H, 11.61; N, 7.53.

N-(2,2-Dimethyl-4-pentenylidene)benzylamine N-oxide (5a): oil (39%); ^{1}H NMR δ 7.41-7.23 (m, 5 H), 6.49 (s, 1 H), 5.78-5.51 (m, 1 H), 5.18-4.90 (m, 2 H), 4.80 (s, 2 H), 2.42 (d, 2 H, J = 7.3 Hz), 1.25 (s, 6 H); ^{13}C NMR δ 143.4, 134.2, 128.6, 128.4, 128.3, 117.3, 70.3, 42.4, 35.9, 23.7. MS *m/z* (relative intensity) 217 (16), 172 (15), 118 (50), 117 (100), 115 (13), 105 (15), 91 (31), 70 (15), 41 (10). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.47; H, 8.90; N, 6.38.

N-(2,2-Dimethyl-4-pentenylidene)butylamine N-oxide (5b): oil (20%); ^{1}H NMR δ 6.41 (s, 1 H), 5.71 (ddt, 1 H, J = 7.4, 10.0, 17.1 Hz), 5.13-5.0 (m, 2 H), 3.7 (t, 2 H, J = 7.0 Hz), 2.46 (d, 2 H, J = 7.4 Hz), 1.87 (quint, 2 H, J = 7.2 Hz), 1.31 (sext, 2 H, J = 7.5 Hz), 1.27 (s, 6 H), 0.95 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 143.2, 134.6, 117.4, 66.2, 42.8, 35.9, 29.4, 23.9, 23.8, 19.4, 13.5. MS *m/z* (relative intensity) 183 (13), 127 (13), 126 (100), 95 (16), 84 (30), 70 (51), 57 (34), 56 (45), 42 (16), 41 (36). Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55; N, 7.64. Found: C, 71.98; H, 11.64; N, 7.57.

Cyclization of Alkenyl Nitrones. General Procedure. Crystalline phenylselenenyl bromide (4.5 mmol) was added portionwise to the solution of the alkenyl nitrone (3 mmol) in dichloromethane (10 ml) at room temperature. The progress of the reaction was monitored by TLC. After 1-1.5 h, methanol (10 ml) and sodium borohydride (4 mmol) were added. In the other experiments methanol (10 ml), water (10 ml) or sodium cyanide (4 mmol) were added. The resulting mixtures were stirred at room temperature for 1-2 h and then poured on water and worked up in the usual way. The reaction products were obtained in a pure form by column chromatography on silica gel using dichloromethane and methanol (99:1) as eluant. Reaction yields are reported in the Schemes. Physical and spectral data are reported below. In the mass spectra only the peaks of the most abundant ^{80}Se isotope are reported.

3,4,5,6-Tetrahydro-2-benzy-3-methyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (7a): oil; *minor isomer:* ^{1}H NMR δ (C_6D_6) 7.4-6.9 (m, 10 H), 4.06 (ddt, 1 H, J = 4.0, 6.3, 10.5 Hz), 4.0 (d, 1 H, J = 13.8 Hz), 3.5 (d, 1 H, J = 13.8 Hz), 3.02 (dd, 1 H, J = 6.6, 12.5 Hz), 2.85 (dd, 1 H, J = 6.6, 12.5 Hz), 2.73 (ddq, 1 H, J = 3.6, 4.1, 6.4 Hz), 1.75-1.55 (m, 1 H), 1.5-1.2 (m, 3 H), 0.95 (d, 3 H, J = 6.4 Hz); ^{13}C NMR δ 138.4, 132.3, 128.9, 128.7, 128.0, 126.7, 126.5, 77.6, 58.9, 55.3, 31.0, 29.9, 25.8, 12.5. MS *m/z* (relative intensity) 361 (1), 262 (1), 204 (3), 150 (36), 134 (10), 91 (100), 41 (4). Anal. Calcd for $C_{19}H_{23}NOSe$: C, 63.33; H, 6.43; N, 3.89. Found: C, 63.21; H, 6.48; N, 3.85; *major isomer:* ^{1}H NMR δ 7.4-7.1 (m, 10 H), 4.15 (d, 1 H, J = 14.4 Hz), 3.9 (dddd, 1 H, J = 2.3, 6.1, 6.9, 10.4 Hz), 3.61 (d, 1 H, J = 14.4 Hz), 2.94 (dd, 1 H, J = 6.9, 12.3 Hz), 2.76 (dd, 1 H, J = 6.1, 12.3 Hz) 2.66 (ddq, 1 H, J = 2.8, 6.2, 10.1 Hz), 1.85-1.12 (m, 4 H), 1,08 (d, 3 H, J = 6.2 Hz); ^{13}C NMR δ 132.2, 128.9, 127.9, 126.6, 126.5, 77.8, 58.9, 58.4, 33.0, 31.4, 31.1, 19.2. MS *m/z* (relative intensity) 361 (1), 204 (4), 150 (45), 91 (100), 55 (6), 41 (7). Anal. Calcd for $C_{19}H_{23}NOSe$: C, 63.33; H, 6.43; N, 3.89. Found: C, 63.30; H, 6.37; N, 3.94.

