Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 4313–4324

TETRAHEDRON: *ASYMMETRY*

Regio- and diastereoselective boron-mediated aldol reactions of chiral α,β,γ,δ-unsaturated *N*-acyloxazolidinones

James M. Takacs,* Mohamad R. Jaber, Benjamin J. Swanson and Steven J. Mehrman

Department of Chemistry, University of Nebraska-Lincoln, Lincoln, NE 68588-0304, USA

Received 17 September 1998; accepted 27 October 1998

Abstract

Chiral *N*-acyloxazolidinones derived from conjugated dienoic acids undergo boron-mediated aldol condensation in good yield and with high regio- and diastereoselectivity to provide a convenient method for introducing a 1,3-diene subunit. The condensation of a homologous triene derivative is also described.

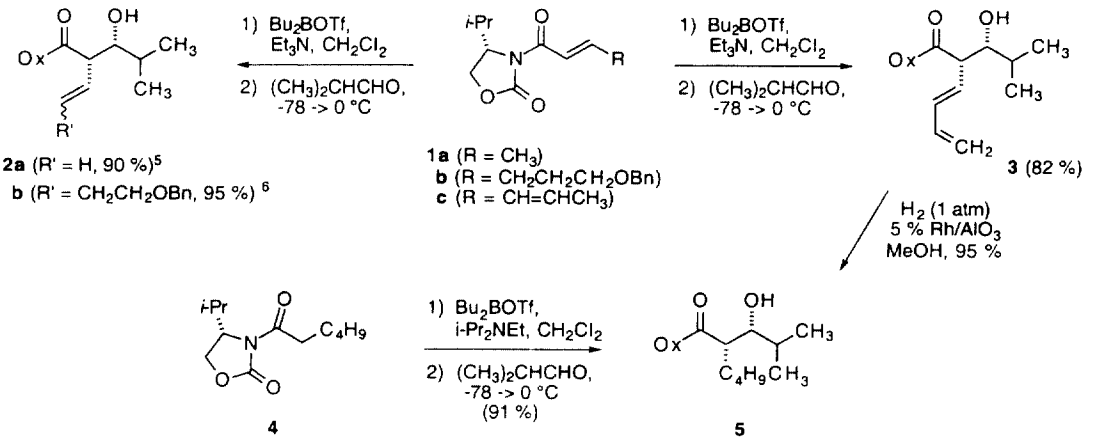
In the course of other studies, we require ready access to substrates bearing one or more 1,3-diene subunits within their structures.[1] While there are a number of reliable methods for the construction of conjugated dienes,[2] the development of new methods, particularly one applicable to enantioselective synthesis, still presents a timely challenge.[3,4]

Evans and co-workers reported the regio- and diastereoselective boron-mediated aldol condensation of crotonic acid derived *N*-acyloxazolidinones.[5] Condensation occurs at the alpha position of the presumed extended enolate to afford β,γ-unsaturated products with high diastereoselection. For example, *N*-acyloxazolidinone **1a** is reported to condense with isobutyraldehyde to afford **2a** in 90% yield and greater than 98% isomeric purity. One limitation to the method is that higher homologues of **1**, that is α,β-unsaturated substrates leading to vicinal disubstituted alkene-containing products, afford a mixture of double bond isomers. For example, *N*-acyloxazolidinone **1b** affords an *E*:*Z* mixture of products **2b** (95% yield).[6,7] In spite of this potentially problematic lack of stereochemical control, we prepared the *N*-acyloxazolidinone (*E*,*E*)-**1c** derived from sorbic acid and examined its reaction with isobutyraldehyde. Under the conditions reported by Evans for the reaction of **1a**, treatment of **1c** with dibutylboron triflate[8] (−78°C, 15 min) and triethylamine (1h at −78°C, 15 min at 0°C) followed by the addition of isobutyraldehyde (1 h at −78°C, 1 h at 0°C) and oxidative work-up (H_2O_2) affords the β,γ,δ,ε-unsaturated condensation product **3** in good yield (82%) and high regio- and diastereoselectivity. As is the case for the other examples described in this paper, the product is of greater than 95% isomeric purity as judged by analysis of the ^1H and ^{13}C NMR spectra. The *E* double bond stereochemistry in **3** was

* Corresponding author. E-mail: jtakacs@unl.edu

0957-4166/98/$ - see front matter
PII: S0957-4166(98)00459-5

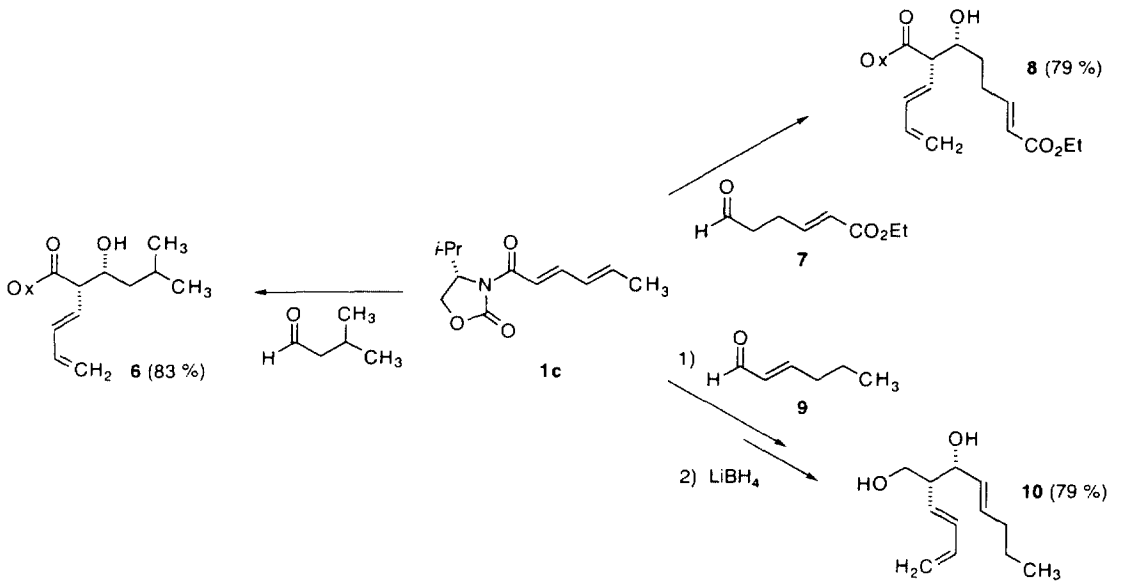
assigned based on the relevant vicinal coupling constant (14.9 Hz). The remaining stereochemistry shown in structure **3** was assigned by hydrogenation and comparison of the product to an authentic sample of **5** prepared via the boron-mediated condensation of **4** with isobutyraldehyde (Scheme 1).



