Enantioselective Construction of Cyclic Ethers by An Aldol-Cyclization Sequence

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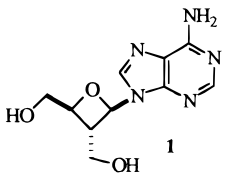
We have modified the substrate used in deconjugative aldol-cyclizations by incorporating the Evans chiral auxiliary. The deconjugative aldol step, using boron enolates, gave the expected products with complete *syn*-aldol stereochemistry. These compounds could then undergo an iodine-mediated cyclization to form optically active products. Oxetanes and fused ring tetrahydrofurans were easily assembled with a variety of substitution patterns and with excellent enantiocontrol. The deconjugation of acyclic chiral enimides resulted in the loss of control of olefin geometry. However, these compounds did appear to cyclize with excellent enantiocontrol.

Introduction

Substituted cyclic ethers, oxetanes and tetrahydrofurans, in particular, are a common structural subunit found in a variety of natural products. Oxetanocin[2] (**1**) and paclitaxel[3] (**2**) incorporate the oxetane ring, while the more common tetrahydrofuran ring can be found in such compounds as (−)-nonactic acid[4] (**3**), citreoviral[5] (**4**), and monensin[6] (**5**). From this small sample, one can see the varied substitution pattern and stereochemical arrangements that need to be addressed in the synthesis of these and other compounds. Consequently, new methods for the assembly of these fragments in a stereospecific and ultimately enantiospecific manner is desirable.



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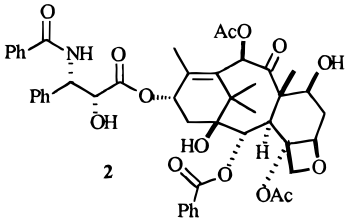

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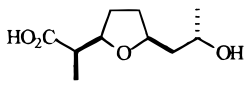

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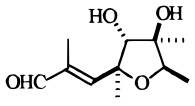

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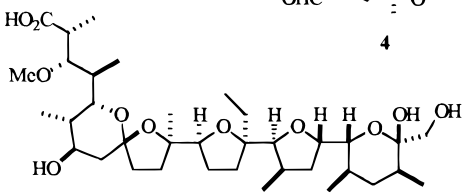

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The varied substituents, substitution pattern, and stereochemistry superimposed upon the conformational mobility of the tetrahydrofuran ring or the strain of the oxetane ring provides a challenge in synthesis to the chemist. Solutions to this challenge have resulted in a variety of ingenious methods for their construction. These methods[7,8] include electrophile-induced (proton, halogen, metal, and chalogenide) reactions, oxidative cyclizations, ester enolate Claisen reactions, radical reactions, epoxide ring opening reactions, Michael additions, cycloadditions, and the use of carbohydrate precursors. In recent years, a renaissance in the electrophile-mediated cyclization of unsaturated alcohols has occurred.[9,10] However, this resurgence has focused on the

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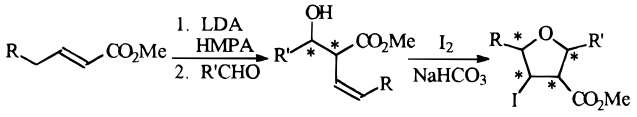
Scheme 1



5-*endo-trig* mode of ring closure rather than the 5-*exo-trig* mode that is predicted by Baldwin's rules. We and others[9,10] have shown the feasibility of this method for the assembly of these systems. In synthetic terms, the endo mode of ring closure provides for increased functionality in the ring, i.e., the iodine, after cyclization, resides on the ring rather than on some pendent substituent. This results in an additional functional group by which the ring may be further elaborated.

We have developed a deconjugative aldol−cyclization sequence[10] (see Scheme 1) for the construction of cyclic ethers. This involved dienolate formation followed by kinetic aldolization at the α-position to generate a species with a homoallylic moiety. This unsaturated alcohol substructure could undergo an iodine-mediated cyclization to afford the cyclic ether derivative. This sequence provided ready access to these compounds in two steps with excellent relative stereocontrol of the resultant four stereocenters. Proper choice of aldol diastereomer (*syn* or *anti*) and olefin geometry (*E* or *Z*) would allow one to essentially construct all the possible isomers for any substitution pattern. A combinatorial library of these compounds could be used as a repository of building blocks in the synthesis of various natural products. For example, in an approach to polyether antibiotics, if R or R′ (see Scheme 1) was, or could be converted to, a carbonyl function (aldehyde or ketone), then the product of the cyclization step could serve as the electrophile in a subsequent deconjugative aldol step. In such a fashion, a polyether antibiotic could be assembled by an iterative manner. A benefit of this approach is that one could easily assemble analogues for structure-function relationships.

In an effort to expand the scope of this method, we wished to extend the chemistry into the chiral manifold, i.e., develop a variation of this sequence for the synthesis of optically active cyclic ethers. In order to exert enantiocontrol over our method, we needed to address the potential sites of control in both steps. From an examination of our earlier work, it became obvious that if control of absolute stereochemistry could be accomplished in the deconjugative aldol step, then excellent enantiocontrol could be obtained in the cyclization step by chiral induction. The chirality generated in the aldol product would direct the cyclization by controlling the allowed conformations that could be adopted in the transition state of the cyclization reaction. Furthermore, the enantioselectivity of the deconjugative aldol step would have to address the double bond geometry in the deconjugation process. Since the cyclization appears to obey the Stork−Eschenmoser hypothesis, in that net *anti* addition of the alcohol and iodine across the alkene is observed, complete control of olefin geometry is crucial for high enantiocontrol in this step. Consequently, it was decided that the most facile procedure would be to make use of the vast amount of information associated with the use of chiral auxiliaries in the aldol reaction.[11] While the majority of this work was on saturated systems, there was one example of an unsaturated system.[12] Therefore, it was decided to make use of the Evans' chiral auxiliary, since they are readily available and have been shown to exhibit great enantiocontrol.[11] We now wish to report our studies in which the enantiospecific variation of our deconjugative aldol-cyclization sequence has been accomplished.

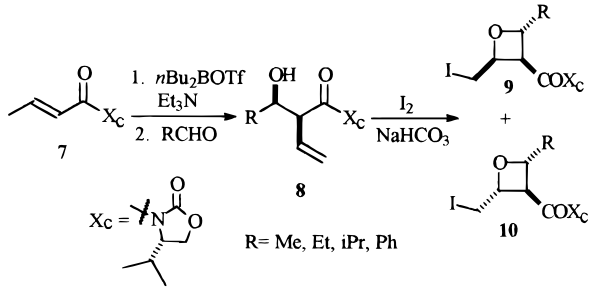
Table 1. Results of Sequence on Imide 7

entry	R	**8** (% yield)[a]	% yield[a] (**9**/**10** ratio)
1	Me (**a**)	90	47 (12:1)
2	Et (**b**)	88	48 (19:1)
3	iPr (**c**)	74	40 (24:1)
4	Ph (**d**)	76	na[b]

[a] Based on isolated, chromatographically pure material. [b] Reaction products decomposed.

Result and Discussion

These investigations began by constructing the chiral imide of crotonic acid. Following the procedure of Evans,[12] crotonyl chloride was treated with the lithiated oxazolidinone derived from L-valine to produce imide **7**. This substrate permitted us to examine the two-step sequence without the further complication of the olefin geometry. Aldol reactions with a series of aldehydes via the boron enolate gave the desired *syn* aldols **8** in good to excellent yields (see Table 1). The chiral auxiliary performed its function without perturbing the deconjugation chemistry.



With these compounds in hand, we were now able to study the cyclization step with the chiral auxiliary intact. Cyclization using the standard conditions, 3 equivalents each of iodine and sodium bicarbonate in acetonitrile, afforded oxetanes **9** and **10** (see Table 1). No tetrahydrofuran formation was observed. This stands in sharp contrast to our previous results with the methyl ester, in which a mixture of oxetane and tetrahydrofuran was obtained.[10a] For compounds **9**, **10**, **13**, and **14**, the

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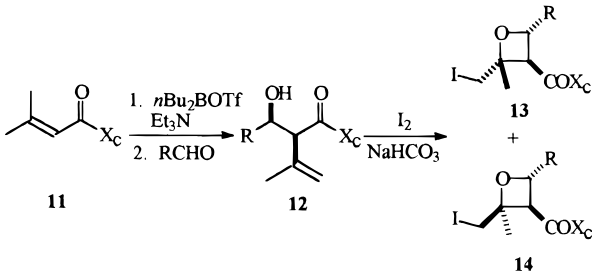
Table 2. Results of Sequence on Imide 11

entry	R	**12** (% yield)[a]	% yield[a] (**13**/**14** ratio)
1	Me (**a**)	70	63 (>98:<2)
2	Et (**b**)	72	84 (82:18)
3	64	64	40 (81:19)
4	Ph (**d**)	70	20[b]

[a] Based on isolated, chromatographically pure material. [b] Reaction product decomposed but appeared to be a single isomer.

formation of the oxetane is easily discerned via the primary iodide moiety. The carbon of the primary iodide is very diagnostic and appears between −24 ppm for methyl iodide to about +10 ppm for alkyl iodides due to the heavy atom effect.[13] We have observed this same chemical shift attribute in several of our other compounds.[10,14,15] The corresponding tetrahydrofuran would contain a secondary iodide, which would show a carbon shift significantly further downfield (ca. 20−40 ppm).



One can also note from Table 1 that excellent facial selectivity was obtained in the cyclization step. The relative stereochemistry was determined by NOE measurements, while the absolute stereochemistry is assumed to be that which one would expect to be induced by the chiral auxiliary (the latter was shown to be true in an other system by X-ray analysis, *vide infra*). The inability to isolate products from the phenyl derivative in the analogous methyl ester series was also observed in our earlier work.[10] Since phenyl products can be obtained in other systems (see Table 2 and our previous work[10]), this would tend to indicate that the phenyl ring does not perturb the cyclization chemistry. However, the phenyl substituent, in this system, may render the product less stable, thus giving rise to decomposition products. Figure 1 shows the potential transition structures for the observed products. The structure leading to the major product experiences an $A^{1,3}$ strain between the vinyl hydrogen and the imide group. This interaction is absent in the transition structure leading to the minor product; however, there appears be a 1,3-transannular interaction between the iodomethyl and R groups in the developing oxetane ring. This nonbonding interaction may override the allylic strain, giving rise to the observed product. This is substantiated by the fact that as the R group becomes more sterically demanding one observed

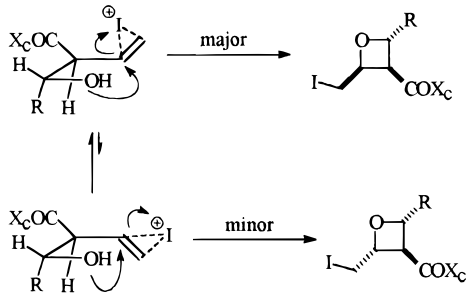


Figure 1.

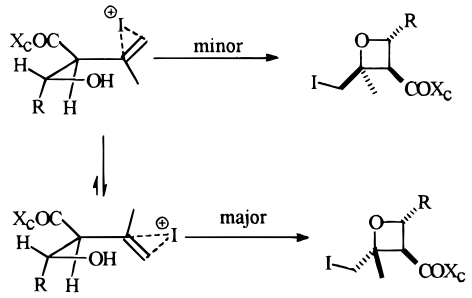


Figure 2.

