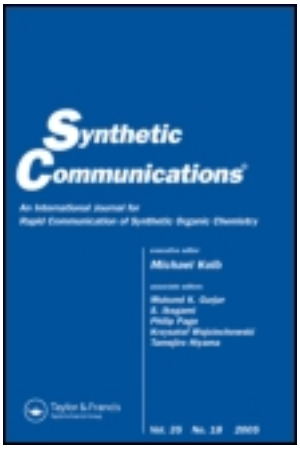

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Chiral N-Acetyl Selone-Promoted Aldol Reactions

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Abstract: The chiral oxazolidineselone functionality was found to be an excellent partner in the stereospecific acetate aldol reaction with aldehydes via the titanium enolates. Good stereocontrol was obtained as determined by NMR spectroscopy. The oxazolidineselone also provided a straightforward way to establish the stereopurity of the coupling reaction through ^{77}Se NMR spectroscopy.

Keywords: Acetate aldol, enolate structure, selenocarbonyl, ^{77}Se NMR spectroscopy

INTRODUCTION

The aldol reaction was reported by Wurtz in 1872[1] and involves a carbon–carbon bond-forming process between an enolate and a β-carbonyl to give rise to a β-hydroxy carbonyl functionality. This reaction has

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proven to be one of the most useful methods of stererospecifically creating two contiguous chiral carbon centers. The development of methods for improved chiral auxilaries,[2] organo-catalytic processes,[3] novel coreactants (e.g., Lewis acids/bases),[4] and recently reported "green" aqueous aldol reactions[5] continues to be of interest in the research community.

Chiral auxiliaries were developed in the early 1980s to provide for a predictable stereochemical result in the aldol bond-forming process. The chiral oxazolinedinone amide boron bases enolate process developed by Evans[6] has been pivotal for gaining easy access to syn-propionates (Evans aldol). By simply using titanium(IV)-based enolates it was discovered that the opposite syn-propionate could be selected (non-Evans aldol). The use of thiazolidinethione-based systems by Crimmins[7] demonstrated that both syn products could be obtained by using 1 or 2 equiv of the enolizing base. Access to the anti-aldol manifold has proven to be more difficult, although some successful methods have been reported.[8]

We have been interested in developing new techniques for carbon–carbon bond-formation using the chiral selone auxilary. The selone-promoted Ti aldol reaction was found to give high stereroselectivety in good to excellent yields. In addition, under certain conditions this chiral auxiliary promoted a rare *anti*-aldol process. The selone functionality has also served as an exquistely sensitive NMR reporter[9] for the determination of chirality at remotely disposed chiral centers and has been pivotal in efforts to help define the solution state of the key Ti enolate in the aldol process.[10] It has provided a straightforward general synthetic route for the construction of the (^{2}H and ^{13}C) isotopomers of ribose and deoxyribose used in the synthesis of labeled nucleic acids.[11]

Compared to other functional groups on the aldol donor, the use of the acetate moiety is rare,[12] mostly because of varying stereoselectivity in the resulting product. To attack this problem, designer molecular scaffolds have been created to increase the compactness and rigidity of the transition state, thereby increasing the effects of strategically placed groups on the energetically prefered conformation. Notable advances have been reported by the Osorio-Lozada[13] and Ghosh[14] groups. The Osorio-Lozada group recently reported that the incorporation of a thiocarbonyl group into an oxazolidinone framework gives rise to very good stereoselectivities in the selected aldol examples.

The success of some chiral auxiliaries with acetate side groups in effecting stereoselective products prompted us to investigate the use of the oxazolidineselone. In addition, the stereoselectivity of the reaction could be interogated immediately upon reaction completion using ^{77}Se NMR spectroscopy.[15] The selenium nucleus is exquistly sensitive to its electronic enviroment. It has a spin $I = 1/2$, just as ^{1}H, has a chemical shift range of more than 3500 ppm, has a relative receptivity of 2.98

compared to ^{13}C, and has a natural abundance of 7.5%. In these systems, the observing selenium nucleus has been shown to detect chiral centers removed by as many as eight bonds.

