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Wittig Rearrangements of Boron-Based Oxazolidinone Enolates

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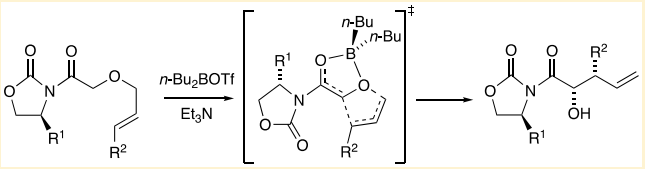
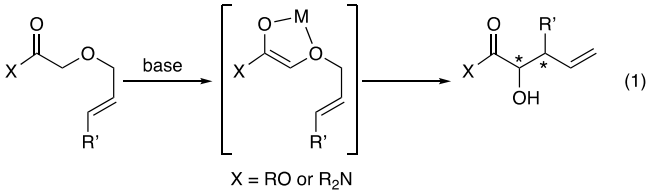
Supporting Information

ABSTRACT: [2,3]-Sigmatropic rearrangements (Wittig rearrangements) of α-alkoxy oxazolidinone enolates are described. Whereas alkali metal enolates fail, owing to facile deacylation, boron enolates generated from di-*n*-butylboron triflate and triethylamine rearranged in good yields and high selectivities with exceptions noted. IR and NMR spectroscopies show the boron is chelated by the α-alkoxy group rather than the more distal oxazolidinone carbonyl in the complex and enolate. The rearrangement product contains a boron alkoxide that remains unchelated by either carbonyl. Optimization was guided by density functional theory computations, suggesting that valine-derived oxazolidinones would be superior to the phenylalanine-derived analogues.



INTRODUCTION

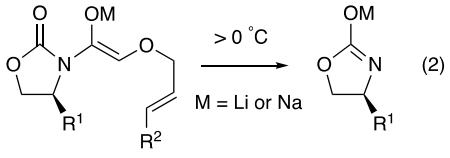
Wittig rearrangements of allyloxy-substituted enolates and related carbanions have enjoyed considerable popularity (eq 1).[1] Several aspects of this reaction captured our imagination.



(1)

First, the aggregation of lithium enolates presents the possibility of rearranging within an aggregate, especially given mounting evidence that enolate aggregates equilibrate slowly on laboratory time scales.[2a] The consequences to stereochemistry would be considerable and pose some challenging but interesting questions. Second, our interest in the chemistry of oxazolidinone-derived Evans enolates[3] previously revealed that, while the lithium enolates in THF are highly aggregated,[2b] TMEDA-solvated sodium enolates are monomeric,[2c] raising the prospect of probing aggregation effects from two extremes. Lastly, there are no reports that describe the use of the Evans oxazolidinone auxiliaries for such [2,3]-sigmatropic rearrangements.[4]

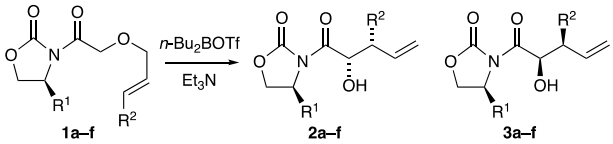
Ultimately, the allure of employing sodium and lithium Evans enolates in the [2,3]-sigmatropic rearrangement proved for naught: both substrates failed to rearrange, owing to competing deacylation pathways (eq 2).[2c] While this explained the absence of such rearrangements, it also brought into focus a more basic question: How would one carry out such a rearrangement?



(2)

After briefly exploring titanium enolates with little luck,[3] we were naturally drawn to boron enolates, owing to reports of boron-based [2,3]-sigmatropic rearrangements on simpler systems,[5] boron-based aldol additions of Evans enolates including α-alkoxy cases,[3d,6] and our previous structural and mechanistic studies of the boron-based Evans enolates.[2d,7]

We describe herein structural, rate, and computational studies of the [2,3]-sigmatropic rearrangement outlined in eq 3. Although our interests are largely structural and mechanistic, we offer select examples that illustrate efficacy, applications, and logical steps toward optimization.



(3)

a; R^1 = Bn, R^2 = H **b**; R^1 = *i*-Pr, R^2 = H **c**; R^1 = Bn, R^2 = Me **d**; R^1 = *i*-Pr, R^2 = Me **e**; R^1 = *i*-Pr, R^2 = *i*-Pr **f**; R^1 = *i*-Pr, R^2 = Ph

RESULTS AND DISCUSSION

Methods. Emblematic results are illustrated in eq 3 and Table 1, with several more specialized examples discussed below (eqs 8−11). Dichloromethane (CH_2Cl_2) and $CDCl_3$ are used interchangeably. Substrates **1a−1f** were prepared from the alkoxy-substituted acids using standard protocols as described by eq 4.[8−10] The absolute and relative stereochemistries were determined by converting **2a** to triol **5**,[11] **2d** to lactone **6**,[12] and **2e** to lactone **7**.[12a] A quaternization (**23**, vide infra) was correlated with γ-lactone **8**.[13] The stereochemistries of the remaining products were inferred by analogy. Stereocontrol in the rearrangement is discussed at greater length in a section below.

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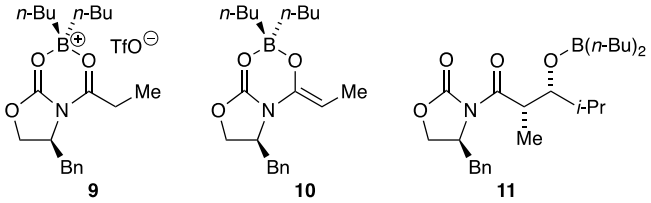
Table 1. [2,3]-Sigmatropic Rearrangements of Oxazolidinone-Derived Boron Enolates

entry	substrate	R^1	R^2	temp (°C)	2:3	yield (%)
1	**1a**	Bn	H	0 to rt	2:1	90
2	**1b**	*i*-Pr	H	0 to rt	3:1	81
3	**1c**	Bn	Me	0 to rt	5:1	90
4	**1d**	*i*-Pr	Me	0 to rt	>15:1[a]	82
5	**1e**	*i*-Pr	*i*-Pr	0 to rt	>30:1	71
6	**1f**	*i*-Pr	Ph	−78 to rt	>30:1	91

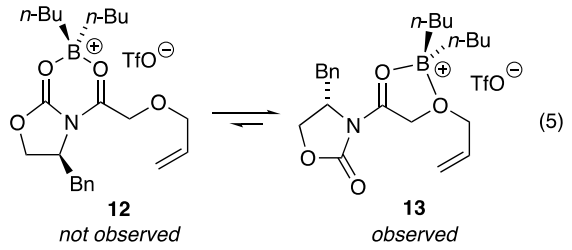
[a]Starting substrate **1d** contains 6% cis-isomer, which affords an anti-isomer.



Previous studies showed that boron NMR spectroscopy would not be useful for studying oxazolidinone-derived intermediates **9**−**11**,[2d] whereas IR spectroscopy proved critical.[14] In the current study, we again rely on IR spectroscopy and augment the assignments with standard two-dimensional ^{1}H and ^{13}C NMR spectroscopies (COSY, HSQC, HMBC, and ROESY). Comparisons of key intermediates with propionate-derived species **9**−**11** reveal the relative importance of the alkoxy and oxazolidinone carbonyl as ligands for boron.

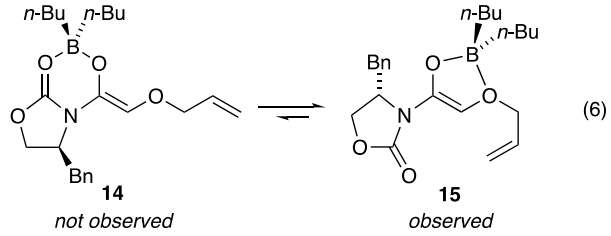
Density functional theory (DFT) calculations were carried out at the B3LYP/6-31G(d) level with single-point calculations at the MP2/6-31G(d) level of theory.[15] Transition structures display single negative frequencies. Allusions to results without further elaboration are documented in the Supporting Information.

Oxazolidinone-Boron Complex. We first studied the [2,3]-Wittig rearrangement of the simplest substrate, **1a**. IR spectroscopy showed that treatment of **1a** with 1.0−2.0 equiv of *n*-Bu_2BOTf at 0 °C causes oxazolidinone and carboxamide carbonyl absorbances of **1a** at 1783 and 1719 cm^{-1} (Figure 1a) to be replaced by absorbances at 1825 and 1613 cm^{-1}, respectively (Figure 1b). Given that the carboxamide and oxazolidinone carbonyls of propionate-derived complex **9** both appear at 1727 cm^{-1}, we conclude that complex **13**, with a complexed carboxamide and a relatively unperturbed oxazolidinone carbonyl, is formed to the exclusion of **12**, in which the oxazolidinone is complexed (eq 5). The full complement of 2D NMR spectroscopies show correlations, including those derived from the B−CH_2 and allyloxy O−CH_2 protons, that are consistent with the assignment of this intermediate as **13**.



