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Optically active isoxazolidines and 1,3-amino alcohols by asymmetric selenocyclization reactions of *O*-allyl oximes

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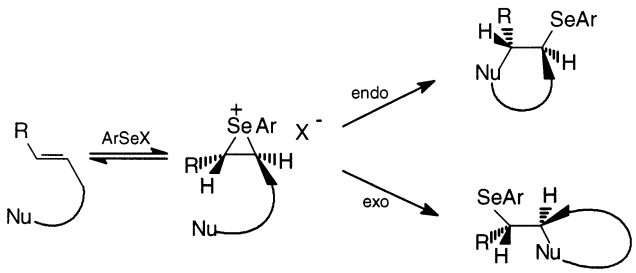
Abstract—The selenyl triflate generated from the reaction of di-2-[(1*S*)-1-(methylthio)ethyl]phenyl diselenide with silver triflate reacts with various substituted *O*-allyl oximes to promote ring closure, which affords optically active isoxazolidines in high yields and with good diastereoselectivity (up to 93:7). Enantiomerically enriched 1,3-amino alcohols can be easily obtained by *N*–*O* bond cleavage of these heterocycles, which was readily effected by treatment with zinc in aqueous acetic acid.

1. Introduction

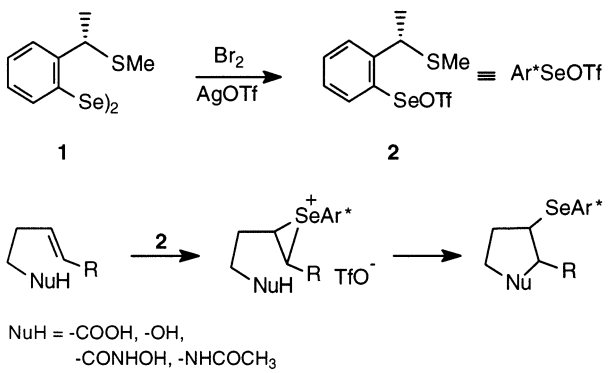
Organoselenium reagents have been widely employed in organic synthesis to effect unconventional conversions of functional groups under mild experimental conditions.[1,2] In recent years many research groups have devoted their attention to the selenocyclization reactions in which an organoselenium electrophile promotes the conversion of an alkene containing a suitably positioned oxygen or nitrogen atom into a heterocyclic compound, through the formation of a carbon–oxygen or a carbon–nitrogen bond, respectively.[1,2] As indicated in Scheme 1 the *exo*- or *endo*-cyclization products are the result of stereospecific *anti*-addition.



Scheme 1.

Recently the introduction of several optically active diselenides has considerably increased the importance of this synthetic procedure. In fact, the addition of a chiral non-racemic selenylating agent to the alkene occurs with good facial selectivity and therefore the subsequent cyclization step generates the heterocyclic compound stereoselectively and in a non-racemic form.[3,4]

Our research group has recently described the preparation of chiral, non-racemic tetrahydrofurans, lactones, lactams and *N*-protected pyrrolidines,[5] induced by the selenyl triflate **2** (generated by treatment of di-2-[(1*S*)-1-(methylthio)ethyl]phenyl diselenide **1** with bromine and silver triflate, Scheme 2). In all cases the cyclization reactions occurred in good chemical yield and with complete regioselectivity and high diastereoselectivities.



Scheme 2.

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Carbon–nitrogen bond forming reactions are of particular interest since they offer a useful synthetic route to several types of chiral nitrogen-containing heterocycles in non-racemic form. Despite the numerous examples of asymmetric selenocyclization reactions reported in the literature, such cyclizations remain somewhat unexplored.[5–10] We have therefore undertaken an investigation in which the enantiomerically pure electrophilic reagent **2** was employed to induce the conversion of the *O*-allyl oximes **3** into the corresponding non-racemic isoxazolidines **6** (Scheme 3). This conversion has already been described by our research group using phenylselenyl sulfate,[11] where racemic isoxazolidines were obtained in very good yields. Reactions with the homochiral electrophilic reagent **2** should proceed in a similar way. Thus, as indicated in Scheme 3, the reaction of **2** with *O*-allyl oximes **3** affords the seleniranium intermediates **4** which are trapped by the weakly nucleophilic imino nitrogen to produce the cyclic imminium salts **5**. These generate the expected mixture of diastereomeric isoxazolidines **6** and the ketones **7** by simple hydrolysis in situ.