Table 3. Results of Sequence on Imide 15

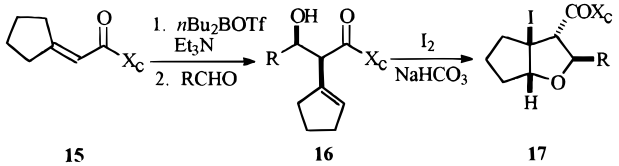
entry	R	**16** (% yield)[a]	**17** (% yield)[a]
1	Me (**a**)	87	83
2	Et (**b**)	88	81
3	iPr (**c**)	86	61
4	Ph (**d**)	84	83

[a] Based on isolated, chromatographically pure material.

increased selectivity in the cyclization (see Table 1). These results indicated that the sequence could be carried out using the chiral auxiliary, so we proceeded to examine other substrates.

We next constructed **11** by coupling the chiral imide and 3,3-dimethylacrylic acid. Exposure of **11** to the two-step sequence gave the oxetanes **13** and **14** by way of aldol **12**. The results for this series are summarized in Table 2. The aldol reaction gave exclusively the α-alkylated deconjugated product with excellent enantiocontrol. The control observed in our earlier work with the methyl esters eroded in the cyclizations of **12**.[10b] While **12a** cyclized with complete control, and in improved yield, to the corresponding oxetane, **12b** and **12c** exhibited average stereocontrol in the cyclization step. Unexpectedly, **12d** proved to be problematic, and the inability to isolate a stable product was contrary to our previous efforts.[10b] In this last case, the poor yield could be partly rationalized by the fact this compound tended to undergo a retro-aldol reaction, as judged by the formation of benzaldehyde in the reaction. The relative stereochemistry (see Figure 2) of the major product could still be rationalized on steric grounds using a transition state based on similar arguments as before.

In a series related to **11**, **15** was subjected to the same sequence of steps to produce **17** by way of **16** (see Table 3). The aldol reaction proceeded in excellent yield with



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(15) In compounds **14a**, **13**/**14c**, and **13d**, the shift of the primary iodide carbon comes at about 14 ppm. This downfield shift can easily be rationalized if one considers the fact that for these compounds this carbon is also neopentyl. The "β-effect" due to the additional methyl substituent is sufficient to cause the observed change in chemical shift (~6 ppm).[13] This value is still far removed from where we have been observing THF iodide shifts (20−30 ppm).

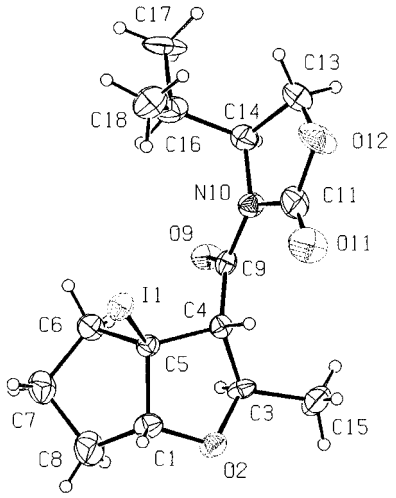


Figure 3. X-ray structure of **17a**.

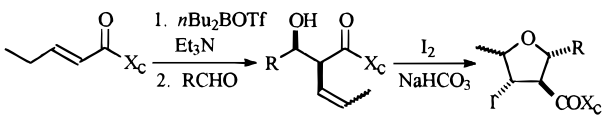
Table 4. Results of Sequence on Imide 18

entry	R	**19** (% yield) (*Z*:*E*)[a]	**20** (% yield)[a]
1	Me (**a**)	98 (70:30)	74
2	Et (**b**)	70 (69:31)	77
3	iPr (**c**)	81 (69:31)	81
4	Ph (**d**)	84 (69:31)	63

[a] Based on isolated, chromatographically pure material.

only one product being detected. Contrary to the situation with **11**, the cyclizations proceeded in excellent yield and with excellent stereocontrol. However, now the only product formed was the fused-ring tetrahydrofuran. No oxetane could be isolated. This structural assignment constitutes a correction of our initially published work on the methyl ester derivative.[10b] A similar occurrence was experienced by workers in related work.[9j] The initial NOE measurements lead us to the conclusion that a spiro-oxetane system had resulted. Subsequently, we have been able to obtain crystals of **17a**, which unambiguously confirm the formation of the fused-ring system (see Figure 3). This X-ray structure provided confirmation of the absolute stereochemistry in addition to the stereochemistry generated in the aldol step. The predicted *syn* aldol diastereomer would give rise to the observed tetrahydrofuran stereochemistry.

The final series investigated was (*E*)-pentenimide **18**. While the aldol reaction proceeded in good to excellent yield with only one aldol isomer being isolated, loss of double bond geometry was now witnessed (see Table 4) with (*Z*)-**19** as the major isomer isolated. In all the other systems, we always had observed complete inversion of double bond geometry in these deconjugative aldol reactions, including the methyl ester derivative of **18**.[10a]



Attempts to equilibrate the olefinic mixture all failed. Since this mixture could not be separated by chromatography, it was subjected to the conditions for cyclization. This resulted in the formation of **20** as a mixture of diastereomers, the ratio of which matched the starting olefinic ratio. Presumably, these two diastereomers were formed from the two olefinic geometries in **19**. If this is so, then cyclization of pure **19** should give rise to **20** with excellent enantiocontrol. The origin of this loss of olefin geometry is currently under scrutiny, and preliminary results have been published.[16]

Conclusions

We have demonstrated that the deconjugative aldol-cyclization sequence can be extended by the use of chiral auxiliaries for the construction of optically active products. Oxetanes and fused ring tetrahydrofurans can easily be assembled with a variety of substitution patterns with excellent enantiocontrol. The deconjugation of chiral pentenimides resulted in the loss of control of olefin geometry. However, these compounds did appear to cyclize with excellent enantiocontrol.

Experimental Section

General Procedures and Materials. Melting points were taken on a Fischer-Johns melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 400 and 100 MHz, respectively, unless specified otherwise. Combustion analyses were performed by M-H-W Laboratories, Phoenix, AZ. All solvents used for chromatography were distilled prior to use. Reactions were monitored by TLC using E. Merck precoated silica gel 60 F-250 (0.25 mm thickness) aluminum-backed plates. The plates were visualized by immersion in *p*-anisaldehyde solution and warming on a hotplate. E. Merck silica gel 60 (70-230 mesh) was used for column chromatography. All solvents were reagent grade, and anhydrous solvents were dried prior to use as follows: CH_2Cl_2 was distilled from CaH_2, while ether and THF were distilled from benzophenone ketyl. Compounds obtained from commercial sources were used directly as received.

General Protocol for Asymmetric Aldol Reactions. To a −78 °C solution of the imide in dry dichloromethane (4 mL/mmol) was added dibutylboryl triflate (1.2 equiv) and stirred for 5 min. The solution was then treated with dry triethylamine (1.4 equiv). After 1 h at −78 °C and 15 min at 0 °C, the solution was recooled to −78 °C and treated with the appropriate aldehyde (1−1.4 equiv). After 1 h at −78 °C and 1 h at 0 °C, the solution was partitioned between 30 mL each of 1 M sodium bisulfate and ethyl acetate/hexanes (1:1). The organic layer was washed with brine and concentrated in vacuo. The resulting oil was redissolved in ether (5 mL), cooled to 0 °C, and treated with 1 mL each of pH 7 phosphate buffer and 30% hydrogen peroxide. After being stirred for 1 h at 0 °C, the reaction mixture was poured into water (25 mL) and ethyl acetate/hexanes (1:1) (25 mL), extracted with ether (3×), washed once with saturated sodium bicarbonate, dried (anhydrous sodium sulfate), filtered, and concentrated in vacuo.

Compounds **7** and **8a**−**d** have been previously prepared,[11a] but to our knowledge the optical rotations for **8** have not been reported. The optical rotations we obtained for these compounds were as follows. **(2′*S*,3′*R*,4*S*)-3-(2′-Ethenyl-3′-hydroxy-1′-oxobutyl)-4-(methylethyl)-2-oxazolidinone (8a)**: $[\alpha]_D = -8.9°$ (*c* 0.247, $CHCl_3$). **(2′*S*,3′*R*,4*S*)-3-(2′-Ethenyl-3′-hydroxy-1′-oxopentyl)-4-(methylethyl)-2-oxazolidinone (8b)**: $[\alpha]_D = -13.1°$ (*c* 0.420, $CHCl_3$). **(2′*S*,3′*R*,4*S*)-3-(2′-Ethenyl-3′-hydroxy-4′-methyl-1′-oxobutyl)-4-(methylethyl)-2-oxazolidinone (8c)**: $[\alpha]_D = -17.3°$ (*c* 0.486, $CHCl_3$). **(2′*S*,3′*R*,4*S*)-3-(2′-Ethenyl-3′-hydroxy-1′-oxobutyl-3′-phenyl)-4-(methylethyl)-2-oxazolidinone (8d)**: $[\alpha]_D = -19.6°$ (*c* 0.224, $CHCl_3$).

General Protocol for Iodoetherification of α-Vinyl *β*-Hydroxy Imides 8a−d. To a solution containing dry acetonitrile (5 mL), iodine (3.0 equiv), and sodium bicarbonate (3.0 equiv) was added α-vinyl *β*-hydroxy imide **8**. The mixture was stirred for 24 h and then quenched with 0.2 M sodium thiosulfate and extracted with ether (3×). The ether layer was

(16) Galatsis, P.; Manwell, J. J.; Millan, S. D. *Tetrahedron Lett.* **1996**, *37*, 5261.

washed once with brine, dried (anhydrous sodium sulfate), filtered and concentrated *in vacuo*.

Cyclization of 8a. The general procedure was followed using iodine (3.93 mmol, 997 mg), sodium bicarbonate (3.93 mmol, 330 mg) and **8a** (1.31 mmol, 300 mg). Chromatography (20% ethyl acetate/80% hexanes) on 25 g of silica gel afforded **9a** (202 mg, 43%) and **10a** (18.5 mg, 4%, mp 131−132 °C). **(*2S*,3*S*,4*R*)-2-(Iodomethyl)-4-methyl-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (9a):** IR (CCl_4)-2968, 2931, 2901, 2876, 1791, 1759, 1710, 1484, 1470, 1420, 1386, 1354, 1339, 1310, 1252, 1215, 1177, 1134, 1067, 1038, 1021, 954, 911, 868 cm^{-1}; ^1H NMR δ 4.65 (ddd, 1H, J = 8.8, 6.0, 1.6 Hz). 4.51 (q, 1H, J = 6.4 Hz), 4.25 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 7.2 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 44.2 Hz), 4.05 (ddd, 1H, J = 7.2, 5.2, 3.6 Hz), 3.19 (dd, 1H, J = 10.4, 6.0 Hz), 3.02 (dd, 1H, J = 10.4, 8.8 Hz), 2.96 (m, 1H), 2.26 (m, 1H), 1.49 (d, 3H, J = 6.8 Hz), 0.96 (d, 3H, J = 6.0 Hz), 0.94 (d, 3H, J = 6.0 Hz); ^{13}C NMR δ 165.8, 120.0, 72.9, 71.6, 69.5, 58.7, 47.8, 30.1, 18.5, 17.1, 16.9, 3.6; HRMS exact mass for $C_{12}H_{18}IN0_4$ (M − I) calcd 240.1236, found 240.1245; $[\alpha]_D$ = +24.1° (*c* 0.216, $CHCl_3$). **(2*R*,3*S*,4*R*)-2-(Iodomethyl)-4-methyl-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (10a):** IR (film) 2957, 2936, 2921, 2872, 1765, 1695, 1493, 1463, 1418, 1401, 1367, 1342, 1297, 1242, 1221, 1203, 1180, 1166, 1141, 1121, 1101, 1066, 1050, 1032, 988, 968, 870, 858, 809, 765, 728 cm^{-1}; ^1H NMR δ 4.92 (dt, 1H, J = 8.0, 6.8 Hz), 4.77 (dq, 1H, J = 6.8, 6.8 Hz), 4.48 (dt, 1H, J = 8.0, 3.6 Hz), 4.28 (dd, 1H, J = 6.8, 6.0 Hz), 4.26 (AB portion of an ABX, 2H, J_{ab} = 8.8 Hz, J_{ax} = 8.8 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 28.0 Hz), 3.44 (AB portion of an ABX, 2H, J_{ab} = 9.6 Hz, J_{ax} = 6.0 Hz, J_{bx} = 8.0 Hz, $\Delta\nu_{ab}$ = 31.4 Hz), 2.42 (m, 1H), 1.53 (d, 3H, J = 6.4 Hz), 0.93 (d, 3H, J = 6.8 Hz), 0.89 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 169.7, 153.8, 77.5, 75.5, 63.5, 58.4, 51.3, 28.2, 23.6, 17.9, 14.8, 10.1; HRMS exact mass for $C_{12}H_{18}INO_4$ (M − I) calcd 240.1236, found 240.1234; $[\alpha]_D$ = +24.1° (*c* 0.384, $CHCl_3$).

