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Synthesis of Unnatural Selenocystines and β-Aminodiselenides via Regioselective Ring-Opening of Sulfamidates Using a Sequential, One-Pot, Multistep Strategy

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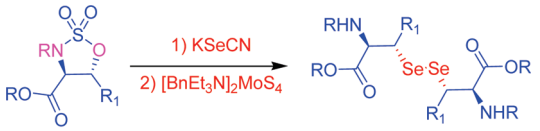

Selenocystines

A variety of *N*-alkyl-β-aminodiselenides have been synthesized in high yield from sulfamidates under mild reaction conditions using potassium selenocyanate and benzyltriethylammonium tetrathiomolybdate ($[BnNEt_3]_2MoS_4$) in a sequential, one-pot, multistep reaction. The tolerance of multifarious protecting groups under the reaction conditions is discussed. The methodology was successfully extended to the synthesis of selenocystine, 3,3′-dialkylselenocystine, and 3,3′-diphenylisoselenocystine and their direct incorporation into peptides.

Introduction

Organoselenium chemistry has led to the emergence of an exceptional class of structures in recent years due to its pivotal role in the synthesis of a large number of biologically active compounds and their importance in therapeutics.[1]

Recent advances in the synthesis of organoselenium compounds have been propelled by the interesting reactivities[2] and their potential pharmaceutical significance.[3] Although several methods are available for the synthesis of organoselenium compounds,[4] there still exist challenges and demands to develop new versatile selenating reagents which can perform regio- and stereocontrolled selenium-transfer reactions. These challenges arise partly because of the relative instability of the existing selenating reagents even at room temperature. Conventional selenating reagents generally yield monoselenides and triselenides as byproducts.[5] Among the many classes of organoselenium compounds, the chiral diselenides have received special attention due to their higher stability and ease of handling relative to the parent selenols. They have been used in the stereoselective ring-opening of epoxides[6] and in the electrophilic selenenylation of alkenes.[7] Most importantly, chiral diselenides have been employed as

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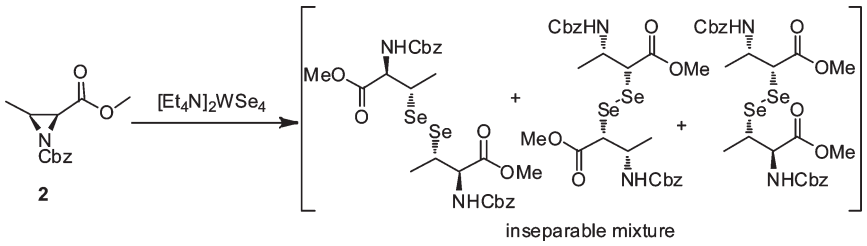
SCHEME 1



useful ligands and catalysts in various asymmetric transformations such as diethylzinc addition to aldehydes,[8] asymmetric hydrosilylation,[9] and 1,4 addition of Grignard reagents to enones.[10]

The synthesis of peptides containing selenocysteine is gaining interest with the discovery of an increasing number of proteins containing this amino acid.[11,12] Selenocysteine derivatives can also serve as convenient precursors to dehydroamino acids,[13] which are useful electrophilic handles for the chemoselective preparation of peptide conjugates.[14] Selenocystine has also been used in protein ligation to incorporate selenocysteine in the active site of a metalloprotein.[15] To the best of our knowledge, only very few methods are reported for the synthesis β-aminodiselenides and selenocystine. Braga et al. reported the synthesis of β-amino diselenides from *N*-Boc-aziridines and *N*-Boc-2-oxazolidinone using Li_2Se_2 as a selenating reagent,[8c,16] whereas selenocystine was synthesized by the reaction of β-L-bromo or iodoalanine with Li_2Se_2.[14,17] This reaction takes more time, gives moderate yields, and is limited to the synthesis of *N*-carbamato-β-aminodiselenides. In addition, Li_2Se_2 has to be prepared in situ for each reaction and leads to monoselenides and triselenides as by products which are very difficult to purify. In our laboratory, we have developed an efficient method for the synthesis of *N*-tosyl β-aminodiselenides, selenocystine, and their higher homologues using tetraethylammonium tetraselenotungstate, $[Et_4N]_2WSe_4$.[18] Our efforts to extend the same methodology for the synthesis of 3,3′-dimethylselenocystine were unsuccessful. The bromo or tosyl derivatives of diprotected threonine were found to be inert to the reaction with tetraselenotungstate, and longer reaction time led to the formation of the corresponding dehydroamino acids. The reaction of aziridine carboxylates **2** with tetraselenotungstate gave inseparable mixture of products (Scheme 1).

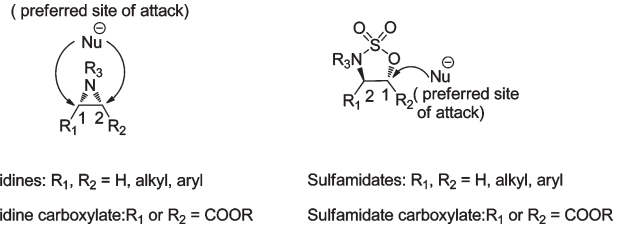


FIGURE 1. Regioselectivity in the ring-opening of sulfamidates over the aziridines with nucleophiles.

Sulfamidates are emerging as important intermediates in organic synthesis[19] and considered as a synthetic equivalent to aziridines. They have certain advantages over the aziridines: (a) they have only one site for nucleophilic attack, i.e., C_1, which renders the reactivity independent of the nature of R_1 and R_2 in contrast to the regioselectivity problem associated with aziridines (Figure 1); (b) the reactivity of sulfamidates is independent of the nature of R_3, while aziridines themselves are classified as activated and nonactivated aziridines based on the nature of R_3.

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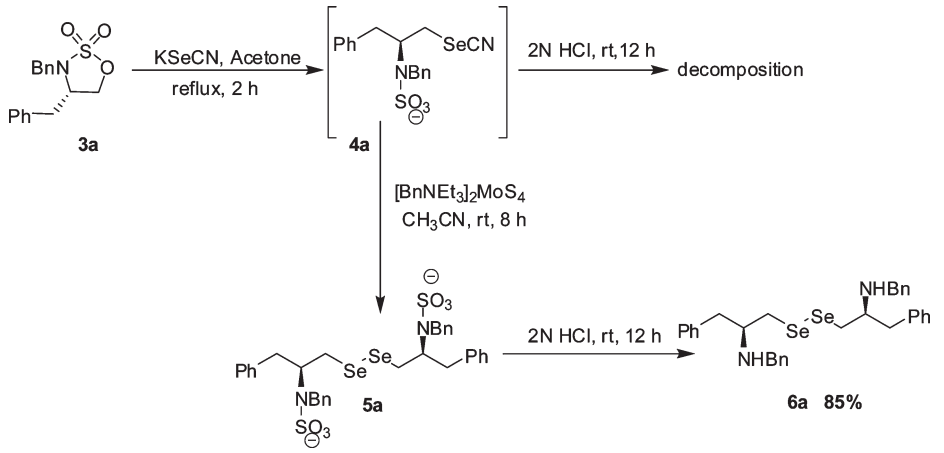
SCHEME 2. Synthesis of *N*-Benzyl-*β*-aminodiselenide



Recently, we have demonstrated the use of benzyltriethylammonium tetrathiomolybdate $[BnNEt_3]_2MoS_4$, **1**, as a useful sulfur-transfer reagent for the synthesis of *β*-amino disulfides[20] and *β*-sulfonamidodisulfides[21] as well as a reagent that can mediate reductive dimerization of alkyl azides,[22] organic thiocyanates,[23] and organic selenocyanates.[24] In exploring further the utility of induced internal redox reactions[23−25] of tetrathiomolybdate **1** in organic synthesis, it appeared quite attractive to study the sequential nucleophilic ring-opening of sulfamidates with potassium selenocyanate followed by reductive dimerization in one pot. Herein, we present the results of such an investigation.

Results and Discussion

We began our investigation with the reaction of sulfamidate **3a**[20](1.0 equiv) with KSeCN (2.0 equiv, reflux, 2 h), which undergoes regioselective ring-opening to afford the *N*-benzyl-*β*-amino selenocyanate **4a** in the form of a salt. Our attempts to hydrolyze **4a** and isolate the corresponding *N*-benzyl-*β*-amino selenocyanate before proceeding to reductive dimerization were unsuccessful as the selenocyanate decomposes during hydrolysis with dilute HCl. To overcome this problem, we changed our strategy and subjected the salt **4a** to reductive dimerization by treatment with tetrathiomolybdate **1**[24] (1.2 equiv, CH_3CN, 28 °C, 8 h), which gave the *N*-benzyl-*β*-aminodiselenide **6a** after hydrolysis in 85% yield (Scheme 2). In order to demonstrate the general utility of this methodology, we prepared a number of *N*-benzylsulfamidates **3a**−**h**.[20] They were then subjected to a one-pot, multistep process involving the regioselective ring-opening with KSeCN, reductive dimerization using tetrathiomolybdate **1**, followed by hydrolysis to give the corresponding *N*-benzyl-*β*-amino diselenides **6a**−**h**.The results of this investigation are summarized in Table 1. From the Table 1, it is clear that this method is general, and all the reactions proceed smoothly under mild reaction conditions to afford the desired *N*-benzyl-*β*-amino diselenides in very good yields. The reactivity of the sulfamidate with KSeCN was found to be substrate dependent; the sulfamidates **3a**−**g** took 2 h for the reaction to reach completion, whereas substituted sulfamidate **3h** derived from (1*S*,2*R*)-1-amino-2,3-dihydro-1*H*-inden-2-ol did not react completely even after refluxing for 48 h with excess of KSeCN. However, reductive dimerization and hydrolysis for all the substrates were equally efficient. The milder conditions and excellent yields obtained in this process encouraged us to study the scope and generality of this methodology with various protecting groups used for the protection of amino groups in sulfamidates. With this objective, we synthesized the sulfamidates **3i**−**l** starting from (*S*)-2-aminobutanol. The reaction of these sulfamidates **3i**−**l** with KSeCN followed by reductive dimerization with **1** and hydrolysis gave the corresponding *β*-aminodiselenides **6i**−**l** in good to excellent yields (Table 1).