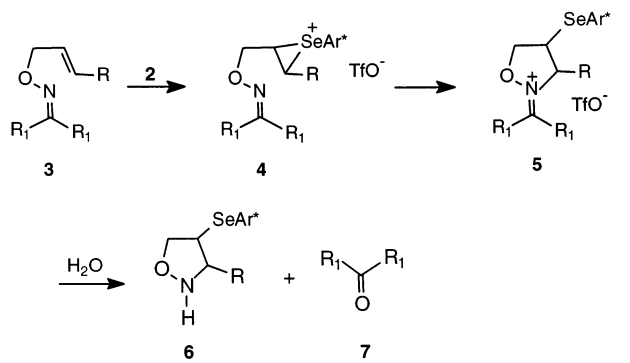
2. Results and discussion

The first experiments were carried out with *O*-allyl oxime **3a**. As indicated in Scheme 4 the reactions were carried out at −70 or at −50°C (entries 1 and 2) by adding **3a** to a solution of Ar*SeOTf **2** (prepared from **1** by treatment with bromine and then with silver triflate; method A) in dichloromethane.

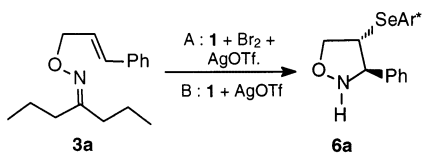
Under these conditions, the isoxazolidines **6a** were obtained in good diastereomeric ratios in both cases (94:6 and 88:12). However, reaction yields were very poor (51% at −70°C and 35% at −50°C). No improvements were seen when using longer reaction times or a large excess of the selenylating agent. However, when the reagent **2** was produced in the absence of bromine from the direct reaction of **1** with silver triflate (Method B), the isoxazolidines **6a** were formed (entry 3) in good yield (77%) and in high diastereomeric ratio (93:7). Very likely, the reaction of **1** with silver triflate generates the Ar*SeOTf, **2**, and Ar*SeAg. This represents a convenient new method to produce arylselenyl triflates and we have also tested the applicability of the method to other diselenides. Thus, in a parallel experiment, we treated PhSeSePh with an equimolar amount of silver triflate in dichloromethane and we obtained PhSeOTf (as demonstrated by the formation of PhCH(OMe)-CH_2SePh after addition to styrene in methanol) and a yellow precipitate. This was identified as PhSeAg[12] by elemental analysis and chemical means. In fact, when a suspension of this salt was treated with cinnamyl bromide in refluxing DMF the substitution product, phenyl (2*E*)-3-phenylprop-2-enyl selenide, was formed quantitatively. Moreover, when treated with bromine, this salt afforded PhSeBr.

This simple and effective method was therefore employed in all of the other experiments described in this paper. These experiments were carried out according to the following general procedure. Silver triflate was added to a solution of the diselenide **1** in dichloromethane, cooled at −50°C. The resulting yellow suspension was stirred at the same temperature for 30 min. During this time the reaction mixture changed progressively to a deep orange solution. The starting oximes **3** were added and after 8 h the temperature was allowed to slowly rise to −20°C. Stirring was continued overnight. The reaction was quenched with a 10% aqueous NaOH solution and extracted with dichloromethane. The reaction products were isolated by column chromatography on silica gel. The isoxazolidines **6** were obtained as mixtures of the two enantiomerically pure diastereoisomers which could not be separated. The diastereomeric ratios of the products were determined by ^{1}H NMR spectra. Reaction yields and diasteromeric ratios are reported in Table 1. (The *O*-allyl oximes used in the present investigation were easily prepared by alkylation[13] of commercial or easily available oximes).

Some preliminary experiments were performed in order to investigate the effect of the groups R_1 on the diastereoselectivity of the process. The results reported



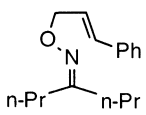
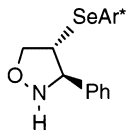
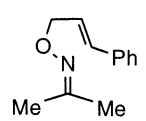
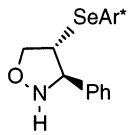
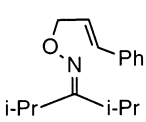
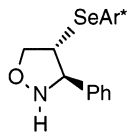
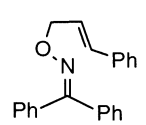
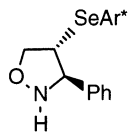
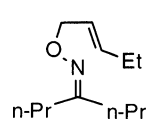
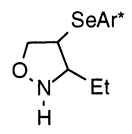
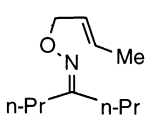
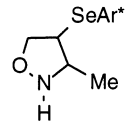
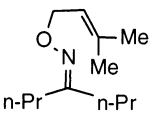
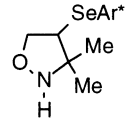
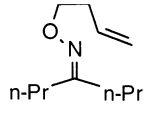
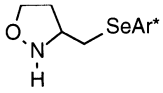
Scheme 3.



Entry	T °C	Method	Yield (%)	D.r.
1	- 70	A	51	94:6
2	- 50	A	35	88:12
3	- 50	B	77	93:7

Scheme 4.