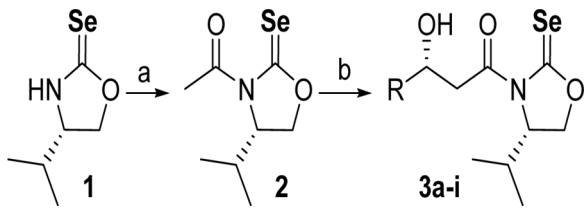
RESULTS AND DISCUSSION

Synthesis (Scheme 1) of N-acetyl valine derived selone was accomplished through reaction of **1**[16] with acetyl chloride and Hunig's base in CH_2Cl_2. Reaction of **2** with $TiCl_4$ and Hunig's base at 0 °C gave the enolate, which was treated with a variety of aldehydes at −78 °C to give aldol products **3a–3i**, Scheme 1. After workup, the crude products were examined by ^{77}Se NMR spectroscopy to determine diastereomeric ratios (dr).

The absolute stereochemistry of the product for **3i** was determined through concurrent cleavage of the auxiliary and formation of the methyl ester, followed by reaction with Mosher's acid chloride.[17] NMR values for both diastereomers were compared to literature values, and the major isomer is shown in Scheme 1.

We found that **2** reacted somewhat sluggishly when only 1.1–1.2 equiv of $TiCl_4$ were used. If, however, 1.7 equiv of $TiCl_4$ were employed, then only a trace amount of starting material was observed in the crude NMR spectra. Yields and stereoselectivities were independent of the amount of aldehyde added.

In general, crude yields and stereoselectivities were quite good for aldehydes that had R groups capable of complexing Ti (entries **a–e**, Table 1). For those aldehydes with saturated alkyl groups, reduced stereoselectivity was alleviated by easy separation using column chromatography, and good combined yields were obtained. The selone auxiliary compares well with other known auxiliaries in both isolated yield and stereoselectivity, although the oxazolidinethione developed by Guz and Phillips[12a] is more consistently selective across different aldehyde types.



Scheme 1. Selone-promoted acetate aldol: (a) acetyl chloride, Hunig's base; (b) $TiCl_4$, Hunig's base followed by RCHO. R = aryl alkyl, alkenyl, and benzyloxy.

Table 1. Selone-promoted Ti aldol reactions of **2** with representative aldehydes

Entry	Aldehyde	dr	Yield
a	PhCHO	96:4	95
b	4-FPhCHO	96:4	93
c	$CH_3CH_2CH=CH(CH_3)CHO$	93:7	90
d	$CH_3CH=CHCHO$	88:12	85
e	$BnOCH_2CHO$	91:9	90
f	2,4,6-$(CH_3)_3$PhCHO	77:23	83
g	$CH_3(CH_2)_2CHO$	77:23	93
h	$(CH_3)_2CHCHO$	74:26	88
i	$(C_6H_{11})CHO$	65:35	86

In Fig. 1, a representative example of the observation of the mixture of aldol diastereomers through the observing selenium nucleus is shown. The spectrum was taken on the crude material before silica-gel flash-column chromatography. The spectrum also provides for an assessment of the overall course of the chemical processing. A very minor peak was observed, which was centered around 120 ppm. This peak corresponds to the unacylated (acetate cleavage) selone. Moreover, the diasteromeric ratio can be interrogated immediately upon quenching of the reaction. This measurement at this time obviates the possible retroaldol or other reactions occurring during purification, which could alter the amount of each diastereomer present. Direct evaluation of the reaction solution can also be