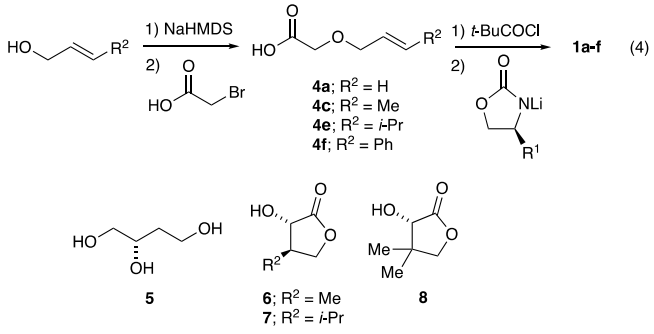
DFT computations show an 11.9 kcal/mol preference for **13**, which seems large but probably a consequence of the net charge. The computed structure of **13** shows a marked 180° rotation of the oxazolidinone moiety about the C−N bond relative to **12**.

Boron Enolate. Treatment of complex **13** with Et_3N at −30 °C causes immediate formation of boron enolate **15**, with absorbances for the oxazolidinone and enolate at 1781 and 1713 cm^{-1}, respectively (Figure 1c). Once again, the minor shift of the oxazolidinone absorbance when compared with enolate **10** (1706 cm^{-1}) in the propionate series is consistent with ether-based chelate **15** and an uncomplexed oxazolidinone, rather than **14**. Two-dimensional NMR spectroscopies show a single *Z*-isomeric enolate **15**. DFT computations predict a 1.6 kcal/mol preference for **15** versus **14**.



Sigmatropic Rearrangement. Warming enolate **15** to 25 °C causes rearrangement following a clean, first-order decay (Figure 2) with formation of alkoxide **17** as a 2:1 mixture of diastereomers (confirmed after workup) in 90% isolated yield. The absorbances for **17** at 1779 and 1711 cm^{-1}, respectively (Figure 1d), show that the boron alkoxide is not chelated by either carbonyl. DFT computations predict a 4.9 kcal/mol preference for open (unchelated) three-coordinate alkoxide **17** (analogous to **11**) relative to the chelate **16**.

The rearrangement in eq 7 represents the simplest mechanism we have ever studied. The first-order decay is operationally the entire rate law. The first-order rate constant is independent of initial concentration and unaffected by excess Et_3N. DFT computations were carried out on four isomeric transition structures **18** (Scheme 1). The barrier from the precomplex **15** to transition structure $\mathbf{18_A}$ is 12.2 kcal/mol. The benzyl moiety appears to not only be an inadequate stereochemical



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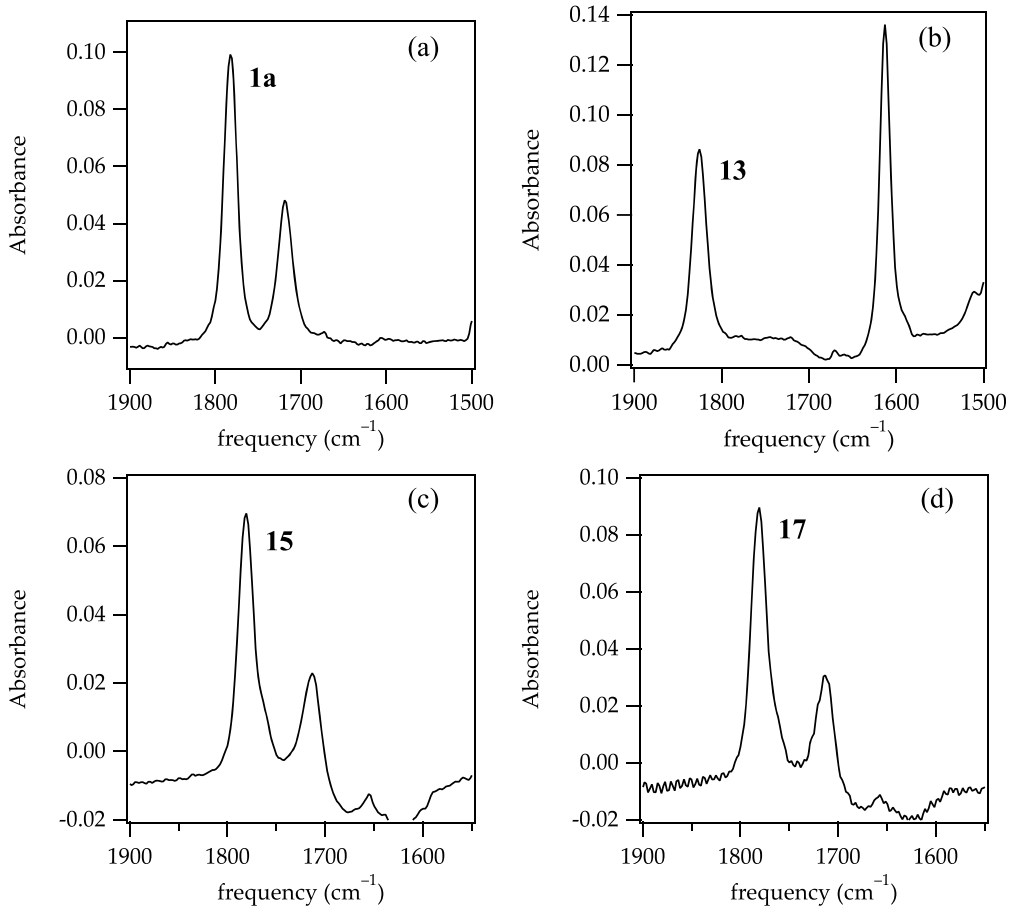


Figure 1. IR spectra of 0.030 M **1a** in CH_2Cl_2 recorded at 0 °C with (a) no additive, (b) 0.060 M *n*-Bu_2BOTf, affording **13**, (c) 0.060 M *n*-Bu_2BOTf and 0.10 M Et_3N, affording **15**, and (d) product **17** after warming to 25 °C.

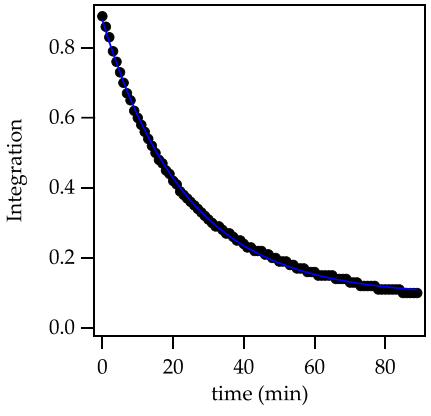
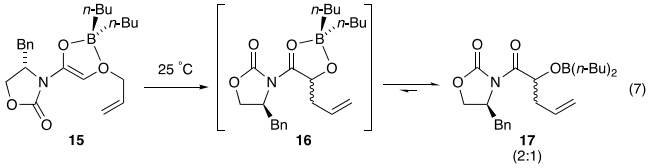
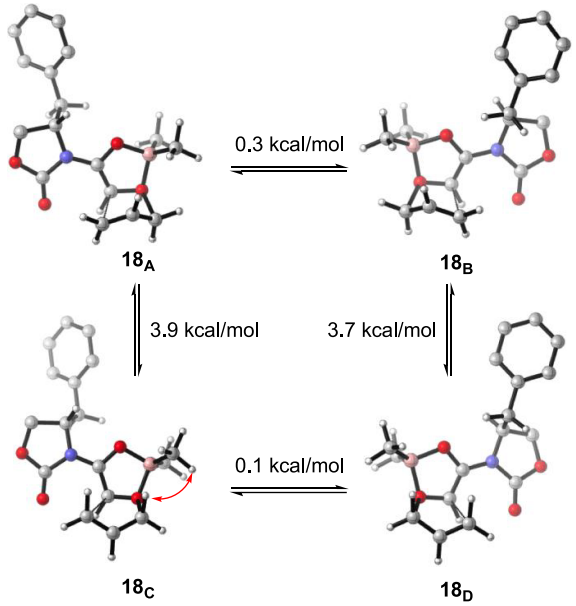


Figure 2. First-order decay of the rearrangement of enolate **15** to give alkoxide **17**.



Scheme 1. DFT Computed Stereoisomers of Transition Structure 18 Using Methyls as Surrogates for *n*-Butyls for the Rearrangement of 1a to Major and Minor Products 2a and 3a (Table 1, Entry 1)



determinant in this simple case but seemed likely to remain so even with substituents placed on the allyloxy fragment. A significant preference for half-chair conformers $\mathbf{18}_A$ and $\mathbf{18}_B$ relative to $\mathbf{18}_C$ and $\mathbf{18}_D$ appears to derive from unfavorable OC*H*−*H*CB interactions (see arrow) in the latter two. The cleaving C−O bond and forming C−C bond are 2.0−2.1 and 2.8

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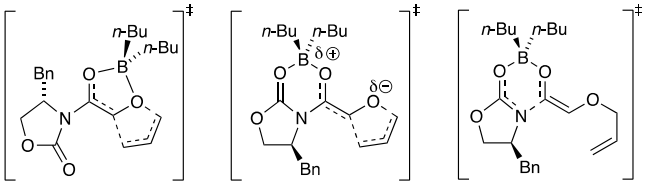
Å, respectively, for all of the transition structures described herein.

