# Synthesis and Characterization of Acylated Chiral Oxazolidine-2-selones: Selone Chiral Derivatizing Agents for the Detection and Quantitation of Remotely Disposed Chiral Centers[1]

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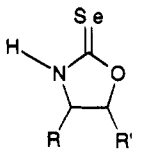
Racemic and chiral carboxylic acids and acid chlorides are coupled cleanly to oxazolidine-2-selone chiral derivatizing agents (CDA's) with yields ranging from 85 to 99%. $^{77}$Se NMR spectroscopy provides a highly sensitive method for the determination of the enantiomeric excesses of these remotely disposed chiral centers. The geometrical relationship between the selenocarbonyl and the adduct carbonyl (*syn* or *anti*) appears to have a profound effect on the chemical shift difference ($\Delta\delta_{Se}$) observed for pairs of adduct diastereomers. Crystallographic and solution state NMR studies suggest that the *syn* orbital overlap enhances the $\Delta\delta_{Se}$.

## Introduction

The development of convenient methods for the determination of enantiomeric excesses and absolute configurations of chiral compounds has been of growing interest due, in part, to the pressure put on the pharmaceutical industry to develop and deliver drugs which are enantiomerically pure[6] as well as to recent advances made in chiral synthesis. The detection and quantitation of chirality at remotely disposed chiral centers by $^{77}$Se NMR spectroscopy has previously been disclosed.[7] In this report, we describe the synthesis and characterization of carboxylic acid adducts of a series of selenium-containing chiral derivatizing agents (CDA's) and the physical parameters which optimize the NMR evaluation of these adducts.

Interest in the development of new NMR spectroscopic methods and reagents for the determination of enantiomeric excesses (ee) is considerable.[8] Usually, the enantiomeric mixture is coupled to a chiral molecule to form a pair of diastereomers, which have different NMR chemical shifts. The ee can be determined by integrating the NMR resonances. Both fluorine- and phosphorus-containing CDA's are commonly used because of their relatively large natural abundance, high sensitivity, and large NMR chemical shift dispersions.[9]

To accurately determine enantiomeric purity, both the CDA coupling reactions and the NMR instrumentation have to meet several criteria. The CDA must be in an enantiomerically pure form, and the coupling reaction must be controlled to avoid kinetic resolution. Usually, a quantitative coupling reaction ensures that the product will reflect the original enantiomeric ratio. In the process of coupling, racemization or epimerization must not occur, and purification of the product must use methods that do not selectively enrich one diastereomer. In addition, the difference in chemical shifts ($\Delta\delta$) between the CDA-derived diastereomeric products should be great enough to allow for accurate NMR integration. Furthermore, recovery of the CDA via chemical cleavage is desirable.




1a-1i

**Figure 1.**

Our oxazolidine-2-selone CDA's (Figure 1) highlight the exceptional chemical shift sensitivity of the $^{77}$Se nucleus and the ability of $^{77}$Se NMR to provide a fast, accurate determination of the ee of chiral molecules. We have systematically ascertained the proper choice of coupling conditions and NMR parameters for the successful quantitation of chirality in carboxylic acids and acid chlorides. The results of the studies herein provide guidelines for optimizing future $^{77}$Se NMR quantitation experiments.

## Results and Discussion

In order to test the applicability of the selone CDA's for the determination of the ee of chiral acid chlorides,

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(6) Stinson, S. C. *Chem. Eng. News* **1994**, *72* (Sept 19), 38.
(7) Wu, R.; Odom, J. D.; Dunlap, R. B.; Silks, L. A. *Tetrahedron: Asymmetry* **1995**, *6*, 833 and references cited therein.
(8) Nagasawa, K.; Yamashita, A.; Katoh, S.; Ito, K.; Wada, K. *Chem. Pharm. Bull.* **1995**, *43*, 344 and references cited therein.
(9) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1968**, *90*, 3732. For a remarkable use of MTPA, see: Williams, R. M.; Glinka, T.; Kwast, E.; Coffman, H.; Stille, J. K. *J. Am. Chem. Soc.* **1990**, *112*, 808. Takeuchi, Y.; Itoh, N.; Satoh, T.; Koizumi, T.; Yamaguchi, K. *J. Org. Chem.* **1993**, *58*, 1812. Takeuchi, Y.; Itoh, N.; Kawahara, S.; Koizumi, T. *Tetrahedron* **1993**, *49*, 1861. Takeuchi, Y.; Ogura, H.; Ishii, Y.; Koizumi, T. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1721. Takeuchi, Y.; Oagura, H.; Ishii, Y.; Koizumi, T. *Chem. Parm. Bull.* **1990**, *38*, 2404. Takeuchi, Y.; Itoh, N.; Note, H.; Koizumi, T.; Yamaguchi, K. *J. Am. Chem. Soc.* **1991**, *113*, 6318. House, K. L.; O'Connor, M. J.; Silks, L. A.; Dunlap, R. B.; Odom, J. D. *Chirality* **1994**, *6*, 196.

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**Table 1. NMR Quantitation of (*R*)- and (*S*)-Acid Chlorides Coupled to Selones 1a–i**

| entry | selone 1a–i | R[d] | R'[d] | acid chloride composition (R'')[e] | adduct ratio by $^1$H NMR | adduct ratio by $^{77}$Se NMR | adduct yield (%) |
|---|---|---|---|---|---|---|---|
| 1 | **a** | Me (R) | Ph | 1:1 (H)[a] | 49.9:50.1 | 49.6:50.4 | 96 |
| 2 | **b** | $CMe_3$ | H | 1:1 (H)[a] | 49.8:50.2 | 49.8:50.2 | 97 |
| 3 | **c** | $CHMe_2$ | H | 1:1 (H)[a] | 49.6:50.4 | 49.9:50.1 | 86 |
| 4 | **d** | $CH_2Ph$ | H | 1:1 (H)[a] | 50.0:50.0 | 49.9:50.1 | 98 |
| 5 | **e** | $CH_2CHMe_2$ | H | 1:1 (H)[a] | 49.8:50.2 | 49.6:50.4 | 92 |
| 6 | **f** | Ph | Ph (R) | 1:1 (H)[a] | 49.9:50.1 | 49.9:50.1 | 98 |
| 7 | **g** | Ph (R) | H | 1:1 (H)[a] | 49.8:50.2 | 49.8:50.2 | 99 |
| 8 | **h** | $(CH_2)_2Me$ | H | 1:1 (H)[a] | 49.8:50.2 | 49.9:50.1 | 95 |
| 9 | **i** | $(CH_2)_3Me$ | H | 1:1 (H)[a] | 49.4:50.6 | 49.8:50.2 | 98 |
| 10 | **a** | Me (R) | Ph | 96.8:3.2 (Me)[b] | 97.0:3.0 | 97.4:2.6 | 98 |
| 11 | **a** | Me (R) | Ph | 92.2:7.8 (Me)[b] | 92.4:7.6 | 91.5:8.5 | 98 |
| 12 | **a** | Me (R) | Ph | 55.5:44.5 (Me)[b] | 54.1:45.9 | 55.9:44.1 | 99 |
| 13 | **a** | Me (R) | Ph | 50.0:50.0 (Me)[b] | 50.4:49.6 | 50.3:49.7 | 98 |
| 14 | **a** | Me (R) | Ph | 60.2:39.8 (Me)[c] | 63.3:36.7 | 62.2:37.8 | 98 |

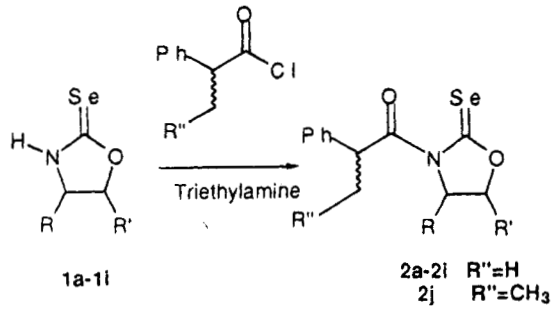
[a] The racemate was used. [b] Ratios (by weight) were calculated using 93.6% ee for the acid chloride ($[\alpha]_D = -86.11$ ($c = 5.8 \times 10^{-3}$, 1,2-dichloroethane)).[10] [c] An excess of acid chloride was used. [d] The absolute configurations are *S* unless noted. [e] Entries 1–9, R'' = H; entries 10–14, R'' = $CH_3$.

**Table 2. $\Delta\delta_{Se}$ (ppm) of (*R,S*)-2-Phenylpropanoyl-Acylated Selones 2a–g**

| compound | $\Delta\delta_{Se}$ ([$^2$H]chloroform)[a] | $\Delta\delta_{Se}$ ([$^2H_6$]benzene) |
|---|---|---|
| **2a** | 40.9 | 38.2 |
| **2b** | 43.3 | 45.6[b] |
| **2c** | 32.0 | 29.3 |
| **2d** | 25.1 | 24.1 |
| **2e** | 38.6 | 41.3 |
| **2f** | 3.5 | 4.8 |
| **2g** | 35.0 | 37.0[b] |

[a] The $^{77}$Se NMR spectra were obtained on a Bruker 300 or AM-200 instrument. Measurements were made at, or near, ambient probe temperature in 5 mm NMR tubes. All spectra were acquired in the proton-decoupled mode; generally, 0.15–0.30 M solutions were used, and 128–1024 scans were acquired using a pulse angle of 30° and a recycle time of 2.2 s. A resolution of 0.1 ppm was obtained using a 32K data table and a spectral width of 100 ppm. [b] [$^2H_8$]Toluene.

racemic mixtures of (*R*)-and (*S*)-2-phenylpropanoyl chloride were coupled to selones **1a–i** (eq 1, Table 1). Most




1a-1i 2a-2i R''=H 2j R''=$CH_3$

pairs of diastereomers exhibited $\Delta\delta_{Se}$ values ranging from 24.1 to 45.6 ppm, with most values distributed in the range of 35–39 ppm (Table 2). However, the diphenyl selone adduct (**2f**) exhibited an anomalously small $\Delta\delta_{Se}$ value of only 3.5 ppm in [$^2$H]chloroform.

We used the following protocol for the coupling of selones **1a-i** to acid chlorides. Generation of the acid chloride from the acid was accomplished using oxalyl chloride (2 equiv) at room temperature over a period of 4–12 h. Coupling of the acid chlorides with the selone was performed at 0 °C with 1.2 equiv of the selenium CDA in the presence of 1.2 equiv of triethylamine in methylene chloride. Although the reaction proceeded very rapidly, the mixtures were allowed to stir for a period of 1 h. Purification by silica gel flash column chromatography was particularly easy because the products were bright yellow.