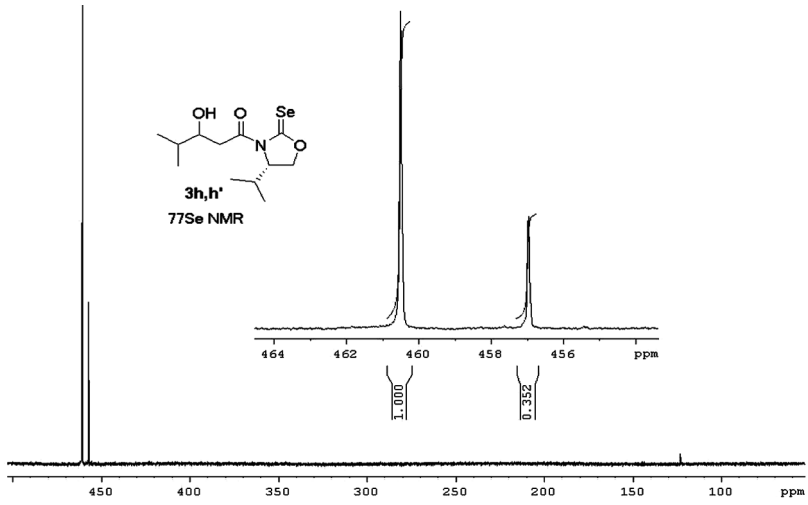


Figure 1. 1D ^{77}Se NMR spectrum of the crude mixture of **3**.

assessed through the observing selenium nucleus by simply taking an aliquot of the solution and immediately recording the NMR spectrum.

We have been particularily interested in gaining an understanding for the basis of the stereochemical preference in our selone systems both computationally and with 2D NMR. Solution structural information should provide a logical basis for further auxiliary design improvements. In addition, to the best of our knowledge, there is a general lack of positional information for the amine base partner in the enolate complex. Evans et al.[18] speculated the complexes are aggregated with the amine and intimately associated with the enolate, possibly through ion pairing. Recently Nebot[19] and coworkers studied pentanone enolate systems in an effort to elucidate if these systems exist as "real" enolates or ate-complexes and also to determine the fate of the amine base and the disposition of the ligands around the metal. In a more recent study, Moreira and coworkers[20] have found, for the complexes studied, there is an apparent biradical character to the titainium enolate (at varying temperatures up to 100 K). Figure 2 shows the proton NMR spectrum of the enolate, which was generated in CD_2Cl_2 using $TiCl_4$ and Hunig's base at 0 °C. All proton resonances were assigned, and the complex was found to be stable for at least 24 h (deteremined by the general lack of observable additional peaks over time). Remarkably, the excess Hunig's base was observed as distinct

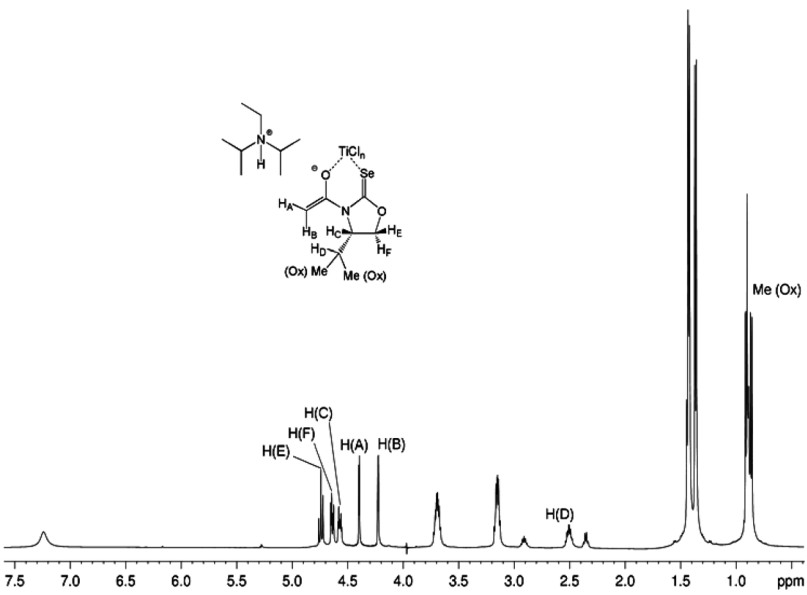


Figure 2. Proton NMR spectrum of the enolate complex.

resonances from the complexed Hunig's base, and the ammonium proton resonance at 7.25 ppm was observed as a broad singlet. Further refinement of the NMR data with DFT calculations are under way.