The chelation serves several purposes. In theory, it provides organization for stereocontrol, which bore no fruit for substrate **1a**, owing to an absence of stereochemically determining interactions. It also, however, allows for a smooth transition from enolate **15** to alkoxide **16** with minimal atomic movement or charge development. Contrast this with the developing charge in transition structure **19** derived from chelate **14**, which causes a large spike in its computed energy. The ether-based chelate also may competitively inhibit the boron-assisted deacylation via a transition structure such as **20**.

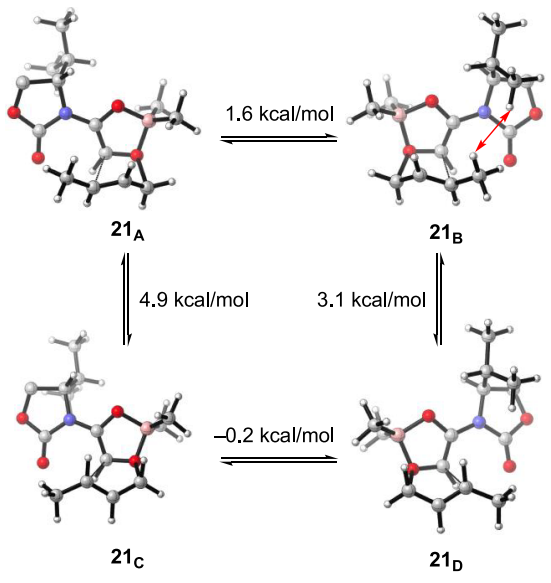


18 **19** **20**

Optimizing Stereoselectivity. The near stereorandom rearrangement of **1a** and computational support for this observed stereorandomness amounted to an inauspicious first effort. It would be more expedient to carry out a simple allylation of α-alkoxy Evans enolates via direct allylation.[16] However, inspection of the cyclic transition structures (Scheme 1), along with follow-up computational studies, led us to hypothesize that improved stereocontrol might be achieved through installation of a vinylic substituent at the 3-position (R^2) and replacement of the oxazolidinone benzyl group with an isopropyl moiety.

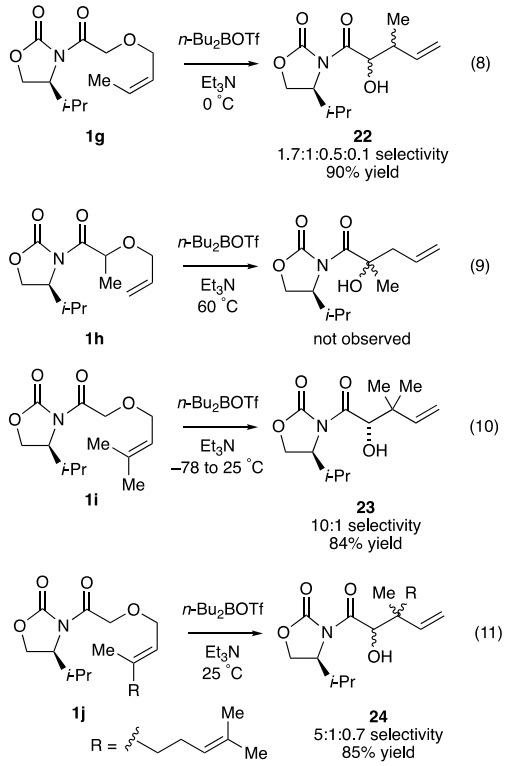
Table 1 (entries 2–4) confirmed this supposition. Thus, *trans*-crotyl ether **1c** rearranges to yield a modest 5:1 mixture of **2c** and **3c** to the exclusion of two other possible isomers (entry 3). Rearrangement of the valine-derived variant **1d** occurs with a significantly improved 15:1 selectivity (entry 4). The origin of this enhanced selectivity is reflected in the DFT computations (Scheme 2). The most stable isomeric transition structure, $\mathbf{21_A}$, corresponds to the major product (**2d**), while the second most stable isomer, $\mathbf{21_B}$, corresponds to the syn product **3d** (eq 1). A 2.6 Å CH_3–CH_3 contact in $\mathbf{21_B}$ (see arrow) absent in $\mathbf{21_A}$ appears to be the source of the facial selectivity.

Scheme 2. DFT Computed Stereoisomers of Transition Structure 21 Using Methyls as Surrogates for *n*-Butyls for the Rearrangement of 1d to the Four Diastereomers (Table 1, Entry 4)



Rearrangement of the *i*-propyl and phenyl-substituted allyl ethers gave excellent results (entries 5 and 6). In the latter case, it was essential to maintain the reaction temperature at −78 °C until after the addition of Et_3N to avoid decomposition of the cinnamyl ether-based substrate **1f** by an apparent solvolysis.

We pressed our luck with a few additional substrates not shown in Table 1. The *cis*-crotyl ether **1g** (eq 8) rearranged to



give two dominant anti-isomers albeit with a poor 1.7:1.0:0.5:0.1 stereocontrol. DFT computations are consistent with the modest reversal. Quaternization of the α carbon was largely a disaster (eq 9). Quaternization of the β carbon afforded **23** in 10:1 selectivity in a high yield (eq 10),[17] but that did not translate particularly well to a stereochemically controlled quaternization (eq 11).

CONCLUSION

The Evans-boron-enolate-based [2,3]-sigmatropic reaction is an effective protocol using *trans*-allylic ethers and showed some promise for the 2,2-disubstituted allylic ethers. A combination of spectroscopic and computational studies helped us understand the structures of the intermediates along the reaction coordinate (Scheme 3) and guided us to a functional protocol where none seemed to exist in the early stages. The intermediate enolate, chelated by the alkoxy moiety rather than the oxazolidinone carbonyl, is common to a number of boron-based aldol additions of such α-alkoxy Evans enolates.[3,6]

EXPERIMENTAL SECTION

Reagents and Solvents. CH_2Cl_2, $CHCl_3$, and $CDCl_3$ were distilled from molecular sieves. Trialkylamines were distilled from sodium benzophenone ketyl. *n*-Bu_2BOTf was used from a commercial

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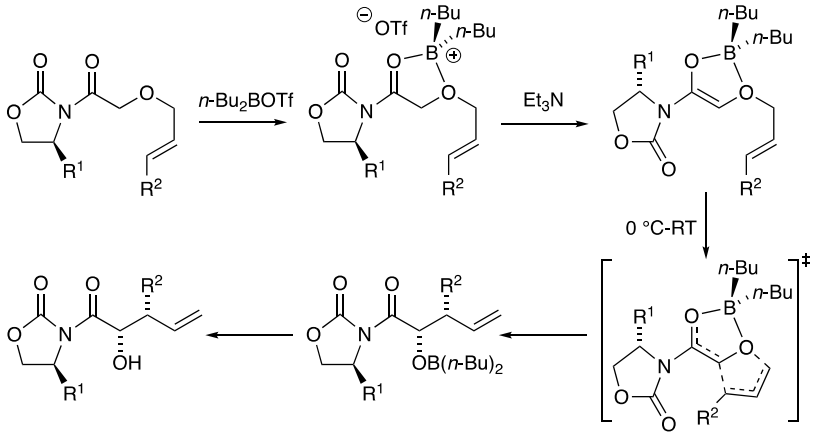
Scheme 3. Summary of the Boron-Enolate-Based [2,3]-Sigmatropic Rearrangement

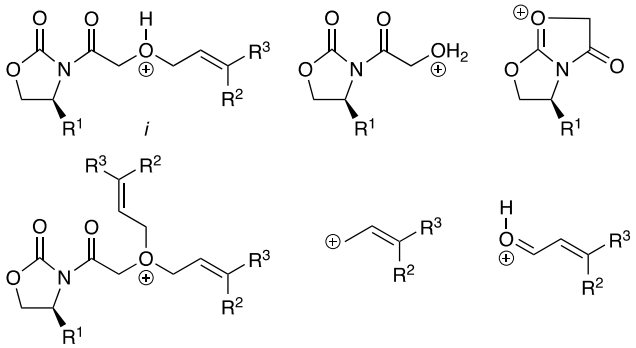


1.0 M n-Bu_2BOTf solution in CH_2Cl_2. Air- and moisture-sensitive materials were manipulated under argon using standard glovebox, vacuum line, and syringe techniques. While the reported yields of rearranged products were optimized, those of the starting materials and correlation products were not.