Cyclization of 8b. The general procedure was followed using iodine (2.59 mmol, 656 mg), sodium bicarbonate (2.59 mmol, 217 mg), and **8b** (0.862 mmol, 220 mg). Chromatography (20% ethyl acetate/80% hexanes) on 25 g of silica gel afforded **9b** (108 mg, 33%, mp 106−107 °C) and **10b** (50 mg, 15%, mp 92−93 °C). Both compounds were recrystallized from hexanes−ethyl acetate (2:1). **(2*S*,3*S*,4*R*)-4-Ethyl-2-(iodomethyl)-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (9b):** IR (film) 2969, 2938, 2896, 2875, 1707, 1487, 1448, 1420, 1392, 1362, 1353, 1328, 1316, 1283, 1239, 1214, 1190, 1177, 1119, 1084, 1056, 1047, 1019, 994, 971, 957, 910, 897, 887, 859, 797, 781, 753, 707, 665, 646, 623 cm^{-1}; ^1H NMR δ 4.59 (ddd, 1H, J = 8.8, 5.6, 1.2 Hz), 4.23 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 7.2 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 10.4 Hz), 4.21 (t, 1H, J = 7.2 Hz), 4.03 (ddd, 1H, J = 7.6, 5.6, 3.6 Hz), 3.18 (dd, 1H, J = 10.0, 5.6 Hz), 3.06 (brs, 1H), 2.99 (dd, 1H, J = 10.0, 8.8 Hz), 2.26 (m, 1H), 1.96 (m, 1H), 1.69 (m, 1H), 1.01 (t, 3H, J = 7.6 Hz), 0.95 (d, 3H, J = 6.4 Hz), 0.93 (d, 3H, J = 7.6 Hz); ^{13}C NMR δ 165.7, 119.6, 78.2, 72.0, 69.5, 58.8, 45.9, 30.1, 24.3, 18.5, 16.9, 9.8, 3.7; HRMS exact mass for $C_{13}H_{20}INO_4$ (M − 1) calcd 254.1397, found 254.1400; $[\alpha]_D$ = +29.4° (*c* 0.384, $CHCl_3$). **(2*R*,3*S*,4*R*)-4-Ethyl-2-(iodomethyl)-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (10b):** IR (film) 2958, 2941, 2885, 1769, 1695, 1494, 1473, 1451, 1423, 1402, 1378, 1337, 1310, 1293, 1231, 1201, 1166, 1141, 1057, 1038, 968, 938, 894, 867, 818, 772, 721, 693 cm^{-1}; ^1H NMR δ 4.89 (dt, 1H, J = 8.0, 6.0 Hz), 4.62 (q, 1H, J = 6.0 Hz), 4.48 (dt, 1H, J = 8.0, 3.6 Hz), 4.38 (t, 1H, J = 6.0 Hz), 4.26 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 4.0 Hz, $\Delta\nu_{ab}$ = 25.6 Hz), 3.43 (AB portion of an ABX, 2H, J_{ab} = 10.0 Hz, J_{ax} = 6.0 Hz, J_{bx} = 7.6 Hz, $\Delta\nu_{ab}$ = 24.8 Hz), 2.43 (m, 1H), 1.88−1.74 (m, 2H), 0.93 (d, 3H, J = 7.2 Hz), 0.92 (t, 3H, J = 7.2 Hz), 0.89 (d, 3H, J = 6.4 Hz); ^{13}C NMR δ 170.0, 153.8, 79.8, 78.1, 63.5, 58.5, 49.0, 29.9, 28.2, 17.9, 14.8, 9.8, 8.1; HRMS exact mass for $C_{13}H_{20}INO_4$ (M − I) calcd 254.1392, found 254.1397; $[\alpha]_D$ = +67.5° (*c* 0.114, $CHCl_3$).

Cyclization of 8c. The general procedure was followed using iodine (2.23 mmol, 565 mg), sodium bicarbonate (2.23 mmol, 187 mg), and **8c** (0.743 mmol, 200 mg). Chromatography (20% ethyl acetate/80% hexanes) on 25 g of silica gel afforded **9c** (113 mg, 38%) and **10c** (6 mg, 2%). **(2*S*,3*S*,4*R*)-2-(Iodomethyl)-4-(methylethyl)-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (9c):** IR (CCl_4) 2962, 2 934, 2879, 1785, 1713, 1470, 1426, 1392, 1354, 1313, 1287, 1253, 1212, 1172, 1122, 1067, 1044, 1024, 994, 966, 911, 865 cm^{-1}; ^1H NMR δ 4.57 (ddd, 1H, J = 10.0, 5.6, 1.2 Hz), 4.23 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 7.2 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 41.4 Hz), 4.03 (ddd, 1H, J = 6.8, 4.8, 3.2 Hz), 3.80 (d, 1H, J = 9.6 Hz), 3.23 (brs, 1H), 3.18 (dd, 1H, J = 10.4, 5.6 Hz), 2.97 (dd, 1H, J = 10.0, 10.0 Hz), 2.27 (m, 1H), 2.07 (m, 1H), 1.10 (d, 3H, J = 6.8 Hz), 0.95 (d, 3H, J = 6.4 Hz), 0.94 (d, 3H, J = 6.4Hz), 0.93 (d, 3H, J = 6.4 Hz); ^{13}C NMR δ 166.8, 119.6, 82.5, 72.2, 69.5, 58.9, 44.7, 30.1, 29.3, 19.7, 18.6, 18.3, 16.9, 3.8; HRMS exact mass for $C_{14}H_{22}INO_4$ (M − I) calcd 268.1549, found 268.1538; $[\alpha]_D$ = +23.5° (*c* 0.340, $CHCl_3$). **(2*R*,3*S*,4*R*)-2-(Iodomethyl)-4-(methylethyl)-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl] oxetane (10c):** IR (CCl_4) 2964, 2930, 2877, 1785, 1742, 1695, 1487, 1470, 1389, 1368, 1339, 1302, 1281, 1232, 1203, 1125, 1099, 1070, 1047, 983, 917, 868, 720 cm^{-1}; ^1H NMR δ 4.78 (dt, 1H, J = 7.6, 6.8 Hz), 4.50 (m, 2H), 4.43 (t, 1H, J = 7.6 Hz), 4.26 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 24.0 Hz), 3.43 (AB portion of an ABX, 2H, J_{ab} = 10.0 Hz, J_{ax} = 6.4 Hz, J_{bx} = 7.6 Hz, $\Delta\nu_{ab}$ = 14.6 Hz), 2.42 (m, 1H), 1.94 (m, 1H), 0.96 (d, 3H, J = 6.8 Hz), 0.94 (d, 3H, J = 6.8 Hz), 0.90 (d, 3H, J = 6.8 Hz), 0.84 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 170.3, 153.7, 83.1, 78.4, 63.4, 58.6, 47.2, 33.8, 28.3, 18.0, 16.7, 16.1, 14.9, 9.6; HRMS exact mass for $C_{14}H_{22}INO_4$ (M − I) calcd 268.1549, found 268.1540; $[\alpha]_D$ = +64.8° (*c* 0.650, $CHCl_3$).

(4*S*)-3-(3′-Methyl-1′-oxo-2′-butenyl)-4-(1-methylethyl)-2-oxazolidinone (11). To a solution containing dry tetrahydrofuran (50 mL) and the oxazolidinone at −78 °C was added *n*-butyllithium (12.2 mmol, 4.9 mL, 2.5 M in hexanes) dropwise via syringe. After being stirred for 1 h, freshly distilled 3,3-dimethylacryloyl chloride (12.2 mmol, 1.45 g) was added via syringe. The yellow solution was stirred at −78 °C for 45 min and then warmed to room temperature and quenched with saturated ammonium chloride solution. The bulk of the tetrahydrofuran was stripped off under vacuum and the resulting solution poured into water and extracted with ether (3×). The combined organic layers were washed once with 15% sodium hydroxide, once with brine, dried (anhydrous sodium sulfate), filtered, and concentrated *in vacuo*. Chromatography (20% ethyl acetate/80% hexanes) on 45 g of silica gel afforded a white solid. Recrystallization from hexanes afforded **11** (1.90 g, 88%, mp 38−39 °C): IR (film) 3098, 2966, 2932, 2882, 1775, 1682, 1632, 1489, 1391, 1365, 1302, 1255, 1211, 1185, 1144, 1123, 1102, 1084, 1055, 1027, 1006, 980, 928, 858, 777, 756, 720 cm^{-1}; ^1H NMR δ 6.94 (s,1H), 4.47 (dt, 1H, J = 8.8, 3.6 Hz), 4.20 (AB portion of an ABX, 2H, J_{ab} = 8.4 Hz, J_{ax} = 8.4 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 27.4 Hz), 2.38 (m, 1H), 2.16 (d, 3H, J = 1.2 Hz), 1.97 (d, 3H, J = 1.2 Hz), 0.91 (d, 3H, J = 6.8 Hz), 0.87 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 165.0, 159.0, 154.0, 115.8, 63.1, 58.3, 28.5, 28.0, 21.3, 18.0, 14.7; $[\alpha]_D$ = +91.7° (*c* 0.504, $CHCl_3$). Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.07. Found: C, 62.66; H, 8.11.