In conclusion, we have extended the utility of the oxazolidineselone auxiliary to aldol reactions, giving rise to good dr values.

EXPERIMENTAL

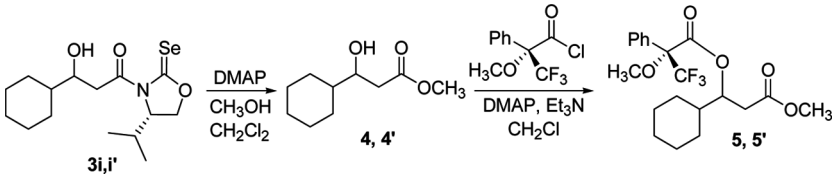
All one-dimensional product characterization NMR experiments were performed in $CDCl_3$, unless otherwise noted, on a DRX 300 MHz NMR spectrometer equipped with triple-axis gradient and a tunable broadband probe. ^1H and ^{13}C spectra were referenced to the TMS signal at 0.00 ppm through the spectrometer's lock frequency. ^{77}Se spectra were referenced to diphenylselenide at 465 ppm. ^1H spectra were recorded at 300.1300056 MHz, ^{13}C spectra at 75.4677506 MHz, and ^{77}Se spectra at 57.2397200 MHz. Mass spectra were obtained on a Thermo Finnegan LCQ Deca XP Plus mass spectrometer. Chemicals were obtained from commercial sources, were used without purification, and were of reagent quality or better.

Typical Procedure, Oxazolidineselone-Based Acetate Aldol

To a flame-dried, round-bottom flask, **2** (100 mg, 0.43 mmol) and dry CH_2Cl_2 (10 mL) were added under Ar. The yellow solution was cooled to 0 °C, and $TiCl_4$ (0.75 mL, 1 M in CH_2Cl_2) was added dropwise. The orange solution was stirred 5 min, and then *i* Pr_2NEt (0.10 mL, 0.57 mmol) was added. The dark mixture was stirred 1 h, then chilled to −78 °C. The aldehyde (6.9 mmol) was added dropwise as a solution in CH_2Cl_2 (2 mL). The mixture was stirred 1 hour, then allowed to warm to 0 °C. After 30 min at 0 °C, saturated aq. NH_4Cl was added until red precipitate was observed. The mixture was diluted with 10% EtOAc in CH_2Cl_2 (~10 mL), then vacuum filtered through silica gel, eluting with 10% EtOAc in CH_2Cl_2. Solvent was evaporated from the filtrate, and purification by column chromatography (5% EtOAc in CH_2Cl_2) gave aldol products **3a–e**, along with minor amounts of starting **2** in some cases. NMR (^1H, ^{13}C, ^{77}Se) and MS analysis were consistent with the product structures.

Derivative Analysis: Mosher's Acid Chloride Adduct of the Aldol Product

Compounds **3i** (150 mg, 0.43 mmol) and **3i′** (100 mg, 0.29 mmol) were separately treated under argon with 4-*N*,*N*-dimethylaminopyridine



Scheme 2. Mosher's acid adduct of the aldol product.