It is reasonable to visualize the nucleophilic attack of KSeCN exclusively at the C−O bond of **3** in a highly stereospecific (S_N2) manner to give **4** followed by the attack of MoS_4^{2-} on the selenium of selenocyanate **4** leading to mononuclear molybdenum species of the type $\mathbf{X_1}$. The second stage of the reaction can be represented as an induced internal electron-transfer from a sulfur ligand to Mo(VI) to produce Mo(IV) species $\mathbf{X_2}$. The reaction of $\mathbf{X_2}$ with **1** results in the formation of alkyl diselenide **5** and $Mo_2S_8^{2-}$. The intermediate **5** on hydrolysis gives *β*-aminodiselenide **6**. This mechanistic rationale is based on our earlier work[23,24] and that of Steifel[25a] (Scheme 3).

In order to demonstrate further the scope of this methodology, we synthesized various chiral diols **7m**−**q** starting from the corresponding L-amino acids.[26] The reaction of diols **7m**−**q** with Burgess reagent ($Et_3NSO_2NCOOMe$) gave sulfamidates **3m**−**q** (Scheme 4) in excellent yields.[27] These sulfamidates **3m**−**q** when subjected to the reaction with KSeCN and **1** followed by hydrolysis gave the corresponding

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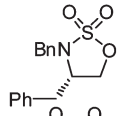
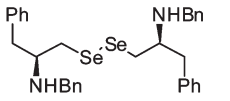
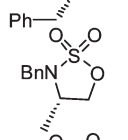
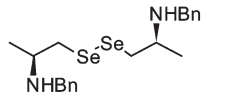
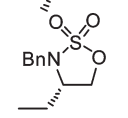
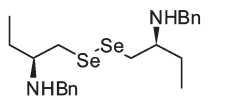
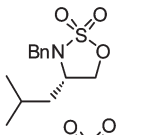
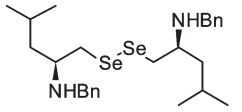
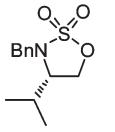
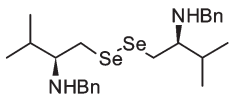
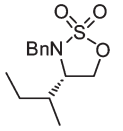
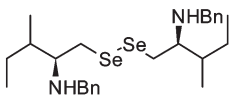
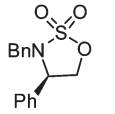
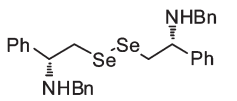
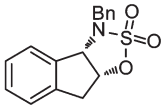
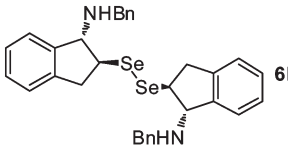
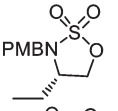
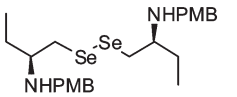
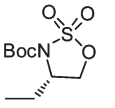
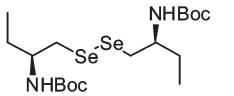
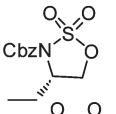
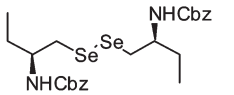
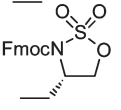
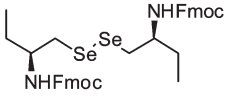
TABLE 1. Synthesis of *N*-Benzyl-*β*-aminodiselenides

Entry	Sulfamidates		Time[a]	Product		Yield[b]
1		**3a**	10 h		**6a**	85%
2		**3b**	10 h		**6b**	72%
3		**3c**	10 h		**6c**	75%
4		**3d**	10 h		**6d**	80%
5		**3e**	10 h		**6e**	84%
6		**3f**	10 h		**6f**	85%
7		**3g**	10 h		**6g**	87%
8		**3h**	32 h		**6h**	30%[c]
9		**3i**	10 h		**6i**	77%
10		**3j**	10 h		**6j**	79%[d]
11		**3k**	10 h		**6k**	85%[d]
12		**3l**	10 h		**6l**	88%[d]

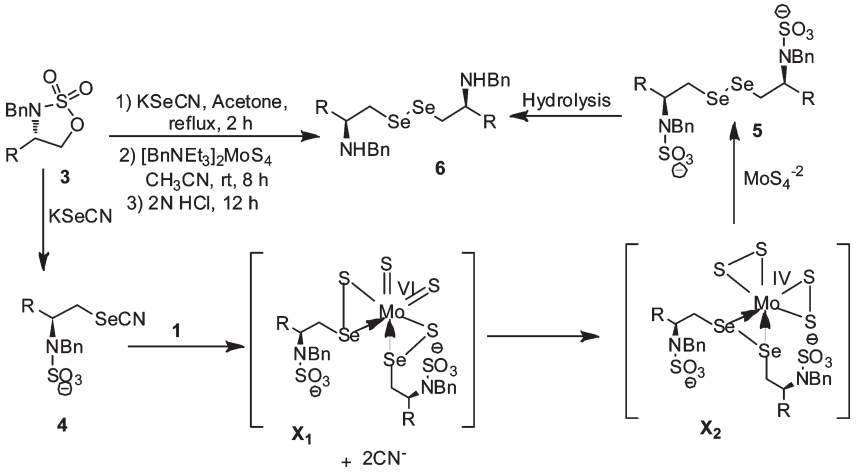
[a]Time required for the formation of selenocyanate and its reductive dimerization. [b]Reaction conditions: (i) KSeCN, acetone, reflux, 2 h; (ii) $[BnEt_3N]_2MoS_4$, CH_3CN, rt, 8 h; (iii) 2 N HCl, rt, 12 h. [c]Reaction conditions: isolated yield after 24 h of reflux with KSeCN followed by reaction with $[BnEt_3N]_2MoS_4$. [d]Reaction conditions: (i) KSeCN, acetone, reflux, 2 h; (ii) $[BnEt_3N]_2MoS_4$, CH_3CN, rt, 8 h; (iii) satd citric acid, 2 h.

substituted *β*-aminodiselenides **6m**−**q** in quantitative yields. Since the sulfamidate **3q** is derived from a racemic diol, it gave 1:1 diastereomeric mixture of the corresponding *β*-aminodiselenide $\mathbf{6q_1}$ and $\mathbf{6q_2}$ as deduced from the proton NMR spectra (Table 2).

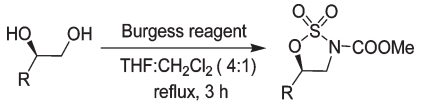
Synthesis of Selenocystines. In order to elaborate this methodology for the synthesis of selenoamino acids, we synthesized sulfamidates **9** by treating the diprotected serine and their 3-alkyl derivative **8** with $SOCl_2$ followed by oxidation with $NaIO_4$ (Scheme 5).

The sulfamidates **9a**−**g** were treated with KSeCN to give the corresponding selenocyanates which on reductive dimerization with tetrathiomolybdate **1** followed by hydrolysis gave the corresponding selenocystine derivatives **10** (Scheme 6) in very good yields. The reactivity of sulfamidates with KSeCN was found to be dependent on the substituents

SCHEME 3. Tentative Mechanism for the Formation of β-Aminodiselenide 6 from 3

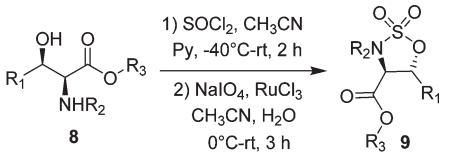


SCHEME 4. Synthesis of Sulfamidates 3m−q from Diols Using Burgess Reagent



R = Bn, **7m** — R = Bn, **3m**
R = *i*Bu, **7n** — R = *i*Bu, **3n**
R = *i*Pr, **7o** — R = *i*Pr, **3o**
R = *s*Bu, **7p** — R = *s*Bu, **3p**
R = *n*Hex, **7q** — R = *n*Hex, **3q**

SCHEME 5. Synthesis of Sulfamidate 9a−g



8 **9**

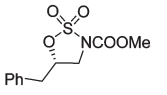
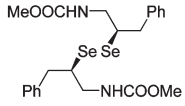
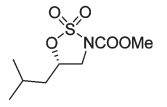
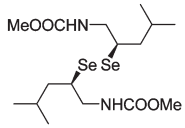
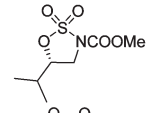
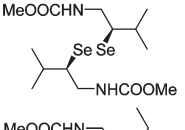
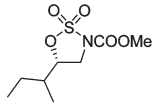
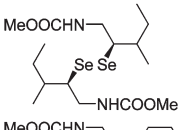
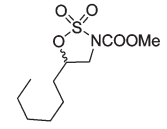
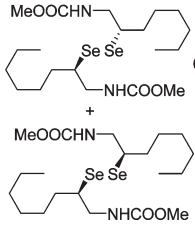
R_1 = H, Me, Ph
R_2 = Bn, Boc, Cbz, Fmoc
R_3 = Me, Bn

present at the β-position. Serine-derived sulfamidate **9a** took 2 h to react with KSeCN in acetone under reflux, whereas methyl-substituted sulfamidates **9b−f** required 5 h to react with KSeCN. The sulfamidate derived from (±) 3-phenyl serine **9g** took only 2 h to react with KSeCN in refluxing acetone. This may be due to the electron withdrawing nature of the phenyl group which enhances the reactivity of sulfamidate **9g** toward the incoming nucleophile. The reductive dimerization and hydrolysis for all the selenocyanate intermediates were found to be equally efficient to give the corresponding selenocystine derivatives **10a−g**.[29] From Table 3 it can be seen that this method is general and could be utilized for the synthesis of orthogonally protected selenocystine and *N*-alkyl selenocystine derivatives like **10e**.

Direct Incorporation of 3,3′-Dimethyl Selenocystine into Peptides. In order to demonstrate the scope of this methodology for the direct incorporation of selenocystine and its derivatives into peptides, we synthesized the peptide derived sulfamidates **13a−d** by DCC-mediated coupling of sulfamidate **11** with amino acid methyl ester **12a−d** (Scheme 7). The sulfamidates **13a−d** were treated with KSeCN followed by reductive dimerization with tetrathiomolybdate **1** and hydrolysis to give the peptide-containing 3,3′-dimethylselenocystine **14a−d** in very good yields (Table 4).