Table 1. Synthesis of isoxazolidines **6a–h** from the *O*-allyl oximes **3a–h** promoted by Ar*SeOTf **2** in CH_2Cl_2

Entry	Starting material		Isoxazolidine[a]		Yield (%)	D.r.[b]
1		**3a**		**6a**	77	**93:7**
2		**3b**		**6a**	63	**93:7**
3		**3c**		**6a**	74	**91:9**
4		**3d**		**6a**	58	**88:12**
5		**3e**		**6e**	93	**88:12**
6		**3f**		**6f**	58	**90:10**
7		**3g**		**6g**	82	**81:19**
8		**3h**		**6h**	80	**60:40**

a) The two diastereoisomers could not be separated.

b) Diastereomeric ratios were determined from the proton NMR spectra after purification by column cromatography.

in Table 1 indicate that the oximes containing different alkyl groups (entries 1–3) afforded the isoxazolidines **6a** with similar diastereomeric ratios. Only in the case of substrate **3d** (entry 4) poorer yield and lower diastereomeric ratio were observed. On the basis of these results all the other experiments were therefore performed on variously substituted heptan-4-one oximes. The results of these cyclization reactions are also shown in Table 1 (entries 5–8).

Poor diastereoselectivity was observed in the reaction of the oxime **3h** (entry 8, D.r. 60:40). This result was not completely unexpected. In fact, it has already been observed in other cases that the addition of an optically active selenylating agent to a monosubstituted alkene occurs with poor facial selectivity.[5] In all of the other cases (entries 5–7) the isoxazolidines **6** were obtained in good yields and with high diastereomeric ratios, the best results being observed with the oximes **3a–3c** in

which a phenyl group is linked to the carbon–carbon double bond and R_1 is an alkyl group. In Table 1, the absolute configuration of the major isomer of the obtained isoxazolidines is indicated only in the case of the product **6a**. For this product, in fact, the absolute configuration was determined by conversion into a known compound as reported below. Under the reasonable assumption that the facial selectivity of the selenocyclization does not change on moving from **3a** to **3e** and **3f** it can be suggested that compounds **6e** and **6f** have the same configuration as **6a**. Similar behavior has been observed in the case of the selenocyclization of the closely related alkenoic acids.[5]

The isoxazolidines obtained with the present method can be employed as starting product for the synthesis of other useful optically enriched compounds. Thus, for instance, the isoxazolidines can be easily converted into 1,3-amino alcohols by the reductive cleavage of the *N–O* bond. We have effected these reductive cleavages in the case of the isoxazolidine **6a** which was a 93:7 mixture of the two diastereoisomers. Although several reducing agents,[14] such as Ni Raney, H_2 and Pt or Pd, or $LiAlH_4$, are reported in the literature to be very efficient, we have found that in the present case the best results are obtained using zinc and a 1:1 mixture of acetic acid and water.[15]

As indicated in Scheme 5, under these experimental conditions, the isoxazolidine **6a** gave rise to the 1,3-amino alcohol **8** which was obtained in excellent yield and without any loss of enantiomeric purity. Compound **8** still contains the arylseleno group and can therefore be easily converted into several derivatives by taking advantage of the versatile chemistry of organoselenium compounds.[1,2]

The reductive cleavage of the *N–O* bond was also employed as the crucial step to assign the absolute configuration of the isoxazolidine **6a**. For this purpose, compound **6a** was first treated with benzyl bromide and was thus transformed into the *N*-benzyl isoxazolidine **9** in 65% yield. This was subjected to reductive deselenylation, using Ph_3SnH and a catalytic amount of AIBN in refluxing benzene,[5] which afforded the isoxazolidine **10**. The reduction[15] of this product gave rise to the known[16] (*S*)-β-amino alcohol **11** in good yields. The enantiomeric excess of **11** (86%) was in perfect agreement with the diastereomeric excess of the starting isoxazolidine.

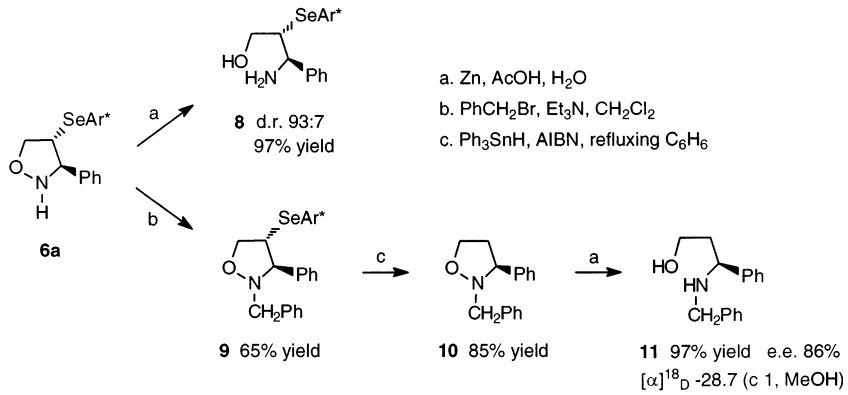
In conclusion, the strongly electrophilic reagent **2**, obtained from the corresponding diselenide **1** by simple treatment with silver triflate, is particularly efficient in promoting asymmetric *endo* cyclization reactions of *O*-allyl oximes. Because of the easily accessible starting materials and the simple procedure employed, this method can find useful synthetic applications. For instance, the reductive removal of the organoselenium moiety from the isoxazolidine **6a** generated **10**, a useful intermediate in the preparation of anxiolytics.[17] The reductive cleavage of the *N–O* bond can be used to obtain enantiomerically enriched amino alcohols. This reaction can also be effected on the arylseleno isoxazolidines thus obtaining 1,3-amino alcohols which still contain the versatile organoselenium group.