The results of some of our ee determinations are presented in Table 1. With a racemic acid chloride as starting material, the selone adduct ratios were determined from integration of the $^{77}$Se and $^1$H resonances. Both the integrated values and the yields of the coupled products are listed. An experiment which employed a variety of enantiomeric ratios of acid chloride was also carried out. Samples were prepared by adding known amounts of (*R*)-2-phenylbutanoyl chloride to its racemic mixture. The optical purity of the (*R*)-acid chloride was predetermined by comparing the rotation value of the compound with the reported value. The measured rotation revealed that a 3.2% racemization occurred during the chlorination process.[10] The compositions of the acid chloride samples after the addition of the (*R*)-enantiomer were determined on the basis of this number. Diastereomeric ratios from the integrals of the $^1$H and $^{77}$Se NMR resonances were also compared with the calculated compositions of the original acid chlorides in Table 1. The data suggest that the coupling reaction proceeds quantitatively and without detectable racemization or epimerization. It is also apparent that the integrated $^{77}$Se NMR resonances accurately represent the enantiomeric purity of the acids. However, using a deficient amount of the selone resulted in a large error in $^{77}$Se signal integrals (Table 1, entry 14). This result suggests that the enantiomers react with the selenium CDA at different rates, resulting in partial kinetic resolution. To ensure accurate results, it is advisable to use an excess (1.2 equiv) of selone in the coupling reaction.[11]

**I. Physical Parameters Which Affect the NMR Experiment.** Performing a number of NMR physical studies in an effort to find the optimal conditions for obtaining the greatest $\Delta\delta_{Se}$ has provided guidelines for designing future NMR experiments and has given insight into the physical and structural properties of selones and selone derivatives. We chose a racemic mixture of (*R,S*)-3-phenylbutanoic acid which was coupled to selone **1a** for these model studies (**(R,S)-3c**). In addition, we also prepared the (*S*)-3-phenylbutanoyl adduct (**(S)-3c**). A comparison of the $^{77}$Se spectra of the (*S*)-diastereomer and the (*R,S*)-mixture revealed that the downfield resonance can be assigned to the (*S*)-isomer.

(10) Feibush, B.; Figueroa, A.; Charles, R.; Onan, K. D.; Feibush, P.; Karger, B. L. *J. Am. Chem. Soc.* **1986**, *108*, 3310. These authors observed 2.1% racemization in the acid chloride generation.

(11) When the chiral center is remotely disposed, this condition is probably no longer required.

Table 3. Solvent Effect on $\delta_{Se}$ (ppm) for 3c

| solvent [$^2$H][a] | $\delta_{Se}$ ((S)-3c) | $\delta_{Se}$ ((R)-3c) | $\Delta\delta_{Se}$ | $P_M/V_M$ |
|---|---|---|---|---|
| cyclohexane | 496.2 | 491.2 | 5.01 | 0.254 |
| carbon tetrachloride | 496.2 | 491.9 | 4.31 | 0.291 |
| benzene | 483.7 | 478.7 | 5.01 | 0.299 |
| toluene | 486.9 | 482.4 | 4.50 | 0.315 |
| chloroform | 467.6 | 464.0 | 3.57 | 0.559 |
| tetrahydrofuran | 466.3 | 463.2 | 3.14 | 0.681 |
| dichloromethane | 465.7 | 462.3 | 3.38 | 0.725 |
| pyridine | 462.8 | 459.4 | 3.43 | 0.786 |
| acetone | 453.2 | 450.4 | 2.82 | 0.868 |
| acetonitrile | 447.5 | 444.7 | 2.83 | 0.920 |
| dimethyl sulfoxide | 448.3 | 445.8 | 2.49 | 0.938 |

[a] The samples were prepared as 0.52 M solutions in the chosen solvents.

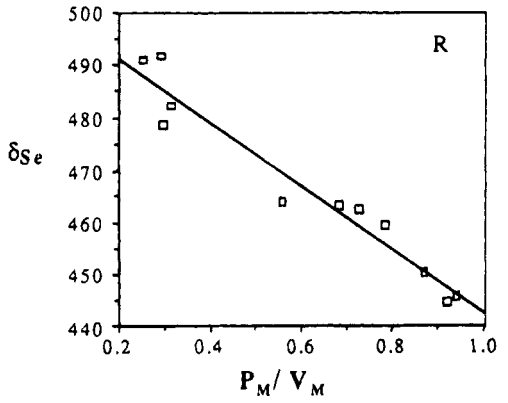



**Figure 2.** $\delta_{Se}$ of acylated 2-oxazolindineselones from (*R*,*S*)-3-phenylbutanoic acid (**3c**) as a function of solvent [((**S**)-**3c**) $R^2 = 0.952$, ((**R**)-**3c**) $R^2 = 0.946$]. Plot of the (**S**)-**3c** $\delta_{Se}$ dependency not shown.

**(A) Solvent Effects.** The $\delta_{Se}$ of compounds (**S**)-**3c** and (**R**)-**3c** in 11 organic solvents are presented in Table 3. The solvent-induced shifts cover a range of 49 ppm for compound (**S**)-**3c** and 47 ppm for (**R**)-**3c** with the extremes being defined by dimethyl sulfoxide and acetonitrile (most shielding) and cyclohexane and carbon tetrachloride (most deshielding).

To investigate the correlation between the $\delta_{Se}$ of our compounds and the intrinsic properties of a variety of solvents, $\delta_{Se}$ was plotted against the following solvent parameters: (1) dielectric constant, $\epsilon$; (2) reciprocal of dielectric constant, $1/\epsilon$; (3) molar polarization, $P_M = (\epsilon - 1)V_M/(\epsilon + 2)$ where $V_M$ is the molar volume defined by the ratio of molecular weight/density;[12] and, (4) molar polarization/molar volume, $P_M/V_M = (\epsilon - 1)/(\epsilon + 2)$. Among these, the best correlation was found for property 4 above. The plots of the $\delta_{Se}$ values of (**S**)-**3c** and (**R**)-**3c** versus $P_M/V_M$ are shown in Figure 2. An increase in the shielding of the $^{77}$Se resonance was found for both (**S**)-**3c** and (**R**)-**3c** in solvents of increasing $P_M/V_M$. A similar trend has been found for $Me_2Se$. The high degree of correlation between the $\delta_{Se}$ and $P_M/V_M$ values of the solvent implies that intermolecular interactions are the single most important contributors to the solvent-induced $\delta_{Se}$ changes.

It has been reported that both the $\delta_{Se}$ and the n $\rightarrow \pi^*$ transition energy of selenocarbonyls are related to their excitation energy ($\Delta E$). For a series of selone compounds, a linear relationship between $\delta_{Se}$ (in [$^2$H]chloroform) and $\lambda_{max}$ (n $\rightarrow \pi^*$) ($R^2 \geq 0.99$) was found.[13] Because this correlation was observed, the solvent-induced $\delta_{Se}$ for **3c** could also relate to changes in the average $\Delta E$. To help determine this dependency in our selones, (**S**)-**3c** was dissolved in the same, but nondeuterated, solvents which were used in the $^{77}$Se NMR studies. The maximum wavelengths of the transition band at around 410 nm in the selected solvents were recorded (Table 4). The observed blue shift with increasing solvent polarity ($\lambda_{max}$ moving to shorter wavelength in a polar solvent) confirmed that the observed bands were typical n $\rightarrow \pi^*$ transitions.[14] A plot of the $\delta_{Se}$ values of (**S**)-**3c** in different solvents versus the $\lambda_{max}$ (n $\rightarrow \pi^*$ transition) in different solvents showed that the correlation is indeed linear (Figure 3). The relatively large deviation from linearity compared with the values previously reported for selone compounds is probably due to the complexity of different solvent systems which were used in this study. The results support the assumption that the solvent-induced $\delta_{Se}$ is associated with the change of the mean average excitation energy, $\Delta E$.

Evidently, solvents do not affect the two epimers equally, as seen from the different slopes of the lines in Figure 2. It appears that a polar solvent more strongly interacts with (**S**)-**3c** than with (**R**)-**3c**, and the $\delta_{Se}$ of (**S**)-**3c** moves toward shielding faster. A plot of $\Delta\delta_{Se}$ versus $P_M/V_M$ gives a straight line with a slope of $-3.2$, suggesting that the resolution of signals is also solvent dependent.

**(B) Temperature Effects.** Although literature reports of temperature studies of $\delta_{Se}$ are rare, there is no

Table 4. Correlation of $\delta_{Se}$ and Wavelength for (S)-3c

| solvent | $\delta_{Se}$ (ppm) | $\lambda$ (nm) |
|---|---|---|
| cyclohexane | 496.2 | 420 |
| carbon tetrachloride | 496.2 | 416 |
| toluene | 486.9 | 414 |
| benzene | 483.7 | 413 |
| chloroform | 467.6 | 406 |
| tetrahydrofuran | 466.3 | 410 |
| dichloromethane | 465.7 | 406 |
| pyridine | 462.8 | *a* |
| acetone | 453.2 | *a* |
| acetonitrile | 447.5 | 402 |
| dimethyl sulfoxide | 448.3 | *a* |

[a] The solvent has a strong background in the observed region.

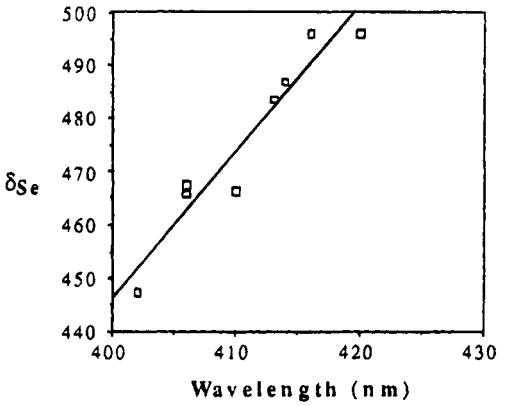



**Figure 3.** $\delta_{Se}$ of (**S**)-**3c** as a function of wavelength and solvent ($R^2 = 0.92$).

(12) Moore, W. J. In *Physical Chemistry*, 4th ed.; Prentice-Hall: Englewood Cliffs, NJ, 1972; Chapter 15, p 702.

(13) Wong, T. C.; Guziec, F. S.; Moustakis, C. A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1471.

(14) Drago, R. S. In *Physical Methods in Chemistry*; Saunders: Philadelphia, PA, 1977; p 106.