NMR Spectroscopy. An NMR tube under a vacuum was flame-dried on a Schlenk line and allowed to return to room temperature, backfilled with argon, and placed in a −78 °C dry ice/acetone bath. The appropriate amounts of oxazolidinone, n-Bu_2BOTf, and Et_3N in $CDCl_3$ were added sequentially via syringe. The tube was flame-sealed under a partial vacuum, mixed on a vortex mixer three times for ∼10 s with cooling between each vortexing, and stored in a freezer at −80 °C. Standard ^1H and ^{13}C NMR spectra were recorded on a 500 MHz spectrometer at 500 and 125 MHz, respectively. The ^1H and ^{13}C resonances are referenced to $CDCl_3$ ($CHCl_3$ 7.26 and $CDCl_3$ 77.2 ppm).

IR Spectroscopic Analyses. IR spectra were recorded with an in situ IR spectrometer fitted with a 30-bounce, silicon-tipped probe. The spectra were acquired in 16 scans at a gain of 1 and a resolution of 4 cm^{-1}. A representative reaction was carried out as follows: The IR probe was inserted through a nylon adapter and O-ring seal into an oven-dried, cylindrical flask fitted with a magnetic stir bar and a T-joint. The T-joint was capped with a septum for injections and a nitrogen line. After evacuation under full vacuum, heating, and flushing with nitrogen, the flask was charged with CH_2Cl_2 and cooled in a 0 °C ice bath. After a background spectrum was recorded, oxazolidinone **1a** (41.3 mg, 0.15 mmol) was added as a 1.0 M solution in CH_2Cl_2 with stirring, followed by 1.0 M n-Bu_2OTf (0.30 mL, 0.30 mmol) and neat Et_3N (70 μL, 0.50 mmol). IR spectra were recorded every 15 s with monitoring of the absorbance at 1783 and 1825 cm^{-1} over the course of the reaction.

Mass Spectrometry. The high-resolution mass spectra (HRMS) were measured using a DART-Orbitrap. The α-alkoxy oxazolidinones showed relatively minor parent ions (corresponding to ***i*** below) and numerous fragmentation products. The structures listed below are emblematic.



*(S,E)-3-(2-(But-2-en-1-yloxy)acetyl)-4-isopropyloxazolidin-2-one (**1d**).* To a solution of NaHMDS (40 mmol, 7.3 g) in THF (20 mL) was added crotyl alcohol (20 mmol, 1.7 mL, 15:1 *trans*/*cis*) followed by stirring under argon for 15 min at rt. A solution of α-bromo acetic acid (18 mmol, 2.5 g) in THF (10 mL) was added. After stirring for 12 h, the reaction was quenched by KOH solution (1.0 M, 20 mL) and extracted three times with KOH solution. The combined aqueous layers were acidified to pH = 1 using concentrated HCl at 0 °C and extracted six times with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (30% ethyl acetate/hexanes) afforded the acid **4c** as a light yellow oil (1.3 g, 56% yield). ^1H NMR (500 MHz, $CDCl_3$): δ 5.77 (dqt, J = 15.4, 6.6, 1.2 Hz, 1H), 5.58 (dtq, J = 15.0, 6.6, 1.6 Hz, 1H), 4.10 (d, J = 1.4 Hz, 2H), 4.04 (dp, J = 6.6, 1.2 Hz, 2H), 1.73 (ddt, J = 6.5, 1.9, 1.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 177.2, 131.8, 126.0, 72.3, 66.6, 17.8. To a solution of **4c** (4.0 mmol, 464.5 mg) in THF (5.0 mL) was added triethylamine (4.4 mmol, 613 μL) followed by stirring for 5 min at −78 °C. Trimethylacetyl chloride (4.4 mmol, 542 μL) was added. The mixture was warmed to rt and stirred for an additional 30 min to generate the mixed anhydride. To a solution of (*S*)-4-isopropyl-2-oxazolidinone (4.0 mmol, 516.6 mg) in THF (30 mL) was added n-BuLi (4.0 mmol, 2.5 mL) as a 1.6 M solution in hexane followed by stirring under argon for 15 min at −78 °C. The mixed anhydride solution was cooled to −78 °C, and the solution containing the lithiated oxazolidinone was added by cannula. The reaction was warmed to rt and stirred for an additional 30 min. The mixture was quenched with saturated NH_4Cl solution and extracted three times with diethyl ether. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (25% ethyl acetate/hexanes) afforded **1d** as a colorless oil (673 mg, 70% yield, 15:1 *trans*/*cis*). ^1H NMR (500 MHz, $CDCl_3$): δ 5.80−5.72 (m, 1H), 5.62 (dtd, J = 15.2, 6.5, 1.7 Hz, 1H), 4.64 (d, J = 2.3 Hz, 2H), 4.45 (dt, J = 8.5, 3.6 Hz, 1H), 4.34 (t, J = 8.7 Hz, 1H), 4.26 (dd, J = 9.1, 3.1 Hz, 1H), 4.09−4.00 (m, 2H), 2.43 (heptd, J = 7.3, 3.1 Hz, 1H), 1.72 (d, J = 6.6, 3H), 0.92 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 170.4, 154.2, 131.1, 126.8, 72.3, 69.3, 64.6, 58.3, 28.4, 18.0, 17.9, 14.8. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{12}H_{20}NO_4$, 242.1386; found, 242.1399.

*(S)-3-(2-(Allyloxy)acetyl)-4-benzyloxazolidin-2-one (**1a**).* Following the procedure of **1d** using allyl alcohol and (*S*)-4-benzyl-2-oxazolidinone afforded alkoxy acid **4a** as a yellow liquid (273.1 mg, 47% yield). ^1H NMR (500 MHz, $CDCl_3$): δ 5.91 (ddt, J = 17.2, 10.3, 5.9 Hz, 1H), 5.33 (dq, J = 17.2, 1.6 Hz, 1H), 5.27 (dq, J = 10.4, 1.3 Hz, 1H), 4.15−4.10 (m, 4H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 174.7, 133.3, 119.01, 72.7, 66.7. Further conversion of **4a** affords **1a** as a colorless oil (520.3 mg, 86% yield). ^1H NMR (500 MHz, $CDCl_3$): δ 7.34 (tt, J = 6.9, 1.1 Hz, 2H), 7.31−7.27 (m, 1H), 7.24−7.18 (m, 2H), 5.97 (ddt, J = 17.2, 10.4, 5.8 Hz, 1H), 5.35 (dq, J = 17.2, 1.6 Hz, 1H), 5.26 (dq, J = 10.4, 1.3 Hz, 1H), 4.74−4.64 (m, 3H), 4.33−4.26 (m, 1H), 4.24 (dd, J = 9.1, 3.0 Hz, 1H), 4.21−4.13 (m, 2H), 3.34 (dd, J = 13.5, 3.3 Hz, 1H), 2.82 (dd, J = 13.5, 9.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 170.4, 153.6, 135.1, 134.0, 129.6, 129.2, 127.6, 118.4, 72.7, 69.7, 67.4,

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55.0, 37.9. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{15}H_{18}NO_4$, 276.1230; found, 276.1244.

*(S)-3-(2-(Allyloxy)acetyl)-4-isopropyloxazolidin-2-one (**1b**).* The procedure of **1d** using allyl acohol afforded **1b** as a colorless oil (543.8 mg, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.95 (ddt, J = 16.4, 10.3, 5.8 Hz, 1H), 5.32 (dt, J = 17.3, 1.6 Hz, 1H), 5.27−5.20 (m, 1H), 4.68 (d, J = 3.5 Hz, 2H), 4.45 (dt, J = 8.3, 3.5 Hz, 1H), 4.35 (t, J = 8.8 Hz, 1H), 4.27 (dd, J = 9.2, 3.1 Hz, 1H), 4.18−4.08 (m, 2H), 2.43 (hd, J = 7.0, 3.9 Hz, 1H), 0.93 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 170.3, 154.2, 134.0, 77.4, 72.7, 69.7, 64.6, 58.4, 28.4, 18.1, 14.8. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{11}H_{18}NO_4$, 228.1230; found, 228.1242.

*(S,E)-4-Benzyl-3-(2-(but-2-en-1-yloxy)acetyl)oxazolidin-2-one (**1c**).* The procedure to prepare **1d** using (*S*)-4-benzyl-2-oxazolidinone afforded **1c** as a colorless oil (504.3 mg, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (dd, J = 8.1, 6.5 Hz, 2H), 7.31−7.26 (m, 1H), 7.21 (dd, J = 7.0, 1.8 Hz, 2H), 5.84−5.75 (m, 1H), 5.64 (dtq, J = 14.7, 6.3, 1.6 Hz, 1H), 4.73−4.67 (m, 1H), 4.65 (d, J = 4.3 Hz, 2H), 4.29 (dd, J = 9.2, 7.8 Hz, 1H), 4.23 (dd, J = 9.1, 3.0 Hz, 1H), 4.12−4.04 (m, 2H), 3.33 (dd, J = 13.4, 3.3 Hz, 1H), 2.82 (dd, J = 13.4, 9.5 Hz, 1H), 1.74 (dq, J = 6.5, 1.2 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 170.5, 153.6, 135.1, 131.1, 129.6, 129.2, 127.6, 126.8, 72.4, 69.4, 67.4, 55.0, 37.9, 18.0. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{16}H_{20}NO_4$, 290.1387; found, 290.1397.