3,4,5,6-Tetrahydro-2-butyl-3-methyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (7b): oil; *minor isomer*: ^{1}H NMR δ 7.55-7.42 (m, 2 H), 7.3-7.12 (m, 3 H), 4.07-3.83 (m, 1 H), 3.10-2.7 (m, 3 H), 2.6-2.3 (m, 2 H), 1.9-1.1 (m, 8 H), 0.99 (d, 3 H, J = 6.5 Hz), 0.93 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 132.3, 128.9, 126.5, 77.4, 55.8, 54.8, 32.8, 32.7, 31.7, 29.8, 28.5, 18.8, 14.0. MS *m/z* (relative intensity) 327 (2), 170 (6), 157 (4), 117 (8), 116 (100), 100 (10), 60 (9), 55 (16), 41 (14); *major isomer:* ^{1}H NMR δ 7.55-7.42 (m, 2 H), 7.3-7.12 (m, 3 H), 4.07-3.83 (m, 1 H), 3.29-3.10 (m, 1 H), 3.10-2.7 (m, 3 H), 2.6-2.3 (m, 1 H), 1.9-1.1 (m, 8 H), 1.06 (d, 3 H, J = 6.5 Hz), 0.93 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 132.3, 128.9, 126.5, 77.8, 58.9, 54.6, 31.3, 31.2, 29.3, 26.1, 20.6, 18.8, 14.0. MS *m/z* (relative intensity) 327 (1), 170 (9), 157 (4), 117 (8), 116 (100), 100 (16), 60 (11), 55 (19), 41 (16). Anal. Calcd for $C_{16}H_{25}NOSe$: C, 58.89; H, 7.72; N, 4.29. Found: C, 58.80; H, 7.81; N, 4.26.

3,4,5,6-Tetrahydro-3-methyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (8): oil; *minor isomer*: ^{1}H NMR δ 7.54-7.43 (m, 2 H), 7.30-7.12 (m, 3 H), 5.0 (br s, 1 H), 3.92-3.8 (m, 1 H), 3.3 (dd, 1 H, J = 6.8, 12.3 Hz), 3.18-2.98 (m, 2 H), 1.95-1.55 (m, 2 H), 1.55-1.20 (m, 2 H), 1.17 (d, 3 H, J = 6.7 Hz); ^{13}C NMR δ 132.3, 130.2, 128.8, 126.6, 77.3, 51.3, 30.4, 27.9, 25.8, 17.5. MS *m/z* (relative intensity) 271 (1), 234 (31), 232 (17), 157 (20), 154 (100), 77 (35), 51 (24); *major isomer:*[18] ^{1}H NMR δ 7.55-7.45 (m, 2 H), 7.31-7.15 (m, 3 H), 4.82 (br s, 1 H), 3.7 (dddd, 1 H, J = 2.1, 6.2, 6.5, 10.5 Hz), 3.05 (ddq, 1 H, J = 3.0, 6.4, 10.0 Hz), 3.04 (dd, 1 H, J = 6.5, 12.4 Hz), 2.86 (dd, 1 H, J = 6.2, 12.4 Hz), 1.95-1.65 (m, 2 H), 1.55-1.10 (m, 2 H), 0.95 (d, 3 H, J = 6.4 Hz); ^{13}C NMR δ 132.2, 130.3, 128.8, 126.6, 78.5, 52.6, 31.9, 31.2, 30.5, 17.7. MS *m/z* (relative intensity) 271 (2), 157 (14), 114 (27), 100 (22), 97 (15), 91 (14), 77 (13), 60 (100), 55 (20), 41 (14). Anal. Calcd for $C_{12}H_{17}NOSe$: C, 53.34; H, 6.34; N, 5.18. Found: C, 53.24; H, 6.39; N, 5.27.