Synthesis of 3,3′-Diphenylisoselenocystine. After synthesizing a variety of selenocystine derivatives, we decided to extend this methodology to the synthesis of isoselenocystine. With this objective in mind, we prepared the chiral diol **16** by Sharpless asymmetric dihydroxlation of ethyl cinnamate

TABLE 2. Synthesis of β-Aminodiselenides by the Reaction of Sulfamidate Derived from Diols

[a]Entry	Sulfamidates	[b]Time	Product	Yield
1		**3m** 12 h		**6m** 99%
2		**3n** 12 h		**6n** 98%
3		**3o** 12 h		**6o** 98%
4		**3p** 12 h		**6p** 98%
5		**3q** 12 h		**6q1** 99% (1:1) + **6q2**

[a]Reaction conditions: (i) KSeCN, acetone, reflux, 4 h; (ii) $[BnEt_3N]_2MoS_4$, CH_3CN, rt, 8 h; (iii) satd citric acid, rt, 2 h. [b]Time required for the formation of selenocyanate and its reductive dimerization.

SCHEME 6. Synthesis of Selenocystine Derivatives 10 from Sulfamidates 9

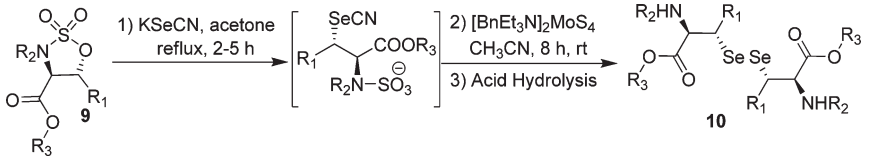
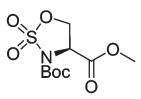
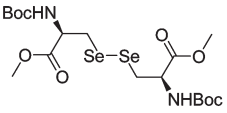
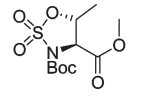
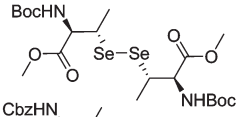
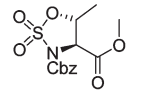
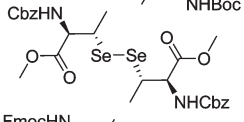
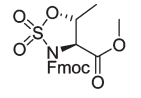
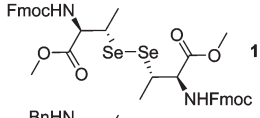
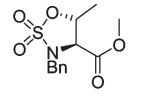
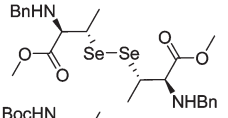
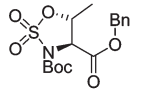
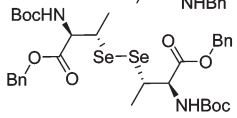
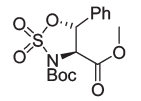
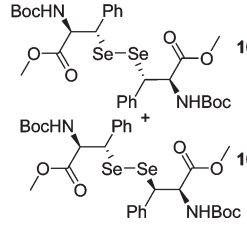


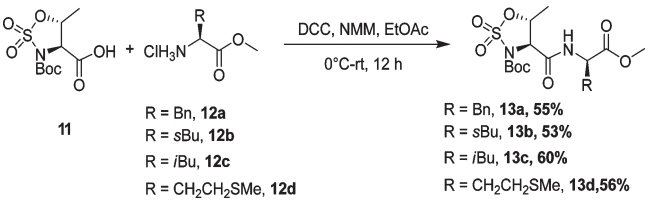
TABLE 3. Synthesis of Selenocystine Derivatives

Entry	Sulfamidates	Time[a]	products	Yield[b]
1		**9a** 10h	 **10a**	85%
2		**9b** 13h	 **10b**	95%
3		**9c** 13h	 **10c**	93%
4		**9d** 13h	 **10d**	95%
5		**9e** 13h	 **10e**	97%[c]
6		**9f** 13h	 **10f**	96%
7		**9g** 10h	 **10g$_1$** **10g$_2$**	97% (1:1)

[a]Time required for the formation of selenocyanate and its reductive dimerization. [b]Reaction condition: (i) KSeCN, acetone, reflux, 2−5 h; (ii) $[BnEt_3N]_2MoS_4$, CH_3CN, rt, 8 h; (iii) satd citric acid, rt, 2 h. [c]Reaction conditions: (i) KSeCN, acetone, reflux, 5 h; (ii) $[BnEt_3N]_2MoS_4$, CH_3CN, rt, 8 h; (iii) 2 N HCl, rt, 12 h.

15 using $(DHQ)_2PHAL$ as the chiral ligand.[28] Refluxing the chiral diol **16** with Burgess reagent ($Et_3NSO_2NCOOMe$) in anhydrous THF gave sulfamidate **17** in 95% yield. The reaction of sulfamidate **17** with KSeCN followed by reductive dimerization with **1** gave 3,3′-diphenylisoselenocystine derivative **18** in very good yield (Scheme 8).

SCHEME 7. Synthesis of Peptide Sulfamidates 13a−d



Synthesis of 3,3′-Dimethylselenocystine-Derived Peptides. The peptides **20a−d** were synthesized from 3,3′-dimethylselenocystine derivative **10b** by coupling with *N*-Cbz-protected amino acids **19a−d** using a conventional peptide coupling reaction (scheme 9). The peptide **20c** was crystallized, and its X-ray crystal structure is shown in Figure 2.

Conclusion

We have demonstrated that a variety of *N*-alkyl-*β*-aminodiselenides can be synthesized in high yield from sulfamidates under mild reaction conditions using potassium selenocyanate and tetrathiomolybdate **1** in a sequential, one-pot, multistep reaction. The tolerance of a variety of protecting groups under the reaction conditions has been discussed. The methodology was successfully extended to the synthesis of selenocystines and their direct incorporation into peptides.

Experimental Section

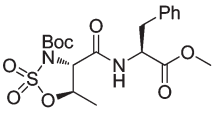
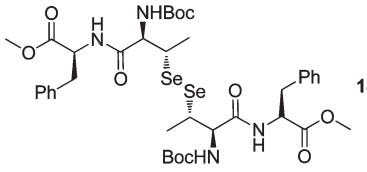
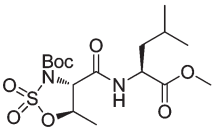
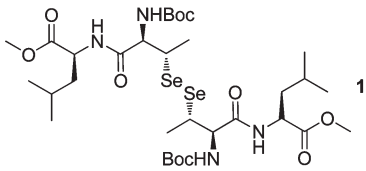
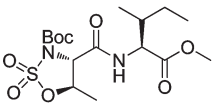
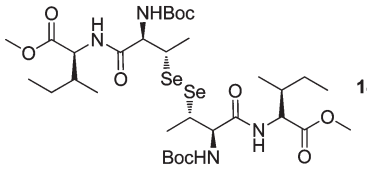
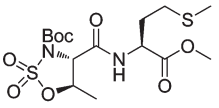
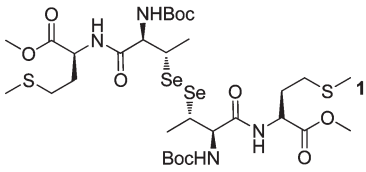
General Methods. All the reactions were performed in oven-dried apparatus and were stirred magnetically. Melting points and optical rotation values (recorded at 25 °C) reported are uncorrected. Infrared spectra were recorded using an FTIR instrument, the frequencies are reported in wavenumbers (cm^{-1}), and intensities of the peak are denoted as s (strong), w (weak), m (medium), broad (br). ^1H and ^{13}C spectra were recorded at 300/400 MHz and 75/100 MHz NMR instruments, respectively. Chemical shifts are reported in parts per million downfield from the internal reference, tetramethylsilane (TMS). Multiplicity is indicated using the following abbreviations: s (singlet), d (doublet), dd (double doublet), t (triplet), m (multiplet), bs (broad singlet). Diphenyl diselenide has been used as an internal standard for ^{77}Se NMR. Mass spectra were recorded on a Q-TOF instrument. References for the compound reported previously are indicated against each of them along with the characterization data.

General Procedure for the Synthesis of Sulfamidates from Diols. Synthesis of Sulfamidate 3m. The diol **7m** (0.076 g, 0.5 mmol, 1.0 equiv) was dissolved in anhydrous THF (5 mL), and methoxycarbonylsulfamoyltriethylammonium hydroxide (0.293 g, 1.25 mmol, 2.5 equiv, 25 °C) was added in a single portion. The resultant solution was immediately warmed to reflux (using a preheated oil bath) and stirred for 2 h. After completion of the reaction, the reaction mixture was cooled to 25 °C, poured into saturated aqueous NH_4Cl (25 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was then washed with water (50 mL) and dried over anhydrous sodium

(28) Sharpless, K, B.; Amberg, W.; Bennani, Y, L.; Crispino, G, A.; Hortung, J.; Jeong, K, S.; Known, H, L; Morikawa, K.; Wang, Z, M.; Xu, D.; Zhang, X, L. *J. Org. Chem.* **1992**, *57*, 2768–2771.

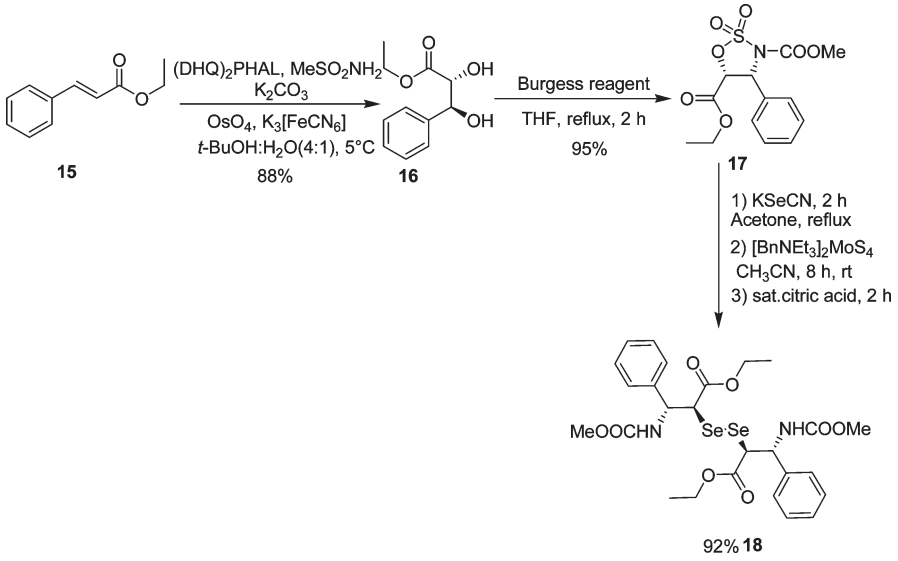
(29) The HPLC analysis for a representative compound **10b** has been recorded using a reversed-phase C-18 column with a gradient flow of 50% MeOH, 50% H_2O (1% TFA). The diastereomeric ratio of **10b** was found to be 92:8. When the HPLC analysis was carried out using a chiral reversed-phase C-18 column, we observed >99% ee of the major diastereomer. See the Supporting Information for further details.