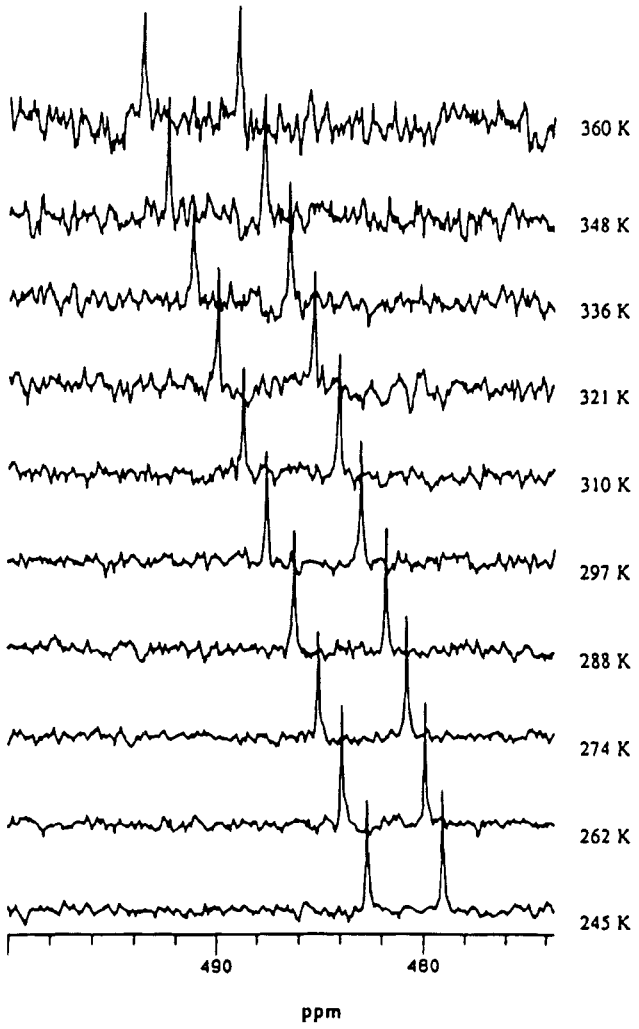



**Figure 4.** $^{77}Se$ NMR spectra of **3c** at different temperatures.

doubt that $\delta_{Se}$ values are temperature dependent. Lardon first noted that $\delta_{Se}$ values change with temperature in melts of aromatic diselenides.[15] Odom later reported the temperature dependence of $\delta_{Se}$ in solution for a variety of biologically important selenium compounds.[16]

Increasing the temperature of the sample results in a deshielding of the $^{77}Se$ resonances, as seen in the spectra in Figure 4. These spectra also clearly reveal that the S/N ratio decreases as temperature increases. The spectra in Figure 4 illustrate that noise increases with increasing temperature, a result of increasing both $T_1$ and the extent of signal saturation as the temperature rises. This temperature dependence clearly demonstrates that chemical shift anisotropy (CSA) is the major mechanism for selenium relaxation at our experimental field (11.7 T) and temperature range. Studies of the $T_1$ values of various selenium compounds have identified spin rotation (SR) and CSA as the most important mechanisms for selenium relaxation.[17]

Over the range studied, the correlations of the $\delta_{Se}$ values of **(S)-3c** and **(R)-3c** with temperature are linear (Table 5). The temperature dependencies of the $\delta_{Se}$ values of epimeric compounds **(S)-3c** and **(R)-3c** were found to be 0.096 and 0.088 ppm $K^{-1}$, respectively, at a

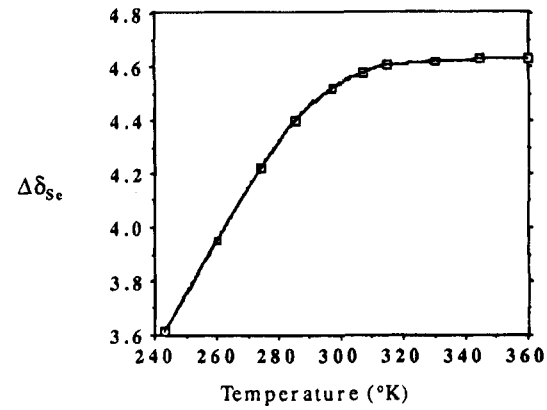



**Figure 5.** $\Delta\delta_{Se}$ (= $\delta_S - \delta_R$) of (*R,S*)-3-phenylbutanoic acid (**3c**) at various temperatures. The samples were prepared as a 0.52 M ([$^2H_8$]toluene) solution in a 5 mm NMR tube. The temperature of the probe was carefully calibrated using a 4% solution of methanol in [$^2H_4$]methanol from 245 to 288 K and an 80% solution of ethylene glycol in [$^2H_6$]dimethylsulfoxide from 297 to 360 K.

**Table 5. $\delta_{Se}$ Temperature Dependence of 3c in [$^2H_8$]Toluene**

| $T$ (K) | $\delta_{Se}$ **((S)-3c)** | $\delta_{Se}$ **((R)-3c)** | $\Delta\delta_{Se}$ |
|---|---|---|---|
| 245 | 482.7 | 479.1 | 3.6 |
| 262 | 483.9 | 479.9 | 4.0 |
| 274 | 485.0 | 480.8 | 4.2 |
| 288 | 486.2 | 481.8 | 4.4 |
| 297 | 487.5 | 483.0 | 4.5 |
| 310 | 488.6 | 484.0 | 4.6 |
| 321 | 489.8 | 485.1 | 4.7 |
| 336 | 491.0 | 486.4 | 4.7 |
| 348 | 492.3 | 487.6 | 4.7 |
| 360 | 493.6 | 488.9 | 4.7 |

field strength of 11.7 T (95.3 MHz). This is smaller than the value reported by Wong[13] (0.34–0.48 ppm $K^{-1}$) on selones (57.2 MHz). This reduction is probably due to the conjugated $\pi$ bonding in **(R or S)-3c**.

In an effort to explore which physical property is most responsible for the temperature shift, the $\delta_{Se}$ values of **(S)-3c** and **(R)-3c** were plotted against the viscosity of toluene at different temperatures.[18] The correlation revealed a smooth but nonlinear curve which suggested that, although viscosity may be one of the factors causing the temperature shift, it is not the sole factor, especially in the higher and lower temperature cases. Plotting $\Delta\delta_{Se}$ ($\delta_{(S)\text{-}3c} - \delta_{(R)\text{-}3c}$) versus temperature (Figure 5) revealed a discrimination of temperature dependence between two diastereomers. Varying the temperature affects **(R)-3c** more strongly than **(S)-3c**, so that the peak of **(R)-3c** moves at a faster rate to a deshielded position as the temperature increases. The resulting $\Delta\delta_{Se}$ increases with increasing temperature and gradually reaches a plateau after 320 K. In practical terms, a better resolution between these diastereomeric peaks could be achieved if the NMR experiments were conducted at a probe temperature of 40–50 °C, rather than at room temperature, as long as the line shape is not significantly changed due to the temperature elevation.

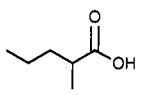
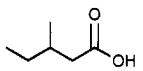
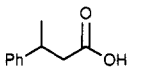
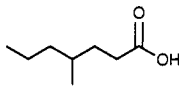
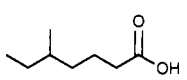
**(C) Concentration Effects.** A concentration dependence of $\delta_{Se}$ has also been observed.[19] The magnitude of this shift is smaller when compared to those of solvent

(15) Lardon, M. A. *Ann. N. Y. Acad. Sci.* **1972**, *192*, 132.
(16) Odom, J. D.; Dawson, W. H.; Ellis, P. D. *J. Am. Chem. Soc.* **1979**, *101*, 5815.
(17) Dawson, W. H.; Odom, J. D. *J. Am. Chem. Soc.* **1977**, *99*, 8352.
(18) *CRC Handbook of Chemistry and Physics*, 72nd ed.; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1991–1992; pp 6–159.
(19) Carr, S. W.; Colton, R. *Aust. J. Chem.* **1981**, *34*, 35–44.

**Table 6. Concentration Effects on $\Delta\delta_{Se}$ for 3c in [$^2$H]Chloroform**

| concentration (M) | $\delta_{Se}$ ((S)-3c) | $\delta_{Se}$ ((R)-3c) | $\Delta\delta_{Se}$ |
|---|---|---|---|
| 0.129 | 468.8 | 465.3 | 3.5 |
| 0.257 | 468.6 | 465.0 | 3.6 |
| 0.515 | 468.2 | 464.3 | 3.9 |
| 0.772 | 467.9 | 463.8 | 4.1 |
| 1.030 | 468.3 | 464.2 | 4.1 |
| 1.287 | 468.2 | 463.8 | 4.4 |

**Table 7. $\Delta\delta_{Se}$ (ppm) of 1a Adducts of Acid Racemates in [$^2$H]Chloroform**

| carboxylic acid | $\delta_{Se}$ | $\Delta\delta_{Se}$ | adduct, no. of bonds[a] |
|---|---|---|---|
|  | 449.4<br>454.5 | 3.1 | **3a**, 4 |
|  | 464.6<br>476.2 | 2.6 | **3b**, 5 |
|  | 465.3<br>468.8 | 3.5 | **3c**, 5 |
|  | 467.1<br>467.5 | 0.4 | **3d**, 6 |
|  | 466.7<br>466.8 | 0.1 | **3e**, 7 |

[a] Number of bonds from the stereogenic center to the selenium atom.

and temperature shifts, usually several ppm. The variation in the $\delta_{Se}$ values of compounds **(S)-3c** and **(R)-3c** in [$^2$H]chloroform solutions as a function of concentration is shown in Table 6. A chemical shift range of approximately 1.5 ppm was found. Although $\delta_{Se}$ is concentration dependent, it is safe to work in a fairly large concentration range without confusing the assignment of resonance peaks by taking advantage of the relatively small magnitude of the concentration shift (~1.5 ppm) compared to the relatively large separation (~3.6 ppm) of the diastereomeric signals.

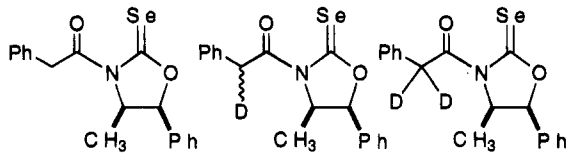
**(D) Effect of Structure.** A series of acylated norephedrine-derived selones were constructed in which the chiral center is sequentially one more bond removed from the observing selenium nucleus (Table 7). As expected, the $\Delta\delta_{Se}$ values for the pair of diastereomers decreased as the chiral center was further removed from the observing selenium nucleus. Interestingly, when the chiral center is moved from five to six bonds from the selenium atom, there is a significant drop in the magnitude of $\Delta\delta_{Se}$. This can be rationalized if the carbonyls are in an *anti* configuration, thereby placing the α- and β-methine groups within close proximity of the selenium atom. However, this "through-space" interaction is significantly diminished in the case of the γ-methine or methylene groups because of the increased distance between the chiral center and the selenium atom. Noteworthy was the fact that, even when the chiral center was seven bonds removed from the selenium, a clear separation of $\Delta\delta_{Se}$ = 0.1 ppm was still achieved for the pair of diastereomers.

**II. Limits of Detection of Remotely Disposed Chiral Centers by $^{77}$Se NMR Spectroscopy.** In an effort to establish the lower limit of detection of remotely disposed stereogenic centers by $^{77}$Se NMR spectroscopy, the racemate of lipoic acid was coupled to a wide variety of selone CDA's mediated by dicyclohexylcarbodiimide (DCC). To the best of our knowledge, other NMR chiral auxiliary agents have failed to distinguish the enantiomers of (*R,S*)-lipoic acid. In the mixture of diastereomers created from the coupling of the selones to racemic lipoic acid, the chiral center of the lipoyl group is eight bonds separated from the selenium atom. Remarkably,

**Table 8. $\Delta\delta_{Se}$ (ppm) of (*R,S*)-Lipoic Acid Adducts of Selones 1a–g[a]**

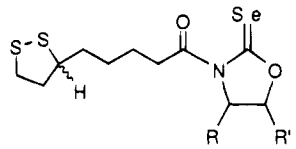
| adduct | parent selone | $\Delta\delta_{Se}$[b] | $\Delta\delta_{Se}$[c] |
|---|---|---|---|
| **6a** | **1g** | 0.4 | 0.2 |
| **6b** | **1c** | 0.3 | 0.3 |
| **6c** | **1a** | 0.1 | 0.2 |
| **6d** | **1d** | 0.2 | 0.1 |
| **6e** | **1b** | 0.3 | 0.06 |
| **6f** | **1e** | 0.3 | 0.2 |
| **6g** | **1f** | 0.3 | 0.06 |

[a] The yields of the DCC-mediated coupling ranged from 85 to 95%. [b] In [$^2$H]chloroform. [c] In [$^2$H$_6$]benzene.