3,4,5,6-Tetrahydro-2-benzylidene-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazinium bromide (9a): ^{1}H NMR δ 10.5 (s, 1 H), 8.45 (d, 2 H, J = 7.7 Hz), 7.9-7.6 (m, 2 H), 7.6-7.1 (m, 6 H), 4.85 (d, 1 H, J

= 12.5 Hz), 4.65-4.5 (m, 1 H), 3.95 (d, 1 H, J = 12.5 Hz), 3.3 (d, 2 H, J = 5.7 Hz), 2.0-1.87 (m, 2 H), 1.2 (s, 3 H), 1.17 (s, 3 H); ^{13}C NMR δ 159.1, 137.1, 135.0, 131.9, 128.8, 128.6, 128.1, 127.6, 126.5, 83.8, 66.0, 40.2, 31.1, 28.9, 26.9, 22.1.

3,4,5,6-Tetrahydro-2-butylidene-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazinium bromide (9b): ^{1}H NMR δ 9.4-9.3 (m, 1 H), 7.8-7.6 (m, 2 H), 7.4-7.15 (m, 3 H), 4.85-4.65 (m, 1 H), 4.3-4.1 (m, 1 H), 3.6-3.4 (m, 1 H), 3.2-2.8 (m, 2 H), 2.2-1.0 (m, 6 H), 1.35 (s, 3 H), 1.25 (s, 3 H), 1.05 (t, 3 H, J = 7.3 Hz); ^{13}C NMR δ 170.0, 133.1, 130.3, 129.3, 127.6, 83.0, 55.1, 41.0, 32.0, 29.0, 28.2, 28.1, 24.9, 24.6, 14.3.

3,4,5,6-Tetrahydro-2-benzyl-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (10a): oil; ^{1}H NMR δ 7.50-7.39 (m, 2 H), 7.38-7.10 (m, 8 H), 4.12 (dddd, 1 H, J = 2.2, 6.0, 6.9, 11.2 Hz), 4.0 (d, 1 H, J = 13.6 Hz), 3.66 (d, 1 H, J = 13.6 Hz), 2.98 (dd, 1 H, J = 6.9, 12.1 Hz), 2.79 (dd, 1 H, J = 6.0, 12.1 Hz), 2.48 (dd, 1 H, J = 1.4, 11.5 Hz), 2.25 (d, 1 H, J = 11.5 Hz), 1.50 (dt, 1 H, J = 2.2, 13.0 Hz) 1.19 (dd, 1 H, J = 11.2, 13.0 Hz), 1.1 (s, 3 H), 0.9 (s, 3 H); ^{13}C NMR δ 137.4, 132.4, 130.8, 128.8, 128.6, 127.9, 126.8, 126.5, 74.8, 66.2, 62.7, 44.0, 31.6, 30.6, 29.4, 25.0. MS *m/z* (relative intensity) 375 (2), 136 (54), 120 (13), 91 (100), 55 (7), 41 (7). Anal. Calcd for $C_{20}H_{25}NOSe$: C, 64.16; H, 6.73; N, 3.74. Found: C, 64.09; H, 6.70; N, 3.81.

3,4,5,6-Tetrahydro-2-butyl-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (10b): oil; ^{1}H NMR δ 7.55-7.45 (m, 2 H), 7.28-7.15 (m, 3 H), 4.07 (dddd, 1 H, J = 2.4, 5.6, 7.5, 11.5 Hz), 3.01 (dd, 1 H, J = 7.5, 12.1 Hz), 2.80 (dd, 1 H, J = 5.6, 12.1 Hz), 2.69 (dt, 1 H, J = 6.8, 12.4 Hz), 2.49 (dt, 1 H, J = 7.3, 12.4 Hz), 2.42 (dd, 1 H, J = 1.7, 11.5 Hz), 2.19 (d, 1 H, J = 11.5 Hz), 1.60-1.28 (m, 5 H), 1.1 (t, 1 H, J = 11.9 Hz), 1.09 (s, 3 H), 0.91 (t, 3 H, J = 7.2 Hz), 0.9 (s, 3 H); ^{13}C NMR δ 132.4, 130.0, 128.8, 126.5, 74.6, 67.3, 58.7, 44.2, 31.8, 30.6, 29.5, 28.9, 25.5, 20.5, 14.0. MS *m/z* (relative intensity) 341 (2), 157 (4), 102 (100), 86 (12), 60 (13), 55 (12), 46 (14), 41 (15). Anal. Calcd for $C_{17}H_{27}NOSe$: C, 59.99; H, 8.00; N, 4.12. Found: C, 60.06; H, 7.93; N, 4.16.