TABLE 4. Direct Incorporation of 3,3′-Dimethylselenocystine into Peptides

Entry	Sulfamidate	Time[a]	Product	Yield[b]
1		**13a** 15h		**14a** 85%
2		**13b** 15h		**14b** 83%
3		**13c** 15h		**14c** 85%
4		**13d** 15h		**14d** 80%

[a]Time required for the formation of selenocyanate and its reductive dimerization. [b]Reaction conditions: (i) KSeCN, acetone, reflux, 7 h; (ii) $[BnEt_3N]_2MoS_4$, CH_3CN, rt, 8 h; (iii) sat citric acid, rt, 2 h.

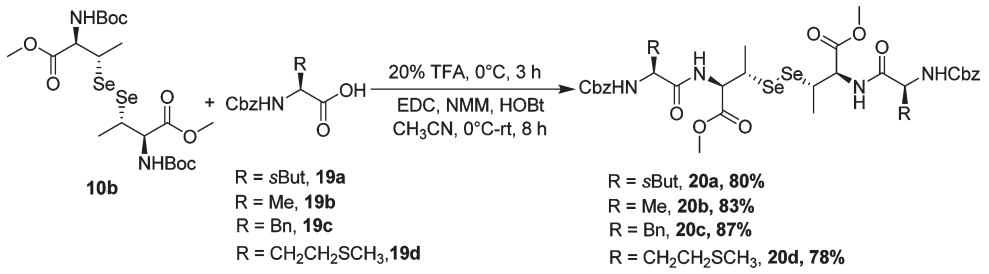
SCHEME 8. Synthesis of 3,3′-Diphenylisoselenocystine



sulfate (Na_2SO_4), and the filtrate was concentrated. The crude product was purified by silica gel (100−200 mesh) column chromatography (eluted with petroleum ether and ethyl acetate) to obtain the compound **3m** as a white solid: yield 90% (0.121 g); mp 78 °C; $[\alpha]^{25}_D$ +7.39 (c = 1, $CHCl_3$); IR (neat) 2962 (m), 2876 (w), 1747 (s), 1444 (m), 1377 (s), 1335 (s), 1195 (s), 1158 (w), 918 (w), 859 (m), 807 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.21 (5H, m), 5.05 (1H, m), 4.02 (1H, dd, J = 8 Hz, J = 16 Hz), 3.88 (3H, s), 3.81 (1H, t, J = 12 Hz), 3.30 (1H, dd, J = 8 Hz, J = 16 Hz), 3.05 (1H, dd, J = 8 Hz, J = 16 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 133.6, 129.7, 129.5, 128.3, 80.2, 55.2, 50.7, 38.8; HRMS calcd for $C_{11}H_{13}NO_5S$ $[M + Na]^+$ 294.0412, found 294.0422.

Compound 3n: yield 88% (0.104 g); white solid; mp 42 °C; $[\alpha]^{25}_D$ +13.79 (c = 1, $CHCl_3$); IR (neat) 2968 (m), 2939 (w), 2883 (w), 1747 (s), 1443 (m), 1377 (s), 1334 (s), 1195 (s), 865 (m), 762 (m), 634 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.96 (1H, m), 4.15 (1H, dd, J = 8 Hz, J = 12 Hz), 3.9 (3H, s), 3.71 (1H, t, J =

SCHEME 9. Synthesis of 3,3′-Dimethylselenocystine-Containing Peptides



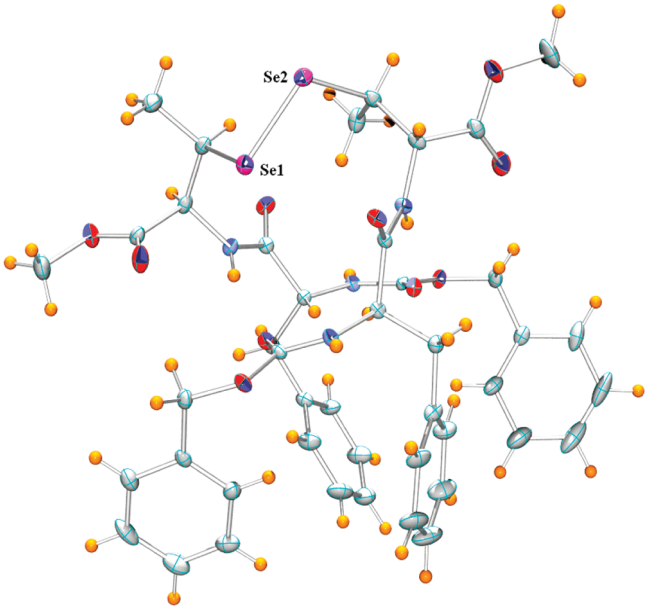


FIGURE 2. ORTEP diagram for compound **20c**.

12 Hz), 1.95−1.77 (2H, m), 1.62−1.54 (1H, m), 0.99 (6H, d, J = 8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 79.0, 54.5, 51.0, 41.0, 24.5, 22.5, 21.9; HRMS calcd for $C_8H_{15}NO_5S$ $[M + Na]^+$ 260.0569, found 260.0556.

Compound 3o: yield 94% (0.104 g); white solid; mp 60 °C; $[\alpha]^{25}_D$ +33.20 (c = 1, $CHCl_3$); IR (neat) 2269 (m), 2883 (w), 1746 (s), 1443 (m), 1376 (s), 1330 (s), 1223 (w), 1194 (s), 996 (w), 955 (w), 853 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57−4.51 (1H, m), 4.07 (1H, dd, J = 5.6 Hz, J = 10 Hz), 3.89 (3H, s), 3.76 (1H, t, J = 10 Hz), 2.11−2.02 (1H, m), 1.08 (3H, d, J = 6.8 Hz), 0.98 (3H, d, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 84.2, 54.6, 49.1, 31.0, 18.2, 16.6; HRMS calcd for $C_7H_{13}NO_5S$ $[M + Na]^+$ 246.0412, found 246.0414.

Compound 3p: yield 95% (0.112 g); white solid; mp 53 °C; $[\alpha]^{25}_D$ +30.38 (c = 1, $CHCl_3$); IR (neat) 2261 (m), 1747 (s), 1443 (m), 1378 (s), 1333 (s), 995 (w), 859 (m), 745 (m), 702 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 (1H, m), 4.07 (1H, dd, J = 5.6 Hz, J = 10 Hz), 3.91 (3H, s), 3.77 (1H, t, J = 10.4 Hz), 1.91 (1H, m), 1.67 (1H, m), 1.29 (1H, m), 0.96 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 83.0, 54.5, 49.1, 37.0, 24.8, 12.8, 10.4; HRMS calcd for $C_8H_{15}NO_5S$ $[M + Na]^+$ 260.0569, found 260.0568.

Compound 3q: yield 85% (0.112 g); gummy solid; IR (neat) 2956 (m), 2932 (s), 2860 (m), 1747 (s), 1444 (s), 1379 (s), 1334 (s), 1195 (s), 1157 (w), 919 (w), 855 (m), 762 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.90−4.82 (1H, m) δ 4.12 (1H, dd, J = 5.7, J = 9 Hz), 3.90 (3H, s), 3.73 (1H, t, J = 9.6), 2.01−1.88 (1H, m), 1.83−1.72 (1H, m), 1.52−1.30 (8H, m), 0.89 (3H, t, J = 6.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 80.2, 54.4, 50.6, 32.2, 31.2, 28.5, 24.3, 22.2, 13.8; HRMS calcd for $C_{10}H_{19}NO_5S$ $[M + Na]^+$ 288.0882, found 288.0887.

Compound 17: yield 95% (0.156 g); gummy solid; $[\alpha]^{25}_D$ +23.50 (c = 1, $CHCl_3$); IR (neat) 2969 (w), 2930 (w), 1749 (s), 1442 (m), 1388 (s), 1315 (s), 1194 (s), 1043 (s), 836 (s), 701 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.36 (5H, m), 5.56 (1H, d, J = 6.3 Hz), 5.53 (1H, d, J = 6.3 Hz), 3.97−3.83 (5H, m), 0.93 (3H, t, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 149.5, 132.9, 129.6, 128.7, 127.6, 77.4, 63.0, 62.5, 54.7, 13.4; HRMS calcd for $C_{13}H_{15}NO_7S$ $[M + Na]^+$ 352.0467, found 352.0461.

General Procedure for the Synthesis of *N*-Boc-, *N*-Cbz-, and *N*-Fmoc-Protected Sulfamidates. Compound 9a. Step I. A solution of $SOCl_2$ (0.47 mL, 6.5 mmol) in dry CH_3CN (15 mL) under nitrogen was cooled to −40 °C, and then Boc-Threo-OMe (1.05 g, 5 mmol) in dry CH_3CN (10 mL) was added dropwise over 10 min and stirring continued for a further 45 min at the same temperature. Dry pyridine (1.9 mL, 25 mmol) was then added. The reaction mixture was further stirred for 1 h and then allowed to warm to room temperature. The reaction mixture was quenched with water and extracted with ethyl acetate (20 mL × 3). The combined organic extract was washed with water, dried over anhydrous sodium sulfate (Na_2SO_4), and concentrated in vacuum to afford the crude sulfamidite. This was used without further purification in the next step.

Step II. To a cooled (ice bath) solution of crude (step I) sulfamidite (5 mmol) in MeCN (30 mL) was added ruthenium(III) chloride (20 mg) followed by $NaIO_4$ (1.60 g, 7.50 mmol) and then water (30 mL). The mixture was stirred at 0 °C for 2 h and diluted with ether, and the phases were separated. The aqueous phase was extracted with ether. The combined organic portions were washed with $NaHCO_3$ solution and then brine. The solution was dried over anhydrous (Na_2SO_4) and concentrated. The crude product was purified by silica gel (100−200 mesh) column chromatography: yield 76% (1.06 g); white solid; mp 71 °C; $[\alpha]^{25}_D$ −39.38 (c = 1, $CHCl_3$); IR (neat) 2984 (m), 1746 (s), 1459 (m), 1440 (w), 1385 (s), 1334 (s), 1194 (m), 1150 (m), 1024 (m), 977 (m), 830 (s), 786 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.84−4.68 (3H, m), 3.86 (3H, s), 1.55 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 147.9, 86.1, 67.4, 57.3, 53.4, 27.7; HRMS calcd for $C_9H_{15}NO_7S$ $[M + Na]^+$ 304.0467, found 304.0540.