Scheme 1. The regio- and diastereoselective aldol condensation of the sorbic acid derived chiral *N*-acyloxazolidinone **1c**

N-Acyloxazolidinone **1c** undergoes efficient boron-mediated aldol condensation with several other simple aldehydes to afford diene-containing products with good efficiency. The results are summarized in Scheme 2. For example, condensation with isovaleraldehyde affords compound **6** (83% yield). Condensation with the γ,δ-unsaturated aldehyde **7** proceeds in 79% yield to afford compound **8**. We see no evidence for competing cycloaddition under the reaction conditions employed, but this example illustrates how the method might be used to efficiently assemble substrates for subsequent intramolecular Diels–Alder cycloaddition or other cyclization reactions.[9] The condensation of **1c** with a prototypical α,β-unsaturated aldehyde proves more difficult. Retro-aldol proceeds readily in the case of (*E*)-2-hexenal and somewhat different reaction conditions need to be employed. The presumed boron enolate is generated from **1c** as described earlier, but after addition of 2-hexenal, the reaction is held at low temperature (1 h at −78°C, 3 h at −50°C) then quenched cold. In addition, the labile aldol adduct is immediately reduced by treatment of the crude product with $LiBH_4$. Under these conditions diol **10** is isolated in good overall yield (79%) and as a single diastereomer as judged by NMR. The embedded 1,5-diene moiety within diol **10** suggests that this methodology should be useful for preparing substrates suitable for examining novel oxy-Cope rearrangements, a strategy that has been developed for enoate derived substrates.[10]

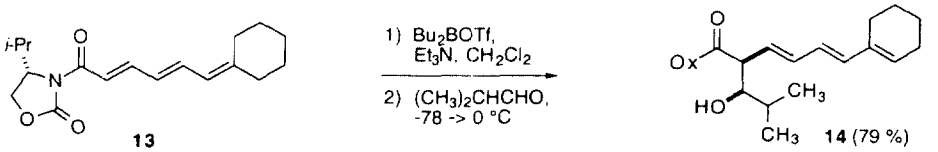
The scope and limitations with respect to the oxazolidinone component have also been briefly surveyed. The results are summarized in Table 1. The norephedrine derived oxazolidinone **11a** affords the condensation product corresponding to **3** but possessing the opposite absolute configuration at the newly formed tetrahedral stereocenters. An additional substituent at the 5-position of the starting oxazolidinone is tolerated, whether that substituent is an acyclic group (entry b, 83%) or part of a cyclic ring system (entry c, 55%). Entry d reveals a limitation to the method, similar to that reported for compound **1b** and related substrates.[6,7] The propyl substituent in substrate (*E,E*)-**11d** affords a near 1:1 mixture of double bond isomers in product **12d** (84%). From the NMR spectrum, we determined that the products are isomeric only at the δ,ϵ-double bond as indicated in structure **12d**. It should be noted however, that in contrast to the lack of diastereoselectivity exhibited by the (*E*)-2-hexenoate derivative **1b**, Schneider found that (*E*)- and (*Z*)-3-pentenoate derivatives (i.e. β,γ-unsaturated rather than α,β-unsaturated oxazolidinone starting materials) retain their double bond stereochemistry upon



Scheme 2. Condensations involving several representative aldehyde partners

boron-mediated aldol condensation.[10] Thus, in analogy to the Schneider work, it may prove possible to prepare products such as **12d** with control of the double bond geometry by starting with a partially deconjugated dienoate derivative. Finally, the isopropyl substituted derivative **11e** shows that it is feasible to prepare products possessing a trisubstituted alkene as part of the newly formed 1,3-diene moiety.

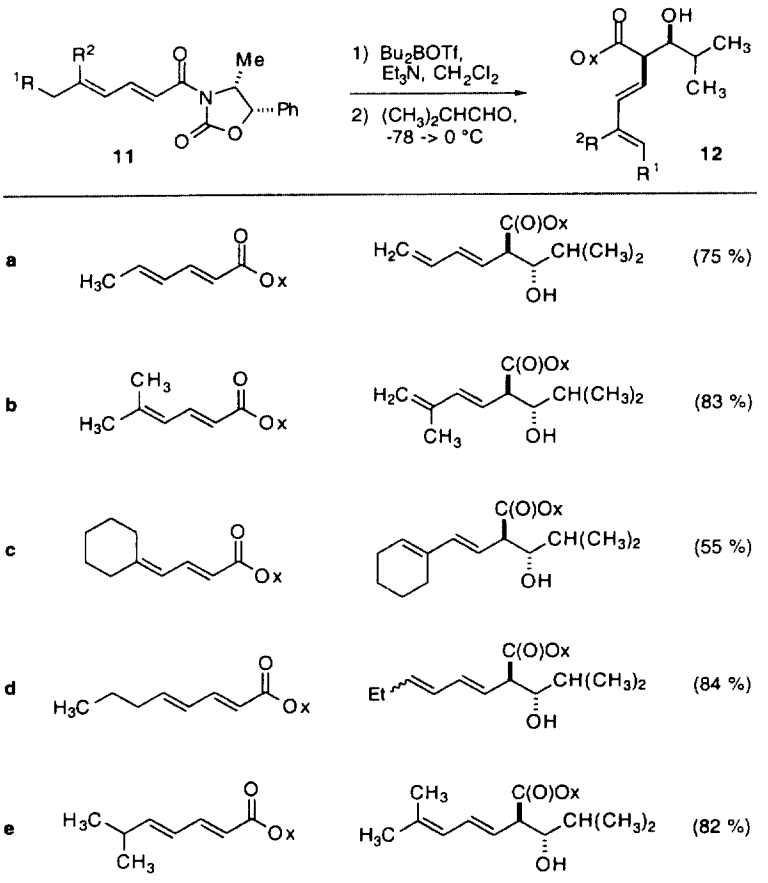
We wondered whether this aldol strategy could be further extended to the preparation of longer conjugated polyene systems. As a simple test case, we prepared triene **13** and found that it too undergoes a facile regio- and stereoselective aldol condensation with isobutyraldehyde to afford the triene-containing product **14** in 79% yield and high isomeric purity.