3,4,5,6-Tetrahydro-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (11): oil; ^{1}H NMR δ 7.55-7.43 (m, 2 H), 7.28-7.12 (m, 3 H), 5.30 (br s, 1 H), 3.9 (dddd, 1 H, J = 2.0, 6.1, 6.5, 11.5 Hz), 3.0 (dd, 1 H, J = 6.5, 12.3 Hz), 2.91 (d, 1 H, J = 12.8 Hz), 2.79 (dd, 1 H, J = 6.1, 12.3 Hz), 2.52 (dd, 1 H, J = 2.0, 12.8 Hz), 1.59 (dt, 1 H, J = 2.0, 13.1 Hz), 1.21 (dd, 1 H, J = 11.5, 13.1 Hz), 1.05 (s, 3 H), 0.91 (s, 3 H); ^{13}C NMR δ 132.4, 130.3, 128.9, 126.7, 75.4, 59.6, 43.7, 31.6, 29.4, 29.0, 23.5. MS *m/z* (relative intensity) 285 (14), 158 (65), 157 (38), 155 (27), 128 (45), 111 (17), 91 (52), 83 (81), 82 (62), 77 (35), 67 (15), 55 (76), 51 (27), 46 (100), 41 (81). Anal. Calcd for $C_{13}H_{19}NOSe$: C, 54.93; H, 6.74; N, 4.93. Found: C, 54.87; H, 6.81; N, 4.98.

5,6-Dihydro-2-benzyl-4,4-dimethyl-6-[(phenylseleno)methyl]-4H-1,2-oxazinium bromide (12a): ^{1}H NMR δ 10.35 (s, 1 H), 7.6-7.15 (m, 10 H), 5.62 (d, 1 H, J = 13.7 Hz), 5.42 (d, 1 H, J = 13.7 Hz), 4.45-4.30 (m, 1 H), 3.17 (dd, 1 H, J = 5.8, 13.4 Hz), 3.02 (dd, 1 H, J = 6.4, 13.4 Hz), 2.05 (d, 1 H, J = 14.2 Hz), 1.79 (dd, 1 H, J = 11.7, 14.2 Hz), 1.49 (s, 3 H), 1.47 (s, 3 H); ^{13}C NMR δ 166.0, 133.2, 129.8, 129.3, 129.1, 127.9, 80.9, 64.6, 36.5, 33.3, 28.3, 27.1, 25.7.

5,6-Dihydro-2-butyl-4,4-dimethyl-6-[(phenylseleno)methyl]-4H-1,2-oxazinium bromide (12b): ^{1}H NMR δ 9.10 (s, 1 H), 7.60-7.40 (m, 2 H), 7.35-7.12 (m, 3 H), 4.60-4.45 (m, 1 H), 4.0 (t, 2 H, J = 6.9 Hz), 3.30-3.10 (m, 2 H), 2.10-1.20 (m, 6 H), 1.27 (s, 3 H), 1.25 (s, 3 H), 0.82 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 163.7, 134.2, 132.6, 130.0, 128.8, 81.1, 61.6, 36.1, 33.8, 30.1, 27.9, 26.9, 25.6, 18.8, 13.1.

3,4,5,6-Tetrahydro-2-benzyl-3-hydroxy-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (13a): oil; ^{1}H NMR δ 7.50-7.10 (m, 10 H), 4.17 (dddd, 1 H, J = 2.4, 5.9, 6.3, 8.7 Hz), 4.05 (d, 1 H, J = 13.7 Hz), 3.81 (d, 1 H, J = 13.7 Hz), 3.71 (d, 1 H, J = 10.8 Hz), 2.95 (dd, 1 H, J = 6.3, 12.5 Hz), 2.82 (dd, 1 H, J = 5.9, 12.5 Hz), 2.68 (d, 1 H, J = 10.8 Hz), 1.50-1.39 (m, 1 H), 1.30-1.12 (m, 1 H), 1.1 (s, 3 H), 1.0 (s, 3 H); ^{13}C NMR δ 137.2, 132.5, 128.9, 128.7, 128.1, 126.9, 126.7, 88.0, 74.7, 57.2, 39.0, 35.0, 30.9, 27.2, 25.0. MS *m/z* (relative intensity) 373 (M-18, 1) 202 (15), 157 (4), 106 (6), 91 (100), 83 (26), 55 (22). Anal. Calcd for $C_{20}H_{25}NO_2Se$: C, 61.53; H, 6.45; N, 3.59. Found: C, 61.41; H, 6.53; N, 3.64.