3. Experimental

New compounds were characterized by MS, ^1H and ^{13}C NMR spectroscopy. GLC analyses and MS spectra were carried out with an HP 6890 gaschromatograph (25 m dimethyl silicone capillary column) equipped with an HP 5973 Mass Selective Detector; for the ions containing selenium only the peaks arising from the selenium–80 isotope are given. ^1H and ^{13}C NMR spectra were recorded at 400 and 100.62 MHz, respectively, on a Bruker DRX 400 instrument; unless otherwise specified, $CDCl_3$ was used as solvent and TMS as standard. Optical rotations were measured with a Jasco DIP-1000 digital polarimeter. Elemental analyses were carried out on a Carlo Erba 1106 Elemental Analyzer.

3.1. Synthesis of *O*-allyl oximes

The preparation of the *O*-allyl oximes was effected by alkylation of acetone oxime, 4-heptanone oxime, 2,4-dimethylpentan-3-one oxime and benzophenone oxime, following the general procedure reported in the literature.[13] Acetone oxime is commercially available. 4-Heptanone oxime, 2,4-dimethylpentan-3-one oxime and benzophenone oxime were prepared from the corresponding ketone using a standard procedure.[18]



Scheme 5.

Compounds **3a**, **3b** and **3f** have identical spectral data to those previously reported in the literature;[13] physical and spectral data for the other starting oximes are reported below.

3.1.1. 2,4-Dimethylpentan-3-one *O*-[(2*E*)-3-phenylprop-2-enyl] oxime 3c. Oil; ^{1}H NMR: δ 7.48–7.20 (m, 5H), 6.60 (dt, 1H, J=1.2, 16.0 Hz), 6.35 (dt, 1H, J=5.9, 16.0 Hz), 4.65 (dd, 2H, J=1.2, 5.9 Hz), 3.05 (sept, 1H, J=7.0 Hz), 2.52 (sept, 1H, J=6.9 Hz), 1.15 (d, 6H, J=7.0 Hz), 1.10 (d, 6H, J=6.9 Hz). ^{13}C NMR: δ 168.6, 137.0, 132.1, 128.5 (two carbons), 127.5, 126.5 (two carbons), 126.3, 73.8, 31.2, 28.1, 21.2 (two carbons), 19.1 (two carbons). MS m/z (rel. int.): 245 (<1), 117 (100), 103 (3), 91 (5), 77 (3). Anal. calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71. Found: C, 78.24; H, 9.53; N, 5.67%.

3.1.2. Diphenylmethanone *O*-[(2*E*)-3-phenylprop-2-enyl]-oxime 3d. Mp 67–68°C; ^{1}H NMR: δ 7.82–7.69 (m, 2H), 7.69–7.38 (m, 13H), 6.84 (dt, 1H, J=1.2, 16.0 Hz), 6.62 (dt, 1H, J=5.9, 16.0 Hz), 5.09 (dd, 2H, J=1.2, 5.9 Hz). ^{13}C NMR: δ 157.0, 136.9, 136.7, 133.5, 133.0, 129.5 (two carbons), 129.4, 128.9, 128.7 (two carbons), 128.4 (two carbons), 128.2 (two carbons), 128.1 (two carbons), 127.8, 126.7 (two carbons), 125.9, 75.4. Anal. calcd for $C_{22}H_{19}NO$: C, 84.31; H, 6.11; N, 4.47. Found: C, 84.30; H, 6.13; N, 4.36%.

3.1.3. Heptan-4-one *O*-[(2*E*)-pent-2-enyl]oxime 3e. Oil; ^{1}H NMR: δ 5.80–5.51 (m, 2H), 4.45–4.38 (m, 2H), 2.28–2.19 (m, 2H), 2.15–1.97 (m, 4H), 1.61–1.37 (m, 4H), 0.98 (t, 3H, J=7.4 Hz), 0.89 (t, 3H, J=7.4 Hz), 0.88 (t, 3H, J=7.3 Hz). ^{13}C NMR: δ 160.9, 135.7, 125.1, 73.9, 36.0, 29.9, 25.3, 19.9, 18.6, 14.1, 13.2, 12.6. Anal. calcd for $C_{12}H_{23}NO$: C, 73.05; H, 11.75; N, 7.10. Found: C, 73.10; H, 11.82; N, 7.05%.