1. Conclusions

We have extended the methodology introduced by Evans and co-workers for the regio- and diastereoselective boron-mediated aldol condensation of crotonic acid derived *N*-acyloxazolidinones to chiral *N*-acyloxazolidinones derived from dienoic acids. These substrates undergo boron-mediated aldol condensation in good yield, and with the exception of **12d**, the product obtained is of 95% or greater diastereomeric purity as judged by NMR. The method provides a convenient way to introduce a 1,3-diene subunit, and we have shown that the strategy can be extended to the preparation of longer conjugated polyene systems.

Table 1
Some of the scope with respect to the *N*-acyloxazolidinone partner



2. Experimental

2.1. General

All solvents were distilled immediately before use under nitrogen. THF was distilled from Na/benzophenone, and dichloromethane (DCM) was distilled from CaH_2. Flash column chromatography used 60–200 mesh silica gel. NMR spectra were recorded on General Electric Omega 500 and 300. ^1H NMR spectral data in $CDCl_3$, unless otherwise mentioned, are reported in ppm from an internal standard tetramethylsilane or residual chloroform (δ 7.25 ppm). ^{13}C spectra are decoupled and reported in ppm from an internal standard deuterochloroform. FT-IR spectra were recorded using the attenuate total reflectance (ATR, ZnSe crystal) technique and reported in cm^{-1}. High resolution mass spectral determinations were performed by the Nebraska Center for Mass Spectrometry, UNL, Lincoln, Nebraska, USA.

2.2. General procedure for the preparation of N-acyloxazolidinones

To a stirred, cooled (−78°C) solution of the dienoic acid (1 equiv.) and Et_3N (1.25 equiv.) in THF (ca. 0.2 M in acid) was added pivaloyl chloride (1.05 equiv.). The resulting slurry was stirred for 15 min at −78°C, and 45 min at 0°C, and then recooled to −78°C. In a separate flask, a stirred, cooled (−78°C) solution of (4*S*)-isopropyl-2-oxazolidinone or (4*R*,5*S*)-4-methyl-5-phenyl-2-oxazolidinone (1.1 equiv. relative to dienoic acid) in THF (ca. 0.2 M in oxazolidinone) was treated with *n*-BuLi (2.50 M solution in hexane, 1.1 equiv. relative to dienoic acid). The resulting metalated oxazolidinone was added, via cannula, to the dienoate slurry. The resulting viscous slurry was stirred for 20 min at −78°C, and then warmed to room temperature and stirred for 15 h. The reaction mixture was quenched by the addition of H_2O and the organic solvents removed via rotovap. The residue was taken up in DCM and washed successively with portions of 0.5 N HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4), filtered and concentrated. Flash column chromatography on silica gel afforded the diene oxazolidinone.

2.2.1. Preparation of **1c**

(4*S*)-Isopropyl-2-oxazolidinone (1.26 g, 9.81 mmol) was condensed with (2*E*,4*E*)-2,4-hexadienoic acid (sorbic acid, 1.00 g, 8.92 mmol) via the general procedure described earlier, using pivaloyl chloride (2.60 ml, 21.1 mmol), Et_3N (1.57 ml, 11.2 mmol), and *n*-BuLi (3.92 ml, 2.50 M solution in hexane, 9.81 mmol) to afford the *N*-acyloxazolidinone **1c** (1.50 g, 75%) as a viscous oil after flash chromatography (4:1 hexane:EtOAc): TLC analysis (7:3 hexane:EtOAc) R_f=0.36; $[\alpha]_D$ +87.8 (c 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (1H, dd, *J*=10.9, 4.0 Hz), 7.13 (1H, d, *J*=14.9 Hz), 6.21 (1H, dd, *J*=11.3, 4.0 Hz), 6.15–6.07 (1H, m), 4.45–4.38 (1H, m), 4.20 (1H, t, *J*=8.9 Hz), 4.11 (1H, dd, *J*=2.8, 6.0 Hz), 2.40–2.30 (1H, m), 1.77 (3H, d, *J*=6.4 Hz), 0.83 (3H, d, *J*=6.8 Hz), 0.78 (3H, d, *J*=6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1 (s), 153.8 (s), 146.2 (d), 140.4 (d), 130.1 (d), 117.9 (d), 63.1 (t), 58.3 (d), 28.3 (d), 18.4 (q), 17.6 (q), 14.3 (q); FTIR (ATR) 1767 (s, C=O), 1677 (s, C=O), 1635 (s, C=C), 1600 (s, C=C); HRMS analysis (EI, $C_{12}H_{17}NO_3$=223.1208) found 223.1209 *m/z*.

2.2.2. Preparation of **11a**

(4*R*,5*S*)-4-Methyl-5-phenyl-2-oxazolidinone (3.93 g, 22.5 mmol) was condensed with (2*E*,4*E*)-2,4-hexadienoic acid (2.44 g, 21.8 mmol) via the general procedure described earlier using pivaloyl chloride (2.60 ml, 21.1 mmol), Et_3N (3.60 ml, 25.8 mmol), and *n*-BuLi (10.00 ml, 2.35 M solution in hexane, 23.5 mmol) to afford the *N*-acyloxazolidinone (3.97 g, 69%) as a viscous oil after flash chromatography (19:1 hexane:EtOAc): TLC analysis (19:1 hexane:EtOAc) R_f=0.18; $[\alpha]_D$ +36.0 (c 0.66, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.20 (7H, m), 6.33–6.18 (2H, m), 5.66 (1H, d, *J*=7.2 Hz), 4.83–4.78 (1H, m), 1.85 (3H, d, *J*=6.4 Hz), 0.9 (3H, d, *J*=6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1 (s), 152.9 (s), 146.6 (d), 140.9 (d), 133.6 (s), 130.3 (d), 128.5 (two aromatic resonances overlapping, d), 125.6 (d), 117.9 (d), 78.8 (d), 54.8 (d), 18.7 (q), 14.5 (q); FTIR (ATR) 1750 (s, C=O), 1677 (s, C=O), 1635 (s, C=C), 1601 (s, C=C); HRMS analysis (EI, $C_{16}H_{17}NO_3$=271.1208) found 271.1218 *m/z*.