Compound 9b: yield 85% (1.25 g); gummy solid; $[\alpha]^{25}_D$ −20.12 (c = 1, $CHCl_3$); IR (neat) 2985 (m), 1741 (s), 1441 (w), 1376 (m), 1326 (w), 1151(s), 1012 (s), 890 (w), 828 (m), 780 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.87 (1H, m), 4.50 (1H, d, J = 6 Hz), 3.85 (3H, s), 1.71 (3H, d, J = 8 Hz), 1.55 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 148.9, 86.7, 64.1, 54.0, 28.3, 19.4; HRMS calcd for $C_{10}H_{17}NO_7S$ $[M + Na]^+$ 318.0623, found 318.0613.

Coumpound 9c: 87% (1.43 g); gummy solid; $[\alpha]^{25}_D$ −30.51 (c = 1, $CHCl_3$); IR (neat) 2983 (w), 1739 (s), 1440 (w), 1384 (s), 1326 (s), 1192 (s), 1074 (m), 1018 (w), 751 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (5H, m), 5.37 (1H, d, J = 12 Hz), 5.35−5.25 (1H, m), 4.95-.4.87 (1H, m), 4.55 (1H, d, J = 6 Hz), 3.75 (3H, s), 1.70 (3H, d, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 149.3,

134.1, 128.6, 128.5, 127.9, 77.8, 69.6, 63.7, 53.7, 18.8; HRMS calcd for $C_{13}H_{15}NO_7S$ $[M + Na]^+$ 352.0467, found 352.0454.

Compound 9d: 79% (1.64 g); gummy solid; $[\alpha]^{25}_D$ −17.28 (c = 1, $CHCl_3$); IR (neat) 3066 (s), 3038 (w), 2957 (w), 1749 (s), 1451 (s), 1390 (s), 1316 (s), 1200 (s), 969 (m), 820 (m), 758 (s), 741 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76−7.68 (4H, m), 7.43−7.24 (4H, m), 4.97 (1H, m), 4.61−4.46 (3H, m); 4.33 (1H, t, J = 7.2 Hz), 3.80 (3H, s), 1.73 (3H, d, J = 6.3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 149.5, 142.8, 141.2, 127.9, 127.2, 125.2, 119.9, 78.1, 70.5, 63.7, 53.5, 46.4, 19.0; HRMS calcd for $C_{20}H_{19}NO_7S$ $[M + Na]^+$ 440.0780, found 440.0770.

Compound 9f: 85% (1.57 g); gummy solid; $[\alpha]^{25}_D$ −26.52 (c = 1, $CHCl_3$); IR (neat) 2983 (w), 1737 (s), 1455 (w), 1325 (m), 1325 (m), 1190 (s), 1151 (m), 826 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (5H, s), 5.31 (1H, d, J = 12 Hz), 5.20 (1H, d, J = 12 Hz), 4.87−4.79 (1H, m), 4.51 (1H, d, J = 6 Hz), 1.67 (3H, d, J = 6 Hz), 1.48 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 148.1, 134.4, 128.7, 128.7, 128.3, 86.1, 77.2, 68.3, 63.7, 27.7, 18.9; HRMS calcd for $C_{16}H_{21}NO_7S$ $[M + Na]^+$ 394.0936 found 394.0941.

Compound 9g(±): 79% (1.41 g); white solid; mp 175 °C; (neat) 2893 (w), 1743 (s), 1459 (s), 1388 (s), 1321 (m), 1197 (s), 1147 (s), 881 (m), 825 (m), 761 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (5H, s), 5.68 (1H, d, J = 6 Hz), 4.85 (1H, d, J = 6 Hz), 3.82 (3H, s), 1.55 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 147.9, 132.5, 130.5, 129.2, 126.6, 86.3, 80.8, 64.1, 53.4, 27.7; HRMS calcd for $C_{15}H_{19}NO_7S$ $[M + Na]^+$ 380.0780, found 380.0791.

Synthesis of Peptide Sulfamidates. Synthesis of 13a. A solution of **11** (1.0 g, 3.55 mmol), $HCl\cdot NH_2$-Phe-OMe **12a** (0.765 g, 4.2 mmol, 1.2 equiv), and *N*-methylmorpholine (1.16 mL, 10.6 mmol, 3 equiv) in ethyl acetate (50 mL) was cooled to 0 °C, and DCC (1.09 g, 5.32 mmol, 1.5 equiv) was added in small portions. The reaction mixture was brought to room temperature (28 °C) and stirred for 12 h. The reaction mixture was cooled and filtered. The filtrate was washed with saturated citric acid solution (25 mL), saturated Na_2CO_3 (25 mL), and brine solution (25 mL). Ethyl acetate was removed under vacuum, and the sulfamidate peptide **13a** was purified by silica gel (100−200 mesh) column chromatography: yield 55% (0.863 g); gummy solid; $[\alpha]^{25}_D$ +2.90 (c = 1, $CHCl_3$); 3064 (w), 2982 (w), 2934 (m), 2556 (w), 1743 (s), 1701 (s), 1684 (s), 1541 (m), 1455 (w), 1372 (m), 1327 (m), 1196 (m), 1149 (m), 1051 (w), 828 (w), 702 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.16 (3H, m), 7.16−7.13 (2H, m), 6.81 (1H, d. J = 8.1 Hz), 4.93−4.86 (1H, m), 4.68−4.60 (1H, m), 4.35 (1H, d, J = 4.8 Hz), 3.74 (3H, s), 3.21 (1H, dd, J = 5.4 Hz, J = 15 Hz), 3.01 (1H, dd, J = 7.2 Hz, J = 12 Hz), 1.61 (3H, d, J = 6 Hz), 1.51 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 165.6, 148.3, 135.2, 129.2, 128.6, 127.1, 86.6, 78.6, 64.5, 53.1, 52.4, 37.8, 27.6; HRMS calcd for $C_{19}H_{26}N_2O_8S$ $[M + Na]^+$ 465.1308, found 465.1319.

Compound 13b: yield 60% (0.869 g); white solid; mp 117 °C; $[\alpha]^{25}_D$ −19.33 (c = 1, $CHCl_3$); IR (neat) 3373 (br), 2959 (m), 1744 (s), 1708 (s), 1549 (w), 1390 (m), 1326 (m), 1197 (m), 1151 (m), 1052 (w), 885 (w), 831 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.81 (1H, d, J = 7.8 Hz), 5.06−4.98 (1H, m), 4.66−4.6 1 (1H, m), 3.73 (3H, s), 1.72−1.45 (15H, m), 0.93 (3H, d, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 165.8, 148.6, 86.7, 78.8, 64.6, 52.3, 51.0, 41.1, 27.7, 24.7, 22.7, 21.6, 18.9; HRMS calcd for $C_{16}H_{28}N_2O_8S$ $[M + Na]^+$ 431.1464, found 431.1446.

Compound 13c: yield 53% (0.767 g); white solid; mp 102 °C; $[\alpha]^{25}_D$ −8.53 (c = 1, $CHCl_3$); IR (neat) 2968 (w), 2936 (m), 2879 (w), 1742 (s), 1700 (s), 1544 (m), 1372 (s), 1327 (s), 1196 (m), 1148 (m), 886 (w), 856 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.0(1H, bs), 5.05 (1H, m), 4.59 (1H, dd, J = 4.8 Hz, J = 9 Hz), 4.49 (1H, d, J = 4.5 Hz), 3.74 (3H, s), 1.99−1.90 (1H, m), 1.72 (3H, d, J = 6 Hz), 1.57 (9H, s), 1.47−1.33 (1H, m), 1.31−1.14 (1H, m), 0.94−0.89 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 165.9, 148.5, 86.6, 78.9, 64.5, 56.7, 52.1, 37.7, 27.6, 24.7, 18.9, 15.3, 11.4; HRMS calcd for $C_{16}H_{28}N_2O_8S$ $[M + Na]^+$ 431.1464, found 431.1475.

Compound 13d: yield 56% (0.846 g); white solid; mp 117 °C; $[\alpha]^{25}_D$ −19.3 (c = 1, $CHCl_3$); IR (neat) 3315 (br), 2980 (m), 2931 (m), 2856 (w), 1740 (s), 1702 (s), 1539 (m), 1371 (m), 1195 (m), 1158 (m), 1053 (w), 886 (w), 875 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22 (1H, d, J = 7.5 Hz), 5.06−4.98 (1H, m), 4.77−4.70 (1H, m), 4.46 (1H, d, J = 4.8 Hz), 3.76 (3H, s), 2.51 (3H, t, J = 7.2 Hz), 2.26−1.98 (2H, m), 2.11 (3H, s), 1.72 (3H, d, J = 6 Hz), 1.57 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 165.9, 148.5, 86.7, 78.9, 64.7, 52.6, 51.8, 33.8, 29.6, 27.7, 18.8,15.3; HRMS calcd for $C_{15}H_{26}N_2O_8S_2$ $[M + Na]^+$ 449.1028, found 449.1022.

General Procedure for the Synthesis of β-Aminodiselenides. Synthesis of 6a. To a solution of sulfamidate **3a** (0.151 g, 0.5 mmol) in acetone (5 mL) was added KSeCN (0.144, 2 equiv, 1 mmol), and the reaction mixture was refluxed for 2 h. The reaction mixture was allowed to come to room temperature, and the volume was reduced to 1 mL. To this solution was added acetonitrile (4 mL) followed by $[BnEt_3N]_2MoS_4$ (1.5 equiv), and stirring was continued for a further 8 h. After the completion of dimerization, the salt was hydrolyzed with 2 N HCl (12 h) or saturated citric acid solution (2 h).The reaction mixture was neutralized with NH_4OH and extracted with ethyl acetate (3 × 25 mL). The combined organic portions were washed with brine. The solution was dried over anhydrous sodium sulfate (Na_2SO_4) and concentrated. The crude product was purified by silica gel (100−200 mesh) column chromatography (eluted with petroleum ether and ethyl acetate) to obtain compound **6a** as a gummy solid: 85%; $[\alpha]^{25}_D$ +39.62 (c = 1, $CHCl_3$); IR (neat) 3428 (br), 3026 (w), 2926 (m), 2856 (m), 1578 (w), 1458 (m), 1117 (m), 744 (m), 698 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30−7.12 (10H, m), 3.81 (1H, d, J = 12 Hz), 3.74 (1H, d, J = 12 Hz), 3.15−2.94 (3H, m), 2.87−2.74 (2H, m), 1.25 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 138.4, 129.3, 128.4, 128.3, 128.1, 126.9, 126.3, 58.4, 51.0, 40.4, 36.2; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 265.94; HRMS calcd for $C_{32}H_{36}N_2Se_2$ $[M + H]^+$ 609.1287, found 609.1305.