(2′*S*,3′*R*,4*S*)-3-(3′-Hydroxy-2′-(1-methylethenyl)-1′-oxobutyl)-4-(methylethyl)-2-oxazolidinone (12a). The general protocol for the asymmetric aldol reaction was followed using imide **11** (1.42 mmol, 300 mg), dibutylboryl triflate (1.70 mmol, 0.47 mL), triethylamine (1.99 mmol, 0.28 mL), and acetaldehyde (1.99 mmol, 0.16 mL). Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded **12a** (254 mg, 70%): IR (film) 3518, 3092, 2971, 2933, 2879, 1780, 1691, 1642, 1492, 1457, 1370, 1303, 1209, 1109, 1063, 1026, 977, 937, 902, 859, 786, 757, 727 cm^{-1}; ^1H NMR δ 5.12 (brs, 1H), 5.04 (s, 1H), 4.48 (dt, 1H, J = 8.4, 3.2 Hz), 4.45 (d, 1H, J = 6.4 Hz), 4.26 (m, 2H), 4.20 (dd, 1H, J = 9.2, 3.6 Hz), 2.63 (brs, 1H), 2.30 (m, 1H), 1.90 (s, 3H), 1.22 (d, 3H, J = 6.4 Hz), 0.90 (d, 3H, J = 7.6 Hz), 0.81 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 173.9, 153.3, 139.6, 117.4, 67.0, 62.9, 58.0, 56.5, 28.1, 22.3, 20.7, 17.9, 14.3; HRMS exact mass for $C_{13}H_{21}NO_4$ (M − MeCHO) calcd 211.1208, found 211.1154; $[\alpha]_D$ = −30.8° (*c* 0.312, $CHCl_3$).

(2′*S*,3*R*,4*S*)-3-(3′-Hydroxy-2′-(1-methylethenyl)-1′-oxopentyl)-4-(methylethyl)-2-oxazolidinone (12b). The general protocol for the asymmetric aldol reaction was followed

using imide **11** (1.42 mmol, 300 mg), dibutylboryl triflate (1.70 mmol, 0.47 mL), triethylamine (1.99 mmol, 0.28 mL), and propanal (1.99 mmol, 0.20 mL). Chromatography (20% ethyl acetate/80% hexanes) on 25 g of silica gel afforded **12b** (201 mg, 72%): IR (film) 3521, 3088, 2967, 2936, 2882, 1783, 1695, 1643, 1487, 1466, 1389, 1370, 1302, 1204, 1149, 1124, 1062, 1026, 982, 906, 859, 775, 753, 726 cm^{-1}; ^1H NMR δ 5.12 (t, 1H, J = 1.2 Hz), 5.04 (s, 1H), 4.54 (d, 1H, J = 6.4 Hz), 4.49 (dt, 1H, J = 8.8, 3.2 Hz), 4.24 (AB portion of an ABX, 2H, J_{ab} = 8.8 Hz, J_{ax} = 8.8 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 29.8 Hz), 4.00 (m, 1H), 2.68 (m, 1H), 2.31 (dsept, 1H, J = 7.2, 4.0 Hz), 1.90 (brs, 3H), 1.52 (m, 2H), 1.00 (t, 3H, J = 7.4 Hz), 0.91 (d, 3H, J = 7.2 Hz), 0.82 (d, 3H, J = 7.2 Hz); ^{13}C NMR δ 173.2, 153.3, 139.6, 117.2, 72.2, 62.8, 58.0, 54.7, 28.0, 27.7, 22.4, 17.9, 14.3, 10.3; HRMS exact mass for $C_{14}H_{23}NO_4$ (M − H_2O) calcd 251.1521, found 251.1518; $[\alpha]_D$ = −34.2° (*c* 0.424, $CHCl_3$).

(2′*S*,3′*R*,4*S*)-3-(3′-Hydroxy-2′-(1-methylethenyl)-4′-methyl-1′-oxopentyl)-4-(methylethyl)-2-oxazolidinone (12c). The general protocol for the asymmetric aldol reaction was followed using imide **11** (0.946 mmol, 200 mg), dibutylboryl triflate (1.14 mmol, 0.29 mL), triethylamine (1.33 mmol, 0.19 mL), and isobutyraldehyde (1.33 mmol, 0.12 mL). Chromatography (20% ethyl acetate/80% hexanes) on 25 g of silica gel afforded **12c** (172 mg, 64%): IR (film) 3537, 3090, 2975, 2934, 2877, 1781, 1693, 1639, 1495, 1470, 1374, 1199, 1108, 1007, 978, 908, 860, 789, 753, 721, 648 cm^{-1}; ^1H NMR δ 5.10 (m, 1H), 5.09 (brs, 1H), 4.76 (d, 1H, J = 7.2 Hz), 4.47 (dt, 1H, J = 8.8, 3.2 Hz), 4.24 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 2.8 Hz, $\Delta\nu_{ab}$ = 31.6 Hz), 3.86 (m, 1H), 2.35 (d, 1H, J = 3.6 Hz), 2.29 (dsept, 1H, J = 7.2, 4.0 Hz), 1.87 (brs, 3H), 1.70 (m, 1H), 0.97 (d, 3H, J = 7.2 Hz), 0.93 (d, 3H, J = 6.4 Hz), 0.88 (d, 3H, J = 6.8 Hz), 0.80 (d, 3H, J = 7.2 Hz); ^{13}C NMR δ 172.8, 153.3, 140.1, 117.6, 75.2, 62.8, 58.0, 52.6, 30.9, 28.0, 21.8, 19.9, 17.8, 16.7, 14.3; HRMS exact mass for $C_{15}H_{25}NO_4$ (M − iPrCHO) calcd 211.1208, found 211.1171; $[\alpha]_D$ = −28.3° (*c* 0.805, $CHCl_3$).

(2′*S*,3′*S*,4*S*)-3-[3′-Hydroxy-1′-oxo-(3′-methylbutenyl)-3′-phenyl]-4-(methylethyl)-2-oxazolidinone (12d). The general protocol for the asymmetric aldol reaction was followed using imide **11** (1.42 mmol, 300 mg), dibutylboryl triflate (1.70 mmol, 0.47 mL), triethylamine (1.99 mmol, 0.28 mL), and benzaldehyde (1.43 mmol, 0.15 mL). Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded a white solid that was recrystallized from hexanes to give **12d** (315 mg, 70%, mp 95−96 °C): IR (film) 3507, 3088, 3063, 3034, 2970, 2927, 2880, 1783, 1697, 1643, 1488, 1457, 1391, 1374, 1305, 1205, 1145, 1105, 1068, 1028, 979, 910, 862, 787, 764, 704, 627 cm^{-1}; ^1H NMR δ 7.43−7.38 (m, 2H), 7.35−7.24 (m, 3H), 5.16 (m, 2H), 5.14 (d, 1H, J = 2.4 Hz), 4.96 (d, 1H, J = 8.0 Hz), 4.21 (dt, 1H, J = 8.8, 3.2 Hz), 4.02 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 2.8 Hz, J_{bx} = 8.8 Hz, $\Delta\nu_{ab}$ = 40.6 Hz), 2.76 (d, 1H, J = 2.4 Hz), 2.25 (dsept, 1H, J = 6.8, 3.6 Hz), 1.80 (s, 3H), 0.85 (d, 3H, J = 6.8 Hz), 0.78 (d, 3H, J = 7.2); ^{13}C NMR δ 171.8, 153.2, 141.3, 139.8, 128.3, 127.9, 126.8, 117.3, 73.2, 62.9, 58.1, 57.2, 28.2, 21.8, 17.9, 14.5. Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30. Found C, 68.20; H, 7.13; $[\alpha]_D$ = −48.3° (*c* 0.352, $CHCl_3$).

General Protocol for Iodoetherification of α-Propenyl *β*-Hydroxy Imides 12a−d. To a solution containing dry acetonitrile (5 mL), iodine (3.0 equiv), and sodium bicarbonate (3.0 equiv) was added α-propenyl *β*-hydroxy imide **12**. The mixture was stirred for 12−48 h and then quenched with 0.2 M sodium thiosulfate solution and extracted with ether (3×). The ether layer was washed once with brine, dried (anhydrous sodium sulfate), filtered, and concentrated *in vacuo*.

Cyclization of 12a. The general protocol was followed using iodine (2.07 mmol, 525 mg), sodium bicarbonate (2.07 mmol, 174 mg), and **12a** (0.689 mmol, 176 mg) for 12 h. Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded **14a** (166 mg, 63%). **(2*R*,3*S*,4*R*)-2,4-Dimethyl-2-(iodomethyl)-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (14a):** IR (film) 2972, 2929, 2874, 1785, 1739, 1692, 1490, 1542, 1392, 1340, 1206, 1122, 1048, 982, 947, 920, 876, 786, 753, 720 cm^{-1}; ^1H NMR δ 5.17 (dq, 1H, J = 6.0, 6.0 Hz), 4.44 (dt, 1H, J = 8.0, 3.2 Hz), 4.27 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 22.2 Hz), 4.22 (d, 1H, J = 6.8 Hz), 3.75 (ABq, 2H, J_{ab} = 10.4 Hz, $\Delta\nu_{ab}$ = 7.5 Hz), 2.40 (m, 1H), 1.45 (s, 3H), 1.44 (d, 3H, J = 6.0 Hz), 0.94 (d, 3H, J = 6.8 Hz), 0.88 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 168.5, 154.0, 80.0, 70.6, 63.8, 58.7, 52.3, 28.4, 22.8, 22.4, 20.6, 18.0, 14.7; HRMS exact mass for $C_{13}H_{20}INO_4$ (M − I) calcd 254.1392, found 254.1394; $[\alpha]_D$ = +53.2° (*c* 0.438, $CHCl_3$).

Cyclization of 12b. The general protocol was followed using iodine (1.67 mmol, 424 mg), sodium bicarbonate (1.67 mmol, 140 mg), and **12b** (0.557 mmol, 150 mg) for 13 h. Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded two inseparable isomers **13b** and **14b** (4.6:1) (184 mg, 84%). **(3*S*,4*R*)-4-Ethyl-2-(iodomethyl)-2-methyl-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]-oxetane (13b, 14b):** IR (film) 2973, 2932, 2881, 1787, 1738, 1695, 1490, 1467, 1389, 1366, 1306, 1214, 1121, 1061, 1041, 983, 946, 871, 781, 756, 721 cm^{-1}; ^1H NMR δ 4.94 (dt, 1H, J = 7.2, 7.2 Hz), 4.88 (dt, 1H, J = 6.8, 6.8 Hz), 4.45 (dt, 1H, J = 8.4, 3.2 Hz), 4.41 (dt, 1H, J = 8.0, 3.2 Hz), 4.28 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 2.8 Hz, $\Delta\nu_{ab}$ = 25.0 Hz), 4.32−4.24 (m, 3H), 4.21 (d, 1H, J = 6.8 Hz), 3.74 (ABq, 2H, J_{ab} = 10.8 Hz, $\Delta\nu_{ab}$ = 16.2 Hz), 3.47 (ABq, 2H, J_{ab} = 9.6 Hz, $\Delta\nu_{ab}$ = 38.7 Hz), 2.52−2.36 (m, 2H), 1.92−1.76 (m, 2H), 1.77 (s, 3H), 1.76−1.62 (m, 2H), 1.47 (s, 3H), 0.95 (d, 3H, J = 7.2 Hz), 0.94 (d, 3H, J = 6.8 Hz), 0.92−0.85 (m, 12H); ^{13}C NMR δ 169.1, 168.6, 154.0, 153.9, 80.7, 80.2, 76.2, 75.2, 63.8, 63.6, 59.1, 58.7, 50.5, 50.0, 29.6, 29.6, 29.3, 28.4, 28.2, 22.9, 20.4, 18.2, 18.0, 15.0, 14.7, 12.7, 8.3, 8.2; HRMS exact mass for $C_{14}H_{22}INO_4$ (M − I) calcd 268.1549, found 268.1546.