2.2.3. Preparation of **11b**

(4*R*,5*S*)-4-Methyl-5-phenyl-2-oxazolidinone (1.97 g, 11.3 mmol) was condensed with (2*E*)-5-methyl-2,4-hexadienoic acid[11] (1.29 g, 10.3 mmol) via the general procedure described earlier using pivaloyl chloride (1.35 ml, 11.0 mmol), Et_3N (1.80 ml, 12.9 mmol), and *n*-BuLi (4.51 ml, 2.5 M in hexane, 11.3 mmol) to afford the *N*-acyloxazolidinone (2.07 g, 72%) as a white solid after flash chromatography (19:1 hexane:EtOAc): TLC analysis (7:3 hexane:EtOAc) R_f=0.43; m.p.=99–101°C; $[\alpha]_D$ +23.6 (c 1.65,

$CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (1H, dd, J=11.7, 3.2 Hz), 7.40–7.19 (6H, m), 6.11 (1H, dd, J=0.7, 11.0 Hz), 5.65 (1H, d, J=7.3 Hz), 4.83–4.78 (1H, m), 1.87 (6H, d, J=9.7 Hz), 0.90 (3H, d, J=6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4 (s), 152.9 (s), 148.2 (s), 142.5 (d), 133.4 (s), 128.5 (two aromatic resonances overlapping, d), 125.5 (d), 124.3 (d), 117.4 (d), 78.7 (d), 54.8 (d), 26.6 (q), 18.9 (q), 14.5 (q); FTIR (ATR) 1769 (s, C=O), 1670 (s, C=O), 1626 (s, C=C), 1590 (s, C=C); HRMS analysis (FAB, $C_{17}H_{19}NO_3$+H=286.1443) found 286.1444 *m/z*.

2.2.4. *Preparation of* ***11c***

(4*R*,5*S*)-4-Methyl-5-phenyl-2-oxazolidinone (300 mg, 1.65 mmol) was condensed with (2*E*)-5-cyclohexyl-2,4-pentadienoic acid[12] (250 mg, 1.50 mmol) via the general procedure described earlier using pivaloyl chloride (0.20 ml, 1.62 mmol), Et_3N (0.26 ml, 1.87 mmol), and *n*-BuLi (0.66 ml, 2.50 M solution in hexane, 1.65 mmol) to afford the *N*-acyloxazolidinone (360 mg, 76%) as a yellow solid after flash chromatography (19:1 hexane:EtOAc): TLC analysis (19:1 hexane:EtOAc) R_f=0.13; m.p.=118–120°C; $[\alpha]_D$ +16.1 (c 0.74, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (1H, dd, J=11.7, 2.9 Hz), 7.42–7.2 (6H, m), 6.07 (1H, d, J=11.9 Hz), 5.65 (1H, d, J=7.5 Hz), 4.84–4.80 (1H, m), 2.44–2.38 (2H, m), 2.25–2.18 (2H, m), 1.63–1.58 (6H, m), 0.90 (3H, d, J=6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6 (s), 156.3 (s), 152.9 (s), 142.0 (d), 133.4 (s), 128.5 (d), 125.5 (d), 125.5 (d), 121.7 (d), 117.6 (d), 78.7 (d), 54.8 (d), 37.7 (t), 29.8 (t), 28.4 (t), 27.9 (t), 26.3 (t), 14.5 (q); FTIR (ATR) 1740 (s, C=O), 1698 (s, C=O), 1618 (s, C=C), 1591 (s, C=C); HRMS analysis (FAB, $C_{20}H_{23}NO_3$+H=326.1756) found 326.1745 *m/z*.

2.2.5. *Preparation of* ***11d***

(4*R*,5*S*)-4-Methyl-5-phenyl-2-oxazolidinone (2.41 g, 13.6 mmol), was condensed with (2*E*,4*E*)-2,4-octadienoic acid[13] (1.59 g, 11.3 mmol) via the general procedure described earlier using pivaloyl chloride (1.54 ml, 12.5 mmol), Et_3N (1.90 ml, 13.6 mmol), and *n*-BuLi (5.79 ml, 2.35 M solution in hexane, 13.6 mmol) to afford the *N*-acyloxazolidinone (3.00 g, 88%) as a viscous oil after flash chromatography (85:15 hexane:EtOAc): TLC analysis (3:1 hexane:EtOAc) R_f=0.50; $[\alpha]_D$ +37.1 (c 1.64, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50–7.20 (7H, m), 6.28 (1H, dd, J=10.9, 4.0 Hz), 6.20–6.15 (1H, m), 5.64 (1H, d, J=7.7 Hz), 4.85–4.70 (1H, m), 2.14 (2H, q, J=7.2 Hz), 1.43 (2H, m), 0.90–0.80 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0 (s), 152.8 (s), 146.5 (d), 145.9 (d), 133.4 (s), 129.0 (d), 128.4 (d), 125.5 (d), 125.4 (d), 118.2 (d), 78.7 (d), 54.7 (d), 34.9 (t), 21.6 (t), 14.4 (q), 13.4 (q); FTIR (ATR) 1772 (s, C=O), 1677 (s, C=O), 1631 (s, C=C), 1602 (s, C=C); HRMS analysis (EI, $C_{18}H_{21}NO_3$=299.1521) found 299.1511 *m/z*.

2.2.6. *Preparation of* ***11e***

2.2.6.1. *(2E,4E)-6-Methyl-2,4-heptadienoic acid.* Ethyl-(2*E*,4*E*)-6-methyl-2,4-heptadienoate[14] (1.25 g, 7.4 mmol) was treated with KOH (0.97 mg, 17 mmol) in methanol:water (30:5 ml). The mixture was stirred for 15 h at room temperature. The methanol was removed via rotovap. Standard acid–base extractive workup afforded the title acid as a yellow solid (1.03 g, quantitative): TLC analysis (70:30 hexane:EtOAc) R_f=0.24; m.p.=34–36°C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.31 (1H, m), 6.15–6.14 (2H, m), 5.79 (1H, d, J=15.3 Hz), 2.45–2.38 (1H, m), 1.03 (6H, d, J=6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0 (s), 152.5 (d), 147.7 (d), 125.3 (d), 118.5 (d), 31.5 (d), 21.6 (q); FTIR (ATR) 3500 (br s, OH), 1682 (s, C=O), 1675 (s, C=C); HRMS analysis ($C_8H_{12}O_2$+H=141.0915) found 141.0914 *m/z*.