Compound 6b: 72%; yellow gummy solid; $[\alpha]^{25}_D$ +158.75 (c = 1, $CHCl_3$); IR (neat) 3305 (br), 2962 (m), 2920 (m), 1453 (s), 733 (s), 697 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32−7.21 (5H, m), 3.82 (1H, d, J = 12 Hz), 3.74 (1H, d, J = 12 Hz), 3.12−2.90 (3H. m), 1.73 (1H, bs), 1.17 (3H, d, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 128.3, 128.0, 126.9, 52.4, 51.1, 38.7, 20.3; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 268.66; HRMS calcd for $C_{20}H_{28}N_2Se_2$ $[M + H]^+$ 457.0661, found 457.0667.

Compound 6c: 75%; yellow gummy solid; $[\alpha]^{25}_D$ −45.69 (c = 1, $CHCl_3$); IR (neat) 3335 (br), 2959 (m), 2942 (m), 867 (w), 1452 (s), 1200 (m), 733 (m), 697 (s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.23 (5H, m), 3.78 (2H, s), 3.18 (1H, dd, J = 6 Hz, J = 12 Hz), 3.04 (1H, dd, J = 6 Hz, J = 12 Hz), 2.75 (1H, m), 1.63−1.52 (3H, m), 0.91 (3H, t, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4, 128.3, 128.1, 126.9, 58.4, 50.9, 36.5, 26.6, 10.0; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 264.80; HRMS calcd for $C_{22}H_{32}N_2Se_2$ $[M + H]^+$ 485.0974, found 485.0994.

Compound 6d: 80%; yellow gummy solid; $[\alpha]^{25}_D$ +15.13 (c = 1, $CHCl_3$); IR (neat) 3315 (br), 3060 (m), 3026 (w), 2954 (s), 2919 (s), 2868 (s), 1493 (w), 1262 (m), 1454 (m), 737 (m), 698 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.23 (5H, m), 3.81 (1H, d, J = 12 Hz), 3.74 (1H, d, J = 12 Hz), 3.24 (1H, dd, J = 6 Hz, J = 12 Hz), 3.06 (1H, dd, J = 6 Hz, J = 12 Hz), 2.86, (1H, m), 1.77 (1H, bs), 1.69 (1H, m), 1.49−1.25 (2H, m), 0.88 (3H, t, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 128.3, 128.2, 126.9, 55.1, 50.8, 43.7, 37.5, 24.9, 22.8; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 264.83; HRMS calcd for $C_{26}H_{40}N_2Se_2$ $[M + H]^+$ 541.1600, found 541.1632.

Compound 6e: 84%; yellow gummy solid; $[\alpha]^{25}_D$ +49.27 (c = 1, $CHCl_3$); IR (neat) 3305 (br), 3024 (m), 2954 (s), 2920

(s), 2862 (m), 1460 (m), 1081 (w), 738 (m), 697 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.20 (5H, m), 3.78 (2H, s), 3.15 (1H, dd, J = 6 Hz, J = 12 Hz), 3.04 (1H, dd, J = 6 Hz, J = 12 Hz), 2.63 (1H, m), 1.95 (1H, m), 1.73 (1H, bs), 0.91 (3H, d, J = 3 Hz), 0.89 (3H, d, J = 3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.4, 128.2, 128.1, 126.8, 62.6, 51.4, 33.8, 29.8, 18.7, 17.9; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 271.13; HRMS calcd for $C_{24}H_{36}N_2Se_2$ $[M + H]^+$ 513.1287, found 513.1287.

Compound 6f. 85%; yellow gummy solid; $[\alpha]^{25}_D$ +20.63 (c = 1, $CHCl_3$); IR (neat) 3365 (br), 3027 (w), 2926 (s), 2870 (m), 1457 (s), 1050 (w), 736 (m), 697 (s) cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.22 (5H, m), 3.80 (1H, d, J = 12 Hz), 3.73 (1H, d, J = 12 Hz), 3.10 (1H, dd, J = 4.5 Hz, J = 12 Hz), 2.97 (1H, dd, J = 3.6 Hz, J = 12 Hz), 2.75 (1H, m), 1.74 (2H, bs), 1.43 (1H, m), 1.21 (1H, m), 0.90 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 128.3, 128.2, 126.8, 61.2, 51.3, 36.4, 33,5, 26.0, 14.0, 12.0; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 270.44; HRMS calcd for $C_{26}H_{40}N_2Se_2$ $[M + H]^+$ 541.1600, found 541.1605.

Compound 6g: 87%; yellow gummy solid; $[\alpha]^{25}_D$ −19.38 (c = 1, $CHCl_3$); IR (neat) 3432 (br), 2923 (w), 1642 (m), 1453 (m), 737 (m), 699 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34−7.20 (10H, m), 3.86 (1H, m), 3.68 (1H, dd, J = 6 Hz, J = 15 Hz), 3.50 (1H, dd, J = 6 Hz, J = 15 Hz), 3.15−3.07 (2H, m), 2.07 (1H, bs); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4, 140.1, 128.6, 128.3, 128.1, 127.5, 127.2, 126.9, 61.8, 51.3, 38.9; ^{77}SeNMR (76 MHz, $CDCl_3$) δ 282.47; HRMS calcd for $C_{30}H_{32}N_2Se_2$ $[M + H]^+$ 581.0974, found 581.0977.

Compound 6h. 30%; yellow gummy solid; $[\alpha]^{25}_D$ −2.40 (c = 1, $CHCl_3$); IR (neat) 3404 (br), 2953 (m), 2923 (s), 2853 (m), 1605 (m), 1457 (m), 1320 (w), 747 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.22 (10H, m), 4.38 (1H, d, J = 6 Hz), 3.89 (2H, s), 3.86−3.77 (2H, m), 3.46 (1H, dd, J = 7.5 Hz, J = 16.8 Hz), 3.03 (1H, dd, J = 5.4 Hz, J = 16.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.21, 141.42, 140.41, 128.39, 128.13, 128.01, 126.99, 124.74, 70.12, 50.75, 46.19, 39.17; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 386.80; HRMS calcd for $C_{32}H_{32}N_2Se_2$ $[M + Na]^+$ 627.0794, found 627.0797.

Compound 6i: 77%; yellow gummy solid; $[\alpha]^{25}_D$ −56.68 (c = 1, $CHCl_3$); IR (neat) 3335 (br), 2920 (m), 2862 (w), 1610 (w), 1509 (s), 1457 (m), 1244 (s), 1171 (w), 1032 (m), 823 (m), 705 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (2H, d, J = 9 Hz), 6.84 (2H, d, J = 9 Hz), 3.78 (3H, s), 3.72 (2H, s), 3.18 (1H, dd, J = 6 Hz, J = 12 Hz), 3.03 m (1H, dd, J = 6 Hz, J = 12 Hz), 2.75 (1H, m), 2.09 (1H, bs), 1.57 (2H, m), 0.97 (3H, t, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 132.37, 129.3, 113.8, 58.3, 55.2, 50.3, 36.3, 26.5, 10.0; HRMS calcd for $C_{24}H_{36}N_2O_2Se_2$ $[M + H]^+$ 545.1185, found 545.1185.

Compound 6j: 79%; yellow gummy solid; $[\alpha]^{25}_D$ +47.40 (c = 1, $CHCl_3$); IR (neat) 3337 (br), 2969 (m), 2930 (m), 1694 (s), 1510 (m), 1366 (m), 1279 (w), 1170 (s), 1098 (w), 987 (w), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.88 (1H, bs), 3.72 (1H, bs), 3.20−3.08 (2H, m), 1.67 (1H, m), 1.45 (10H, s), 0.95 (3H, t, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.56, 79.29, 52.59, 36.45, 28.46, 27.09, 10.43; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 283.96; HRMS calcd for $C_{18}H_{36}N_2O_4Se_2$ $[M + Na]^+$ 527.0903, found 527.0927.

Compound 6k: 85%; yellow gummy solid; $[\alpha]^{25}_D$ −1.8 (c = 1, $CHCl_3$); IR (neat) 3320 (br), 2964 (m), 2930 (w), 1695 (s), 1532 (m), 1274 (m), 1239 (m), 1101 (m), 737 (m), 696 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.74−3.25 (5H, m), 5.19−5.06 (3H, m), 3.78 (1H, bm), 3.16−3.02 (2H, m), 1.65−1.42 (2H, m), 0.92 (3H, t, J = 6 Hz), ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 136.5, 128.4, 127.9, 66.5, 53.2, 36.1, 27.1, 10.3; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 289.34; HRMS calcd for $C_{24}H_{32}N_2O_4Se_2$ $[M + Na]^+$ 595.0590, found 595.0593.

Compound 6l: 88%; yellow gummy solid; $[\alpha]^{25}_D$ −11.24 (c = 1, $CHCl_3$); IR (neat) 3328 (br), 2962 (m), 2925 (m), 1693 (s). 1531 (m), 1447 (m), 1274 (s), 1241 (m), 1106 (m), 1080 (m), 757(m), 737(m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (4H, d, J = 8 Hz), 7.56 (4H, d, J = 8 Hz), 7.39−7.25 (8H, m), 5.09 (2H, bs), 4.38 (4H, bd, J = 8 Hz), 4.19 (2H, bs), 3.12 (4H, bm), 1.6−1.4 (4H, m), 0.92 (6H, bs); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.0, 143.9, 141.3, 127.6, 126.9, 125.0, 119.9, 66.52, 53.3, 47.2, 35.9, 27.2, 10.3; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 288.48; HRMS calcd for $C_{38}H_{40}N_2O_4Se_2$ $[M + Na]^+$ 771.1216, found 771.1254.