Cyclization of 12c. The general protocol was followed using iodine (1.16 mmol, 298 mg), sodium bicarbonate (1.16 mmol, 98 mg), and **12c** (0.388 mmol, 110 mg) for 14 h. Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded a mixture of two inseparable isomers **13c** and **14c** (5.2:1) (119 mg, 75%). **(3*S*,4*R*)-2-(Iodomethyl)-2-methyl-4-(methylethyl)-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (13c, 14c):** IR (film) 2965, 2930, 2873, 1782, 1735, 1691, 1491, 1467, 1392, 1367, 1300, 1276, 1212, 1223, 1093, 1054, 990, 874, 783, 752, 719 cm^{-1}; ^1H NMR δ 4.63 (dd, 1H, J = 8.8, 7.2 Hz), 4.60 (dd, 1H, J = 8.4, 7.6 Hz), 4.46 (dt, 1H, J = 8.4, 3.2 Hz), 4.43 (dt, 1H, J = 7.6, 3.6 Hz), 4.39 (d, 1H, J = 7.2 Hz), 4.35−4.24 (m, 2H), 4.29 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 26.6 Hz), 4.24 (d, 1H, J = 6.8 Hz), 3.73 (ABq, 2H, J_{ab} = 10.4 Hz, $\Delta\nu_{ab}$ = 18.1 Hz), 3.49 (ABq, 2H, J_{ab} = 9.6 Hz, $\Delta\nu_{ab}$ = 15.3 Hz), 2.50 (m, 1H), 2.41 (m, 1H), 2.00 (m, 1H), 1.89 (m, 1H), 1.76 (s, 3H), 1.47 (s, 3H), 0.96 (d, 3H, J = 6.4 Hz), 0.95 (d, 3H, J = 7.2 Hz), 0.95−0.93 (m, 9H), 0.89 (d, 3H, J = 7.2 Hz), 0.79 (d, 3H, J = 6.4 Hz), 0.77 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 169.2, 168.7, 154.0, 153.8, 80.3, 80.1, 79.7, 78.9, 63.7, 63.6, 59.2, 58.8, 49.3, 48.6, 34.0, 33.8, 29.3, 28.4, 28.1, 22.9, 20.1, 18.3, 18.1, 17.4, 17.3, 16.2, 16.1, 15.0, 14.7, 12.4; HRMS exact mass for $C_{15}H_{24}INO_4$ (M − I) calcd 282.1705, found 282.1692.

Cyclization of 12d. The general protocol was followed using iodine (1.89 mmol, 480 mg), sodium bicarbonate (1.89 mmol, 159 mg), and **12d** (0.630 mmol, 200 mg) for 48 h. Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded **13d** (56 mg, 20%). **(3*S*,4*S*)-2-(Iodomethyl)-2-methyl-4-phenyl-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]oxetane (13d):** IR (film) 3086, 3065, 3032, 2968, 2928, 2876, 1780, 1696, 1486, 1451, 1388, 1351, 1304, 1272, 1209, 1181, 1144, 1123, 1102, 1039, 995, 913, 874, 815, 757, 736, 701 cm^{-1}; ^1H NMR δ 7.42−7.28 (m, 5H), 6.10 (d, 1H, J = 7.2 Hz), 4.48 (dt, 1H, J = 8.0, 3.2 Hz), 4.37 (d, 1H, J = 7.6 Hz), 4.28 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 18.0 Hz), 3.84 (ABq, 2H, J_{ab} = 10.8 Hz, $\Delta\nu_{ab}$ = 31.0 Hz), 2.46 (m, 1H), 1.58 (s, 3H), 0.97 (d, 3H, J = 6.8 Hz), 0.92 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 168.1, 153.9, 141.3, 128.6, 128.0, 125.0, 80.7, 74.2, 63.9, 58.9, 53.9, 28.5, 23.0, 19.6, 18.1, 14.7; HRMS exact mass for $C_{17}H_{22}INO_4$ (M − I) calcd 316.1549, found 316.1538.

(4*S*)-3-(1′-Oxo-2′-cyclopentenylethyl)-4-(1-methylethyl)-2-oxazolidinone (15). To a solution containing dry tetrahydrofuran (40 mL) and the oxazolidinone at −78 °C was added *n*-butyllithium (6.92 mmol, 2.7 mL, 2.5 M in hexanes) dropwise

via syringe. After 30 min of stirring, freshly distilled acid chloride (6.92 mmol, 1.00 g) was added via syringe. The solution was stirred at −78 °C for 30 min and then warmed to room temperature and quenched with saturated ammonium chloride solution. The bulk of the tetrahydrofuran was stripped off under vacuum and the resulting solution poured into water and extracted with ether (3×). The combined organic layers were washed once with 15% sodium hydroxide and brine, dried (anhydrous sodium sulfate), filtered, and concentrated *in vacuo*. Chromatography (20% ethyl acetate/80% hexanes) on 30 g of silica gel afforded a solid. Recrystallization from hexanes afforded **15** (1.16 g, 85%, mp 54−55 °C): IR (film) 2966, 2876, 1781, 1678, 1634, 1490, 1453, 1380, 1306, 1249, 1202, 1065, 1041, 1005, 981, 951, 871, 760, 710 cm^{-1}; ^1H NMR δ 7.21 (brs, 1H), 4.48 (dt, 1H, J = 8.8, 3.6 Hz), 4.21 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 25.0 Hz), 2.79 (m, 2H), 2.53 (brt, 2H, J = 7.6 Hz), 2.39 (m, 1H), 1.76 (m, 2H), 1.67 (m, 2H), 0.91 (d, 3H, J = 6.8 Hz), 0.87 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ173.2, 164.8, 154.1, 110.8, 63.0, 58.3, 36.8, 33.9, 28.5, 26.4, 25.4, 18.0, 14.6; $[\alpha]_D$ = +89.6° (*c* 1.29, $CHCl_3$). Anal. Calcd for $C_{13}H_{19}N0_3$: C, 65.80; H, 8.07. Found: C, 65.61; H, 8.06.

(2′*S*,3′*R*,4*S*)-3-[2′-(1-Cyclopentenyl)-3′-hydroxy-1′-oxobutyl]-4-(methylethyl)-2-oxazolidinone (16a). The general protocol for the asymmetric aldol reaction was followed using imide **15** (1.26 mmol, 300 mg), dibutylboryl triflate (1.52 mmol, 0.38 mL), triethylamine (1.77 mmol, 0.25 mL), and acetaldehyde (2.48 mmol, 0.14 mL). Chromatography (30% ethyl acetate/70% hexanes) on 25 g of silica gel afforded **16a** (307 mg, 87%):. IR (film) 3516, 2972, 2927, 2876, 2848, 1782, 1694, 1495, 1466, 1370, 1304, 1200, 1145, 1100, 1062, 1020, 980, 951, 858, 797, 776. 715 cm^{-1}; ^1H NMR δ 5.75 (t, 1H, J = 1.6 Hz), 4.62 (d, 1H, J = 5.2 Hz), 4.47 (dt, 1H, J = 8.4, 3.2 Hz), 4.25−4.20 (m, 1H), 4.21 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 32.0 Hz), 2.97 (s, 1H), 2.54 (m, 1H), 2.38−2.20 (m, 4H), 1.86 (m,2H), 1.17 (d, 3H, J = 6.8 Hz), 0.88 (d, 3H, J = 7.2 Hz), 0.78 (d, 3H, J = 6.4 Hz); ^{13}C NMR δ 173.7, 153.2, 137.4, 131.9, 67.0, 62.8, 57.9, 51.4, 34.9, 32.4, 27.9, 23.3, 20.5, 17.8, 14.2; HRMS exact mass for $C_{15}H_{23}NO_4$ (M − H_2O) calcd 263.1521, found 263.1523; $[\alpha]_D$ = −30.3° (*c* 0.984, $CHCl_3$).

(2′*S*,3′*R*,4*S*)-3-[2′-(1-Cyclopentenyl)-3′-hydroxy-1′-oxopentyl]-4-(methylethyl)-2-oxazolidinone (16b). The general protocol for the asymmetric aldol reaction was followed using imide **15** (1.26 mmol, 300 mg), dibutylboryl triflate (1.52 mmol, 0.38 mL), triethylamine (1.77 mmol, 0.25 mL), and propanal (1.77 mmol, 0.13 mL). Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded **16b** (328 mg, 88%): IR (film) 3528, 3055, 2966, 2934, 2878, 2848, 1786, 1695, 1489, 1467, 1374, 1305, 1201, 1104, 1060, 1030, 978, 780, 714 cm^{-1}; ^1H NMR δ 5.75 (t, 1H, J = 2.0 Hz), 4.72 (d, 1H, J = 4.4 Hz), 4.49 (dt, 1H, J = 8.4, 3.2 Hz), 4.23 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 31.2 Hz), 3.97 (m, 1H), 3.03 (d, 1H, J = 2.0 Hz), 2.57 (m, 1H), 2.38−2.22 (m, 4H), 1.95−1.75 (m, 2H), 1.49 (m, 2H), 0.98 (t, 3H, J = 7.2 Hz), 0.90 (d, 3H, J = 6.8 Hz), 0.79 (d, 3H, J = 7.2 Hz); ^{13}C NMR δ 174.0, 153.2, 137.5, 131.9, 72.4, 62.8, 58.0, 49.6, 34.9, 32.4, 28.0, 27.5, 23.4, 17.9, 14.2, 10.3; HRMS exact mass for $C_{16}H_{25}NO_4$ (M − H_2O) calcd 277.1678, found 277.1669; $[\alpha]_D$ = −22.4° (*c* 0.348, $CHCl_3$).

(2′*S*,3′*R*,4*S*)-3-[2′-(1-Cyclopentenyl)-3′-hydroxy-4′-methyl-1′-oxopentyl]-4-(methylethyl)-2-oxazolidinone (16c). The general protocol for the asymmetric aldol reaction was followed using imide **15** (1.26 mmol, 300 mg), dibutylboryl triflate (1.52 mmol, 0.38 mL), triethylamine (1.77 mmol, 0.25 mL), and isobutyraldehyde (1.77 mmol, 0.16 mL). Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded **16c** (335 mg, 86%): IR (film) 3530, 3056, 2965, 2874, 2850, 1785, 1696, 1494, 1467, 1387, 1303, 1201, 1147, 1120, 1098, 1063, 1026, 1007, 975, 856, 829, 775, 716, 700 cm^{-1}; ^1H NMR δ 5.80 (t, 1H, J = 2.0 Hz), 4.96 (1H, J = 5.2 Hz), 4.48 (dt, 1H, J = 8.4, 3.6 Hz), 4.24 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 2.8 Hz, $\Delta\nu_{ab}$ = 32.4 Hz), 3.76 (ddd, 1H, J = 6.8, 5.2, 2.4 Hz), 2.91 (d, 1H, J = 2.8 Hz), 2.58 (m, 1H), 2.38−2.22 (m, 4H), 1.85 (m, 2H), 1.68 (m, 1H), 0.97 (d, 3H, J = 6.4 Hz), 0.96 (d, 3H, J = 6.8 Hz), 0.90 (d, 3H, J = 7.2 Hz), 0.79 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 173.9, 153.2, 137.8, 132.2, 75.7, 62.8, 58.0, 47.5, 34.5, 32.3, 31.1, 28.0, 23.4, 19.6, 17.9, 17.7, 14.2; HRMS exact mass for $C_{17}H_{25}NO_4$ (M − H_2O) calcd 291.1834, found 291.1837; $[\alpha]_D$ = −23.6° (*c* 0.488, $CHCl_3$).