*(S,E)-4-iIsopropyl-3-(2-((4-methylpent-2-en-1-yl)oxy)acetyl)-oxazolidin-2-one (**1e**).* *trans*-4-Methylpent-2-en-1-ol was prepared by a literature procedure as follows.[18] To a solution of ethyl (triphenylphosphoranylidene)acetate (20 mmol, 6.97 g) in CH_2Cl_2 (40 mL) was added isobutyraldehyde (25 mmol, 2.3 mL), and the mixture was stirred at rt overnight. The mixture was concentrated in vacuo, dissolved in hexanes, and filtered. The solution was concentrated in vacuo to afford the ester precursor as a colorless liquid (1.2 g, 42% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.94 (dd, J = 15.7, 6.6 Hz, 1H), 5.76 (dd, J = 15.7, 1.5 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 2.45 (dpd, J = 13.5, 6.8, 1.5 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.06 (d, J = 6.8 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 167.2, 155.6, 118.8, 60.3, 31.1, 21.4, 14.4. To a solution of the ester (8.5 mmol, 1.2 g) in toluene (20 mL) was added diisobutylaluminum hydride (20 mmol, 20 mL) as 1.0 M solution in toluene at −78 °C. The reaction was warmed to rt and stirred for an additional 12 h. The reaction was quenched with saturated NH_4Cl and acidified with concentrated HCl until all solids dissolved. The mixture was extracted three times with diethyl ether. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo to afford the alcohol precursor as a colorless liquid (648 mg, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.67 (ddt, J = 15.4, 6.2, 1.2 Hz, 1H), 5.59 (dtd, J = 15.5, 5.8, 1.2 Hz, 1H), 4.09 (dt, J = 6.0, 1.1 Hz, 2H), 2.36 (s, 1H), 2.34−2.26 (m, 1H), 1.00 (dd, J = 6.7, 0.8 Hz, 6H). Following the procedure of **1d**, *trans*-4-methylpent-2-en-1-ol was converted to alkoxy acid **4e** as a light yellow liquid (312 mg, 32% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.73 (ddt, J = 15.5, 6.5, 1.2 Hz, 1H), 5.50 (dtd, J = 15.5, 6.5, 1.4 Hz, 1H), 4.09 (s, 2H), 4.06 (dt, J = 6.6, 1.0 Hz, 2H), 2.38−2.27 (m, 1H), 1.00 (d, J = 6.7 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 171.45, 144.01, 121.83, 72.62, 66.33, 30.94, 22.21. Alkoxy acid **4e** was converted to **1e** as a colorless liquid (295 mg, 52% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.75 (ddt, J = 15.5, 6.4, 1.2 Hz, 1H), 5.57 (dtd, J = 15.6, 6.4, 1.4 Hz, 1H), 4.67 (d, J = 1.8 Hz, 2H), 4.50−4.45 (m, 1H), 4.37 (t, J = 8.8 Hz, 1H), 4.29 (dd, J = 9.1, 3.1 Hz, 1H), 4.12−4.05 (m, 2H), 2.46 (heptd, J = 7.0, 3.9 Hz, 1H), 2.40−2.29 (m, 1H), 1.02 (d, J = 6.8 Hz, 6H), 0.95 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 170.3, 154.1, 143.0, 122.4, 72.4, 69.3, 64.4, 58.2, 30.8, 28.2, 22.1, 22.1, 17.9, 14.7. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{14}H_{24}NO_4$, 270.1700; found, 270.1707.

*(S)-3-(2-(Cinnamyloxy)acetyl)-4-isopropyloxazolidin-2-one (**1f**).* The procedure of **1d** using cinnamyl alcohol afforded **4f** as a yellow solid (488 mg, 51% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43−7.37 (m, 2H), 7.35−7.31 (m, 2H), 7.29−7.27 (m, 1H), 6.67−6.62 (m, 1H), 6.28 (dt, J = 15.9, 6.3 Hz, 1H), 4.29 (dd, J = 6.4, 1.3 Hz, 2H), 4.17 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 171.4, 136.2, 134.6, 128.8, 128.3, 126.8, 124.2, 72.4, 66.6. Compound **1f** was obtained as a light yellow solid (283 mg, 37% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (dd, J = 7.4, 1.8 Hz, 2H), 7.32 (td, J = 7.6, 1.7 Hz, 2H), 7.24 (dd, J = 7.8, 1.6 Hz, 1H), 6.64 (d, J = 15.9 Hz, 1H), 6.33 (dtd, J = 15.9, 6.3, 1.7 Hz, 1H), 4.72 (d, J = 2.1 Hz, 2H), 4.45 (dt, J = 8.1, 3.3 Hz, 1H), 4.34−4.24 (m, 4H), 2.47−2.37 (m, 1H), 0.92 (dd, J = 7.1, 1.6 Hz, 3H), 0.86 (dd, J = 6.9, 1.6 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 170.2, 154.1, 136.4, 133.6, 128.6, 127.9, 126.6, 125.0, 72.2, 69.5, 64.4, 58.2, 28.3, 17.9, 14.6. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{17}H_{22}NO_4$, 304.1543; found, 304.1557.

*(S,Z)-3-(2-(But-2-en-1-yloxy)acetyl)-4-isopropyloxazolidin-2-one (**1g**).* The procedure of **1d**, except using 2-butyn-1-ol, afforded the alkoxy acid **4g** as a light yellow liquid (805 mg, 33% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.27 (q, J = 2.4 Hz, 2H), 4.23 (s, 2H), 1.86 (t, J = 2.3 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.3, 84.6, 73.6, 65.8, 59.3, 3.7. Alkoxy acid **4g** was converted to the acylated oxazolidinone as a colorless oil (987 mg, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.76 (s, 2H), 4.48−4.42 (m, 1H), 4.35 (t, J = 8.7 Hz, 1H), 4.30−4.24 (m, 3H), 2.42 (heptd, J = 7.0, 4.0 Hz, 1H), 1.85 (t, J = 2.3 Hz, 3H), 0.93 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 169.95, 154.2, 83.9, 74.2, 68.6, 64.6, 59.1, 58.4, 28.4, 18.0, 14.8, 3.8. Lindlar hydrogenation was carried out according to a modified literature procedure as follows.[19] To a solution of acylated oxazolidinone (2 mmol, 479 mg) in MeOH (10 mL) was added Lindlar catalyst (0.10 mmol, 212 mg), and the mixture was stirred under H_2 (1.0 atm) at rt for 18 h. The reaction was filtered through Celite and concentrated in vacuo. Flash chromatography (25% ethyl acetate/hexanes, R_f = 0.30) afforded **1g** as a colorless oil (409 mg, 85%, 12:1 *cis*/*trans*). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.73 (dqt, J = 10.9, 6.9, 1.3 Hz, 1H), 5.65−5.58 (m, 1H), 4.66 (d, J = 4.5 Hz, 2H), 4.46 (ddd, J = 8.3, 4.0, 3.1 Hz, 1H), 4.34 (dd, J = 9.2, 8.5 Hz, 1H), 4.26 (dd, J = 9.2, 3.0 Hz, 1H), 4.24−4.15 (m, 2H), 2.44 (dtt, J = 14.0, 7.0, 3.5 Hz, 1H), 0.93 (d, J = 7.1 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 170.4, 154.2, 129.3, 126.0, 69.6, 66.7, 64.6, 58.3, 28.4, 18.0, 14.8. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{12}H_{20}NO_4$, 242.1387; found, 242.1396.

*(4S)-3-(2-(Allyloxy)propanoyl)-4-isopropyloxazolidin-2-one (**1h**).* To a solution of **1b** (0.50 mmol, 114 mg) in THF (3 mL) was added NaHMDS (0.6 mmol, 110 mg) in THF (2 mL) under argon at −78 °C. After stirring for 15 min, methyl iodide (1.0 mmol, 62 μL) was added and the mixture was warmed to 0 °C. The mixture was stirred for another 30 min. The reaction was quenched with NH_4Cl and extracted three times with diethyl ether. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (25% ethyl acetate/hexanes, R_f = 0.30) afforded **1h** as a colorless oil (65 mg, 54%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.93 (ddt, J = 17.2, 10.3, 5.8 Hz, 1H), 5.29 (dq, J = 17.2, 1.6 Hz, 1H), 5.19 (dq, J = 10.3, 1.3 Hz, 1H), 5.11 (q, J = 6.6 Hz, 1H), 4.51 (ddd, J = 8.5, 4.1, 3.2 Hz, 1H), 4.34 (t, J = 8.8 Hz, 1H), 4.25 (dd, J = 9.2, 3.2 Hz, 1H), 4.07 (ddt, J = 12.3, 5.8, 1.4 Hz, 1H), 3.92 (ddt, J = 12.3, 6.0, 1.3 Hz, 1H), 2.34 (pd, J = 6.9, 4.1 Hz, 1H), 1.49 (d, J = 6.7 Hz, 3H), 0.92 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 173.7, 153.7, 134.4, 117.9, 73.7, 71.3, 64.3, 58.3, 28.6, 19.0, 18.0, 15.0. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{12}H_{20}NO_4$, 242.1387; found, 242.1399.