4

**Figure 6.**



6a-6g

the $^{77}$Se NMR spectrum of the diastereomeric mixture featured two clearly resolved resonances in all cases, and some exhibited a $\Delta\delta_{Se}$ greater than 20 Hz (Table 8). As is the case with other acylated selones where the stereogenic center is in closer proximity to the observing nucleus, the use of [$^2$H$_6$]benzene as the NMR solvent did not serve to enhance $\Delta\delta_{Se}$. Examination of Table 8 reveals that the phenyl glycinol-derived selone **1g** gives rise to the greatest $\Delta\delta_{Se}$.

In an attempt to further elucidate the limits of this method, the deuterated acylated selone **4** was constructed (Figure 6). The $^{77}$Se NMR spectrum (in [$^2$H]chloroform) exhibited four resonances. The largest peak has been assigned to the fully protonated species, which has a chemical shift at $\delta_{Se}$ = 471.7 ppm.[20] The diastereomeric monodeuterated species exhibited observable $\Delta\delta_{Se}$ differences of 5 Hz. The most shielded peak has been assigned to the bis-deuterated species which resonates at $\delta_{Se}$ = 470.4 ppm. Not only is it remarkable that the selenium nucleus has the special ability to distinguish between a hydrogen and a deuterium five atoms removed, but it can also discern the presence of four different species (with $\Delta\delta_{Se}$ = 1.3 ppm). Clearly, from these results, we readily determined that deuterium incorporation was fortuitously incomplete even though the integration of the parent carboxylic acid $^1$H spectrum indicated ~95% deuterium incorporation.

In addition, we have constructed compound **5** (Figure 7), which contains an allenic stereogenic center, and we

(20) Silks, L. A.; Dunlap, R. B.; Odom, J. D. *J. Am. Chem. Soc.* **1990**, *112*, 4979.

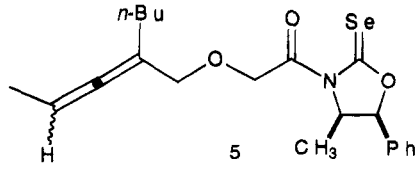



**Figure 7.**

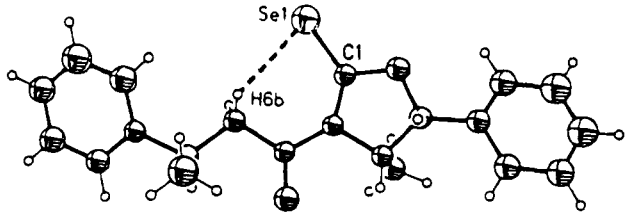



**Figure 8.** ORTEP diagram of **3c**.

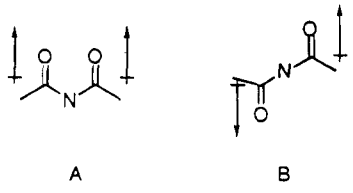



**Figure 9.**

have observed a measurable $\Delta\delta_{Se} = 10$ Hz. The detection and quantitation of chirality for allenes has traditionally been a difficult process. Again, the selenium reporter group of the norephedrine-derived selone is capable of detecting the stereogenic center which is eight bonds removed from the observed selenium nucleus.[21]

**III. Solid and Solution State Structures. Unusual Conformational Differences.** We have obtained crystal structures of two different acylated selones **3c** and the (*R*)-Mosher's acid (MTPA = α-methoxy-α-(trifluoromethyl)phenyl acetic acid) adduct of **(S)-1g**. The structure of epimer **3c** is provided in Figure 8. The crystal was orthorhombic with a unit cell $a = 9.150$ Å, $b = 23.664$ Å, $c = 8.451$ Å and a space group of $P2_12_12_1$. It was found that the distance between the selenium atom and C1 was 1.78 Å, which is shorter than that of the parent selone (1.82 Å). This discovery supports the theory of participation of the π orbitals from the adjacent carbonyl group in the acid moiety. The heterocyclic ring exists in a nearly planar conformation, suggesting an extended π-conjugated system. The selenocarbonyl and the carbonyl groups are *anti* to each other. Lee and Kumler[22] reported from dipole moment studies in cyclic carbamates that the *anti* conformation of carbonyls was preferred. A higher dipole moment would arise as the two carbonyl groups line up in the same direction, as shown in structure A (Figure 9). This orientation would be unfavorable due to electrostatic repulsion. The *anti* conformation of B has the two carbonyl groups farther apart and would, therefore, be the electrostatically favored arrangement. As a result of the *anti* conformation of the carbonyls, the α-methylene protons are ~2.87 Å from the selenium atom. This can be considered a "hard contact."

The structure of the (*R*)-MTPA adduct of **(S)-1g** is illustrated in Figure 10. The crystal was monoclinic with

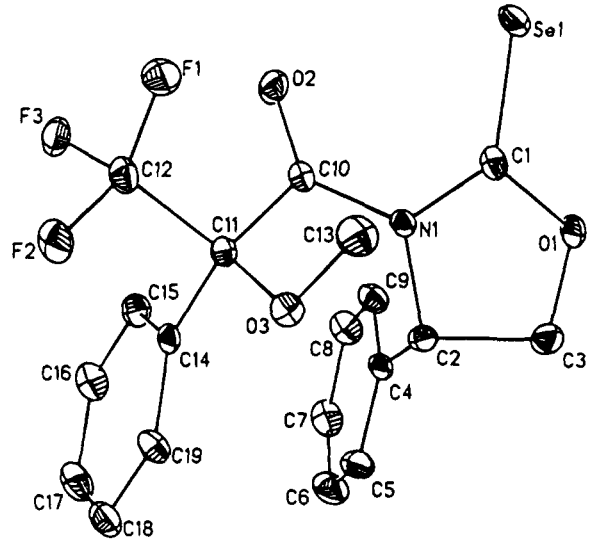



**Figure 10.** ORTEP diagram of (*R*)-MTPA–**1g**.

a unit cell $a = 18.538$ Å, $b = 6.138$ Å, and $c = 16.399$ Å and a space group of *C*2. It was found that the distance between the selenium atom and C1 was 1.79 Å, which is shorter than that observed in the selone. The heterocyclic ring is nearly planar. In contrast to **3c**, the carbonyl groups are in a *syn* orientation. This conformation allows for stacking of the aromatic rings which are 3.85 Å apart. However, it should be noted that the aromatic groups are not symmetrically stacked, with the MTPA phenyl group being slightly skewed out of plane. Using the X-ray coordinates for (*R*)-MTPA–**1g** and performing a rigid body rotation (optimized from the X-ray data[23] ) about the amide bond, we found that molecular modeling suggests that, for the (*R*)-MTPA derivatives, both the steric hindrance of the $OCH_3$ group with the selenium atom and the additional stabilization derived from the interaction of phenyl groups is sufficient to cause the carbonyls to adopt a *syn* orientation. It was found that, if the identical process was performed for the (*S*)-MTPA–**1g** adduct, the *anti* conformation was slightly favored. In addition, these data suggest that the barrier to rotation from the *syn* to *anti* conformation in (*R*)-MTPA–**1g** is greater than 200 kcal/mol.

Examination of the IR spectral data for the (*S*)-MTPA derivatives of both **1c** and **1g** indicates that the absorbances in the 1700 $cm^{-1}$ regions for both are similar, with a single absorbance noted for each. However, for the (*R*)-MTPA derivatives, the IR spectra (neat) possess multiple absorbances centered around 1700 $cm^{-1}$, which are indicative of the *syn* conformation. This anomaly can be explained if the (*S*)-MTPA adducts adopt an *anti* carbonyl arrangement in which there is one distinct chromophore, while the (*R*)-MTPA derivatives contain the *syn* conformation and therefore exhibit more than one carbonyl absorbance due to the lack of sigificant π overlap (and only one chromophore). The (*S*)-MTPA derivatives show shielded selenium resonances compared to the (*R*)-derivatives, signaling additional π overlap. The selone ring C4 proton for the (*S*)-MTPA adducts is deshielded ($\Delta\delta_H = 0.9$ for MTPA–**1g**, $\Delta\delta_H = 0.55$ ppm for MTPA–**1c**). The greatest $\Delta\delta_H$, however, is observed for the (*S*)-MTPA–**1c** methine proton which is deshielded compared to that of the (*R*)-MTPA diastereomer by 2.5 ppm. This

(21) The parent carboxylic acid was kindly provided by Professor James A. Marshall.
(22) Lee, C. M.; Kumler, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 4596.
(23) The molecular-modeling studies were performed on a Macintosh II fx running CAChe.

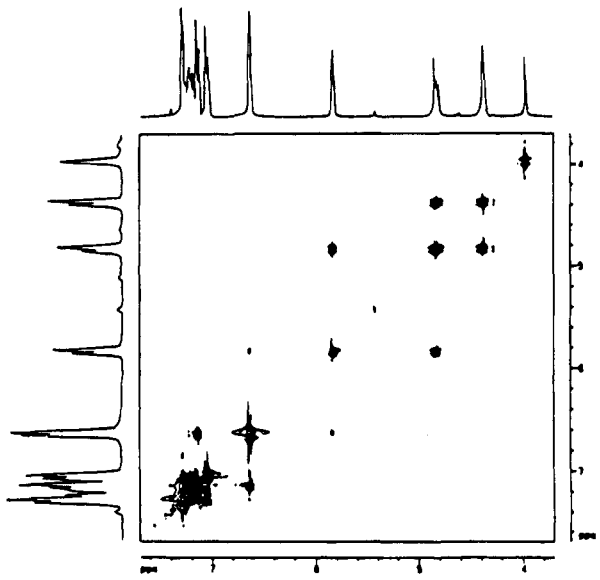


**Figure 11.** Two-dimensional $^1H,^1H$ COSY of (*R*)-MTPA–**1g**.

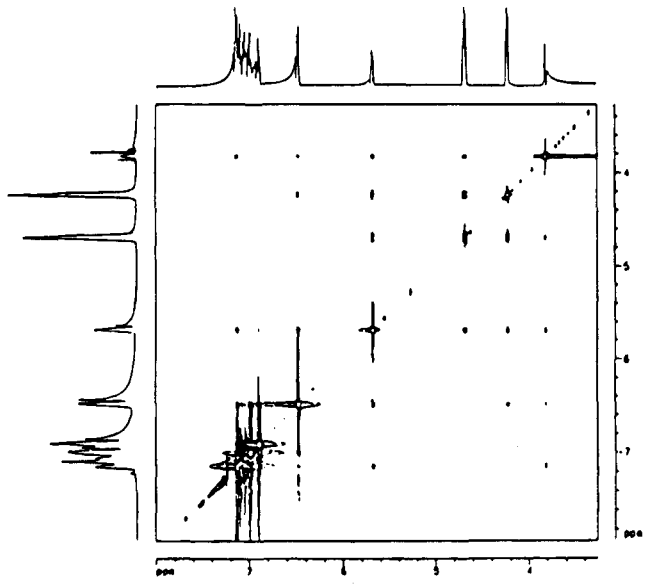


**Figure 12.** Two-dimensional $^1H,^1H$ NOESY of (*R*)-MTPA–**1g**.

extreme $\Delta\delta_H$ value can be explained if the methine proton is in the O–C–N plane and in close proximity to the *anti* acyl oxygen. Molecular-modeling results suggest that this is the case. In addition, it is now clear that the large $\Delta\delta_{Se}$ difference (113 ppm; largest to date) observed for the (*R*,*S*)-MTPA adducts of **1c** and **1g** is not due to their chirality differences, but mainly to the *anti* and *syn* conformations. Furthermore, it is now evident that the lack of a $\Delta\delta_F$ is primarily due to the large distance between the $CF_3$ group and the selone chiral center. In an effort to confirm the solution state conformation of both diastereomers, we have measured the two-dimensional $^1H,^1H$ NOESY and COSY spectra of (*R*)- and (*S*)-MTPA adducts of selone **1g**. In Figure 11, it is evident from the $^1H,^1H$ COSY for the (*R*)-MTPA–**1c** adduct that the phenyl group which is attached to the heterocylic ring can be assigned and that the ortho protons are coupling to the C4 methine proton on the ring. In addition, the 5(*R*)-methylene proton on the oxazolidine-2-selone ring is shielded compared to the 5(*S*) proton. It is clear from Figure 12 ($^1H,^1H$ NOESY) that the methoxy group is proximal to both the C4 and the 5(*S*)-protons, thereby suggesting a *syn* carbonyl relationship. The (*R*)-MTPA adduct lacks this type of NOE, thus suggesting *anti* carbonyls.