2.2.6.2. *Compound* ***11e***. (4*R*,5*S*)-4-Methyl-5-phenyl-2-oxazolidinone (777 mg, 4.46 mmol) was condensed with (2*E*,4*E*)-6-methyl-2,4-heptadienoic acid (450 mg, 3.21 mmol) via the general procedure

described earlier using pivaloyl chloride (0.55 ml, 4.5 mmol), Et_3N (0.71 ml, 5.1 mmol), and *n*-BuLi (1.80 ml, 2.5 M in hexane, 4.5 mmol) to afford the *N*-acyloxazolidinone (932.7 mg, 97%) as a viscous oil after flash chromatography (85:15 hexane:EtOAc): TLC analysis (4:1 hexane:EtOAc) R_f=0.53; $[\alpha]_D$ +31.6 (c 0.55, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.42–7.18 (7H, m), 6.25–6.11 (2H, m), 5.6 (1H, d, *J*=9.3 Hz), 4.81–4.76 (1H, m), 2.42–2.39 (1H, m), 1.00 (6H, d, *J*=6.6 Hz), 0.87 (3H, d, *J*=6.5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9 (s), 152.8 (s), 152.6 (d), 146.8 (d), 133.3 (s), 128.4 (two aromatic resonances overlapping, d), 125.9 (d), 125.5 (d), 118.3 (d), 78.7 (d), 54.7 (d), 31.3 (d), 21.5 (q), 14.4 (q); FTIR (ATR) 1769 (s, C=O), 1676 (s, C=O), 1631 (s, C=C), 1601 (s, C=C); HRMS analysis (FAB, $C_{18}H_{21}NO_3$+H=300.1560) found 300.1601 *m/z*.

2.2.7. Preparation of ***13***

2.2.7.1. *Ethyl-(2E,4E)-7-cyclohexyl-2,4,6-heptatrienoate.* A suspension of (2*E*)-5-cyclohexyl-2,4-pentadienal[15] (1.87 g, 12.5 mmol), triethyl phosphonocrotonate (3.08 g, 13.7 mmol), lithium hydroxide monohydrate (576.0 mg) and 4A molecular sieves (beads, 19.0 g) in THF (75 ml) was heated at reflux for 3 h.[16] The reaction mixture was filtered through a short plug of silica gel (ether), concentrated via rotovap and the residue subjected to flash chromatography (19:1 hexane:EtOAc) to afford the title ester (1.82 g, 66%) as a white solid: TLC analysis (9:1 hexane:EtOAc) R_f=0.55; m.p. 55–57°C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (1H, dd, *J*=11.3, 4.0 Hz), 6.69 (1H, dd, *J*=11.7, 2.8 Hz), 6.07 (1H, dd, *J*=11.3, 3.2 Hz), 5.74 (1H, d, *J*=11.3 Hz), 5.67 (1H, d, *J*=15.3 Hz), 4.04 (2H, q, *J*=6.8 Hz), 2.20–2.15 (2H, m), 2.10–2.00 (2H, m), 1.50–1.40 (6H, m), 1.14 (3H, t, *J*=7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5 (s), 149.2 (s), 144.7 (d), 136.1 (d), 127.4 (d), 121.8 (d), 118.9 (d), 59.5 (t), 37.2 (t), 29.2 (t), 28.2 (t), 27.4 (t), 26.2 (t), 13.9 (q); FTIR (ATR) 1725 (s, C=O), 1610 (s, C=C); HRMS analysis (EI, $C_{14}H_{20}NO_2$=220.1463) found 220.1461 *m/z*.

2.2.7.2. *(2E,4E)-7-Cyclohexyl-2,4,6-heptatrienoic acid.* Ethyl-(2*E*,4*E*)-7-cyclohexyl-2,4,6-heptatrienoate (1.57 g, 7.13 mmol) was treated with KOH (939.7 mg, 16.8 mmol) in methanol:water (30:5 ml). The mixture was stirred for 15 h at room temperature. Standard acid–base extractive work-up afforded the desired acid as a white solid (1.01 g, 74%): TLC analysis (9:1 hexane:EtOAc) R_f=0.10; m.p. 109–111°C; ^1H NMR (500 MHz, $CDCl_3$) δ 11.50 (1H, br s), 7.43 (1H, dd, *J*=11.7, 3.6 Hz), 6.88 (1H, dd, *J*=11.3, 3.2 Hz), 6.24 (1H, dd, *J*=11.7, 2.8 Hz), 5.90 (1H, d, *J*=11.7 Hz), 5.81 (1H, d, *J*=15.3 Hz), 2.40–2.30 (2H, m), 2.20–2.10 (2H, m), 1.60–1.50 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9 (s), 151.0 (s), 147.6 (d), 137.9 (d), 127.4 (d), 122.0 (d), 118.2 (d), 37.6 (t), 29.6 (t), 28.5 (t), 27.8 (t), 26.5 (t); FTIR (ATR) 3500 (br s, OH), 1682 (s, C=O), 1605 (s, C=C); HRMS analysis (FAB, $C_{12}H_{16}NO_2$=192.1150) found 192.1151 *m/z*.