Compound 6m: 99%; yellow gummy solid; $[\alpha]^{25}_D$ +88.49 (c = 1, $CHCl_3$); IR (neat) 3332 (br), 2960 (s), 2930 (m), 2874 (m), 1704 (s), 1533 (s), 1260 (s), 1057 (w), 777 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32−7.13 (5H, m), 5.25 (1H, bs), 3.66 (3H, s), 3.43−3.26 (3H, m), 2.96−2.78 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 138.6, 129.0, 128.5, 126.6, 25.2, 47.0, 45.5, 39.7; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 310.40; HRMS calcd for $C_{22}H_{28}N_2O_4Se_2$ $[M + Na]^+$ 567.0277, found 567.0275.

Compound 6n: 98%; yellow gummy solid; $[\alpha]^{25}_D$ +54.28 (c = 1, $CHCl_3$); IR (neat) 3337 (br), 2955 (s), 2926 (s), 2856 (s), 1713 (s), 1537 (s), 1435 (s), 1257 (m), 1193 (w), 854 (w), 777 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.39 (1H, bs), 3.68 (3H, s), 3.50−3.31 (2H, m), 3.25−3.05 (1H, m), 1.88−1.76 (1H, m), 1.53−1.37 (2H, m), 0.93 (3H, d, J = 6 Hz), 0.90 (3H, d, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 52.1, 46.1, 43.5, 42.3, 26.2. 22.7, 21.9; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 294.90; HRMS calcd for $C_{16}H_{32}N_2O_4Se_2$ $[M + Na]^+$ 499.0599, found 499.0580.

Compound 6o: 98%; yellow gummy solid; $[\alpha]^{25}_D$ +86.50 (c = 1, $CHCl_3$); IR (neat) 3335 (br), 2959 (s), 2930 (m), 2872 (m), 1713 (s), 1537 (s), 1531 (s), 1368 (m), 1260 (m), 1021 (w), 777 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.24 (1H, bs), 3.68 (3H, s), 3.63−3.59 (1H, m), 3.43−3.34 (1H, m), 3.06 (1H, dd, J = 6 Hz, J = 12 Hz), 1.98−1.88 (1H, m), 1.07 (3H, d, J = 6 Hz), 0.99 (3H, d, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.9, 56.7, 52.1, 44.1, 30.9, 20.8, 19.8; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 295.88; HRMS calcd for $C_{14}H_{28}N_2O_4Se_2$ $[M + Na]^+$ 471.0277, found 471.0278.

Compound 6p: 98%; yellow gummy solid; $[\alpha]^{25}_D$ +103.2 (c = 1, $CHCl_3$); IR (neat) 3334 (br), 2925 (m), 2853 (w), 1704 (s), 1531 (m), 1257 (s), 1193 (w), 1147 (w), 777 (w), 747 (w), 700 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.33 (1H, bs), 3.68 (3H, s), 3.63−3.54 (1H, m), 3.48−3.39 (1H, m), 0.95−0.89 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 55.5, 52.1, 44.6, 37.4, 27.8, 16.2, 11.6; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 296.74; HRMS calcd for $C_{16}H_{32}N_2O_4Se_2$ $[M + Na]^+$ 499.0890, found 499.0581

Compounds $6q_1$ and $6q_2$: (1:1 dr) 99%; yellow gummy solid; IR (neat) 3334 (br), 2955 (m), 2926 (s), 2855 (m), 1704 (s), 1530 (s), 1463 (m), 1257 (s), 1194 (m), 1016 (w), 777 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.34 (1H, bs), 5.26 (1H, bs), 3.64 (6H,s), 3.47−3.24 (4H, m), 3.03 (2H, bm), 1.67−1.36 (2H, m), 0.84 (6H, t, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 52.1, 50.2, 46.6, 45.9, 45.8, 45.63, 33.1, 31.8, 31.5, 28.9, 28.8, 27.7, 27.7, 27.6, 22.5, 13.9, ^{77}Se NMR (76 MHz, $CDCl_3$) δ 302.89, 294.11; HRMS calcd for $C_{20}H_{40}N_2O_4Se_2$ $[M + Na]^+$ 555.1216, found 555.1210.

Compound 10b: yield 95% (0.140 g); yellow gummy solid; $[\alpha]^{25}_D$ +43.19 (c = 1, $CHCl_3$); IR (neat) 3368 (br), 2977 (w), 1739 (m), 1713 (s), 1502 (m), 1367 (w), 1162 (m), 1078 (w), 1017 (w), 735 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.25 (1H,d, J = 9 Hz), 4.62 (1H, dd, J = 3.6 Hz, J = 9 Hz), 3.76 (3H, s), 3.64−3.51 (1H, m), 1.45 (9H, s), 1.43 (3H, d, J = 6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 155.7, 80.7, 58.3, 53.0, 41.5, 28.7, 18.4; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 374.05; HRMS calcd for $C_{20}H_{36}N_2O_8Se_2$ $[M + Na]^+$ 615.0700, found 615.0719.

Compound 10c. yield 93% (0.153 g); yellow gummy solid; $[\alpha]^{25}_D$ +10.00 (c = 1, $CHCl_3$); IR (neat) 3347 (br), 2952 (w), 1721 (s), 1520 (m), 1213 (s), 1055 (w), 1024 (w), 698 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−3.26 (5H, m), 5.48 (1H, d, J = 8.7 Hz), 5.11 (2H, s), 4.70 (1H, dd, J = 4.2 Hz, J = 9 Hz), 3.7 (3H, s), 3.64−3.55 (1H, m), 1.41 (3H, d, J = 6 Hz); ^{13}C NMR (75

MHz, $CDCl_3$) δ 170.7, 155.9, 136.0, 128.5, 128.2, 128.1, 67.2, 58.4, 52.5, 41.0, 17.9; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 375.01; HRMS calcd for $C_{26}H_{32}N_2O_8Se_2$ $[M + Na]^+$ 683.0387, found 683.0409.

Compound 10d: yield 95% (0.198 g); yellow solid; mp 112 °C; $[\alpha]^{25}_D$ +19.58 (c = 1, $CHCl_3$); IR (neat); 3334 (w), 3054 (w), 2951 (w), 1722 (s), 1449 (m), 1509 (m), 1212 (s), 1085 (w), 1027 (w), 758 (w), 739 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (2H, d, J = 7.2 Hz), 7.59 (2H, d, J = 7.2 Hz), 3.41−7.28 (4H, m), 5.52 (1H, d, J = 9 Hz) 4.72 (1H, dd, J = 4.2 Hz, J = 9 Hz), 4.38 (2H, m), 4.23 (1H, t, J = 6.6 Hz), 3.76 (3H, s), 3.66−3.59 (1H, m), 1.45 (3H, d, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 155.8, 143.7, 141.2, 127.7, 127.0, 125.07, 119.9, 67.3, 58.3, 52.6, 47.1, 40.9, 18.0; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 373.88; HRMS calcd for $C_{40}H_{40}N_2O_8Se_2$ $[M + Na]^+$ 859.1013, found 859.1096.

Compound 10e: yield 97% (0.138 g); yellow gummy solid; $[\alpha]^{25}_D$ +47.47 (c = 1, $CHCl_3$); IR (neat) 3332 (bs), 3028 (w), 2952 (m), 1734 (s), 1455 (m), 1201 (m), 1178 (m), 1152 (m), 986 (w), 742 (w), 698 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.24 (5H, m), 3.88 (1H, d, J = 12.9 Hz), 3.71 (3H, s), 3.65 (1H, d, J = 12 Hz), 3.57 (1H, d, J = 5.1 Hz), 3.51−3.41 (1H, m), 2.03 (1H, bs), 1.41 (3H, d, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 139.4, 128.34, 128.31, 127.1, 64.8, 52.5, 51.8, 43.6, 18.1; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 391.25; HRMS calcd for $C_{24}H_{32}N_2O_4Se_2$ $[M + H]^+$ 573.0770, found 573.0795.

Compound 10f: yield 96% (0.178 g); yellow gummy solid; $[\alpha]^{25}_D$ +16.25 (c = 1, $CHCl_3$); IR (neat) 3366 (br), 2977 (m), 2926 (w), 1718 (s), 1498 (m), 1455 (w), 1367 (m), 1159 (s), 1063 (w), 752 (w), 698 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (5H, s), 5.24−5.16 (3H, m), 4.60 (1H, bs), 1.43 ((9H, s), 1.36 (3H, d, J = 6 Hz);); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 155.1, 135.1, 128.5, 128.44, 128.41, 80.2, 67.3, 58.0, 41.2, 28.2, 17.9; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 377.06; HRMS calcd for $C_{32}H_{44}N_2O_8Se_2$ $[M + Na]^+$ 769.1326, found 769.1346.

Compound 10g(±): yield 97% (0.172 g); yellow solid; mp 115 °C; IR (neat) 3320 (m), 2959 (s), 2930 (m), 1747 (s), 1700 (s), 1540 (s), 1522 (s), 1367 (m), 1250 (m), 1165 (s), 1017 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.20 (3H, m), 7.19−7.13 (2H, m), 4.98−4.87 (2H, m), 4.20 (1H, m), 3.66−3.65 (3H, 2s), 1.40−1.39 (9H, 2s); ^{77}Se NMR (76 MHz, $CDCl_3$) δ 407.92; HRMS calcd for $C_{30}H_{40}N_2O_8Se_2$ $[M + Na]^+$ 739.1013, found 739.1038.

Compound 14a: yield 85% (0.188 g); yellow solid; mp 147 °C; $[\alpha]^{25}_D$ +66.9 (c = 1, $CHCl_3$); IR (neat) 3317 (br), 3063 (w), 2976 (w), 2930 (m), 1745 (s), 1662 (s), 1519 (s), 1367 (m), 1166 (s), 1078 (w), 739 (w), 700 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (1H, d, J = 7.5 Hz), 7.26−7.14 (5H, m), 5.50 (1H, d, J = 9 Hz), 4.89−4.81 (2H, m). 3.70−3.58 (1H, m), 3.65 (3H, s), 3.20 (1H, dd, J = 6 Hz, J = 15 Hz), 3.01 (1H, dd, J = 6 Hz, 12 Hz), 1.44 (9H, s), 1.27 (3H, d, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 169.5, 155.7, 136.3, 129.0, 128.4, 126.8, 80.0, 58.5, 53.6, 522.1, 37.7, 33.9, 28.3, 17.0; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 402.54; HRMS calcd for $C_{38}H_{54}N_4O_{10}Se_2$ $[M + Na]^+$ 907.2068, found 907.2097.