From these experiments, it is now clear why selone **1a** CDA is capable of observing "diastereotopic deuterons" in compound **4**. With the carbonyls in the *anti* position, compound **4**'s α-methylene protons are within ~2.8 Å of the observing selenium nucleus, thereby placing the selenium atom in a hard contact arrangement, and the selenium atom is able to sense small differences at this stereogenic center. In addition, we are now able to rationalize the small $\Delta\delta_{Se}$ value observed for **2f** and other acylated derivatives of selone **1f**. The diphenyl substituents could force the carbonyls into a *syn* conformation, placing the chiral center further from the observing selenium nucleus. The selenium atom would no longer benefit from a close through-space interaction and would have to rely on through-bond differences between the diastereomers to reveal the nature of the chiral center.

## Conclusion

The results presented underscore the importance of chiral selones as a new generation of CDA's which have at least halved the limits of detection of the agents currently employed. They are complementary to most of the existing CDA's in that they are useful with a variety of different functional groups, including carboxylic acids. Overall, these data indicate that the limits of detection of the remotely disposed centers with these CDA's remain to be elucidated. X-ray and NMR studies have uncovered an unusual *syn*/*anti* event in the (*R*)- and (*S*)-MTPA selone adducts which provides for an understanding of the large chemical shift differences observed for these compounds. Studies to increase the nature and number of functional groups which can be coupled and subsequently evaluated by $^{77}Se$ NMR spectroscopy with this new class of chiral CDA's are ongoing.

## Experimental Section

**General.** The $^1H$, $^{13}C$, $^{19}F$, and $^{77}Se$ NMR spectra were recorded as [$^2H$]chloroform solutions on IBM NR-80 or Bruker AM-200, AC-250, WM-300, AM-300, AM-500, or AMX-500 NMR spectrometers. $\delta_H$ values are expressed in parts per million with respect to tetramethylsilane at 0.0 ppm. $\delta_C$ values are referenced with respect to internal [$^2H$]chloroform ($\delta$ = 77.0 ppm with respect to tetramethylsilane at 0.0 ppm). $\delta_F$ values are referenced with respect to $CFCl_3$. $\delta_{Se}$ values are expressed in ppm with respect to a 60% (v/v) solution of $(CH_3)_2Se$ in [$^2H$]-chloroform (0 ppm).[24] Positive chemical shifts denote resonances deshielded with respect to the reference. IR spectra were recorded on a BioRad FTIR instrument unless otherwise noted. Mass spectra were measured on a VG 70SQ GC/MS spectrometer. Microanalyses were performed on a Perkin-Elmer elemental analyzer (CST-4, Los Alamos National Laboratory). Analytical thin-layer chromatography (TLC) was carried out on glass plates (silica gel 60, 250 μm thickness) obtained from Analtech. TLC visualization was accomplished with a UV lamp, $I_2$ staining, and an ethanolic solution of phosphomolybdic acid. Liquid chromatography separations were carried out on silica gel using the Still protocol.[25]

The acids, oxalyl chloride, and MTPA acid chlorides were obtained from Aldrich Chemical Co. and used without purification. DCC was purchased from Aldrich Chemical Co. and

(24) Luthra, N. P.; Dunlap, R. B.; Odom, J. D. *J. Magn. Reson.* **1983**, *52*, 318–322.
(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

distilled prior to use. Triethylamine was purchased from Sigma Chemical Co. and distilled from calcium hydride and stored over KOH. Methylene chloride was distilled from calcium hydride. Tetrahydrofuran was distilled from potassium benzophenone ketyl prior to use.

X-ray structure determinations were obtained on ENRAF-Nonius CAD4 and Seimens P3F diffractometers with crystals obtained from methylene chloride solutions. Details of data collection and structural refinement and tables of atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre and are available as supporting information.[26]

When possible, pairs of diastereomeric selone adducts were separated and isolated. This allowed for the unambiguous and simple data reduction of the spectra. The chromatography ratio of the distance moved by the substance and the distance moved by the solvent front, $R_f1$ and $R_f2$, is used to indicate either the slower or faster moving diastereomer, respectively. The accurate mass was calculated using either the $^{76}Se$ (9.36% natural abundance) or $^{80}Se$ (49.61% natural abundance) isotope. These were then compared to the values experimentally determined from the HRMS (using the natural abundance $^{76}Se$ or $^{80}Se$ from the compound "footprint" peaks).

**General Procedure for Selone Carboxylic Acid Adduct Formation.** To a dichloromethane solution containing 1.2 equiv of freshly distilled DCC was added dropwise a dichloromethane solution of the acid, at 0 °C. The mixture was then stirred at 0 °C for 1 h. To this mixture were added dropwise 1.2 equiv of triethylamine (neat) and a catalytic amount of *N,N'*-dimethylaminopyridine (5 mol %), followed by the selone. Generally for unhindered carbonyls, the reaction was complete in 1 h, during which time the solution became bright yellow (the progress of the reaction was also monitored by TLC). The product was purified using flash chromatography.

**(4*R*,5*S*)-3-(1-Oxo-2-phenylpropyl)-4-methyl-5-phenyloxazolidine-2-selones (2a):** IR ([$^2$H]chloroform) 3067, 3032, 2983, 2935, 1790, 1705, 1498, 1455, 1339, 1301, 1270, 1216, 1179, 1151, 1123, 962, 945 cm$^{-1}$; $^1$H NMR ([$^2$H]chloroform) $R_f1$ $\delta$ 0.69 (d, $J$ = 6.9 Hz, 3H), 1.58 (d, $J$ = 6.9 Hz, 3H), 4.97 (quint, $J$ = 6.4 Hz, 1H), 5.69 (d, $J$ = 6.9 Hz, 1H), 6.38 (q, $J$ = 6.9 Hz, 1H), 7.10–7.43 (m, 10H); $^{13}$C NMR $\delta$ 13.6, 18.9, 44.2, 59.4, 85.2, 126.2, 127.4, 128.3, 128.6, 129.0, 132.2, 139.5, 176.2, 188.4; $^1$H NMR $R_f2$ $\delta$ 1.00 (d, $J$ = 6.4 Hz, 3H), 1.57 (d, $J$ = 6.8 Hz, 3H), 4.83 (quint, $J$ = 6.9 Hz, 1H), 5.49 (d, $J$ = 6.9 Hz, 1H), 6.42 (q, $J$ = 6.8 Hz, 1H), 7.26–7.43 (m, 10H); $^{13}$C NMR $\delta$ 14.1, 19.2, 43.1, 60.8, 84.8, 125.9, 127.3, 128.2, 128.6, 129.0, 131.7, 140.1, 176.1, 188.2; $^{77}$Se NMR $\delta$ 477.3 ($R_f2$), 429.3 ($R_f1$); HRMS $m/z$ calcd for $C_{19}H_{19}NO_2{}^{80}Se$ 373.0581, found 373.0579. Anal. Calcd for $C_{19}H_{19}NO_2Se$: C, 61.29; H, 5.14; N, 3.76. Found: C, 61.03; H, 5.26; N, 3.22.

**(4*S*)-3-(1-Oxo-2-phenylpropyl)-4-*tert*-butyloxazolidine-2-selones (2b):** IR 2971, 2934, 1708, 1482, 1454, 1349, 1323, 1277, 1211, 1175, 1128, 1052, 1030, 930 cm$^{-1}$; $^1$H NMR ([$^2$H]-chloroform) $R_f1$ $\delta$ 0.61 (s, 9H), 1.49 (d, $J$ = 6.7 Hz, 3H), 4.24 (dd, $J$ = 9.6, 8.1 Hz, 1H), 4.36 (dd, $J$ = 9.6, 2.0 Hz, 1H), 4.76 (dd, $J$ = 9.6, 2.0 Hz, 1H), 6.62 (q, $J$ = 6.7 Hz), 7.18–7.53 (m, 5H); $^{13}$C NMR $\delta$ 18.6, 25.3, 36.0, 42.3, 65.7, 70.8, 127.5, 128.6 (2C), 140.1, 176.1, 190.6; $^1$H NMR $R_f2$ $\delta$ 0.91 (s, 9H), 1.55 (d, $J$ = 7.1 Hz, 3H), 4.03 (dd, $J$ = 7.4, 9.4 Hz, 1H), 4.33 (dd, $J$ = 1.5, 9.7 Hz, 1H), 4.65 (dd, $J$ =1.5, 9.7 Hz, 1H), 6.40 (q, $J$ = 6.7 Hz), 7.19–7.27 (m, 5H); $^{13}$C NMR $\delta$ 20.3, 25.9, 36.2, 42.6, 66.9, 70.6, 127.2, 128.5 (2C), 139.9, 175.6, 191.5; $^{77}$Se NMR $\delta$ 447.8 ($R_f1$), 490.9 ($R_f2$); HRMS $m/z$ calcd for $C_{16}H_{21}NO_2{}^{76}Se$ 335.0764, found 335.0753.