2.2.7.3. *Compound* ***13.*** (4*S*)-Isopropyl-2-oxazolidinone (687.3 mg, 5.32 mmol), was condensed with (2*E*,4*E*)-7-cyclohexyl-2,4,6-heptatrienoic acid (930.0 mg, 4.84 mmol) via the general procedure described earlier using pivaloyl chloride (0.64 ml, 5.2 mmol), Et_3N (0.85 ml, 6.1 mmol), and *n*-BuLi (2.26 ml, 2.35 M solution in hexane, 5.3 mmol) to afford the *N*-acyloxazolidinone (752.2 mg, 52%) as a yellow solid after flash chromatography (4:1 hexane:EtOAc): TLC analysis (3:1 hexane:EtOAc) R_f=0.48; m.p. 140–142°C; $[\alpha]_D$ +90.0 (c 0.85, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (1H, dd, *J*=11.3, 3.6 Hz), 7.20 (1H, d, *J*=14.9 Hz), 6.84 (1H, dd, *J*=11.7, 2.8 Hz), 6.27 (1H, dd, *J*=11.7, 2.8 Hz), 5.85 (1H, d, *J*=11.3 Hz), 4.45–4.38 (1H, m), 4.20 (1H, t, *J*=8.9 Hz), 4.11 (1H, dd, *J*=2.8, 6.0 Hz), 2.40–2.30 (3H, m), 2.20–2.10 (2H, m), 1.60–1.50 (6H, m) 0.85 (3H, d, *J*=6.8 Hz), 0.79 (3H, d, *J*=6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0 (s), 153.8 (s), 150.6 (s), 146.7 (d), 137.8 (d), 128.1 (d), 122.0 (d), 117.9 (d), 63.1

(t), 58.3 (d), 37.4 (t), 29.5 (t), 28.3 (d), 28.2 (t), 27.6 (t), 26.3 (t), 17.7 (q), 14.5 (q); FTIR (ATR) 1771 (s, C=O), 1677 (s, C=O), 1596 (s, C=C), 1486 (s, C=C); HRMS analysis (EI, $C_{18}H_{25}NO_3$=303.1834) found 303.1837 *m/z*.

2.3. General procedure for the asymmetric boron-mediated aldol condensation of the dienoate derivatives

To a stirred, cooled (−78°C) solution of *N*-acyloxazolidinone (1 equiv.) in DCM (ca. 0.2 M) was added Bu_2BOTf (1.2 equiv.) dropwise.[8] After 5 min, Et_3N (1.4 equiv.) was added dropwise. After stirring for an additional 1 h (−78°C), the reaction was warmed to 0°C (15 min), and then re-cooled (−78°C). The appropriate aldehyde (1.47 equiv.) was added dropwise, and the resulting mixture was stirred for 1 h (−78°C), and then warmed to 0°C. After ca. 1 h at 0°C (follow by TLC), the reaction was partitioned between 1 M aqueous $NaHSO_4$ and DCM. The organic layer was separated, cooled to 0°C then treated with pH 7 phosphate buffer (ca. 5 ml on a 3 mmol scale reaction) and 30% H_2O_2 (ca. 2 ml on this scale). After stirring rapidly for 1 h, the mixture was partitioned between saturated $NaHCO_3$ and DCM. The organic layer was dried (Na_2SO_4) and concentrated. Flash chromatography on silica afforded the desired β-hydroxyoxazolidinone derivative.

2.3.1. Preparation of **3**

(4*S*)-4-Isopropyl-3((2*E*,4*E*)-1-oxo-2,4-hexadienyl)-2-oxazolidinone (450.0 mg, 2.01 mmol) was condensed with isobutyraldehyde (0.27 ml, 3.0 mmol) via the general procedure described earlier using Bu_2BOTf (0.61 ml, 2.4 mmol) and Et_3N (0.39 ml, 2.8 mmol) to afford the β-hydroxyoxazolidinone (483.8 mg, 82%) as an oil after flash chromatography (4:1 hexane:EtOAc): HPLC analysis (E. Merck LiChrosorb Si 60, 80:20 hexane:EtOAc, 1.0 ml/min) 6.2 (95%), 8.1 (5%); TLC analysis (3:1 hexane:EtOAc) R_f=0.38; $[\alpha]_D$ +47.5 (c 0.59, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.41 (1H, dd, *J*=10.9, 4.4 Hz), 6.33 (1H, dd, *J*=10.1, 6.4 Hz), 5.83 (1H, dd, *J*=9.3, 6.1 Hz), 5.20 (1H, d, *J*=16.9 Hz), 5.08 (1H, d, *J*=10.9 Hz), 4.84 (1H, dd, *J*=3.2, 6.4 Hz), 4.50–4.45 (1H, m), 4.30–4.20 (2H, m), 3.63–3.60 (1H, m), 3.23 (1H, d, *J*=1.2 Hz), 2.40–2.30 (1H, m), 1.75–1.68 (1H, m), 1.00–0.80 (12H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6 (s), 153.2 (s), 136.5 (d), 136.2 (d), 126.5 (d), 117.7 (t), 76.5 (d), 63.0 (t), 58.1 (d), 48.2 (d), 30.9 (d), 28.0 (d), 18.8 (q), 18.3 (q), 17.6 (q), 14.3 (q); FTIR (ATR) 3500 (br s, OH), 1776 (s, C=O), 1687 (s, C=O); HRMS analysis (CI, $C_{15}H_{25}NO_4$+H=296.1862) found 296.1854 *m/z*.

2.3.1.1. *Hydrogenation of* **3**. A sample of **3** (75.0 mg, 0.25 mmol) in EtOH (3 ml) was treated with 5% Rh/alumina (ca. 2 mg) under an atmosphere of H_2 (room temperature, 24 h). The resulting mixture was then filtered through a short plug of silica gel and the solvent was removed under vacuum to give the reduced product (72.1 mg, 95%) which was identical to compound **5** prepared as set out below.

2.3.2. Preparation of **5**

(4*S*)-4-Isopropyl-3-(1-oxohexanoyl)-2-oxazolidinone[17] (500.0 mg, 2.20 mmol) was condensed with isobutyraldehyde (0.22 ml, 2.4 mmol) via the general procedure described earlier using Bu_2BOTf (0.61 ml, 2.4 mmol) and diisopropylethylamine (0.43 ml, 2.5 mmol) to afford the β-hydroxyoxazolidinone (602.1 mg, 91%) as an oil after flash chromatography (4:1 hexane:EtOAc): TLC analysis (3:1 hexane:EtOAc) R_f=0.35; $[\alpha]_D$ +47.2 (c 0.89, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 4.42–4.38 (1H, m), 4.20–4.10 (3H, m), 3.63–3.60 (1H, m), 3.36 (1H, dd, *J*=4.0, 2.8 Hz), 2.30–2.20 (1H, m), 1.80–1.70 (1H, m), 1.60–1.50 (2H, m), 1.30–1.10 (4H, m), 1.00–0.80 (15H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.6 (s), 153.4 (s), 76.6 (d), 62.7 (t), 58.4 (d), 44.5 (d), 31.0 (d), 29.2 (t), 28.1 (d), 26.0 (t), 22.6 (t), 18.9

(q), 18.2 (q), 17.6 (q), 14.2 (q), 13.6 (q); FTIR (ATR) 3500 (br s, OH), 1774 (s, C=O), 1686 (s, C=O); HRMS analysis (FAB, $C_{16}H_{29}NO_4$+H=300.2175) found 300.2178 *m/z*.