(53 mg, 0.43 mmol, and 36 mg, 0.29 mmol, respectively) in 6 mL of 20% methanol in CH_2Cl_2 (Scheme 2). The mixtures were stirred at room temperature for 48 h. Each mixture was filtered through silica gel using CH_2Cl_2 to elute. After evaporation of the solvent, purification by column chromatography (10–20% EtOAc in hexanes) gave the esters **4** (50 mg, 60% yield) and **4′** (30 mg, 54% yield) as slightly yellow oils. NMR analysis was analogous to literature examples.[21]

The esters **4** and **4′** were converted to the corresponding (*S*)-MTPA-esters according to the literature, and the ^{1}H NMR shifts for the MTPA methoxy signals were compared. Resonances at δ 3.70 for **5** and 3.60 for **5′** confirmed the *R* configuration for the major isomer (**3i**, **4**, and **5**) and the *S* configuration for the minor isomer (**3i′**, **4′**, and **5′**). Absolute configurations for **3a–i** were assigned by analogy and analysis of the ^{77}Se NMR shifts.

Data

Compound **3a** (PhCHO)

^{1}H NMR ($CDCl_3$) δ 7.48 (d, $J = 7.2$ Hz, 2H), 7.42 (t, $J = 7.2$ Hz, 2H), 7.34 (t, $J = 7.1$ Hz, 1H), 5.35 (dt, $J = 9.0$, 3.6 Hz, 1H), 4.78 (dt, $J = 8.4$, 3.3 Hz, 1H), 4.47 (dd, $J = 9.5$, 3.0 Hz, 1H), 4.39 (t, $J = 9.5$ Hz, 1H), 4.06 (dd, $J = 17.1$, 3.3 Hz, 1H), 3.95 (dd, $J = 17.1$, 8.4 Hz, 1H), 3.19 (d, $J = 4.2$ Hz, 1H), 2.45–2.34 (m, 1H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.92 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.5, 172.9, 142.3, 128.6, 127.9, 125.9, 70.3, 69.6, 64.2, 46.7, 29.0, 18.2, 15.0; ^{77}Se ($CDCl_3$) δ 461.3; MS (ESI) m/z 341.9 $[M + H]^+$.

Compound **3b** (4-F-PhCHO)

^{1}H NMR ($CDCl_3$) δ 7.48–7.42 (quartet of triplets, $J = 8.4$, 5.4, 2.1 Hz, 2H), 7.09 (triplet of triplets, $J = 8.4$, 2.1 Hz, 2H), 5.32 (dt, 9.3, 3.6 Hz, 1H), 4.79 (dt, $J = 8.7$, 3.3 Hz, 1H), 4.47 (dd, $J = 9.1$, 3.0 Hz, 1H), 4.40 (t, $J = 9.1$ Hz, 1H), 4.06 (dd, $J = 17.4$, 3.3 Hz, 1H), 3.86 (dd, $J = 17.4$,

9.3 Hz, 1H), 3.27 (d, $J = 4.2$ Hz, 1H), 2.43–2.33 (m, 1H), 0.98 (d, $J = 7.2$ Hz, 3H), 0.92 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.5, 172.7, 162.3 (d, $J = 244.4$ Hz), 138.1 (d, $J = 3.2$ Hz), 127.6 (d, $J = 8.1$ Hz), 115.4 (d, $J = 21.3$ Hz), 69.7, 69.6, 64.21, 46.8, 29.0, 18.1, 15.0;^{77}Se ($CDCl_3$) δ 461.4; MS (ESI) m/z 358.6 $[M]^+$.

Compound **3c** (2-Methyl-2-pentenal)

^{1}H NMR ($CDCl_3$) δ 5.54 (t, $J = 7.2$ Hz, 1H), 4.78 (dt, $J = 8.4$, 3.3 Hz, 1H), 4.62 (t, $J = 6.3$ Hz, 1H), 4.47 (dd, $J = 12.6$, 3.0 Hz, 1H), 4.43 (dd, $J = 12.6$, 9.6 Hz, 1H), 3.74 (d, $J = 6.3$ Hz, 2H), 2.73 (br s, 1H), 2.44–2.33 (m, 1H), 2.08 (quintet, $J = 7.2$ Hz, 2H), 1.71 (s, 3H), 1.00 (t, 7.2 Hz, 3H), 0.97 (d, $J = 7.2$ Hz, 3H), 0.92 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.5, 173.2, 134.5, 128.9, 73.1, 69.6, 64.2, 44.0, 29.0, 20.8, 18.2, 15.0, 13.9, 12.1;^{77}Se ($CDCl_3$) δ 455.3; MS (ESI) m/z 332.3 $[M]^+$.