**(4*S*)-3-(1-Oxo-2-phenylpropyl)-4-(1-methylethyl)-oxazolidine-2-selones (2c):** IR 2970, 2934, 1787, 1708, 1482, 1455, 1362, 1311, 1275, 1199, 1184, 1145, 1070, 1012, 932 cm$^{-1}$; $^1$H NMR ([$^2$H]chloroform) $R_f1$ $\delta$ 0.33 (d, $J$ = 7 Hz, 3H), 0.82 (d, $J$ = 7 Hz, 3H), 1.46–1.51 (m, 1H), 4.20–4.34 (m, 2H), 4.68–4.73 (m, 1H), 6.48 (q, $J$ = 7 Hz, 1H), 7.14–7.39 (m, 5H); $^{13}$C NMR $\delta$ 13.8, 18.2, 18.8, 27.9, 43.4, 63.6, 68.8, 127.4, 128.3, 128.5, 139.6, 176.0, 188.9; $^1$H NMR $R_f2$ $\delta$ 0.73 (d, $J$ = 7 Hz, 3H), 0.83 (d, $J$ = 7 Hz, 3H), 2.34–2.40 (m, 1H), 4.09 (dd, $J$ = 8.0, 8.0 Hz, 2H), 4.28 (dd, $J$ = 2.4, 9.4 Hz, 1H), 4.47–4.52 (m, 1H), 6.36 (q, $J$ = 7 Hz, 1H), 7.14–7.31 (m, 5H); $^{13}$C NMR $\delta$ 15.0, 18.1, 19.6, 29.4, 42.9, 65.3, 69.0, 127.3, 128.3, 128.5, 140.0, 176.1, 189.3; $^{77}$Se NMR $\delta$ 412.7 ($R_f1$), 444.4 ($R_f2$); HRMS $m/z$ calcd for $C_{15}H_{19}NO_2{}^{76}Se$ 322.0651, found 322.0612. Anal. Calcd for $C_{15}H_{19}NO_2{}^{77}Se$: C, 55.56; H, 5.91; N, 4.32. Found: C, 55.74; H, 5.89; N, 3.97.

**(4*S*)-3-(1-Oxo-2-phenylpropyl)-4-benzyloxazolidine-2-selones (2d):** IR 3066, 3031, 2962, 2929, 1736, 1703, 1497, 1455, 1350, 1298, 1278, 1196, 1180, 1140, 1096, 1012, 937 cm$^{-1}$; $^1$H NMR ([$^2$H]chloroform) $R_f1$ $\delta$ 1.59 (d, $J$ = 6.7 Hz, 3H), 2.41 (dd, $J$ = 10.7, 13.4 Hz, 1H), 3.05 (dd, $J$ = 3.4, 13.4 Hz, 1H), 4.22–4.30 (m, 2H), 4.90–5.10 (m, 1H), 6.45 (q, $J$ = 6.7 Hz, 1H), 7.03–7.49 (m, 10H); $^{13}$C NMR $\delta$ 19.3, 37.2, 43.4, 60.5, 72.2, 127.3, 127.4, 128.4, 128.6, 128.9, 129.1, 134.8, 139.5, 176.1, 188.6; $^1$H NMR $R_f2$ $\delta$ 1.60 (d, $J$ = 7 Hz, 3H), 2.81 (dd, $J$ = 10.4, 14.3 Hz, 1H), 3.37 (dd, $J$ = 3.2, 10.4 Hz, 1H), 4.04 (dd, $J$ = 7.4, 9.4 Hz, 2H), 4.27 (dd, $J$ = 2.0, 9.4 Hz, 1H), 4.70-4.90 (m, 1H), 6.43 (q, $J$ = 7 Hz, 1H), 7.21–7.41 (m, 10H); $^{13}$C NMR $\delta$ 14.2, 37.4, 42.9, 61.7, 71.7, 127.3, 127.4, 128.2, 128.5, 129.0, 129.3, 135.1, 140.0, 176.1, 188.6; $^{77}$Se NMR $\delta$ 413.6 ($R_f1$), 454.8 ($R_f2$); HRMS $m/z$ calcd for $C_{19}H_{19}NO_2{}^{80}Se$ 373.0581, found 373.0582. Anal. Calcd for $C_{19}H_{19}NO_2Se$: C, 61.29; H, 5.14; N, 3.76. Found: C, 61.48; H, 4.88; N, 3.61.

**(4*S*)-3-[(1-Oxo-2-phenylpropyl)phenyl]-4-(2-methylpropyl)oxazolidine-2-selones (2e):** IR 2963, 2934, 1787, 1704, 1467, 1455, 1356, 1338, 1294, 1276, 1198, 1183, 1140, 1071, 1031, 933 cm$^{-1}$; $^1$H NMR ([$^2$H]chloroform) $R_f1$ $\delta$ 0.84 (d, $J$ = 6.3 Hz, 3H), 0.88 (d, $J$ = 6.1 Hz, 3H), 1.12–1.18 (m, 1H), 1.38–1.46 (m, 2H), 1.56 (d, $J$ = 7.1 Hz, 3H), 4.17 (dd, $J$ = 9.0, 5.1 Hz, 1H), 4.51 ($t_{app}$, $J$ = 9.0 Hz, 1H), 4.70–4.90 (m, 1H), 4.90–5.10 (m, 1H), 6.36 (q, $J$ = 7.1 Hz, 1H), 7.26–7.44 (m, 5H); $^{13}$C NMR $\delta$ 18.8, 21.3, 23.3, 25.0, 40.3, 44.0, 58.6, 73.4, 127.4, 123.4, 128.6, 139.5, 176.2, 188.7; $^1$H NMR $R_f2$ $\delta$ 0.96 (d, $J$ = 6.0 Hz, 6H), 1.56 (d, $J$ = 6.9 Hz, 3H), 1.5–1.6 (m, 2H), 1.7–1.8 (m, 1H), 4.22–4.26 (m, 2H), 4.60–4.65 (m, 1H), 6.40 (q, $J$ = 6.9 Hz, 1H), 7.21–7.39 (m, 5H); $^{13}$C NMR $\delta$ 19.4, 21.3, 23.4, 25.1, 40.5, 42.9, 59.6, 72.8, 127.3, 128.3, 128.6, 140.0, 176.0, 188.7; $^{77}$Se NMR $\delta$ 414.2 ($R_f1$), 452.9 ($R_f2$); HRMS $m/z$ calcd for $C_{16}H_{21}NO_2{}^{80}Se$ 339.0737, found 339.0743. Anal. Calcd for $C_{16}H_{21}NO_2Se$: C, 56.81; H, 6.26; N, 4.14. Found: C, 57.14; H, 6.10; N, 3.86.

**(4*S*,5*R*)-3-[(1-Oxo-2-phenylpropyl)phenyl]-4,5-diphenyloxazolidine-2-selones (2f):** IR 3068, 3034, 2981, 2933, 1791, 1711, 1469, 1456, 1357, 1334, 1264,1173, 1144, 1082, 1046, 1030, 1006, 949, 934 cm$^{-1}$; $^1$H NMR ([$^2$H]chloroform) $R_f1$ $\delta$ 1.56 (d, $J$ = 6.9 Hz, 3H), 5.97 (m, 1H), 6.62 (q, $J$ = 6.9 Hz, 1H), 6.44 (d, $J$ = 6.4 Hz, 2H), 6.93–7.01 (m, 4H), 7.07–7.14 (m, 3H), 7.25–7.35 (m, 5H); $^{13}$C NMR $\delta$ 20.0, 44.3, 67.6, 86.2, 126.3, 126.5, 126.8, 127.2, 128.0, 128.2, 128.3, 128.5, 128.52, 128.6, 132.1, 133.1, 139.3, 175.0, 188.9; $^1$H NMR $R_f2$ $\delta$ 1.53 (d, $J$ = 6.9 Hz, 3H), 5.69 (d, $J$ = 7.3 Hz, 1H), 5.73 (d, $J$ = 7.3 Hz, 1H), 6.44 (q, $J$ = 6.9 Hz, 1H), 6.89–7.07 (m, 3H), 7.12–7.15 (m, 6H), 7.25–7.45 (m, 6H); $^{13}$C NMR $\delta$ 19.2, 43.2, 68.8, 86.0, 126.45, 126.49, 127.4, 128.0, 128.2, 128.36, 128.45, 128.7 (2C), 131.2, 133.8, 140.1, 175.6, 189.3; $^{77}$Se NMR $\delta$ 406.9 ($R_f2$), 464.7 ($R_f1$); HRMS $m/z$ calcd for $C_{24}H_{21}NO_2{}^{80}Se$ 435.0737, found: 435.0746. Anal. Calcd for $C_{24}H_{21}NO_2Se$: C, 66.36; H, 4.87; N, 3.22. Found: C, 66.33; H, 5.02; N, 3.15.

**(4*R*)-3-(1-Oxo-2-phenylpropyl)-4-phenyloxazolidine-2-selones (2g):** IR 3067, 3034, 2976, 2935, 1789, 1713, 1495, 1456, 1375, 1334, 1267, 1195, 1138, 1061, 1031, 929 cm$^{-1}$; $^1$H NMR ([$^2$H]chloroform) isomers could not be separated $\delta$ 1.37 (d, $J$ = 7.0 Hz, 6H), 4.20 (dd, $J$ = 7.1, 9.4 Hz, 1H), 4.31 (dd, $J$ = 3.0, 9.4 Hz, 1H), 4.50 (t, $J$ = 8.6 Hz, 1H), 4.68 (t, $J$ = 9.4 Hz, 1H), 5.47 (dd, $J$ = 3.0, 8.6 Hz, 1H), 5.55 (dd, $J$ = 7.1, 9.4 Hz, 1H), 6.23 (q, $J$ = 7.0 Hz, 1H), 6.33 (q, $J$ = 7.0 Hz), 6.8–7.4 (m, 10H); $^{13}$C NMR $\delta$ 18.6, 19.3, 43.1, 44.4, 63.4, 63.7, 75.4 (2C), 125.9, 126.6, 127.2, 128.3, 128.5, 128.9, 129.3, 136.0, 138.3, 138.7, 139.9, 175.1, 175.5, 188.6 (2C); $^{77}$Se NMR $\delta$ 412.2, 449.4; HRMS $m/z$ calcd for $C_{18}H_{17}NO_2{}^{80}Se$ 359.0424, found

(26) The authors have deposited atomic coordinates for **3c** and the (*R*)-MTPA adduct of **1g** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, DB2 1EZ, U.K.

359.0426. Anal. Calcd for $C_{18}H_{17}NO_2Se$: C, 60.30; H, 4.78; N, 3.91. Found: C, 60.08; H, 5.02; N, 3.65.

**(4*S*)-3-(1-Oxo-2-phenylpropyl)-4-propyloxazolidine-2-selones (2h):** IR 2965, 1707, 1543, 1455, 1354, 1285, 1198, 1142, 917 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) *Rf*1 $\delta$ 0.71 (t, $J$ = 7.1 Hz, 3H), 0.81 ($t_{app}$, $J$ = 7.3 Hz, 1H), 0.90 ($t_{app}$, $J$ = 5.0 Hz, 1H), 1.04–1.17 (m, 1H), 1.19–1.29 (m, 2H), 1.48 (d, $J$ = 6.7 Hz, 3H), 4.12 (dd, $J$ = 5.1, 9.1 Hz, 1H), 4.41 ($t_{app}$, $J$ = 9.1 Hz, 1H), 4.60–4.80 (m, 1H), 6.34 (q, $J$ = 6.7 Hz, 1H), 7.14–7.32 (m, 5H); $^{13}C$ NMR $\delta$ 13.5, 17.4, 18.8, 33.2, 43.8, 59.5, 72.9, 127.4, 128.4, 128.6, 139.6, 176.2, 188.9; $^1H$ NMR *Rf*2 $\delta$ 0.90 (t, $J$ = 7.1 Hz, 3H), 1.20–1.35 (m, 2H), 1.49 (d, $J$ = 6.7 Hz, 3H), 1.60–1.85 (m, 2H), 4.17 (dd, $J$ = 2.0, 5.4 Hz, 2H), 4.45–4.60 (m, 1H), 6.34 (q, $J$ = 6.7 Hz, 1H), 7.14–7.32 (m, 5H); $^{13}C$ NMR $\delta$ 13.7, 17.9, 19.5, 34.1, 43.0, 60.7, 72.6, 127.3, 128.3, 128.6, 140.0, 176.1, 188.8; $^{77}Se$ NMR $\delta$ 406.9 (*Rf*1), 442.4 (*Rf*2); HRMS $m/z$ calcd for $C_{15}H_{19}NO_2{}^{76}Se$ 321.0608, found 321.0608.