(2′*S*,3′*S*,4*S*)-3-[2′-(1-Cyclopentenyl)-3′-hydroxy-1′-oxobutyl-3′-phenyl]-4-(methylethyl)-2-oxazolidinone (16d). The general protocol for the asymmetric aldol reaction was followed using imide **15** (1.26 mmol, 300 mg), dibutylboryl triflate (1.52 mmol, 0.38 mL), triethylamine (1.77 mmol, 0.25 mL), and benzaldehyde (1.27 mmol, 0.13 mL). Chromatography (30% ethyl acetate/70% hexanes) on 25 g of silica gel afforded **16d** (366 mg, 84%, mp 90−91 °C). IR (film) 3503, 3062, 3037, 2965, 2932, 2853, 1781, 1697, 1492, 1456, 1391, 1372, 1301, 1206, 1102, 1063, 1027, 976, 777, 757, 704 cm^{-1}; ^1H NMR δ 7.41−7.22 (m, 5H), 5.84 (brs, 1H), 5.13 (m, 2H), 4.25 (dt, 1H, J = 8.4, 3.2 Hz), 4.04 (AB portion of an ABX, 2H, J_{ab} = 8.8 Hz, J_{ax} = 2.8 Hz, J_{bx} = 8.48 Hz, $\Delta\nu_{ab}$ = 33.0 Hz), 2.94 (d, 1H, J = 1.2 Hz), 2.47 (m, 1H), 2.35 (m, 2H), 2.26 (m, 1H), 2.04 (m, 1H), 1.83 (m, 2H), 0.86 (d, 3H, J = 6.8 Hz), 0.77 (d, 3H, J = 7.2 Hz); ^{13}C NMR δ 172.4, 153.2, 141.3, 137.8, 132.2, 128.2, 127.8, 126.7, 73.1, 62.9, 58.1, 52.6, 34.0, 32.5, 28.1, 23.3, 17.9, 14.4; $[\alpha]_D$ = −21.3° (*c* 0.785, $CHCl_3$). Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34. Found: C, 70.04; H, 7.27.

General Protocol for Iodoetherification α-Cyclopentenyl β-Hydroxy Imides 16a−d. To a solution containing dry acetonitrile (5 mL), iodine (3.0 equiv), and sodium bicarbonate (3.0 equiv) was added α-propenyl β-hydroxy imide **16**. The mixture was stirred for 12−22 h and then quenched with 0.2 M sodium thiosulfate solution and extracted with ether (3×). The ether layer was washed once with brine, dried (anhydrous sodium sulfate), filtered, and concentrated *in vacuo*.

Cyclization of 16a. The general protocol was followed using iodine (1.98 mmol, 503 mg), sodium bicarbonate (1.98 mmol, 167 mg), and **16a** (0.661 mmol, 186 mg) for 12 h. Chromatography (30% ethyl acetate/70% hexanes) on 25 g of silica gel afforded **17a** (223 mg, 83%, mp 100−101 °C) as a solid, which was recrystallized from hexanes. **(1*R*,3*R*,4*S*,5*S*)-5-Iodo-3-methyl-4-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]-2-oxaspiro[3.4]octane (17a):** IR (film) 2967, 2934, 2875, 1780, 1697, 1488, 1468, 1388, 1302, 1236. 1205, 1111, 1062, 1022, 1005, 976, 939, 887, 859, 827, 804, 762, 716 cm^{-1}; ^1H NMR δ 5.10 (d, 1H, J = 9.2 Hz), 4.91 (dd, 1H, J = 6.0 3.2 Hz), 4.57 (dt, 1H, J = 8.4, 3.6 Hz), 4.32 (dq, 1H, J = 9.2, 6.0 Hz), 4.26 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 28.8 Hz), 2.53 (m, 1H), 2.34 (m, 1H), 2.20 (m, 1H), 1.94 (m, 3H), 1.69 (m, 1H), 1.27 (d, 3H, J = 6.0 Hz), 1.02 (d, 3H, J = 7.2 Hz), 0.95 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 170.3, 153.4, 95.6, 76.5, 62.8, 60.9, 58.4, 48.9, 41.1, 31.3, 28.3, 25.2, 19.5, 18.0, 14.9; $[\alpha]_D$ = +34.1° (*c* 0.824, $CHCl_3$). Anal. Calcd for $C_{15}H_{22}INO_4$: C, 44.24; H, 5.44. Found: C, 44.44; H, 5.59. Crystals of **17a**, suitable for single-crystal X-ray analysis, were obtained by recrystallization from hexanes. Details of the crystal structure analysis (cell data, data collection, processing and refinement) are concisely summarized in Table 1 (Supporting Information). Full details are available from the authors or from the Cambridge Crystallographic Data Centre.[17]

Cyclization of 16b. The general protocol was followed using iodine (2.69 mmol, 683 mg), sodium bicarbonate (2.69 mmol, 226 mg), and **16b** (0.897 mmol, 265 mg) for 13 h. Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded **17b** (305 mg, 81%). **(1*R*,3*R*,4*S*,5*S*)-3-Ethyl-5-iodo-4-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]-2-oxaspiro[3.4]octane (17b):** IR (film) 2966, 2939, 2879, 1785, 1738, 1694, 1490, 1467, 1385, 1300, 1207, 1105, 1058, 1020, 1002, 953, 909, 845, 757, 714 cm^{-1}; ^1H NMR δ 5.15 (d, 1H, J = 9.2 Hz), 4.83 (dd, 1H, J = 5.2, 1.6 Hz), 4.57 (dt, 1H, J = 8.4, 4.0 Hz), 4.26 (AB portion of an ABX, 2H, J_{ab} = 8.8 Hz, J_{ax} = 8.8 Hz, J_{bx} = 4.0, $\Delta\nu_{ab}$ = 26.4 Hz), 4.29−4.18 (m,

(17) The author has deposited atomic coordinates for **17a** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

1H), 2.55 (ddd, 1H, J = 14.4, 10.0, 8.0 Hz), 2.34 (m, 1H), 2.19 (m, 1H), 1.92 (m, 3H), 1.75 (dtd, 1H, J = 15.6, 7.6, 2.0 Hz), 1.59 (m, 2H), 1.03 (d, 3H, J = 6.4 Hz), 0.95 (d, 3H, J = 7.2 Hz), 0.88 (t, 3H, J = 7.6 Hz); ^{13}C NMR δ 170.5, 153.4, 95.5, 82.0, 62.8, 58.7, 58.5, 49.4, 40.7, 30.6, 28.3, 27.5, 24.9, 18.0, 14.9, 9.7; HRMS exact mass for $C_{16}H_{24}INO_4$ (M − I) calcd 294.1705, Found 294.1673; $[\alpha]_D$ = +34.9° (*c* 1.23 $CHCl_3$).

Cyclization of 16c. The general protocol was followed using iodine (2.06 mmol, 522 mg), sodium bicarbonate (2.06 mmol, 173 mg), and **16e** (0.685 mmol, 212 mg) for 13 h. Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel afforded **17c** (182 mg, 61%). **(1*R*,3*R*,4*S*,5*S*)-5-Iodo-3-(methylethyl)-4-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]-2-oxaspiro[3.4]octane (17c):** IR (film) 2969, 2939, 2875, 1783, 1742, 1696, 1490, 1468, 1441, 1387, 1303, 1273, 1205, 1102, 1053, 1021, 977, 847, 760, 711 cm^{-1}; ^{1}H NMR δ 5.20 (d, 1H, J = 8.8 Hz), 4.75 (d, 1H, J = 5.2 Hz), 4.56 (dt, 1H, J = 8.8, 3.6 Hz), 4.25 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 4.4 Hz, $\Delta\nu_{ab}$ = 26.0 Hz), 4.10 (m, 1H), 2.54 (ddd, 1H, J = 14.4, 9.6, 8.4 Hz), 2.33 (m, 1H), 2.19 (m, 1H), 1.96 (m, 2H), 1.78 (m, 3H), 1.03 (d, 3H, J = 6.8 Hz), 0.93 (d, 3H, J = 7.2 Hz), 0.88 (d, 3H, J = 6.4 Hz), 0.82 (d, 3H, J = 7.2 Hz); ^{13}C NMR δ 170.7, 153.4, 95.5, 86.0, 62.7, 58.5, 56.3, 50.1, 40.4, 32.5, 29.9, 28.2, 24.5, 18.3, 18.0, 17.9, 14.9; HRMS exact mass for $C_{17}H_{26}INO_4$ (M − I) calcd 308.1862, found 308.1846; $[\alpha]_D$ = +35.0° (*c* 2.67, $CHCl_3$).

Cyclization of 16d. The general protocol was followed using iodine (2.38 mmol, 603 mg), sodium bicarbonate (2.38 mmol, 200 mg), and **16d** (0.792 mmol, 272 mg) for 22 h. Chromatography (20% ethyl acetate/80% hexanes) on 25 g of silica gel afforded **17d** (308 mg, 83%). **(1*R*,3*S*,4*S*,5*S*)-5-Iodo-3-phenyl-4-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]-2-oxaspiro[3.4]octane (17d):** IR (film) 3090, 3066, 3036, 2965, 2934, 2877, 1786, 1737, 1695, 1496, 1459, 1388, 1302, 1206, 1109, 1026, 981, 935, 845, 756, 702, 646 cm^{-1}; ^{1}H NMR δ 7.30 (m, 5H), 5.48 (d, 1H, J = 9.2 Hz), 5.19 (d, 1H, J = 9.6 Hz), 5.14 (dd, 1H, J = 6.4, 2.8 Hz), 4.48 (ddd, 1H, J = 8.0, 4.0, 4.0 Hz), 4.12 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 4.0 Hz, J_{bx} = 9.2 Hz, $\Delta\nu_{ab}$ = 13.0 Hz), 2.70 (m, 1H), 2.31 (m, 2H), 2.03 (m, 3H), 1.84 (m, 1H), 1.01 (d, 3H, J = 6.8 Hz), 0.93 (d, 3H, J = 7.2 Hz); ^{13}C NMR δ 169.6, 152.9, 138.5, 128.6, 128.5, 126.4, 96.6, 81.8, 62.7, 61.1, 58.4, 47.8, 41.1, 31.7, 28.3, 25.2, 18.0, 14.9; HRMS exact mass for $C_{20}H_{24}INO_4$ (M − I) calcd 342.1705, found 342.1703; $[\alpha]_D$ = +70.7° (*c* 0.95, $CHCl_3$).