Compound **3d** (Crotonaldehyde)

^{1}H NMR ($CDCl_3$) δ 5.82 (dq, $J = 15.3$, 6.3 Hz, 1H), 5.64 (ddd, $J = 15.3$, 6.3, 1.5 Hz, 1H), 4.79 (dt, $J = 8.1$, 3.3 Hz, 1H), 4.69 (br s, 1H), 4.48 (dd, $J = 9.4$, 3.0 Hz, 1H), 4.41 (t, $J = 9.4$ Hz, 1H), 3.86 (dd, $J = 17.4$, 3.3 Hz, 1H), 3.62 (dd, $J = 17.4$, 8.7 Hz, 1H), 2.82 (br s, 1H), 2.44–2.34 (m, 1H), 1.77 (d, $J = 6.3$ Hz, 3H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.93 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.4, 172.9, 131.6, 127.7, 69.6, 68.8, 64.2, 45.3, 29.0, 18.2, 17.8, 15.0;^{77}Se ($CDCl_3$) δ 459.0; MS (ESI) m/z 305.1 $[M + H]^+$.

Compound **3e** ($BnOCH_2CHO$)

^{1}H NMR ($CDCl_3$) δ 7.41–7.31 (m, 5H), 4.78 (dt, $J = 8.2$, 3.1 Hz, 1H), 4.64 (s, 2H), 4.47 (dd, $J = 9.5$, 3.1 Hz, 1H), 4.40 (dd, $J = 9.5$, 9.3 Hz, 1H), 3.88 (dd, $J = 17.2$, 9.3 Hz, 1H), 3.72 (dd, $J = 17.2$, 3.8 Hz, 1H), 3.08 (d, $J = 5.0$ Hz, 1H), 2.45–2.35 (m, 1H), 0.98 (d, $J = 7.0$ Hz, 3H), 0.93 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.5, 172.9, 137.9, 128.4, 127.8, 127.7, 73.4, 73.0, 69.5, 67.6, 64.2, 42.2, 28.9, 18.1, 15.0;^{77}Se ($CDCl_3$) δ 455.5; MS (ESI) m/z 384.3 $[M]^+$, 366.1 $[M - H_2O]^+$.

Compound **3f** (Mesitylaldehyde, Major)

^{1}H NMR ($CDCl_3$) δ 6.89 (s, 2H), 5.82 (d, $J = 10.2$ Hz, 1H), 4.81 (dt, $J = 8.1$, 3.0 Hz, 1H), 4.51–4.39 (m, 3H), 3.62 (dd, $J = 18.3$, 2.7 Hz, 1H),

2.73 (d, $J = 3.3$ Hz, 1H), 2.5 (s, 6H), 2.46–2.41 (m, 1H), 2.31 (s, 3H), 1.00 (d, $J = 7.2$ Hz, 3H), 0.94 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.4, 173.2, 137.1, 136.3, 134.6, 130.2, 69.6, 66.8, 64.4, 44.1, 29.1, 20.8, 18.2, 15.0;^{77}Se ($CDCl_3$) δ 460.1; MS (ESI) m/z 382.3 $[M]^+$.