**(4*S*)-3-(1-Oxo-2-phenylpropyl)-4-butyloxazolidine-2-selones (2i):** IR 2962, 1706, 1545, 1455, 1352, 1278, 1142, 914 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) *Rf*1 $\delta$ 0.69 (t, $J$ = 7.0 Hz, 3H), 0.81–0.99 (m, 2H), 1.0–1.2 (m, 2H), 1.2–1.4 (m, 2H), 1.48 (d, $J$ = 6.7, 3H), 4.11 (dd, $J$ = 5.4, 9.1 Hz, 1H), 4.42 ($t_{app}$, $J$ = 9.1 Hz, 1H), 4.60–4.80 (m, 1H), 6.34 (q, $J$ = 6.7 Hz, 1H), 7.15–7.37 (m, 5H); $^{13}C$ NMR $\delta$ 13.7, 18.7, 22.2, 25.9, 30.8, 43.9, 59.6, 72.9, 127.5, 128.4, 128.6, 139.6, 176.2, 188.8; $^1H$ NMR *Rf*2 $\delta$ 0.90 (t, $J$ = 7.1 Hz, 3H), 1.20–1.40 (m, 4H), 1.54 (d, $J$ = 7.0 Hz, 3H), 1.60–1.85 (m, 2H), 4.22 (m, 1H), 4.53–4.58 (m, 1H), 6.39 (q, $J$ = 7.0 Hz, 1H), 7.19–7.37 (m, 5H); $^{13}C$ NMR $\delta$ 13.8, 19.4, 22.2, 26.6, 31.6, 42.9, 50.8, 72.6, 127.3, 128.3, 128.5, 149.0, 176.1, 188.1; $^{77}Se$ NMR $\delta$ 404.4 (*Rf*1), 441.8 (*Rf*2); HRMS $m/z$ calcd for $C_{16}H_{21}NO_2{}^{76}Se$ 335.0764, found 335.0761.

**(4*R*,5*S*)-3-(1-Oxo-2-phenylbutyl)-4-methyl-5-phenyloxazolidine-2-selones (2j):** IR 3067, 3032, 2969, 2934, 2876, 1704, 1498, 1456, 1351, 1338, 1304, 1261, 1178, 1150, 1123, 979, 946 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) (the diastereomers were not separated) $\delta$ 0.65 (d, $J$ = 7 Hz, 3H), 0.92 (t, $J$ = 6.7 Hz, 3H), 0.93 (t, $J$ = 6.7 Hz, 3H), 0.97 (d, $J$ = 7 Hz, 3H), 1.86 (m, 2H), 2.17 (m, 2H), 4.83 (m, 1H), 4.97 (m, 1H), 5.50 (d, $J$ = 7.0 Hz, 3H), 5.89 (d, $J$ = 7.0 Hz, 3H), 6.30 (m, 2H), 7.17–7.42 (m, 10H); $^{13}C$ NMR $\delta$ 11.9, 13.7, 27.2, 51.0, 59.4, 85.1, 126.2, 127.4, 128.5, 128.6, 128.9, 129.0, 132.3, 137.8, 175.6, 188.4; $^{77}Se$ NMR $\delta$ 428.8, 467.6; HRMS $m/z$ calcd for $C_{20}H_{21}NO_2{}^{80}Se$ 387.0737, found 387.0732. Anal. Calcd for $C_{20}H_{21}NO_2Se$: C, 62.17; H, 5.76; N, 3.63. Found: C, 62.19; H, 5.42; N, 3.65.

**(4*S*,5*R*)-3-(2-Methyl-1-oxopentyl)-4-methyl-5-phenyloxazolidine-2-selones (3a):** IR 2961, 1705, 1465, 1339, 1269, 1187, 1145, 972 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) (the diastereomers were not separated) $\delta$ 0.90–1.00 (m, 6H), 1.20–1.30 (m, 4H), 1.30–150 (m, 4H), 4.7–5.1 (m, 2H), 5.60–5.70 (m, 1H), 7.30–7.40 (m, 5H); $^{13}C$ NMR $\delta$ 14.5, 14.6, 14.7, 17.3, 17.4, 20.4, 20.8, 36.2, 36.5, 38.0, 38.2, 60.0, 60.4, 85.2, 85.3, 126.0–132.6 (6C), 179.0, 188.8; $^{77}Se$ NMR $\delta$ 452.5, 449.4; HRMS $m/z$ calcd $C_{16}H_{21}NO_2{}^{80}Se$ 339.0738, found 339.0722 (4 ppm error). Anal. Calcd for $C_{16}H_{21}NO_2Se$: C, 56.81; H, 6.26. Found: C, 57.11; H, 6.30.

**(4*S*,5*R*)-3-(3-Methyl-1-oxopentyl)-4-methyl-5-phenyloxazolidine-2-selones (3b):** IR 2964, 1708, 1456, 1355, 1271, 1187, 1123, 976 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.9–1.0 (m, 9H), 1.2–1.4 (m, 2H), 2.0–2.2 (m, 1H), 3.2–3.6 (m, 2H), 4.99 (m, 1H), 5.70 (d, $J$ = 7.4 Hz, 1H), 7.3–7.4 (m, 5H); $^{13}C$ NMR $\delta$ 11.7, 14.7, 19.5, 29.6, 29.7, 31.8, 31.9, 44.9, 45.0, 60.1, 85.4, 126.4–132.5, 174.0, 189.0; $^{77}Se$ NMR $\delta$ 449.4 (*R*), 454.5 (*S*); HRMS $m/z$ calcd for $C_{16}H_{21}NO_2{}^{80}Se$ 339.0738, found 339.0745. Anal. Calcd for $C_{16}H_{21}NO_2Se$: C, 56.81; H, 6.26. Found: C, 56.98; H, 6.16.

**(4*S*,5*R*)-3-(3-Phenyl-1-oxobutyl)-4-methyl-5-phenyloxazolidine-2-selones (3c):** IR 2963, 1707, 1455, 1355, 1265, 1187, 1148, 987 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) *S* $\delta$ 0.87 (d, $J$ = 6.7 Hz, 3H), 1.37 (d, $J$ = 7.0 Hz, 3H), 3.45 (m, 1H), 3.72 (dd, $J$ = 6.2, 16.6 Hz, 1H), 3.94 (dd, $J$ = 8.4, 16.6 Hz, 1H), 4.78 (m, 1H), 5.46 (d, $J$ = 7.3 Hz, 1H), 7.17–7.42 (m, 10H); $^1H$ NMR *R* $\delta$ 0.79 (d, $J$ = 6.6 Hz, 3H), 1.33 (d, $J$ = 7.0 Hz, 3H), 3.47 (m, 1H), 3.75 (dd, $J$ = 7.5, 16.9 Hz, 1H), 3.86 (dd, $J$ = 6.8, 16.9 Hz, 1H), 4.91 (m, 1H), 5.67 (d, $J$ = 7.5 Hz, 1H), 7.20–7.40 (m, 10H); $^{13}C$ NMR *S* $\delta$ 14.6, 23.0, 37.3, 45.9, 60.2, 85.6, 126.1–146.1, 173.3, 189.1; $^{13}C$ NMR *R* $\delta$ 14.5, 22.7, 36.8, 46.0, 60.0, 85.6, 126.4–146.0, 173.3, 189.0; $^{77}Se$ NMR $\delta$ 465.27 (*R*), 468.82 (*S*); HRMS $m/z$ calcd for $C_{20}H_{21}NO_2{}^{80}Se$ 387.0737, found 387.0742. Anal. Calcd for $C_{20}H_{21}NO_2Se$: C, 62.17; H, 5.76. Found: C, 61.80; H, 5.69.

**(4*S*,5*R*)-3-(4-Methyl-1-oxoheptyl)-4-methyl-5-phenyloxazolidine-2-selones (3d):** IR 2959, 1707, 1456, 1340, 1271, 1186, 1124, 946 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.8–1.0 (m, 9H), 1.1–1.4 (m, 4H), 1.4–1.6 (m, 2H), 1.6–1.8 (m, 1H), 3.3–3.6 (m, 2H), 4.94–4.99 (m, 1H), 5.70 (d, $J$ = 7.4 Hz, 1H), 7.3–7.4 (m, 5H); $^{13}C$ NMR $\delta$ 14.7, 14.75, 19.9, 20.5, 31.9, 32.5, 36.5, 39.5, 60.1, 85.5, 126.4, 129.1, 129.4, 132.5, 175.0, 188.9; $^{77}Se$ NMR $\delta$ 467.1, 467.5; HRMS $m/z$ calcd for $C_{18}H_{25}NO_2{}^{80}Se$ 367.1051, found 367.1055.

**(4*S*,5*R*)-3-(5-Methyl-1-oxoheptyl)-4-methyl-5-phenyloxazolidine-2-selones (3e):** IR 2961, 1707, 1456, 1345, 1271, 1184, 1123, 948 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.8–0.9 (m, 6H), 1.1–1.5 (m, 4H), 1.5–1.8 (m, 3H), 3.3–3.5 (m, 2H), 4.99 (m, 1H), 5.70 (d, $J$ = 7.4 Hz, 1H), 7.3–7.4 (m, 5H); $^{13}C$ NMR $\delta$ 11.7, 14.7, 19.5, 22.7, 29.7, 34.6, 36.2, 38.8, 60.1, 85.5, 126.6, 129.1, 129.2, 133.4, 174.6, 188.9; $^{77}Se$ NMR $\delta$ 466.7, 466.8; HRMS $m/z$ calcd for $C_{18}H_{25}NO_2{}^{76}Se$ 363.1077, found 363.1076. Anal. Calcd for $C_{18}H_{25}NO_2Se$: C, 59.01; H, 6.88. Found: C, 58.72; H, 6.77.

**(4*R*,5*S*)-3-[2-($^1H_2/^1H,^2H/^2H_2$)-2′-Phenyl-1-oxoethyl]-4-methyl-5-phenyl-oxazolidine-2-selones (4):** IR 2929, 1704, 1497, 1454, 1352, 1189, 980, 939 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.93 (d, $J$ = 6.6 Hz, 3H), 4.99 ($dd_{app}$, $J$ = 7.1, 7.4 Hz, 2H), 4.97 (m, 1H), 5.68 (d, $J$ = 7.4 Hz, 1H), 7.29–7.39 (m, 5H); $^2H$ NMR ([$^1H$]chloroform) $\delta$ 4.89 (bs, $1^2H$); $^{13}C$ NMR $\delta$ 14.2, 43.6 (for monodeuterated derivative, $J_{^{13}C\text{-}^2H}$ = 20.4 Hz), 44.0 (for perprotonated derivative), 60.0, 85.2, 126, 127.2, 128.5, 128.7, 129.1, 129.8, 131.9, 133.5, 172.3, 188.7; $^{77}Se$ NMR$\delta$ 471.8 (perprotonated), 471.1 (monodeuterated), 471.0 (monodeuterated), 470.4 (perdeuterated), ([$^2H_6$]benzene) 485.3 (perprotonated), 484.58 (monodeuterated), 484.49 (monodeuterated), 483.8 (perdeuterated); HRMS $m/z$ calcd for $C_{18}H_{17}NO_2{}^{80}Se$ 359.0426, found 359,0424.