(4*S*)-3-[1-Oxo-2′-(*E*)-pentenyl)-4-(1-methylethyl)-2-oxazolidinone (18). Into a dry 100 mL flask containing oxazolidinone (8.4 mmol, 988 mg) and dry tetrahydrofuran (35 mL) at −78 °C was added *n*-butyllithium (10 mmol, 4.0 mL, 2.5 M in hexanes) dropwise via syringe. After the mixture was stirred for 30 min, freshly distilled (*E*)-2-pentenoyl chloride (10 mmol, 1.2 g) was added via syringe. The solution was stirred for 30 min at −78 °C and then warmed to room temperature. The majority of the solvent was stripped off, the remaining solution was diluted with ether, and saturated ammonium chloride was added. The mixture was extracted with ether (3×), washed once with 15% sodium hydroxide, once with brine, dried (anhydrous sodium sulfate), filtered, and concentrated in vacuo. Chromatography (15% ethyl acetate/85% hexanes) on 45 g of silica gel afforded 1.31 g (74%) of a pale yellow oil: IR (film) 3901, 2965, 2936, 2874, 1782, 1684, 1637, 1491, 1464, 1391, 1364, 1303, 1261, 1205, 1151, 1122, 1102, 1061, 1049, 1022, 978, 917, 863, 778, 758, 739, 714, 646 cm^{-1}; ^{1}H NMR δ 7.27 (dt, 1H, J = 15.6, 1.2 Hz), 7.19 (dt, 1H, J = 15.6, 5.6 Hz), 4.50 (dt, 1H, J = 8.4, 2.8 Hz), 4.25 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 8.4 Hz, J_{bx} = 2.8 Hz, $\Delta\nu_{ab}$ = 26.6 Hz), 2.42 (m, 1H), 2.31 (m, 2H), 1.11 (t, 3H, J = 7.6 Hz), 0.93 (d, 3H, J = 7.2 Hz), 0.89 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 165.2, 154.0, 152.8, 119.5, 63.3, 58.5, 28.4, 25.8, 18.0, 14.6, 12.2; HRMS exact mass for $C_{11}H_{17}NO_3$ calcd 211.1208, found 211.1197; $[\alpha]_D$ = +96.1° (*c* 1.42, $CHCl_3$).

(2′*S*,3′*R*,4*S*)-3-[3′-Hydroxy-1′-oxo-2′-(1-methylethenyl)-butyl]-4-(methylethyl)-2-oxazolidinone (19a). The general procedure for the asymmetric aldol reaction was followed using imide **18** (1.35 mmol, 286 mg), dibutylboryl triflate (1.62 mmol, 0.41 mL), triethylamine (2.27 mmol, 0.32 mL), and acetaldehyde (2.27 mmol, 0.13 mL). Chromatography (30% ethyl acetate/70% hexanes) on 20 g silica gel afforded **19a** (277 mg, 81%) as an inseparable mixture of two isomers (cis/trans = 2.3:1): IR (film) 3540, 2972, 2927, 2877, 1780, 1696, 1493, 1454, 1381, 1319, 1206, 1105, 1065, 1021, 981, 931, 869, 762, 717 cm^{-1}; ^{1}H NMR δ 5.89 (dq, 1H, J = 10.8**,** 6.8 Hz), 5.86 (m, 1H), 5.57 (ddq, 1H, J = 15.2, 9.2, 1.6 Hz), 5.49 (ddq, 1H, 10.8, 9.6, 1.6 Hz), 4.92 (dd, 1H, J = 9.6, 3.6 Hz), 4.48 (m, 4H), 4.25 (AB portion of an ABX, 2H, J_{ab} = 8.8 Hz, J_{ax} = 9.2 Hz, J_{bx} = 2.8 Hz, $\Delta\nu_{ab}$ = 35.6 Hz), 4.22 (m, 1H), 4.14 (m, 2H), 2.83 (brs, 2H), 2.33 (m, 2H), 1.75 (ddd, 6H, J = 13.6, 7.2, 2.0 Hz), 1.19 (d, 3H, J = 6.8 Hz), 1.17 (d, 3H, J = 6.0 Hz), 0.90 (d, 6H, J = 7.6 Hz), 0.84 (d, 3H, J = 6.8 Hz), 0.83 (d, 3H, J = 7.2 Hz); ^{13}C NMR δ 175.0, 174.8, 153.6, 153.5, 133.0, 131.5, 123.6. 123.2, 68.5, 67.7, 63.1, 63.0, 58.2, 58.1, 52.1, 47.7, 28.2, 28.0, 19.8, 19.7, 18.2, 17.8, 14.5, 14.4, 13.9; HRMS exact mass for $C_{13}H_{21}NO_4$ (M − H_2O) calcd 237.1365, found 237.1353.

(2′*S*,3′*R*,4*S*)-3-[(3′-Hydroxy-1′-oxo-2′-(l-methylethenyl)-pentyl]-4-(methylethyl)-2-oxazolidinone (19b). The general procedure for the asymmetric aldol reaction was followed using imide **18** (1.42 mmol, 300 mg), dibutylboryl triflate (1.70 mmol, 0.43 mL), triethylamine (1.99 mmol, 0.28 mL), and propanal (1.70 mmol, 0.12 mL). Chromatography (25% ethyl acetate/65% hexanes) on 25 g of silica gel afforded **19b** (268 mg, 70%) as an inseparable mixture of two isomers (cis/trans = 2.2:1): IR (film) 3526, 2966, 2939, 2878, 1781, 1696, 1488, 1466, 1388, 1374, 1301, 1204, 1143, 1124, 1100, 1058, 1024, 981, 862, 794, 777, 757, 719, 646 cm^{-1}; ^{1}H NMR δ 5.85 (m, 2H), 5.57 (ddq, 1H, J = 15.2, 9.2, 1.2 Hz), 5.51 (ddq, 1H, J = 11.2, 9.6, 1.6 Hz), 5.00 (dd, 1H, J = 9.6, 3.6 Hz), 4.54 (dd, 1H, J = 9.2, 3.2 Hz), 4.48 (m, 2H), 4.30−4.18 (m, 2H), 4.24 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 35.2 Hz), 3.86 (m, 2H), 3.13 (d, 1H, J = 2.0 Hz), 2.88 (d, 1H, J = 2.4 Hz), 2.33 (m, 2H), 1.76 (dd, 3H, J = 6.8, 1.2 Hz), 1.72 (dd, 3H, J = 6.8, 1.2 Hz), 1.49 (m, 4H), 0.98 (t, 3H, J = 7.2 Hz), 0.95 (t, 3H, J = 7.2 Hz), 0.89 (d, 6H, J = 7.2 Hz), 0.83 (d, 6H, J = 6.8 Hz); ^{13}C NMR δ 175.3, 175.0, 153.6, 153.4, 132.7, 131.3, 123.6, 123.3, 73.7, 72.9, 63.1, 63.0, 58.2, 58.1, 50.4, 46.3, 28.2, 28.1, 27.0, 26.9, 18.2, 17.8, 14.5, 14.4, 14.0, 10.2, 10.1; HRMS exact mass for $C_{14}H_{23}NO_4$ (M + 1) calcd 270.1705, found 270.1695.

(2′*S*,3′*R*,4*S*)-3-[(3′-Hydroxy-4′-methyl-1′-oxo-2′-(1-methylethenyl)pentyl]-4-(methylethyl)-2-oxazolidinone (19c). The general procedure for the asymmetric aldol reaction was followed using imide **18** (1.42 mmol, 300 mg), dibutylboryl triflate (1.70 mmol, 0.43 mL), triethylamine (1.99 mmol, 0.28 mL), and isobutyraldehyde (1.70 mmol, 0.16 mL). Chromatography (15% ethyl acetate/85% hexanes) on 25 g of silica gel afforded **19c** (327 mg, 81%) as a mixture of isomers (cis/trans = 2.2:1) of which the cis isomer could be separated. **Isomeric mixture:** IR (film) 3524, 2966, 2927, 2877, 1788, 1700, 1478, 1384, 1301, 1207, 1157, 1124, 1091, 975, 870, 781, 726 cm^{-1}; ^{1}H NMR δ 5.90−5.79 (m, 2H), 5.61−5.50 (m, 2H), 5.19 (dd, 1H, J = 10.0, 4.0 Hz), 4.74 (dd, 1H, J = 9.2, 3.2 Hz), 4.47 (m, 2H), 4.24 (AB portion of an ABX, 2H, J_{ab} = 8.8 Hz, J_{ax} = 8.8 Hz, J_{bx} = 3.6, $\Delta\nu_{ab}$ = 35.8 Hz), 4.23 (AB portion of an ABX, 2H, J_{ab} = 8.8 Hz, J_{ax} = 8.8 Hz, J_{bx} = 3.6 Hz, $\Delta\nu_{ab}$ = 30.6 Hz), 3.61 (m, 1H), 3.55 (m, 1H), 3.20 (d, 1H, J = 2.0 Hz), 2.79 (d, 1H, J = 2.0 Hz), 2.31 (m, 2H), 1.76 (dd, 3H, J = 6.8, 1.6 Hz), 1.70 (dd, 3H, J = 6.4, 1.2 Hz), 1.71−1.62 (m, 2H), 0.98 (d, 6H, J = 6.8 Hz), 0.93 (d, 3H, J = 6.8 Hz), 0.89 (d, 3H, J = 6.8 Hz), 0.88 (d, 3H, J = 6.8 Hz), 0.87 (d, 3H, J = 6.8 Hz), 0.81 (d, 6H, J = 7.2 Hz); ^{13}C NMR δ 175.4, 175.1, 153.5, 153.3, 132.4, 131.0, 123.7, 76.8, 76.4, 63.0, 62.9, 58.2, 58.1, 48.2, 44.3, 31.1, 30.8, 28.1, 28.0, 19.4, 19.0, 18.4, 18.2, 18.0, 17.8, 14.6, 14.4, 14.1; HRMS exact mass for $C_{15}H_{25}NO_4$ (M − H_2O) calcd 265.1678, found 265.1677. **Cis isomer**: **(2′*S*,3′*R*,4*S*)-3-[3′-Hydroxy-4′-methyl-1′-oxo-2′-((*Z*)-1-methylethenyl)pentyl]-4-(methylethyl)-2-oxazolidinone**: IR (film) 3530, 3023, 2967, 2937, 2878, 1781, 1695, 1488, 1469, 1449, 1387, 1373, 1341, 1305, 1204, 1149, 1125, 1099, 1062, 1029, 1005, 976, 928, 877, 861, 793, 776, 721 cm^{-1}; ^{1}H NMR δ 5.81 (dq, 1H, J = 10.8, 6.8 Hz), 5.51 (tq, 1H, J = 10.8, 1.6 Hz), 5.16 (dd, 1H, J = 10.0, 3.6 Hz), 4.45 (dt, 1H, J = 8.8, 3.6 Hz), 4.22 (AB portion of an ABX, 2H, J_{ab} = 9.2 Hz, J_{ax} = 9.2 Hz, J_{bx} = 3.2 Hz, $\Delta\nu_{ab}$ = 36.0 Hz), 3.61−3.58 (m, 1H), 2.77 (d, 1H, J = 1.6 Hz), 2.30 (m, 1H), 1.74 (dd,

3H, J = 6.8, 1.6 Hz), 1.65 (m, 1H), 0.96 (d, 3H, J = 6.8 Hz), 0.91 (d, 3H, J = 6.8 Hz), 0.86 (d, 3H, J = 7.2 Hz), 0.80 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 175.1, 153.5, 131.0, 123.6, 76.8, 63.0, 58.2, 44.3, 31.1, 28.1, 19.4, 18.0, 17.8, 14.5, 14.1; HRMS exact mass for $C_{15}H_{25}NO_4$ (M − H_2O) calcd 265.1678, found 265.1677; $[\alpha]_D$ = −29.0° (*c* 1.20, $CHCl_3$).