*(S)-4-Isopropyl-3-(2-((3-methylbut-2-en-1-yl)oxy)acetyl)-oxazolidin-2-one (**1i**).* The procedure of **1d**, except using 3-methyl-2-buten-1-ol, afforded **4i** as a pale yellow oil (573 mg, 40% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.35 (tp, J = 7.1, 1.4 Hz, 1H), 4.11 (d, J = 7.2 Hz, 2H), 4.09 (s, 2H), 1.77 (d, J = 1.5 Hz, 3H), 1.70 (d, J = 1.4 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.6, 139.5, 119.6, 67.9, 66.4, 26.0, 18.2. Compound **1i** was obtained as a white solid (183.5 mg, 36% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.40 (tdt, J = 5.7, 2.8, 1.5 Hz, 1H), 4.65 (d, J = 2.9 Hz, 2H), 4.46 (dt, J = 8.3, 3.5 Hz, 1H), 4.34 (t, J = 8.8 Hz, 1H), 4.26 (dd, J = 9.1, 3.1 Hz, 1H), 4.12 (qd, J = 11.4, 7.1 Hz, 3H), 2.44 (pd, J = 7.0, 3.9 Hz, 1H), 1.76 (d, J = 1.5 Hz, 3H), 1.70 (d, J = 1.4 Hz, 3H), 0.93 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 170.5, 154.2, 138.6, 120.3, 69.5, 67.9, 64.5, 58.3, 28.4, 26.0, 18.2, 18.1, 14.8. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{13}H_{22}NO_4$, 256.1543; found, 256.1556.

*(S,E)-3-(2-((3,7-Dimethylocta-2,6-dien-1-yl)oxy)acetyl)-4-isopropyloxazolidin-2-one (**1j**).* The procedure of **1d** using geraniol afforded

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4j as a colorless oil (835 mg, 39% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.34 (t, J = 7.1 Hz, 1H), 5.08 (t, J = 7.1 Hz, 1H), 4.14 (d, J = 7.1 Hz, 2H), 4.08 (s, 2H), 2.11 (t, J = 7.1 Hz, 2H), 2.08−2.04 (m, 2H), 1.68 (d, J = 2.3 Hz, 6H), 1.60 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 173.7, 142.9, 132.1, 123.8, 119.2, 67.9, 66.3, 39.7, 26.4, 25.8, 17.8, 16.6. Conversion of **4j** to **1j** afforded a colorless oil (468 mg, 38% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.43 (ddt, J = 8.3, 7.0, 1.3 Hz, 1H), 5.15−5.08 (m, 1H), 4.68 (d, J = 2.6 Hz, 2H), 4.48 (dt, J = 8.3, 3.5 Hz, 1H), 4.37 (t, J = 8.8 Hz, 1H), 4.29 (dd, J = 9.2, 3.1 Hz, 1H), 4.17 (qd, J = 11.5, 6.9 Hz, 2H), 2.46 (heptd, J = 7.1, 3.9 Hz, 1H), 2.17−2.10 (m, 2H), 2.07 (dd, J = 9.4, 6.1 Hz, 2H), 1.71 (d, J = 1.4 Hz, 3H), 1.70 (d, J = 1.4 Hz, 3H), 1.62 (s, 3H), 0.95 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 170.5, 154.2, 141.8, 131.9, 124.0, 120.0, 69.5, 68.0, 64.5, 58.3, 39.8, 28.4, 26.5, 25.8, 18.1, 17.8, 16.7, 14.8. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{18}H_{30}NO_4$, 324.2169; found, 324.2185.

*(S)-3-((2S,3R)-2-Hydroxy-3-methylpent-4-enoyl)-4-isopropyloxazolidin-2-one (**2d**).* To a solution of **1d** (0.40 mmol, 96.4 mg) in CH_2Cl_2 (1.0 mL) was added n-Bu_2BOTf (0.80 mmol, 800 μL) as 1.0 M solution in CH_2Cl_2, and the reaction was stirred at 0 °C for 5 min. Triethyamine (1.2 mmol, 168 μL) was added. The reaction was warmed to rt and stirred for an additional 3 h. The reaction was quenched with saturated NH_4Cl and extracted three times with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (20% ethyl acetate/hexanes) afforded **2d** and its minor isomer as a colorless oil (78.9 mg, 82% yield, 15:1 selectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.86 (ddd, J = 17.6, 10.3, 7.6 Hz, 1H), 5.13−5.02 (m, 3H), 4.38 (dt, J = 7.2, 3.4 Hz, 1H), 4.30 (t, J = 8.4 Hz, 1H), 4.26 (dd, J = 9.1, 2.8 Hz, 1H), 3.31 (d, J = 8.9 Hz, 1H), 2.61−2.54 (m, 1H), 2.44 (heptd, J = 7.2, 3.7 Hz, 1H), 1.03 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.3, 153.9, 140.0, 115.5, 73.8, 64.2, 59.2, 41.8, 28.4, 18.1, 14.6, 13.9. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{12}H_{20}NO_4$, 242.1387; found, 242.1399.

*(S)-4-Benzyl-3-((S)-2-hydroxypent-4-enoyl)oxazolidin-2-one (**2a**).* Following the procedure for rearrangement of **1d**, **1a** afforded **2a** and its minor isomer as a colorless oil (90% yield, 2:1 selectivity). Major product ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (dd, J = 8.1, 6.5 Hz, 2H), 7.32−7.27 (m, 1H), 7.24−7.19 (m, 2H), 5.87 (ddt, J = 17.2, 10.2, 7.1 Hz, 1H), 5.21−5.09 (m, 3H), 4.66 (ddt, J = 10.0, 6.7, 3.3 Hz, 1H), 4.31−4.23 (m, 2H), 3.55 (d, J = 7.9 Hz, 1H), 3.32 (dd, J = 13.5, 3.3 Hz, 1H), 2.84 (dd, J = 13.5, 9.4 Hz, 1H), 2.62 (dddt, J = 14.3, 7.1, 4.7, 1.3 Hz, 1H), 2.46 (dtt, J = 14.2, 7.1, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.1, 153.4, 134.9, 133.0, 129.6, 129.2, 127.7, 118.8, 70.4, 67.1, 55.7, 38.4, 37.7. Minor product ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 (dd, J = 8.1, 6.5 Hz, 2H), 7.32−7.27 (m, 1H), 7.24−7.19 (m, 2H), 5.87 (ddt, J = 17.1, 10.1, 7.1 Hz, 1H), 5.23−5.14 (m, 3H), 4.75 (ddt, J = 9.8, 8.1, 3.5 Hz, 1H), 4.31 (t, J = 8.6 Hz, 1H), 4.24 (dd, J = 9.2, 3.4 Hz, 1H), 3.35−3.25 (m, 2H), 2.74 (dd, J = 13.4, 9.8 Hz, 1H), 2.67 (dddd, J = 11.3, 5.8, 2.5, 1.2 Hz, 1H), 2.53−2.45 (m, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.7, 153.1, 134.9, 132.6, 129.5, 129.2, 127.7, 119.1, 70.3, 67.3, 55.2, 39.1, 38.3. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{15}H_{18}NO_4$, 276.1230; found, 276.1243.

*(S)-3-((S)-2-Hydroxypent-4-enoyl)-4-isopropyloxazolidin-2-one (**2b**).* Following the procedure for rearrangement of **1d**, **1b** afforded **2b** and its minor isomer (81% yield, 3:1 selectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.85 (ddt, J = 17.2, 10.2, 7.1 Hz, 1H), 5.19−5.06 (m, 3H), 4.41 (dt, J = 7.7, 3.3 Hz, 1H), 4.34 (t, J = 8.6 Hz, 1H), 4.29 (dd, J = 9.1, 2.9 Hz, 1H), 3.57 (d, J = 8.0 Hz, 1H), 2.59 (dddt, J = 14.3, 7.1, 4.9, 1.3 Hz, 1H), 2.48−2.38 (m, 2H), 0.94 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.0, 154.1, 133.1, 118.6, 70.4, 64.4, 59.1, 38.4, 28.4, 18.1, 14.7. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{11}H_{18}NO_4$, 228.1230; found, 228.1243.