3.1.4. Heptan-4-one *O*-[3-methylbut-2-enyl]oxime 3g. Oil; ^{1}H NMR: δ 5.43 (tsept, 1H, J=1.4, 6.8 Hz), 4.60–4.50 (m, 2H), 2.35–2.25 (m, 2H), 2.25–2.13 (m, 2H), 1.82–1.75 (m, 3H), 1.75–1.70 (m, 3H), 1.70–1.48 (m, 4H), 0.96 (t, 6H, J=7.3 Hz). ^{13}C NMR: δ 161.0, 136.5, 120.7, 69.9, 36.1, 29.9, 25.7, 20.0, 19.2, 18.1, 14.2, 13.8. MS m/z (rel. int.): 197 (4), 180 (8), 154 (8), 130 (4), 129 (3), 114 (5), 101 (4), 73 (8), 70 (15), 69 (100), 68 (8), 67 (4), 55 (4), 53 (4). Anal. calcd for $C_{12}H_{23}NO$: C, 73.05; H, 11.75; N, 7.10. Found: C, 72.95; H, 11.69; N, 6.97%.

3.1.5. Heptan-4-one *O*-but-3-enyloxime 3h. Oil; ^{1}H NMR: δ 5.81 (ddt, 1H, J=6.8, 10.2, 17.0 Hz), 5.15–4.92 (m, 2H), 4.07 (t, 2H, J=6.8 Hz), 2.36 (tq, 2H, J=1.1, 6.8 Hz), 2.27–2.15 (m, 2H), 2.15–2.03 (m, 2H), 1.61–1.38 (m, 4H), 0.91 (t, 6H, J=7.3 Hz). ^{13}C NMR: δ 160.3, 135.0, 116.1, 72.1, 35.6, 33.1, 29.6, 19.8, 19.2, 14.2, 13.7. MS m/z (rel. int.): 183 (13) 168 (94), 155 (14), 138 (18), 127 (56), 114 (16), 110 (29), 96 (21), 73 (31), 70 (100), 55 (56), 43 (93), 41 (86). Anal. calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.75; N, 7.64. Found: C, 71.90; H, 11.79; N, 7.60%.

3.2. General procedure for cyclization reactions

To a solution of the aryldiselenide **1** (1 mmol) in dichloromethane (5 mL) at −50°C was added silver trifluoromethansulfonate (1 mmol). The resulting yellow suspension was stirred at the same temperature for 0.5 h. During this time the reaction mixture progressively turned into a deep orange solution. The starting oxime **3** was added and the mixture stirred for 8 h. The temperature was then allowed to gradually rise to −20°C and stirring was continued overnight. The reaction mixture was poured into a 10% NaOH solution and extracted with dichloromethane. The organic layer was filtered through Celite, dried over Na_2SO_4 and evaporated. The reaction products were obtained in a pure form after column chromatography of the residue on silica gel. In these cases the NMR spectra were recorded in C_6D_6 at 340 K. Broad signals were in fact observed at lower temperatures.

3.2.1. 4-({2-[(1*S*)-1-(Methylthio)ethyl]phenyl}seleno)-3-phenylisoxazolidine 6a. Oil; major (3*R*,4*R*)-diastereoisomer: ^{1}H NMR (C_6D_6, T=340 K): δ 7.52 (dd, 1H, J=1.3, 7.7 Hz), 7.48 (dd, 1H, J=1.3, 7.7 Hz), 7.38–7.32 (m, 2H), 7.21–7.09 (m, 4H), 6.93 (dt, 1H, J=1.3, 7.7 Hz), 5.7 (br s, 1H), 4.66 (q, 1H, J=7.0 Hz), 4.39 (d, 1H, J=4.5 Hz), 4.19 (dd, 1H, J=6.8, 8.3 Hz), 3.92 (ddd, 1H, J=4.5, 5.6, 6.8 Hz), 3.88 (dd, 1H, J=5.6, 8.3 Hz), 1.84 (s, 3H), 1.51 (d, 3H, J=7.0 Hz). ^{13}C NMR (C_6D_6, T=340 K): δ 146.4, 146.0, 139.9, 135.7, 128.5, 128.3, 127.5, 127.3, 127.2 (two carbons), 126.6 (two carbons), 75.8, 70.3, 51.5, 44.4, 21.4, 13.6. Anal. calcd for $C_{18}H_{21}NOSSe$: C, 57.15; H, 5.59; N, 3.70. Found: C, 57.20; H, 5.67; N, 3.51%.