(2′*S*,3′*S*,4*S*)-3-[3′-Hydroxy-1′-oxo-3′-phenyl-2′-(1-methylethenyl)propyl]-4-(methylethyl)-2-oxazolidinone (19d). The general procedure for the asymmetric aldol reaction was followed using imide **18** (0.50 mmol, 106 mg), dibutylboryl triflate (0.61 mmol, 0.16 mL), triethylamine (0.74 mmol, 0.10 mL), and benzaldehyde (0.50 mmol, 0.05 mL). Chromatography (30% ethyl acetate/70% hexanes) on 20 g of silica gel afforded **19d** (150 mg, 94%) as an inseparable mixture of two isomers (cis/trans = 2.3:1): IR (film) 3507, 3093, 3065, 3034, 2968, 2920, 2877, 1781, 1698, 1490, 1386, 1457, 1304, 1201, 1147, 1121, 1098, 1058, 973, 914, 879, 860, 797, 776, 755, 736, 705 cm^{-1}; ^{1}H NMR δ 7.41−7.20 (m, 10H), 5.87−5.75 (m, 1H), 5.85 (dq, 1H, J = 10.8, 6.8 Hz), 5.68−5.57 (m, 1H), 5.60 (tq, 1H, J = 10.0, 2.0 Hz), 5.28 (dd, 2H, J = 9.6, 6.0 Hz), 4.91 (m, 2H), 4.18 (m, 2H), 4.05 (dd, 2H, J = 9.2, 2.8 Hz), 3.88 (m, 2H), 2.83 (brs, 2H), 2.26 (m, 2H), 1.72 (dd, 3H, J = 6.8, 1.3 Hz), 1.54 (dd, 3H, J = 6.8, 1.6 Hz), 0.85 (d, 6H, J = 6.8 Hz), 0.79 (d, 6H, J = 6.8 Hz); ^{13}C NMR δ 173.6, 173.4, 153.3, 153.2, 140.7, 140.6, 133.1, 132.3, 128.1, 127.8, 126.8, 126.7, 124.6, 123.5, 75.3, 74.5, 63.2, 63.1, 58.5, 58.4, 54.0, 49.5, 28.6, 28.4, 18.19, 17.9, 13.5; HRMS exact mass for $C_{18}H_{23}NO_4$ (M − PhCHO) calcd 211.1208, found 211.1164.

General Protocol for Iodoetherification of α-Propenyl *β*-Hydroxy Imides 19a−d. To a solution containing dry acetonitrile (5 mL), iodine (3.0 equiv), and sodium bicarbonate (3.0 equiv) was added α-vinyl *β*-hydroxy imide **19**. The mixture was stirred for 13−38 h, quenched with 0.2 M sodium thiosulfate solution, and extracted with ether (3×). The ether layer was washed once with brine, dried (anhydrous sodium sulfate), filtered, and concentrated *in vacuo*.

Cyclization of 19a. The general protocol was followed using iodine (3.26 mmol, 826 mg), sodium bicarbonate (3.26 mmol, 273 mg), and **19a** (1.08 mmol, 277 mg) for 15 h. Chromatography (25% ethyl acetate/75% hexanes) on 25 g of silica gel yielded a solid that upon recrystallization from hexanes afforded two inseparable isomers (70:30) of **20a** (305 mg, 74%, mp 40−41 °C). **(3*S*,4*R*,5*S*)-2,5-Dimethyl-3-iodo-4-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl] tetrahydrofuran (20a):** IR (film) 2971, 2930, 2877, 1782, 1693, 1486, 1451, 1390, 1338, 1301, 1282, 1242, 1207, 1144, 1101, 1064, 1022, 996, 975, 949, 878, 853, 834, 789, 775, 735, 714 cm^{-1}; ^{1}H NMR δ 4.80 (m, 2H), 4.63 (t, 1H, J = 5.2 Hz), 4.51 (dt, 1H, J = 8.4, 3.6 Hz), 4.46 (dt, 1H, J = 8.4, 3.6 Hz), 4.26 (m, 5H), 4.12 (m, 2H), 3.59 (m, 2H), 2.40 (m, 2H), 1.46 (d, 6H, J = 6.0 Hz), 1.37 (d, 3H, J = 6.4 Hz), 1.36 (d, 3H, J = 6.4 Hz), 0.97 (d, 3H, J = 7.2 Hz), 0.96 (d, 3H, J = 6.8 Hz), 0.95 (d, 3H, J = 7.2 Hz), 0.94 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 172.3, 171.4, 153.5, 153.4, 82.4, 79.0, 77.3, 63.2, 63.1, 59.6, 59.5, 58.9, 58.8, 32.8, 28.2, 28.1, 27.5, 23.7, 21.1, 20.6, 18.0, 17.9, 17.1, 14.7, 14.1; HRMS exact mass for $C_{13}H_{20}INO_4$ (M − I) calcd 254.1392, found 254.1395.

Cyclization of 19b. The general protocol was followed using iodine (2.23 mmol, 565 mg), sodium bicarbonate (2.23 mmol, 187 mg), and **19b** (0.743 mmol, 200 mg) for 13 h. Chromatography (15% ethyl acetate/85% hexanes) on 25 g of silica gel afforded two inseparable isomers (69:31) of **20b** (225 mg, 77%). **(2*S*,3*R*,4*S*)-2-Ethyl-4-iodo-5-methyl-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl] tetrahydrofuran (20b):** IR (film) 2965, 2934, 2878, 1784, 1694, 1488, 1464, 1385, 1305, 1263, 1231, 1202, 1144, 1104, 1059, 1019, 974, 908, 866, 847, 779, 760, 718 cm^{-1}; ^{1}H NMR δ 4.85 (dd, 1H, J = 10.0, 8.0 Hz), 4.83 (dd, 1H, J = 7.2, 5.2 Hz), 4.56 (t, 1H, J = 5.6 Hz), 4.49 (dt, 1H, J = 8.4, 4.0 Hz), 4.45 (dt, 1H, J = 8.0, 3.6 Hz), 4.27 (t, 1H, J = 9.2 Hz), 4.23 (m, 4H), 4.05 (m,1H), 3.98 (m, 2H), 3.62 (dq, 1H, J = 6.0, 6.0 Hz), 2.40 (m, 2H), 1.85−1.59 (m, 4H), 1.36 (d, 3H, J = 6.4 Hz), 1.35 (d, 3H, J = 6.4 Hz), 0.97−0.92 (m, 18H); ^{13}C NMR δ 172.6, 171.8, 153.5, 153.4, 84.2, 77.1, 63.1, 58.9, 57.5, 32.7, 28.3, 28.2, 28.1, 27.9, 23.6, 18.0, 17.0, 14.8, 14.7, 10.3, 9.9; HRMS exact mass for $C_{14}H_{22}INO_4$ (M − I) calcd 268.1549, found 268.1535.

Cyclization of 19c. The general protocol was followed using iodine (2.35 mmol, 595 mg), sodium bicarbonate (2.35 mmol, 197 mg), and **19c** (0.783 mmol, 222 mg) for 13 h. Chromatography (15% ethyl acetate/85% hexanes) on 25 g of silica gel afforded two inseparable isomers (69:31) of **20c** (259 mg, 81%). **(2*S*,3*R*,4*S*)-4-Iodo-5-methyl-2-(methylethyl)-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]tetrahydrofuran (20c):** IR (film) 2968, 2937, 2875, 1787, 1700, 1491, 1468, 1386, 1301, 1278, 1231, 1200, 1142, 1097, 1061, 1019, 974, 911, 868, 849, 773, 757, 712 cm^{-1}; ^{1}H NMR δ 4.96 (dd, 1H, J = 10.4, 8.0 Hz), 4.89 (dd, 1H, J = 7.2, 6.0 Hz), 4.47 (m, 4H), 4.30-4.20 (m, 4H), 3.91 (m, 2H), 3.66 (m, 2H), 2.40 (m, 2H), 1.87 (m, 2H), 1.36 (d, 3H, J = 6.0 Hz), 1.33 (d, 3H, J = 6.0 Hz), 0.99 (d, 3H, J = 6.8 Hz), 0.96 (d, 3H, J = 7.6 Hz), 0.95 (d, 3H, J = 6.8 Hz), 0.94 (d, 3H, J = 6.8 Hz), 0.93 (d, 3H, J = 7.6 Hz), 0.92 (d, 3H, J = 6.8 Hz), 0.88 (d, 3H, J = 6.8 Hz), 0.87 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 172.9, 172.3, 153.4, 88.1, 87.9, 83.2, 76.9, 63.1, 63.0, 58.9, 58.8, 54.5, 54.4, 32.8, 32.6, 32.0, 29.4, 28.2, 23.4, 18.8, 18.4, 18.1, 18.0, 17.8, 17.2, 14.9, 14.8; HRMS exact mass for $C_{15}H_{24}INO_4$ (M − I) calcd 282.1705, found 282.1690.

Cyclization of 19d. The general protocol was followed using iodine (1.89 mmol, 480 mg), sodium bicarbonate (1.89 mmol, 159 mg), and **19d** (0.63 mmol, 200 mg) for 38 h. Chromatography (15% ethyl acetate/85% hexanes) on 25 g of silica gel afforded a mixture of inseparable isomers (69:31) of **20d** (175 mg, 63%, mp 113−115 °C). **(2*R*,3*R*,4*S*)-4-Iodo-5-methyl-2-phenyl-3-[[(4*S*)-4-(methylethyl)-2-oxazolidin-3-yl]carbonyl]tetrahydrofuran (20d):** IR (CCl_4) 3096, 3070, 3033, 3009, 2969, 2931, 2882, 1794, 1695, 1487, 1458, 1380, 1306, 1276, 1241, 1224, 1197, 1142, 1099, 1064, 1024, 995, 969, 908, 873, 859, 717, 700 cm^{-1}; ^{1}H NMR δ 7.30 (m, 10H), 5.27 (dd, 1H, J = 8.8, 2.0 Hz), 5.13 (t, 1H, J = 8.0 Hz), 5.09 (d, 1H, J = 8.8 Hz), 5.00 (d, 1H, J = 6.2 Hz), 4.72 (dd, 1H, J = 7.2, 6.4 Hz), 4.54 (dq, 1H, J = 9.2, 6.0 Hz), 4.42 (m, 2H), 4.20 (dd, 1H, J = 10.4, 9.6 Hz), 4.13 (m, 4H), 3.98 (dq, 1H, J = 6.4, 6.4 Hz), 2.40 (m, 2H), 1.53 (d, 3H, J = 7.2 Hz), 1.47 (d, 3H, J = 7.2 Hz), 0.95 (d, 3H, J = 7.2 Hz), 0.94 (d, 3H, J = 6.8 Hz), 0.93 (d, 3H, J = 7.6 Hz), 0.92 (d, 3H, J = 6.8 Hz); ^{13}C NMR δ 171.3, 170.7, 152.8, 152.8, 139.1, 138.2, 128.6, 128.5, 126.6, 126.1, 84.7, 84.3, 84.2, 77.4, 63.1, 59.0, 58.9, 30.5, 28.5, 28.4, 27.2, 24.1, 18.0, 17.6, 14.9. Anal. Calcd for $C_{18}H_{22}INO_4$: C, 48.77; H, 5.00. Found: C, 48.52; H, 5.24.

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Supporting Information Available: Table 1 (Summary of Data Collection, Structure Solution and Refinement Details) and ^{1}H NMR spectra for compounds **9a−c**, **10a−c**, **12a−c**, **13b−d**, **14a−c**, **16a−c**, **17b−d**, **18**, **19a−d**, and **20a−c** (29 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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