*(S)-4-Benzyl-3-((2S,3R)-2-hydroxy-3-methylpent-4-enoyl)-oxazolidin-2-one (**2c**).* The procedure for **1d** using **1c** afforded **2c** and its minor isomer as a colorless oil (90% yield, 5:1 selectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (dd, J = 8.1, 6.5 Hz, 2H), 7.32−7.27 (m, 1H), 7.24−7.20 (m, 2H), 5.89 (ddd, J = 17.5, 10.3, 7.5 Hz, 1H), 5.16−5.06 (m, 3H), 4.64 (ddt, J = 9.6, 6.4, 3.5 Hz, 1H), 4.26−4.23 (m, 2H), 3.37−3.30 (m, 2H), 2.82 (dd, J = 13.5, 9.6 Hz, 1H), 2.66−2.58 (m, 1H), 1.06 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.4, 153.2, 139.9, 135.0, 129.6, 129.2, 127.7, 115.6, 73.9, 67.0, 55.8, 41.8, 37.7, 13.9. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{16}H_{20}NO_4$, 290.1386; found, 290.1398.

*(S)-3-((2S,3R)-2-Hydroxy-3-isopropylpent-4-enoyl)-4-isopropyloxazolidin-2-one (**2e**).* Following the procedure for rearrangement of **1d**, **1e** afforded **2e** (71% yield, >30:1 selectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.70 (dt, J = 17.1, 10.1 Hz, 1H), 5.23 (t, J = 9.8 Hz, 1H), 5.08 (dd, J = 10.3, 2.2 Hz, 1H), 5.02 (dd, J = 17.1, 2.2 Hz, 1H), 4.33 (q, J = 4.7 Hz, 1H), 4.24 (d, J = 4.8 Hz, 2H), 3.18 (d, J = 10.2 Hz, 1H), 2.39 (heptd, J = 7.0, 3.7 Hz, 1H), 2.24 (dddd, J = 19.2, 13.1, 8.3, 3.5 Hz, 2H), 0.92 (dd, J = 6.9, 1.4 Hz, 6H), 0.89 (d, J = 6.9 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 175.0, 154.4, 134.5, 118.8, 71.9, 64.3, 59.1, 56.5, 28.7, 26.9, 21.5, 18.2, 16.7, 14.8. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{14}H_{24}NO_4$, 270.1670; found, 270.1712.

*(S)-3-((2S,3S)-2-Hydroxy-3-phenylpent-4-enoyl)-4-isopropyloxazolidin-2-one (**2f**).* To a solution of **1f** (0.040 mmol, 12.1 mg) in CH_2Cl_2 (1.0 mL) was added n-Bu_2BOTf (0.080 mmol, 80 μL) as 1.0 M solution in CH_2Cl_2 followed by stirring at −78 °C for 5 min. Triethylamine (0.12 mmol, 17 μL) was added. The reaction was warmed to rt and stirred for an additional 3 h. The reaction was quenched with saturated NH_4Cl and extracted three times with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (20% ethyl acetate/hexanes) afforded **2f** and its minor isomer (11.2 mg, 91% yield, >30:1 selectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35−7.29 (m, 2H), 7.29−7.22 (m, 3H), 6.19 (ddd, J = 17.1, 10.2, 8.2 Hz, 1H), 5.58 (dd, J = 9.2, 6.0 Hz, 1H), 5.20 (dt, J = 17.1, 1.3 Hz, 1H), 5.17 (dt, J = 10.2, 1.2 Hz, 1H), 4.33−4.23 (m, 3H), 3.78−3.71 (m, 1H), 3.21 (d, J = 9.2 Hz, 1H), 2.40 (heptd, J = 7.0, 3.5 Hz, 1H), 0.90 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 173.7, 154.0, 138.9, 137.4, 128.7, 128.6, 127.5, 117.3, 73.7, 64.3, 59.3, 54.5, 28.4, 18.1, 14.7. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{17}H_{22}NO_4$, 304.1543; found, 304.1558.

*(4S)-3-(2-Hydroxy-3-methylpent-4-enoyl)-4-isopropyloxazolidin-2-one (**22**).* Following the procedure for rearrangement of **1d**, **1g** afforded **22** and its minor isomers (90% yield, 1.7:1:0.5:0.1 selectivity). Major product ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.75 (ddd, J = 17.1, 10.4, 8.0 Hz, 1H), 5.11−5.05 (m, 3H), 4.38−4.35 (m, 1H), 4.33−4.30 (m, 1H), 4.30−4.28 (m, 1H), 3.19 (d, J = 8.6 Hz, 1H), 2.69−2.62 (m, 1H), 2.48 (dtd, J = 14.1, 7.0, 3.6 Hz, 1H), 1.21 (d, J = 6.9 Hz, 3H), 0.93 (dd, J = 7.1, 1.6 Hz, 3H), 0.89 (dd, J = 6.9, 1.2 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.3, 153.8, 137.6, 116.6, 74.4, 64.3, 59.4, 41.4, 28.3, 18.1, 17.0, 14.6. Minor product ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.77−5.70 (m, 1H), 5.10−5.06 (m, 2H), 5.04 (ddd, J = 17.2, 1.9, 1.2 Hz, 1H), 4.52 (dt, J = 8.6, 3.4 Hz, 1H), 4.37−4.34 (m, 1H), 4.29−4.26 (m, 1H), 3.01 (d, J = 8.9 Hz, 1H), 2.78 (dtdd, J = 9.4, 8.3, 6.5, 2.6 Hz, 1H), 2.26 (heptd, J = 6.8, 3.4 Hz, 1H), 1.26 (d, J = 6.9 Hz, 3H), 0.94−0.92 (m, 3H), 0.90−0.89 (m, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.8, 153.5, 136.9, 117.1, 74.1, 64.2, 58.3, 42.0, 28.7, 18.1, 17.7, 14.9. HRMS (DART-Orbitrap): m/z [M + H]$^+$ calcd for $C_{12}H_{20}NO_4$, 242.1387; found, 242.1399.

*(S)-3-((S)-2-Hydroxy-3,3-dimethylpent-4-enoyl)-4-isopropyloxazolidin-2-one (**23**).* To a solution of **1i** (0.10 mmol, 25.5 mg) in CH_2Cl_2 (1.0 mL) was added n-Bu_2BOTf (0.15 mmol, 150 μL) as 1.0 M solution in CH_2Cl_2, and the mixture was stirred at −78 °C for 5 min. Triethylamine (0.30 mmol, 42 μL) was added. The reaction was warmed to rt and stirred for an additional 12 h. The reaction was quenched with saturated NH_4Cl and extracted three times with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (20% ethyl acetate/hexanes) afforded **23** and its minor isomer (21.3 mg, 84% yield, 10:1 selectivity). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.94 (dd, J = 17.5, 10.8 Hz, 1H), 5.22 (d, J = 10.0 Hz, 1H), 5.06 (dd, J = 10.8, 1.3 Hz, 1H), 5.02 (dd, J = 17.5, 1.3 Hz, 1H), 4.33 (ddd, J = 7.1, 3.9, 2.9 Hz, 1H), 4.26−4.20 (m, 2H), 3.10 (d, J = 10.0 Hz, 1H), 2.43 (heptd, J = 7.0, 3.8 Hz, 1H), 1.15 (s, 3H), 1.08 (s, 3H), 0.93 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 173.7, 154.1, 143.7, 113.6, 74.7, 64.0, 59.4, 42.3,

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28.7, 24.9, 20.7, 18.2, 14.8. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{13}H_{22}NO_4$, 256.1543; found, 256.1556.

*(S)-3-((2S,3R)-2-Hydroxy-3,7-dimethyl-3-vinyloct-6-enoyl)-4-isopropyloxazolidin-2-one (**24**).* The procedure of **1i** using **1j** afforded **24** (85% yield, 5:1:0.7 selectivity). Major ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.79−5.73 (m, 1H), 5.27 (dd, J = 10.8, 0.8 Hz, 1H), 5.19 (ddd, J = 17.5, 4.1, 0.9 Hz, 1H), 5.08 (tdt, J = 7.1, 2.8, 1.4 Hz, 1H), 4.58 (s, 1H), 4.04 (dt, J = 14.8, 7.5 Hz, 1H), 3.84 (dd, J = 11.8, 3.1 Hz, 1H), 3.75 (ddd, J = 10.1, 8.1, 3.1 Hz, 1H), 2.37 (dp, J = 10.2, 6.7 Hz, 1H), 2.02−1.88 (m, 2H), 1.74 (ddd, J = 13.6, 11.9, 4.8 Hz, 1H), 1.67 (t, J = 1.3 Hz, 3H), 1.59 (d, J = 1.3 Hz, 3H), 1.58−1.54 (m, 1H), 1.21 (s, 3H), 1.03 (d, J = 6.7 Hz, 3H), 0.90−0.87 (m, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 174.0, 154.1, 142.4, 131.7, 124.5, 114.9, 74.2, 64.0, 59.5, 46.0, 38.6, 28.8, 25.8, 22.7, 18.2, 17.8, 15.9, 14.9. Minor ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.94 (dd, J = 17.6, 10.9 Hz, 1H), 5.32 (d, J = 10.2 Hz, 1H), 5.13 (dd, J = 10.9, 1.4 Hz, 1H), 5.10−5.05 (m, 1H), 5.00 (dd, J = 17.6, 1.5 Hz, 1H), 4.29 (ddd, J = 7.8, 3.9, 2.4 Hz, 1H), 4.22 (dd, J = 9.1, 2.4 Hz, 1H), 4.19 (dd, J = 9.1, 7.8 Hz, 1H), 3.01 (d, J = 10.3 Hz, 1H), 2.42 (pd, J = 6.9, 3.8 Hz, 1H), 1.90 (dq, J = 11.8, 6.2 Hz, 2H), 1.70−1.65 (m, 5H), 1.57 (d, J = 1.3 Hz, 3H), 1.03 (s, 3H), 0.92 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 172.7, 155.9, 138.9, 132.3, 123.8, 117.5, 84.2, 61.7, 61.4, 43.8, 36.0, 26.6, 25.8, 22.3, 20.1, 19.9, 18.8, 17.8. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_{18}H_{30}NO_4$, 324.2169; found, 324.2182.