Compound **3f′** (Mesitylaldehyde, Minor)

^{1}H NMR ($CDCl_3$) δ 6.89 (s, 2H), 5.76 (d, $J = 9.6$ Hz, 1H), 4.82 (dt, $J = 8.4$, 3.3 Hz, 1H), 4.55–4.39 (m, 3H), 3.61 (dd, $J = 18.3$, 2.7 Hz, 1H), 2.84 (d, 3.3 Hz, 1H), 2.51 (s, 6H), 2.50–2.44 (m, 1H), 2.31 (s, 3H), 1.02 (d, $J = 6.9$ Hz, 3H), 0.98 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.3, 173.6, 137.2, 136.3, 134.5, 130.2, 69.6, 67.0, 64.3, 44.2, 29.0, 20.8, 18.2, 15.1;^{77}Se ($CDCl_3$) δ 459.2; MS (ESI) m/z 382.2 $[M]^+$ (MS virtually identical to **3e**).

Compound **3g** (Butyraldehyde, Major)

^{1}H NMR ($CDCl_3$) δ 4.78 (dt, $J = 6.8$, 3.1 Hz, 1H), 4.47 (dd, $J = 9.5$, 3.0 Hz, 1H), 4.40 (dd, $J = 9.5$, 8.1 Hz, 1H), 4.25–4.17 (m, 1H), 3.85 (dd, $J = 17.6$, 2.6 Hz, 1H), 3.46 (dd, $J = 17.6$, 9.3 Hz, 1H), 2.84 (d, $J = 3.8$ Hz, 1H), 2.45–2.33 (m, 1H), 1.67–1.44 (m, 4H), 0.99 (t, $J = 6.8$ Hz, 3H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.93 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.5, 173.6, 69.6, 67.8, 64.1, 45.3, 38.6, 29.0, 18.7, 18.1, 15.0, 14.0;^{77}Se ($CDCl_3$) δ 459.0; MS (ESI) m/z 306.3 $[M]^+$, 288.0 $[M - H_2O]^+$.

Compound **3g′** (Butyraldehyde, Minor)

^{1}H NMR ($CDCl_3$) δ 4.81 (dt, $J = 8.2$, 3.4 Hz, 1H), 4.45 (dd, $J = 9.5$, 3.0 Hz, 1H), 4.42 (t, $J = 8.9$ Hz, 1H), 4.22–4.11 (m, 1H), 3.77 (dd, $J = 17.2$, 9.2 Hz, 1H), 3.61 (dd, $J = 17.1$, 3.0 Hz, 1H), 3.01 (d, $J = 4.86$, 1H), 2.45–2.35 (m, 1H), 1.72–1.43 (m, 4H), 1.03 (t, $J = 6.03$ Hz, 3H), 0.99 (d, $J = 6.9$ Hz, 3H), 0.95 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.6, 173.8, 69.6, 68.3, 64.1, 45.1, 38.8, 29.0, 18.7, 18.1, 15.0, 13.0; ^{77}Se ($CDCl_3$) δ 450.6; MS (ESI) m/z 306.3 $[M]^+$, 288.0 $[M - H_2O]^+$ (MS virtually identical to **3g**).

Compound **3h** (Isobutyraldehyde, Major)

^{1}H NMR ($CDCl_3$) δ 4.77 (dt, $J = 8.1$, 3.3 Hz, 1H), 4.46 (dd, $J = 9.3$, 3.0 Hz, 1H), 4.40 (dd, $J = 9.3$, 8.1 Hz), 3.96 (m, 1H), 3.77 (dd, $J = 17.4$,

2.4 Hz, 1H), 3.51 (dd, $J = 17.4$, 9.9 Hz), 2.43–2.33 (m, 1H), 1.88–1.77 (m, 1H), 1.02 (d, $J = 3.9$ Hz, 3H), 1.00 (d, $J = 3.9$ Hz, 3H), 0.96 (d, $J = 6.9$ Hz, 3H), 0.91 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ189.5, 174.0, 72.7, 69.6, 64.2, 42.8, 33.3, 29.0, 18.5, 18.2, 17.8, 15.0;^{77}Se ($CDCl_3$) δ 458.4; MS (ESI) m/z 308.0 $[M + H]^+$.