Compound 14b: yield 85% (0.173 g); yellow solid; mp 115 °C; $[\alpha]^{25}_D$ +33.87 (c = 1, $CHCl_3$); IR (neat) 3318 (br), 2966 (m), 2930 (m), 2875 (w), 1744 (s), 1662 (s), 1522 (s), 1457 (w), 1367 (m), 1165 (m), 1015 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (1H, d, J = 6.6 Hz), 5.53 (1H, d, J = 9 Hz), 4.64 (1H, bs), 4.53 (1H, dd, J = 6 Hz, J = 8.4 Hz), 3.71 (3H, s), 3.66−3.61 (1H, m) 1.95−1.86 (1H, m), 1.43 (9H, s), 1.42−1.10 (5H, m), 0.92−0.85 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 169.9, 155.7, 80.1, 58.6, 56.8, 51.9, 37.0, 28.2, 25.2, 17.7, 15.4, 11.1; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 390.41; HRMS calcd for $C_{32}H_{58}N_4O_{10}Se_2$ $[M + Na]^+$ 841.2381, found 841.2383.

Compound 14c: yield 83% (0.169 g); yellow gummy solid; $[\alpha]^{25}_D$ −2.09 (c = 1, $CHCl_3$); IR (neat) 3367 (br), 2978 (m), 1745 (s), 1716 (s), 1505 (s), 1497 (s), 1367 (m), 1245 (m), 1208 (m), 1163 (s), 1055 (w), 700 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (1H, d, J = 8.1 Hz), 5.63 (1H, d, J = 10.2 Hz), 4.91 (1H, dd, J = 3.9 Hz, J = 9 Hz), 4.66−4.59 (1H, m), 3.73−3.65 (1H, m), 3.69 (3H, s), 1.75−1.53 (3H, m), 1.46 (9H, s), 1.28 (3H, d, J = 6 Hz), 0.91 (3H, d, J = 3 Hz), 0.89 (3H, d, J = 3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 169.6, 155.8, 79.9, 58.2, 52.0, 50.8, 48.4, 40.2, 28.3, 24.9, 22.5, 21.7, 16.8; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 390.41; HRMS calcd for $C_{32}H_{58}N_4O_{10}Se_2$ $[M + Na]^+$ 841.2381, found 841.2353.

Compound 14d: yield 80% (0.170 g); yellow solid; mp 201 °C; $[\alpha]^{25}_D$ +100.75 (c = 1, $CHCl_3$); IR (neat) 3315 (br), 2975 (m), 2926 (m), 1745 (s), 1662 (s), 1516 (s), 1447 (m), 1367 (m), 1271 (m), 1166 (s), 1015 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (1H, d, J = 8.1 Hz), 5.62 (1H, d, J = 9.9 Hz), 4.90 (1H, dd, J = 3.6 Hz, J = 9.9 Hz), 4.78−4.71 (1H, m), 3.71 (3H, s), 3.71−3.62 (1H, m), 2.56−2.46 (2H, m), 2.20 (3H, s), 1.96−1.90 (1H, m), 1.80−1.66 (1H, m), 1.46 (3H, d, J = 6.3, Hz), 1.46 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 169.8, 155.9, 80.1, 58.8, 52.3, 51.4, 33.9, 31.0, 30.6, 28.3, 16.9, 15.4; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 406.59; HRMScalcd for $C_{30}H_{54}N_4O_{10}S_2Se_2$ $[M + Na]^+$ 877.1509, found 877.1529.

Compound 18: yield 92% (0.151 g); yellow color solid; mp 110 °C; $[\alpha]^{25}_D$ −365.04 (c = 1, $CHCl_3$); IR (neat) 3338 (br), 2981 (m), 2955 (m), 2853 (w), 1728 (s), 1535 (s), 1288 (s), 1255 (s), 1175 (m), 1025 (m), 701 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.26, (5H, m), 6.1 (1H, bs), 5.11 (1H, dd, J = 9 Hz, J = 15 Hz), 4.05−3.98 (3H, m), 3.69 (3H, s), 1.05 (3H, t, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 156.3, 139.3, 128.6, 128.1, 127.2, 61.5, 56.2, 52.3, 49.7, 13.7; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 433.12; HRMS calcd for $C_{26}H_{32}N_2O_8Se_2$ $[M + Na]^+$ 683.0387, found 683.0374.

General Procedure for the Synthesis of 3,3′-Dimethylselenocystine Peptides (20a−d). Boc-protected 3,3′-dimethylselenocystine derivative **10b** (0.5 mmol) was dissolved in dichloromethane (4 mL), and TFA (1 mL) was added. The reaction mixture was stirred at 0 °C for 3 h. Dichloromethane and TFA were removed under vacuum, and the crude trifluoroacetate salt was used directly for peptide coupling without purification.

The trifluoroacetate salt (0.5 mmol, obtained as above), *N*-Cbz-amino acid (1.2 mmol), and HOBt (1.2 mmol) were dissolved in acetonitrile (8 mL). The solution was cooled to 0 °C, and *N*-methylmorpholine (1.5 mmol, 3 equiv) was added dropwise. EDC (1.5 mmol, 3 equiv) was added to the reaction mixture, which was allowed to come to rt (28 °C), and stirring was continued for 8 h. The solvent was removed under vacuum, and the residue was extracted with ethyl acetate (25 mL × 3). The combined ethyl acetate layers were washed with saturated citric acid solution, saturated Na_2CO_3 solution, and finally with brine. The crude solution of the peptide was dried over anhydrous Na_2SO_4 and concentrated. The peptides (**20a−d**) were purified by silica gel (100−200 mesh) column chromatography.

Compound 20a: yield 80% (0.177 g); yellow gummy solid; $[\alpha]^{25}_D$ +47.5 (c = 1, $CHCl_3$); IR (neat) 3309 (br), 3032 (m), 2963 (s), 2932 (s), 1744 (s), 1666 (s), 1533 (s), 1455 (m), 1216 (s), 1027 (m) 756 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (1H, d, J = 9 Hz), 7.34−7.26 (5H, m), 5.63 (1H, d, J = 9 Hz), 5.20 (1H, d, J = 12.6 Hz), 5.08 (1H, d, J = 12.6 Hz), 5.01 (1H, dd, J = 3 Hz, J = 5,4 Hz), 4.45 (1H, t, J = 9 Hz), 3.70 (3H, s), 3.63−3.53 (1H, m), 1.80−1.72 (1H, m), 1.61−1.52 (1H, m), 1.38 (3H, d, J = 6 Hz), 1.20−1.05 (1H, m), 0.94 (3H, d, J = 6.6 Hz), 0.86 (3H, t, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 170.0, 156.7, 136.4, 128.4, 127.9, 127.7, 66.9, 59.0, 57.4, 52.3, 38.6, 37.3, 24.6, 18.3, 15.2, 10.8; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 379.31; HRMS calcd for $C_{38}H_{54}N_4O_{10}Se_2$ $[M + Na]^+$ 909.2068 found 909.2136.

Compound 20b: yield 83% (0.166 g); yellow gummy solid; $[\alpha]^{25}_D$ +54.00 (c = 1, $CHCl_3$); IR (neat) 3314 (br), 3032 (w), 2955 (m), 2977 (m), 1738 (s), 1672 (s), 1530 (s), 1454 (m), 1258 (m),

1215 (m), 1027 (m), 753 (m), 698 (w); cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.27 (6H, m), 5.87 (1H, d, J = 9 Hz), 5.15 (2H, 2d, J = 12 Hz), 4.93 (1H, bm), 4.52−4.43 (1H, m), 3.72(3H, s), 3.58−3.50 (1H, m), 1.39 (3H, d, J = 7.5 Hz), 1.37 (3H, d, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 170.2, 156.3, 136.1, 128.4, 128.0, 127.9, 66.9, 57.1, 52.5, 50.2, 39.8, 18.3, 18.0; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 379.57; HRMS calcd for $C_{32}H_{42}N_4O_{10}Se_2$ $[M + Na]^+$ 825.1129, found 825.1164.

Compound 20c: yield 87% (0.207 g); yellow solid; mp 144 °C; $[\alpha]^{25}_D$ +43.50 (c = 1, $CHCl_3$); IR (neat) 3305 (br), 3061 (w), 2929 (w), 1742 (s), 1662 (s), 1536 (s), 1262 (m), 1025 (m), 737(m), 698(s) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41−7.14 (11H, m), 5.72 (1H, d, J = 8.4 Hz), 5.12−4.92 (3H, m), 4.83−4.74 (1H, bm), 3.67 (3H, s), 3.52−3.42 (1H, m), 3.08 (1H. dd, J = 6 Hz, J = 15 Hz), 2.93 (1H, dd, J = 6 Hz, J = 15 Hz), 1.34 d, J = 6 Hz), ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 169.9, 156.3, 136.4, 136.2, 129.3, 128.6, 128.4, 128.0, 127.7, 126.7, 66.9, 57.3, 55.8, 52.4, 38.5, 33.8, 18.3; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 379.69; HRMS calcd for $C_{44}H_{50}N_4O_{10}Se_2$ $[M + Na]^+$ 977.1755, found 977.1761.

Compound 20d: yield 78% (0.179 g); yellow gummy solid; $[\alpha]^{25}_D$ +45.2 (c = 1, $CHCl_3$); IR (neat) 3311 (br), 3033 (w), 2953 (m), 2919 (m), 1740 (s), 1704 (s), 1668 (s), 1531 (s), 1437 (m), 1256 (m), 1216 (s), 1050 (m), 753 (m); ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (1H. bs), 7.32 (5H, s), 5.96 (1H, bs), 5.11 (2H, 2d, J = 12 Hz), 4.94 (1H, bs), 4.01 (1H, bm), 3.72 (3H, s), 3.60−3.51 (1H, m), 2.58 (2H, t, J = 12 Hz), 2.10−1.91 (5H, m), 1.38 (3H, d, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 170.0, 156.4, 136.1, 128.4, 128.8, 127.9, 67.0, 57.2, 53.7, 52.4, 39.2, 31.6,29.5, 18.2, 15.1; ^{77}Se NMR (76 MHz, $CDCl_3$) δ 379.23; HRMS calcd for $C_{36}H_{50}N_4O_{10}S_2Se_2$ $[M + Na]^+$ 945.1196, found 945.1277.

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Supporting Information Available: Experimental procedures, characterization of all new compounds, and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.