Oil; minor (3*S*,4*S*)-diastereoisomer (distinct signals): ^{1}H NMR: δ 7.53 (dd, 1H, J=1.3, 7.7 Hz), 7.49 (dd, 1H, J=1.3, 7.7 Hz), 6.94 (dt, 1H, J=1.3, 7.7 Hz), 4.69 (q, 1H, J=7.0 Hz), 4.41 (d, 1H, J=4.5 Hz), 4.13 (dd, 1H, J=7.0, 8.4 Hz), 3.93 (ddd, 1H, J=4.5, 5.6, 7.0 Hz), 3.87 (dd, 1H, J=5.6, 8.4 Hz), 1.80 (s, 3H), 1.52 (d, 3H, J=7.0 Hz). ^{13}C NMR: δ 76.0, 69.8, 51.4, 44.3.

3.2.2. 3-Ethyl-4-({2-[(1*S*)-1-(methylthio)ethyl]phenyl}-seleno)isoxazolidine 6e. Oil; major diastereoisomer: ^{1}H NMR (C_6D_6, T=340 K): δ 7.55 (dd, 1H, J=1.4, 7.5 Hz), 7.53 (dd, 1H, J=1.4, 7.5 Hz), 7.18 (dt, 1H, J=1.4, 7.5 Hz), 6.99 (dt, 1H, J=1.4, 7.5 Hz), 4.75 (br s, 1H), 4.71 (q, 1H, J=7.0 Hz), 4.13 (dd, 1H, J=7.5, 9.0 Hz), 3.76 (dd, 1H, J=5.8, 9.0 Hz), 3.48 (ddd, 1H, J=4.2, 5.8, 7.5 Hz), 3.16 (ddd, 1H, J=4.2, 5.8, 6.9 Hz), 1.81 (s, 3H), 1.51 (d, 3H, J=7.0 Hz), 1.48–1.25 (m, 2H), 0.82 (t, 3H, J=7.4 Hz). ^{13}C NMR (C_6D_6, T=340 K): δ 146.3, 135.3, 130.4, 128.4, 127.5, 127.3, 76.1, 69.0, 48.5, 44.4, 26.1, 21.5, 13.8, 11.0. Anal. calcd for $C_{14}H_{21}NOSSe$: C, 50.91; H, 6.41; N, 4.24. Found: C, 50.97; H, 6.43; N, 4.20%.

Oil; minor diastereoisomer (distinct signals): ^{1}H NMR: δ 4.10 (dd, 1H, J=7.4, 9.1 Hz), 3.75 (dd, 1H, J=5.8, 9.1 Hz), 3.49 (ddd, 1H, J=4.2, 5.8, 7.5 Hz), 0.83 (t, 3H, J=7.3 Hz). ^{13}C NMR: δ 76.3, 68.6, 48.4.

3.2.3. 3-Methyl-4-({2-[(1*S*)-1-(methylthio)ethyl]phenyl}-seleno)isoxazolidine 6f. Oil; major diastereoisomer: ^{1}H NMR (C_6D_6, $T=340$ K): δ 7.56 (dd, 1H, $J=1.5$, 7.7 Hz), 7.51 (dd, 1H, $J=1.3$, 7.7 Hz), 7.17 (dt, 1H, $J=1.3$, 7.7 Hz), 6.98 (dt, 1H, $J=1.5$, 7.7 Hz), 4.80 (br s, 1H), 4.72 (q, 1H, $J=7.0$ Hz), 4.10 (dd, 1H, $J=7.5$, 9.0 Hz), 3.82 (dd, 1H, $J=5.7$, 9.0 Hz), 3.38–3.32 (m, 2H), 1.87 (s, 3H), 1.56 (d, 3H, $J=7.0$ Hz), 1.01 (d, 3H, $J=6.4$ Hz). ^{13}C NMR (C_6D_6, $T=340$ K): δ 146.8, 135.7, 130.7, 128.8, 127.9, 127.7, 76.5, 63.5, 50.6, 44.9, 22.0, 17.4, 14.2. Anal. calcd for $C_{13}H_{19}NOSSe$: C, 49.37; H, 6.06; N, 4.43. Found: C, 49.35; H, 5.99; N, 4.38%.

Oil; minor diastereoisomer (distinct signals): ^{1}H NMR: δ 4.07 (dd, 1H, $J=7.2$, 8.9 Hz), 1.85 (s, 3H), 1.55 (d, 3H, $J=7.0$ Hz), 1.04 (d, 3H, $J=6.3$ Hz). ^{13}C NMR: δ 76.6, 63.1.