Compound **3h′** (Isobutyraldehyde, Minor)

^{1}H NMR ($CDCl_3$) δ 4.81 (ddd, $J = 8.2$, 3.8, 3.0 Hz, 1H), 4.48 (dd, $J = 9.5$, 3.0 Hz, 1H), 4.41 (dd, $J = 9.5$, 8.2 Hz, 1H), 3.93 (quartet of doublets, $J = 10.2$, 4.9, 2.1 Hz, 1H), 3.82 (dd, $J = 16.5$, 10.0 Hz, 1H), 3.58 (dd, $J = 16.5$, 2.1 Hz, 1H), 3.01 (d, $J = 5.0$ Hz, 1H), 2.45–2.35 (m, 1H), 1.91–1.81 (m, 1H), 1.05 (d, $J = 5.0$ Hz, 3H), 1.03 (d, $J = 5.0$ Hz, 3H), 0.99 (d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.7, 174.2, 73.4, 69.6, 64.1, 42.3, 33.6, 29.0, 18.5, 18.1, 17.8, 15.0;^{77}Se ($CDCl_3$) δ 457.0; MS (ESI) m/z 308.0 $[M + H]^+$ (MS virtually identical to **3h**).

Compound **3i** (Cyclohexane Carboxaldehyde, Major)

^{1}H NMR ($CDCl_3$) δ 4.78 (dt, $J = 8.1$, 3.6 Hz, 1H), 4.47 (dd, $J = 9.4$, 3.0 Hz, 1H), 4.41 (t, $J = 9.4$ Hz, 1H), 4.00–3.95 (m, 1H), 3.80 (dd, $J = 17.5$, 2.1 Hz, 1H), 3.54 (dd, $J = 17.5$, 9.6 Hz, 1H), 2.76 (br s, 1H), 2.45–2.34 (m, 1H), 1.94 (d, $J = 12.6$ Hz, 1H), 1.92–1.70 (m, 4H), 1.58–1.45 (m, 1H), 1.34–1.05 (m, 5H), 0.98 (d, $J = 7.0$ Hz, 3H), 0.95 (d, $J = 6.9$ Hz); ^{13}C NMR ($CDCl_3$) δ 189.5, 174.1, 72.2, 69.6, 64.2, 43.2, 42.9, 29.0, 28.9, 28.4, 26.4, 26.2, 26.1, 18.2, 15.0;^{77}Se ($CDCl_3$) δ 460.2; MS (ESI) m/z 346.0 $[M]^+$.

Compound **3i′** (Cyclohexane Carboxaldehyde, Minor)

^{1}H NMR ($CDCl_3$) δ 4.81 (dt, $J = 8.4$, 3.3 Hz, 1H), 4.49 (dd, $J = 9.6$, 3 Hz, 1H), 4.41 (t, $J = 8.4$ Hz, 1H), 3.95–3.89 (m, 1H), 3.86 (dd, $J = 16.2$, 9.9 Hz, 1H), 3.55 (dd, $J = 16.2$, 1.5 Hz, 1H), 3.01 (d, $J = 4.8$ Hz, 1H), 2.46–2.36 (m, 1H), 1.94 (d, $J = 12.6$ Hz, 1H), 1.85–1.67 (m, 4H), 1.58–1.46 (m, 1H), 1.34–1.07 (m, 5H), 0.98 (d, $J = 7.2$ Hz, 3H), 0.94 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.7, 174.3, 72.9, 69.6, 64.2, 43.4, 42.4, 29.0, 28.9, 28.4, 26.4, 26.2, 26.1, 18.1, 15.0;^{77}Se ($CDCl_3$) δ 455.9; MS (ESI) m/z 346.1 $[M]^+$ (MS virtually identical to **3i**).

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