2.3.3. Preparation of 6

(4*S*)-4-Isopropyl-3((2*E*,4*E*)-1-oxo-2,4-hexadienyl)-2-oxazolidinone (375.7 mg, 1.68 mmol) was condensed with isovaleraldehyde (0.26 ml, 2.5 mmol) via the general procedure described earlier using Bu_2BOTf (0.51 ml, 2.0 mmol) and Et_3N (0.33 ml, 2.4 mmol) to afford the β-hydroxyoxazolidinone (430.2 mg, 83%) as an oil after flash chromatography (4:1 hexane:EtOAc): TLC analysis (3:1 hexane:EtOAc) R_f=0.38; $[\alpha]_D$ +55.8 (c 0.86, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.40–6.20 (2H, m), 5.78 (1H, dd, *J*=9.3, 5.2 Hz), 5.15 (1H, d, *J*=16.9 Hz), 5.03 (1H, d, *J*=10.0 Hz), 4.50 (1H, dd, *J*=3.2, 3.2 Hz), 4.45–4.40 (1H, m), 4.24 (1H, t, *J*=8.9 Hz), 4.15 (1H, dd, *J*=3.2, 6.0 Hz), 4.05–4.00 (1H, m), 3.20 (1H, br s), 2.40–2.30 (1H, m), 1.75–1.68 (1H, m), 1.42–1.38 (1H, m), 1.10–1.00 (1H, m), 0.90–0.85 (12H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4 (s), 153.3 (s), 136.7 (d), 136.2 (d), 126.4 (d), 117.7 (t), 69.5 (d), 63.0 (t), 58.0 (d), 51.0 (d), 43.0 (t), 27.9 (d), 24.1 (d), 23.3 (q), 21.6 (q), 17.6 (q), 14.3 (q); FTIR (ATR) 3500 (br s, OH), 1774 (s, C=O), 1687 (s, C=O); HRMS analysis (FAB, $C_{17}H_{27}NO_4$+Li=316.2100) found 316.2103 *m/z*.

2.3.4. Preparation of 8

(4*S*)-4-Isopropyl-3((2*E*,4*E*)-1-oxo-2,4-hexadienyl)-2-oxazolidinone (170 mg, 0.75 mmol) was condensed with (*E*)-ethyl 6-oxo-hex-2-eneoate[18] (180 mg, 1.1 mmol) via the general procedure described earlier using Bu_2BOTf (0.21 ml, 0.83 mmol) and Et_3N (0.15 ml, 1.1 mmol) to afford the β-hydroxyoxazolidinone (220 mg, 79%) as an oil after flash chromatography (85:15 hexane:EtOAc): TLC analysis (50:50 hexane:EtOAc) R_f=0.52; HPLC analysis (E. Merck LiChrosorb Si 60 column, 70:30 hexane:EtOAc) 9.3 (100%); $[\alpha]_D$ −3.9 (c 0.90, MeOH); ^{1}H NMR (500 MHz, C_6D_6) δ 7.00–6.90 (1H, dd, *J*=15.7 Hz), 6.45 (1H, dd, *J*=10.5 Hz), 6.30 (ddd, 1H, *J*=16.9, 10.1, 10.1 Hz), 5.95–5.85 (1H, m), 5.87 (1H, d, *J*=15.3 Hz), 5.01 (1H, d, *J*=16.9 Hz), 4.87 (1H, d, *J*=10.1 Hz), 4.70 (1H, dd, *J*=9.7, 3.6 Hz), 4.10–3.90 (4H, m), 3.40 (2H, d, *J*=5.6 Hz), 2.30–2.05 (2H, m), 2.00–1.90 (1H, m), 1.70–1.55 (2H, m), 1.00–0.90 (3H, m), 0.42 (3H, d, *J*=6.9 Hz), 0.34 (3H, d, *J*=6.9 Hz); ^{13}C NMR (125 MHz) δ 174.4 (s), 166.6 (s), 153.7 (s), 150.0 (d), 137.1 (d), 137.0 (d), 127.5 (d), 122.2 (d), 118.0 (t), 71.2 (d), 62.8 (t), 60.2 (t), 58.1 (d), 51.5 (d), 32.9 (t), 28.7 (t), 28.2 (d), 17.4 (q), 14.1 (q), 14.0 (q); FTIR (ATR) 3500 (br s, OH), 1776 (s, C=O), 1696 (s, C=O), 1651 (s, C=O); HRMS analysis (FAB, $C_{20}H_{29}NO_6$+H=380.2073) found 380.2073 *m/z*.

2.3.5. Preparation of 10

To a stirred, cooled (−78°C) solution of (4*S*)-4-isopropyl-3((2*E*,4*E*)-1-oxo-2,4-hexadienyl)-2-oxazolidinone (220 mg, 1.0 mmol) in DCM (5 ml) was added Bu_2BOTf (0.30 ml, 1.2 mmol) dropwise. After the Bu_2BOTf dissolved, Et_3N (0.21 ml, 1.4 mmol) was added dropwise. Upon additional stirring for 1 h at −78°C, the mixture was warmed to 0°C for 15 min, then re-cooled to −78°C. Freshly distilled (*E*)-2-hexenal (0.17 ml, 1.5 mmol) was added, and the resulting mixture stirred at −78°C (1 h) and −50°C (3 h). The reaction mixture was partitioned between 1 M $NaHSO_4$ and DCM. The organic layer was separated, dried, and concentrated to afford the crude β-hydroxyoxazolidinone as a yellow oil. A cooled (0°C) solution of the crude product in THF was treated with $LiBH_4$ (10.0 ml, 0.2 M in THF, 2 mmol), which was added dropwise over 5 min. The resulting mixture was stirred at 0°C (1 h), and then quenched by the addition of pH 7 buffer (2 ml) and H_2O_2 (2 ml). After stirring for an additional 1 h at 0°C, the reaction mixture was diluted with Et_2O and washed sequentially with saturated aqueous $NaHCO_3$ (10 ml) and brine (10 ml). The resulting organic layer was dried (Na_2SO_4) and concentrated.