**(4*R*,5*S*)-3-[2(-(2-Butyl-penta-2,3-dienyl)oxy]-1-oxoethyl]-4-methyl-5-phenyloxazolidine-2-selones (5):** IR 2933, 2856, 2119, 1708, 1550, 1450, 1359, 1299, 1192, 1046, 972 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.87 (d, $J$ = 7.1 Hz, 3H), 0.93 (d, $J$ = 6.6 Hz, 3H), 1.1–1.6 (m, 4H), 1.65 (d, $J$ = 5.0 Hz, 3H), 2.18–2.2 (m, 2H), 4.07–4.12 (m, 2H), 5.00–5.29 (m, 4H), 5.76 (d, $J$ = 7.4 Hz, 1H), 7.29–7.39 (m, 5H); $^{13}C$ NMR $\delta$ 14.4, 14.7, 15.2, 22.8, 29.6, 30.1, 60.1, 71.8, 73.5, 86.4, 87.1, 100.1, 126.4, 129.2, 129.6, 132.2, 171.5, 188.1; $^{77}Se$ NMR $\delta$ 473.4, 473.5; low resolution mass spectrum $m/z$ calcd for $C_{21}H_{27}NO_3{}^{80}Se$ 421.1, found 421.1.

**(4*S*)-3-[5-(1,2-Dithiolan-3-yl)-1-oxopentyl]-4-phenyloxazolidine-2-selones (6a):** IR 3370, 3024, 2921, 2854, 1705, 1697, 1643, 1451, 1370, 1334, 1273, 1194, 1146 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 1.25–1.50 (m, 2H), 1.60–1.73 (m, 4H), 1.79–1.90 (m, 1H), 2.35–2.45 (m, 1H), 3.02–3.13 (m, 2H), 4.35 (dd, $J$ = 3.2, 9.1 Hz, 1H), 4.69 (t, $J$ = 9.1 Hz, 1H), 5.61 (dd, $J$ = 3.2, 9.2 Hz, 1H), 7.2–7.4 (m, 5H); $^{13}C$ NMR $\delta$ 24.1, 28.3, 34.5, 38.0, 38.4, 40.1, 56.2, 52.9, 75.7, 126.0, 128.9, 129.2, 138.2, 173.3, 188.6; $^{77}Se$ NMR $\delta$ 461.7, 462.5 ([$^2H_6$]benzene), 454.4, 454.0 ([$^2H$]chloroform); HRMS $m/z$ calcd for $C_{17}H_{21}NO_2S_2{}^{76}Se$ 411.0206, found 411.0204.

**(4*S*)-3-[5-(1,2-Dithiolan-3-yl)-1-oxopentyl]-4-(1-methylethyl)oxazolidine-2-selones (6b):** IR 2959, 2922, 2867, 1781, 1707, 1467, 1372, 1314, 1274, 1182, 1145, 1003, 940 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.84 (d, $J$ = 7.0 Hz, 3H), 0.87 (d, $J$ = 7.0 Hz, 3H), 1.49–1.56 (m, 2H), 1.67–1.72 (m, 4H), 1.84–1.95 (m, 1H), 2.26–2.39 (m, 1H), 2.40–2.50 (m, 1H), 3.02–3.20 (m, 2H), 3.3–3.41 (m, 1H), 3.49–3.56 (m, 2H), 4.33 (dd, $J$ = 9.4 Hz, 9.4, 1H), 4.39 (dd, $J$ = 3.4, 9.4, 1H), 4.63–4.69 (m, 1H); $^{13}C$ NMR $\delta$ 14.7, 17.9, 24.1, 28.2, 28.6, 34.3, 37.6, 38.2, 39.9, 56.0, 63.8, 69.2, 173.4, 188.9; $^{77}Se$ NMR $\delta$ 466.6, 466.2 ([$^2H_6$]benzene), 459.8, 459.5 ([$^2H$]chloroform); HRMS $m/z$ calcd for $C_{14}H_{23}NO_2S_2{}^{76}Se$ 377.0362, found 377.0360. Anal. Calcd for $C_{14}H_{23}NO_2S_2Se$: C, 44.20; H, 6.09; N, 3.68. Found: C, 44.21; H, 6.24; N, 3.56.

**(4*S*,5*R*)-3-[5-(1,2-Dithiolan-3-yl)-1-oxopentyl]-4-methyl-5-phenyloxazolidine-2-selones (6c):** known; $^{77}Se$ NMR $\delta$ 480.0, 479.8 ([$^2H_6$]benzene), 468.1, 468.0 ([$^2H$]chloroform).

**(4*S*)-3-[5-(1,2-Dithiolan-3-yl)-1-oxopentyl]-4-benzyloxazolidine-2-selones (6d):** IR 2979, 2931, 2857, 1730, 1451, 1368, 1299, 1245, 1202, 1139, 1095, 1028 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 1.20–1.40 (m, 2H), 1.64–1.74 (m, 4H), 1.84–1.91 (m, 2H), 2.2-2.47 (m, 2H), 2.72 (dd, $J$ = 9.9, 13.3 Hz, 1H), 3.00–3.20 (m, 3H), 3.30–3.44 (m, 1H), 3.46–3.60 (m, 2H), 4.21 (dd, $J$ = 7.3, 9.4 Hz, 1H), 4.29 (dd, $J$ = 2.7, 9.4 Hz, 1H), 4.89 (m, 1H), 7.14–7.31 (m, 5H); $^{13}C$ NMR $\delta$ 24.1, 28.4, 34.5, 37.4, 37.8, 38.4, 40.1, 56.1, 60.5, 72.0, 127.3, 128.8, 129.2, 134.9, 173.6, 188.5; $^{77}Se$ NMR $\delta$ 480.3, 480.2 ([$^2H_6$]benzene), 466.6, 466.4([$^2H$]chloroform); HRMS $m/z$ calcd for $C_{18}H_{23}NO_2S_2{}^{76}Se$ 425.0362, found 425.0349.

**(4*S*)-3-[5-(1,2-Dithiolan-3-yl)-1-oxopentyl]-4-(2,2-dimethylethyl)-oxazolidine-2-selones (6e):** IR 3016, 2967, 2930, 2873, 1708, 1474, 1350, 1326, 1280, 1211, 1164, 1132, 1066, 971, 930 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.86 (s, 9H), 1.40–1.55 (m, 2H), 1.60–1.75 (m, 2H), 1.87 ($sep_{app}$, $J$ = 6.8 Hz, 1H), 3.03 ($Sep_{app}$, $J$ = 6.8 Hz, 1H), 3.00–3.30 (m, 2H), 3.30–3.60 (m, 3H), 4.22 (dd, $J$ = 7.8, 10.1 Hz, 1H), 4.40 (dd, $J$ = 1.8, 10.1 Hz, 1H), 4.75 (dd, $J$ = 1.8, 7.8 Hz, 1H); $^{13}C$ NMR ([$^2H_6$]benzene) $\delta$ 25.1, 25.7, 28.9, 35.0, 35.9, 38.3, 38.6, 40.2, 56.5, 65.8, 70.5, 173.2, 190.6; $^{77}Se$ NMR $\delta$ 488.83, 488.77 ([$^2H_6$]-benzene), 473.2, 472.9 ([$^2H$]chloroform); HRMS $m/z$ calcd $C_{15}H_{25}NO_2S_2{}^{76}Se$ 391.0519, found 391.0528.

**(4*S*)-3-[5-(1,2-Dithiolan-3-yl)-1-oxopentyl]-4-(2-methylpropyl)oxazolidine-2-selones (6f):** IR 2945, 2922, 2868, 1767, 1706, 1458, 1363, 1340, 1291, 1196, 1140, 1029, 170, 930 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 0.90 (d, $J$ = 2 Hz, 3H), 0.92 (d, $J$ = 2.4 Hz, 3H), 1.40–1.60 (m, 3H), 1.60–1.80 (m, 4H), 1.80–1.90 (m, 1H), 2.27 (t, $J$ = 7.4 Hz, 2H), 2.35–2.46 (m, 1H), 3.01–3.15 (m, 2H), 3.21–3.45 (m, 1H), 3.49–3.61 (m, 2H), 4.27 (dd, $J$ = 2.7, 9.1 Hz, 1H), 4.38 (dd, $J$ = 9.1, 9.4 Hz, 1H), 4.63–4.75 (m, 1H); $^{13}C$ NMR $\delta$ 21.2, 23.2, 24.0, 24.4, 24.8, 28.3, 33.6, 34.4, 37.7, 38.3, 40.0, 40.6, 56.1, 58.3, 73.2, 173.4, 188.5; $^{77}Se$ NMR $\delta$ 472.5, 472.3 ([$^2H_6$]benzene), 455.8, 455.5 ([$^2H$]chloroform). Anal. Calcd for $C_{15}H_{25}NO_2S_2Se$: C, 45.79; H, 6.88; N, 3.55. Found: C, 45.79; H, 6.78; N, 3.49.

**(4*S*,5*R*)-3-[5-(1,2-Dithiolan-3-yl)-1-oxopentyl]-4,5-diphenyloxazolidine-2-selones (6g):** IR 2931, 2850, 2114, 1705, 1453, 1353, 1336, 1262, 1209, 1182, 1147, 1045, 938 $cm^{-1}$; $^1H$ NMR ([$^2H$]chloroform) $\delta$ 1.40–1.60 (m, 2H), 1.60–1.80 (m, 4H), 1.80–1.90 (m, 1H), 2.41–2.46 (m, 1H), 3.06–3.21 (m, 2H), 3.37–3.45 (m, 1H), 3.49–3.61 (m, 2H), 5.87 (d, $J$ = 7.7 Hz, 1H), 5.94 (d, $J$ = 7.7 Hz, 1H), 6.84–6.87 (m, 2H), 6.95–6.98 (m, 2H), 7.09–7.11 (m, 6H); $^{13}C$ NMR $\delta$ 21.2, 23.2, 24.0, 24.4, 24.8, 28.3, 33.6, 34.4, 37.7, 38.3, 40.0, 40.6, 56.1, 58.3, 73.2, 173.4, 188.5; $^{77}Se$ NMR $\delta$ 488.83, 488.77 ([$^2H_6$]-benzene), 473.2, 472.9 ([$^2H$]chloroform); HRMS $m/z$ calcd for $C_{23}H_{25}NO_2S_2{}^{76}Se$ 487.0519, found 487.0516.

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**Supporting Information Available:** Two-dimensional $^1H,^1H$ COSY and NOESY spectrum for (*S*)-MTPA adducts of **1g** and the COSY spectrum of (*R*)-MTPA–**1g** (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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