3.2.4. 3,3-Dimethyl-4-({2-[(1*S*)-1-(methylthio)ethyl]-phenyl}seleno)isoxazolidine 6g. Oil; major diastereoisomer: ^{1}H NMR (C_6D_6, $T=340$ K): δ 7.44 (dd, 1H, $J=1.5$, 7.7 Hz), 7.43 (dd, 1H, $J=1.3$, 7.7 Hz), 7.09 (dt, 1H, $J=1.3$, 7.7 Hz), 6.92 (dt, 1H, $J=1.5$, 7.7 Hz), 4.75 (br s, 1H), 4.62, (q, 1H, $J=7.0$ Hz), 4.23 (t, 1H, $J=8.5$ Hz), 3.81 (t, 1H, $J=8.5$ Hz), 3.34 (t, 1H, $J=8.5$ Hz), 1.78 (s, 3H), 1.46 (d, 3H, $J=7.0$ Hz), 1.19 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (C_6D_6, $T=340$ K): δ 146.6, 135.5, 131.3, 128.6, 127.9, 127.8, 77.1, 63.5, 55.1, 44.7, 24.6, 23.0, 22.0, 14.4. Anal. calcd for $C_{14}H_{21}NOSSe$: C, 50.91; H, 6.41; N, 4.24. Found: C, 50.74; H, 6.40; N, 4.12%.

Oil; minor diastereoisomer (distinct signals): ^{1}H NMR: δ 7.45 (dd, 1H, $J=1.5$, 7.7 Hz), 4.61 (q, 1H, $J=7.0$ Hz), 4.16 (t, 1H, $J=8.5$ Hz), 3.38 (t, 1H, $J=8.5$ Hz), 1.45 (d, 3H, $J=7.0$ Hz), 1.21 (s, 3H), 1.08 (s, 3H). ^{13}C NMR: δ 130.1, 77.5, 54.9, 44.8, 22.1, 14.4.

3.2.5. 3-[({2-[(1*S*)-1-(Methylthio)ethyl]phenyl}seleno)-methyl]isoxazolidine 6h. Oil; major diastereoisomer: ^{1}H NMR (C_6D_6, $T=340$ K): δ 7.60 (dd, 1H, $J=1.5$, 7.8 Hz), 7.58 (dd, 1H, $J=1.5$, 7.8 Hz), 7.17 (dt, 1H, $J=1.5$, 7.8 Hz), 7.02 (dt, 1H, $J=1.5$, 7.8 Hz), 4.90 (br s, 1H), 4.79 (q, 1H, $J=7.0$ Hz), 3.72 (dt, 1H, $J=5.4$, 8.4 Hz), 3.45–3.31 (m, 2H), 3.01 (dd, 1H, $J=6.7$, 12.0 Hz), 2.77 (dd, 1 H, $J=7.1$, 12.0 Hz), 1.93–1.83 (m, 1H), 1.90 (s, 3H), 1.70–1.59 (m, 1H), 1.59 (d, 3H, $J=7.0$ Hz). ^{13}C NMR (C_6D_6, $T=340$ K): δ 146.4, 134.5, 131.7, 127.7, 127.1 (two carbons), 70.0, 60.3, 44.8, 36.2, 33.1, 22.1, 14.3. Anal. calcd for $C_{13}H_{19}NOSSe$: C, 49.37; H, 6.06; N, 4.43. Found: C, 49.43; H, 6.11; N, 4.39%.

Oil; minor diastereoisomer (distinct signals): ^{1}H NMR: δ 4.80 (q, 1H, $J=7.0$ Hz), 3.05 (dd, 1H, $J=6.6$, 12.0 Hz), 2.74 (dd, 1 H, $J=7.1$, 12.0 Hz), 1.91 (s, 3H), 1.58 (d, 3H, $J=7.0$ Hz). ^{13}C NMR: δ 60.3.

3.2.6. 3-Amino-2-({2-[(1*S*)-1-(methylthio)ethyl]phenyl}-seleno)-3-phenylpropan-1-ol 8. Oil; major (2*R*,3*R*)-diastereoisomer: ^{1}H NMR: δ 7.53 (dd, 1H, $J=1.3$, 7.8 Hz), 7.39 (dd, 1H, $J=1.4$, 7.8 Hz), 7.3–7.15 (m, 6H), 7.07 (dt, 1H, $J=1.4$, 7.8 Hz), 4.42 (q, 1H, $J=7.0$ Hz), 4.28 (d, 1H, $J=5.8$ Hz), 3.93 (dd, 1H, $J=2.7$, 12.0 Hz), 3.72 (dd, 1H, $J=5.3$, 12.0 Hz), 3.45 (ddd, 1H, $J=2.7$, 5.3, 5.8 Hz), 3.2 (br s, 3H), 1.86 (s, 3H), 1.46 (d, 3H, $J=7.0$ Hz). ^{13}C NMR: δ 146.1, 142.2, 135.7, 129.8, 128.6 (two carbons), 128.5, 127.8, 127.5, 127.1, 126.6 (two carbons), 64.0, 59.2, 53.8, 44.1, 21.5, 14.1. Anal. calcd for $C_{18}H_{23}NOSSe$: C, 56.83; H, 6.09; N, 3.62. Found: C, 56.90; H, 6,11; N, 3.51%.