*(3S,4R)-3-Hydroxy-4-methyldihydrofuran-2(3H)-one (**6**).* To a solution of **2d** (0.21 mmol, 50.8 mg) in CH_2Cl_2 cooled to −78 °C, O_3 was bubbled through until the solution turned blue. Dimethyl sulfide (13.5 mmol, 1.0 mL) was added gradually until the blue color disappeared. The mixture was warmed to rt and stirred for another 30 min to ensure complete quenching. The reaction was washed three times with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography (40% ethyl acetate/hexanes) afforded the corresponding aldehyde (21.3 mg, 42% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.79 (s, 1H), 5.32 (dd, J = 7.0, 5.3 Hz, 1H), 4.44 (dt, J = 3.8, 2.3 Hz, 1H), 4.39 (t, J = 8.7 Hz, 1H), 4.32 (dd, J = 9.2, 2.6 Hz, 1H), 3.96 (d, J = 7.0 Hz, 1H), 2.95 (qd, J = 7.3, 5.4 Hz, 1H), 2.42 (dtq, J = 11.0, 7.2, 4.0, 3.4 Hz, 1H), 1.15 (d, J = 7.2 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 201.8, 172.2, 154.5, 70.3, 64.7, 59.1, 48.1, 28.4, 18.0, 14.7, 8.5. $NaBH_4$ (1.0 mmol, 37.8 mg) was added to acetic acid (0.5 mL) at 0 °C, warmed to rt, and then stirred for 1.0 h. The aldehyde in acetic acid (0.20 mL) was added, and the mixture was stirred for an additional 30 min. The reaction was quenched by saturated $NaHCO_3$ solution and extracted three times with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Flash chromatography (40% ethyl acetate/hexanes) afforded the cyclized lactone **6** (2 mg, 20%), which was compared to literature data.[12] ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.42 (dd, J = 9.1, 7.9 Hz, 1H), 4.01 (dd, J = 10.6, 2.9 Hz, 1H), 3.80 (dd, J = 10.7, 9.1 Hz, 1H), 2.59−2.48 (m, 2H), 1.26 (d, J = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 177.4, 73.9, 70.7, 39.1, 14.5. $[\alpha]_D^{20}$ −40° (c 1.0, $CDCl_3$). HRMS (DART-Orbitrap): m/z $[M + H - H_2O]^+$ calcd for $C_5H_7O_2$, 99.0440; found, 99.0446.

*(3S,4R)-3-Hydroxy-4-isopropyldihydrofuran-2(3H)-one (**7**).* Following the procedure converting **2d** to lactone **6**, **2e** afforded the intermediate aldehyde as a colorless liquid (15 mg, 42% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.86 (d, J = 1.5 Hz, 1H), 5.10−5.06 (m, 1H), 4.38 (t, J = 8.1 Hz, 1H), 4.30 (d, J = 6.4 Hz, 2H), 3.09 (ddd, J = 9.8, 4.0, 1.5 Hz, 1H), 2.44 (tt, J = 7.3, 3.7 Hz, 1H), 2.32 (dqd, J = 12.0, 6.6, 3.1 Hz, 1H), 1.21 (d, J = 7.3 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.94 (dd, J = 7.2, 1.8 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 203.9, 171.6, 155.3, 68.7, 64.9, 59.0, 57.4, 28.7, 26.2, 21.2, 18.6, 18.0, 14.9. The cyclized lactone **7** was obtained as a colorless liquid (2 mg, 28% yield), which was compared to literature data.[12a] ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.43 (t, J = 8.7 Hz, 1H), 4.15 (dd, J = 10.4, 2.4 Hz, 1H), 3.89 (dd, J = 10.7, 9.2 Hz, 1H), 2.50 (d, J = 2.5 Hz, 1H), 2.23 (tt, J = 10.5, 8.5 Hz, 1H), 1.78 (ddt, J = 14.8, 13.0, 6.6 Hz, 1H), 1.11 (d, J = 6.7 Hz, 3H), 0.95 (d, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 178.0, 71.8, 68.9, 50.2, 30.9, 20.7, 20.3. HRMS (DART-Orbitrap): m/z $[M + H - H_2O]^+$ calcd for $C_7H_{11}O_2$, 127.0754; found, 127.0761.

*(S)-3-Hydroxy-4,4-dimethyldihydrofuran-2(3H)-one (**8**).* The procedure of **6** using **23** afforded the intermediate aldehyde as a white crystal (6.1 mg, 23% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.69 (s, 1H), 4.94 (d, J = 6.9 Hz, 1H), 4.44 (ddd, J = 8.3, 4.1, 2.9 Hz, 1H), 4.37 (dd, J = 9.1, 8.3 Hz, 1H), 4.31−4.28 (m, 2H), 2.33 (hd, J = 6.9, 4.0 Hz, 1H), 1.25 (s, 3H), 1.22 (s, 3H), 0.92 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H). The cyclized lactone **8** as a colorless oil (3 mg, 96% yield) shown to be identical to a known sample.[13] ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.10 (d, J = 3.3 Hz, 1H), 4.03 (d, J = 9.0 Hz, 1H), 3.94 (d, J = 8.9 Hz, 1H), 2.37 (d, J = 3.1 Hz, 1H), 1.24 (s, 3H), 1.08 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 176.8, 76.5, 75.9, 41.1, 23.1, 18.9. HRMS (DART-Orbitrap): m/z $[M + H]^+$ calcd for $C_6H_{12}O_3$, 131.0703; found, 131.0704. $[\alpha]_D^{20}$ −33.3 (c 1.2, $CDCl_3$).

*(S)-Butane-1,2,4-triol (**5**).* To a solution of **2a** (0.07 mmol, 18.5 mg) in CH_2Cl_2 cooled to −78 °C, O_3 was bubbled through until the solution turned blue. Dimethyl sulfide (13.5 mmol, 1.0 mL) was added gradually until the blue color disappeared, and the mixture was warmed to rt and stirred for another 30 min to ensure the complete quenching. The reaction was extracted three times with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography (50% ethyl acetate/hexanes) afforded the aldehyde as a colorless liquid (5.8 mg, 31% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.81 (d, J = 0.9 Hz, 1H), 7.37−7.31 (m, 2H), 7.31−7.27 (m, 1H), 7.21 (dd, J = 7.0, 1.7 Hz, 2H), 4.81 (d, J = 4.6 Hz, 1H), 4.69 (ddt, J = 10.4, 9.2, 3.0 Hz, 1H), 4.31 (dd, J = 9.2, 8.0 Hz, 1H), 4.27−4.24 (m, 2H), 3.85−3.65 (m, 1H), 3.33 (dd, J = 13.5, 3.5 Hz, 1H), 2.85−2.81 (m, 1H). To a solution of the aldehyde in MeOH (0.10 mL) was added $NaBH_4$ (0.05 mmol, 2 mg) at 0 °C and stirred for 1 h after warming to rt. The reaction was concentrated in vacuo. Flash chromatography (ethyl acetate) afforded the triol **5** as a colorless liquid (1.9 mg, 85%), which was compared with literature data.[11] ^{1}H NMR (500 MHz, D_2O): δ 3.75 (ddt, J = 8.5, 6.8, 4.0 Hz, 1H), 3.64 (ddd, J = 7.6, 5.9, 1.6 Hz, 2H), 3.52 (dd, J = 11.8, 3.8 Hz, 1H), 3.41 (dd, J = 11.7, 6.8 Hz, 1H), 1.66 (dtd, J = 14.6, 7.3, 4.3 Hz, 1H), 1.56 (ddt, J = 14.5, 8.9, 6.0 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, D_2O): δ 69.0, 65.6, 58.4, 34.7. $[\alpha]_D^{20}$ − 31.5° (c 1.0, D_2O). HRMS (DART-Orbitrap): m/z $[M + H - HOD]^+$ calcd for $C_4H_7D_2O_2$, 91.0723; found, 91.0728.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b01426.

Spectroscopic, rate, and computational data (PDF)

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