3,4,5,6-Tetrahydro-2-butyl-3-hydroxy-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (13b): oil; ^{1}H NMR δ 7.55-7.45 (m, 2 H), 7.30-7.17 (m, 3 H), 4.1 (dddd, 1 H, J = 5.4, 5.8, 7.0, 10.4 Hz), 3.70 (d, 1 H, J = 10.5 Hz), 2.99 (dd, 1 H, J = 7.0, 12.3 Hz), 3.0-2.8 (m, 1 H), 2.85 (dd, 1 H, J = 5.4, 12.3 Hz), 2.61-2.45 (m, 1 H), 2.60 (d, 1 H, J = 10.5 Hz), 1.60-1.15 (m, 6 H), 1.1 (s, 3 H), 1.0 (s, 3 H), 0.91 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 132.6, 130.0, 129.0, 126.9, 89.3, 74.8, 53.2, 39.5, 35.2, 31.8, 29.1, 27.3, 25.2, 20.5, 14.0. MS *m/z* (relative intensity) 339 (M-18, 1), 182 (26), 168 (40), 157 (19), 154 (16), 140 (18), 111 (28), 83 (100), 82 (21), 77 (12), 69 (17), 57 (22), 55 (65), 43 (15), 41 (52). Anal. Calcd for $C_{17}H_{27}NO_2Se$: C, 57.30; H, 7.64; N, 3.93. Found: C, 57.32; H, 7.71; N, 3.84.

3,4,5,6-Tetrahydro-2-benzyl-3-cyano-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (14a): oil; ^{1}H NMR δ 7.50-7.40 (m, 2 H), 7.40-7.20 (m, 8 H), 4.26 (d, 1 H, J = 12.9 Hz), 4.12 (dddd, 1 H, J = 3.1, 6.3, 6.7, 10.0 Hz), 3.75 (d, 1 H, J = 12.9 Hz), 3.20 (s, 1 H), 3.03 (dd, 1 H, J = 6.7, 12.5 Hz), 2.78 (dd, 1 H, J = 6.3, 12.5 Hz), 1.55 (dd, 1 H, J = 3.1, 13.5 Hz), 1.44 (dd, 1 H, J = 10.0, 13.5 Hz), 1.13 (s, 3 H), 1.12 (s, 3 H); ^{13}C NMR δ 135.2, 132.7, 129.0, 128.5, 127.8, 127.0, 75.4, 63.1, 60.5, 40.8, 33.6, 30.7, 28.3, 24.7. MS *m/z* (relative intensity) 400 (2), 239 (11), 161 (16), 157 (6), 92 (8), 91 (100), 81 (22), 77 (5), 41 (6). Anal. Calcd for $C_{21}H_{24}N_2OSe$: C, 63.15; H, 6.06; N, 7.01. Found: C, 63.21; H, 6.13; N, 7.07.

3,4,5,6-Tetrahydro-2-butyl-3-cyano-4,4-dimethyl-6-[(phenylseleno)methyl]-2H-1,2-oxazine (14b): oil; ^{1}H NMR δ 7.53-7.45 (m, 2 H), 7.30-7.20 (m, 3 H), 4.05 (dddd, 1 H, J = 3.1, 5.8, 7.4, 10.5 Hz), 3.3 (s, 1 H), 3.06 (dd, 1 H, J = 7.4, 12.4 Hz), 3.04-2.91 (m, 1 H), 2.81 (dd, 1 H, J = 5.8, 12.4 Hz), 2.53 (dt, 1 H, J = 7.3, 12.3 Hz), 1.63-1.20 (m, 6 H), 1.19 (s, 3 H), 1,17 (s, 3 H), 0.91 (t, 3 H, J = 7.2 Hz); ^{13}C NMR δ 132.5, 129.0, 128.0, 126.9, 115.6, 75.2, 64.8, 56.5, 40.9, 33.7, 30.8, 28.6, 28.3, 24.9, 20.2, 13.9. MS *m/z* (relative intensity) 366 (9), 238 (41), 209 (12), 183 (13), 158 (11), 157 (15), 127 (100), 83 (27), 82 (40), 57 (20), 55 (17), 41 (17). Anal. Calcd for $C_{18}H_{26}N_2OSe$: C, 59.17; H, 7.17; N, 7.67. Found: C, 59.24; H, 7.12; N, 7.75.

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