Oil; minor (2*S*,3*S*)-diastereoisomer (distinct signals): ^{1}H NMR: δ 7.43 (dd, 1H, $J=1.3$, 7.8 Hz), 7.08 (dt, 1H, $J=1.3$, 7.8 Hz), 4.54 (q, 1H, $J=7.0$ Hz), 4.32 (d, 1H, $J=5.8$ Hz), 3.87 (dd, 1H, $J=2.9$, 12.3 Hz), 3.71 (dd, 1H, $J=5.3$, 12.3 Hz) 1.88 (s, 3H), 1.49 (d, 3H, $J=7.0$ Hz). ^{13}C NMR: δ 146.2, 142.1, 135.6, 129.7, 128.7 (two carbons), 128.6, 127.9, 127.6, 127.2, 126.5 (two carbons), 59.1, 53.6, 44.0.

3.2.7. 2-Benzyl-4-({2-[(1*S*)-1-(methylthio)ethyl]phenyl}-seleno)-3-phenylisoxazolidine 9. Oil; major (3*R*,4*R*)-diastereoisomer: ^{1}H NMR (C_6D_6, $T=340$ K): δ 7.51 (dd, 1H, $J=1.5$, 7.8 Hz), 7.51–7.38 (m, 4H), 7.35 (dd, 1H, $J=1.5$, 7.8 Hz), 7.28–7.12 (m, 6H), 7.1 (dt, 1H, $J=1.5$, 7.8 Hz), 6.84 (dt, 1H, $J=1.5$, 7.8 Hz), 4.70 (q, 1H, $J=7.0$ Hz), 4.42 (dd, 1H, $J=7.4$, 9.0 Hz), 4.19 (dd, 1H, $J=4.7$, 9.0 Hz), 4.03 (d, 1H, $J=14.1$ Hz), 3.94 (d, 1H, $J=7.4$ Hz), 3.93 (d, 1H, $J=14.1$ Hz), 3.89 (dt, 1H, $J=4.7$, 7.4 Hz), 1.81 (s, 3H), 1.46 (d, 3H, $J=7.0$ Hz). ^{13}C NMR (C_6D_6, $T=340$ K): δ 146.7, 139.4, 138.1, 135.8, 130.9, 129.4 (two carbons), 128.9 (two carbons), 128.7, 128.3 (four carbons), 128.2, 127.7, 127.6, 127.3, 77.5, 73.6, 60.4, 53.5, 44.8, 21.9, 14.2. Anal. calcd for $C_{25}H_{27}NOSSe$: C, 64.10; H, 5.81; N, 2.99. Found: C, 64.08; H, 5.74; N, 3.04%.

Oil; minor (3*S*,4*S*)-diastereoisomer (distinct signals): ^{1}H NMR: δ 4.41 (dd, 1H, $J=7.6$, 9.0 Hz), 4.16 (dd, 1H, $J=4.7$, 9.0 Hz), 4.02 (d, 1H, $J=14.1$ Hz), 1.78 (s, 3H), 1.49 (d, 3H, $J=7.0$ Hz). ^{13}C NMR: δ 77.2, 73.3, 53.1.

3.2.8. (3*S*)-2-Benzyl-3-phenylisoxazolidine 10. Oil; $[\alpha]_D^{15}=-95.9$ ($c=0.91$, $CHCl_3$). ^{1}H NMR: δ 7.5–7.25 (m, 10H), 4.18–4.05 (m, 2H), 4.01 (d, 1H, $J=14.0$ Hz), 3.88 (t, 1H, $J=8.1$ Hz), 3.81 (d, 1H, $J=14.0$ Hz), 2.74 (ddt, 1H, $J=6.6$, 8.1, 12.1 Hz), 2.36 (ddt, 1H, $J=6.6$, 8.1, 12.1 Hz). ^{13}C NMR: δ 140.8, 138.3, 128.8 (two carbons), 128.6 (two carbons), 128.3 (two carbons), 128.2 (two carbons), 127.6, 127.1, 69.7, 65.8, 60.1, 38.9. MS m/z (rel. int.): 239 (59), 162 (11), 148 (8), 117 (23), 115 (5), 104 (11), 91 (100), 77 (12), 65 (12). Anal. calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.42; H, 7.22; N, 5.79%.

3.2.9. (3*S*)-3-(Benzylamino)-3-phenylpropan-1-ol 11[16]. Oil; $[\alpha]_D^{18}=-28.7$ ($c=1$, MeOH). MS m/z (rel. int.): 196 (99), 105 (9), 104 (9), 91 (100), 77 (9), 65 (11). Anal. calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.65; H, 7.93; N, 5.79%.

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