Chromatography on silica (70:30 hexane:EtOAc) afforded diol **10** (153 mg, 79%) as a clear viscous oil: TLC analysis (50:50 hexane:EtOAc) R_f=0.23; $[\alpha]_D$ +1.2 (c 0.82, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.29 (1H, ddd, *J*=14.9, 10.3, 10.3 Hz), 6.11 (1H, dd, *J*=15.3, 10.5 Hz), 5.65–5.55 (2H, m), 5.11 (1H, d, *J*=16.9 Hz), 5.00 (1H, d, *J*=10.1 Hz), 4.20 (1H, dd, *J*=4.8, 6.1 Hz), 3.72 (1H, dd, *J*=7.3, 6.9 Hz), 3.60 (1H, dd, *J*=5.6, 5.6 Hz), 3.30–2.90 (2H, m), 2.45–2.35 (1H, m), 2.00–1.95 (2H, m), 1.40–1.30 (2H, m), 0.85 (3H, t, *J*=7.3 Hz); ^{13}C NMR (125 MHz) δ 136.7 (d), 134.4 (d), 133.1 (d), 130.6 (d), 130.1 (d), 116.3 (t), 73.9 (d), 63.7 (t), 50.2 (d), 34.2 (t), 22.2 (t), 13.5 (q); FTIR (ATR) 3500 (br s, OH), 1781 (s, C=O), 1651 (m, C=C); HRMS analysis (FAB, $C_{12}H_{20}O_2$+Li=203.1623) found 203.1619 *m/z*.

2.3.6. Preparation of *12a*

(4*R*,5*S*)-4-Methyl-5-phenyl-3-((2*E*,4*E*)-1-oxo-2,4-hexadienyl)-2-oxazolidinone (**11a**, 537 mg, 2.00 mmol) was condensed with isobutyraldehyde (0.25 ml, 2.8 mmol) via the general procedure described earlier using Bu_2BOTf (2.20 ml, 1.0 M in DCM, 2.20 mmol) and Et_3N (0.35 ml, 2.51 mmol) to afford the β-hydroxyoxazolidinone (515 mg, 75%) as a viscous oil after flash chromatography (85:15 hexane:EtOAc): HPLC analysis (E. Merck LiChrosorb Si 60, 80:20 hexane:EtOAc, 1.0 ml/min) 5.5 (5%), 6.9 (95%); $[\alpha]_D$ +96.3 (c 0.41, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.45–7.22 (5H, m), 6.44–6.30 (2H, m), 5.87–5.82 (1H, m), 5.68 (1H, d, *J*=7.3 Hz), 5.25–5.21 (1H, m), 5.12–5.09 (1H, m), 4.85–4.78 (2H, m), 3.65–3.63 (1H, m), 3.14 (1H, br s), 1.78–1.63 (1H, m), 1.01 (3H, d, *J*=6.9 Hz), 0.95 (3H, d, *J*=6.9 Hz), 0.86 (3H, d, *J*=6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5 (s), 153.0 (s), 136.6 (d), 136.4 (d), 133.0 (s), 128.8 (d), 128.7 (d), 126.1 (d), 125.6 (d), 117.9 (t), 78.8 (d), 76.9 (d), 54.8 (d), 48.6 (d), 31.1 (d), 18.9 (q), 18.5 (q), 14.2 (q); FTIR (ATR) 3500 (br s, OH), 1775 (s, C=O), 1692 (s, C=O); HRMS (FAB, $C_{20}H_{25}NO_4$+Na=366.1681) found 366.1670 *m/z*.

2.3.7. Preparation of *12b*

(4*R*,5*S*)-4-Methyl-5-phenyl-3-((2*E*)-5-methyl-1-oxo-2,4-hexdienyl)-2-oxazolidinone (**11b**, 1.00 g, 3.50 mmol) was condensed with isobutyraldehyde (0.47 ml, 5.4 mmol) via the general procedure described earlier using Bu_2BOTf (0.97 ml, 3.8 mmol) and Et_3N (0.69 ml, 4.9 mmol) to afford the β-hydroxyoxazolidinone (1.04 g, 83%) as a viscous oil after flash chromatography (70:30 hexane:EtOAc): TLC analysis (70:30, hexane:EtOAc) R_f=0.32; $[\alpha]_D$ +138.3 (c 0.84, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.41–7.2 (5H, m), 6.44 (1H, d, *J*=15.7 Hz), 5.77 (1H, dd, *J*=9.3, 6.9 Hz), 5.65 (1H, d, *J*=7.3 Hz), 5.0 (2H, s), 4.78–4.75 (2H, m), 3.63 (1H, dd, *J*=3.2, 4.4 Hz), 3.18 (1H, s), 1.80 (3H, s), 1.70–1.61 (1H, m), 0.98 (3H, d, *J*=6.4 Hz), 0.92 (3H, d, *J*=6.9 Hz), 0.82 (3H, d, *J*=6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3 (s), 152.3 (s), 141.3 (s), 138.2 (d), 133.0 (s), 128.6 (d), 128.5 (d), 125.5 (s), 122.2 (d), 117.0 (t), 78.7 (d), 76.8 (d), 54.6 (d), 48.8 (d), 31.0 (d), 18.3 (q), 18.8 (q), 18.3 (q), 14.0 (q); FTIR (ATR) 3500 (br s, OH), 1778 (s, C=O), 1695 (s, C=O), 1608 (s, C=C); HRMS analysis (FAB, $C_{21}H_{27}NO_4$+Li=364.2100) found 364.2107 *m/z*.

2.3.8. Preparation of *12c*

(4*R*,5*S*)-4-Methyl-5-phenyl-3-((2*E*)-5-cyclohexyl-1-oxo-2,4-pentadienyl)-2-oxazolidinone (**11c**, 980.0 mg, 3.00 mmol) was condensed with isobutyraldehyde (0.40 ml, 4.4 mmol) via the general procedure described earlier using Bu_2BOTf (0.82 ml, 3.3 mmol) and Et_3N (0.59 ml, 4.2 mmol) to afford the β-hydroxyoxazolidinone (660.0 mg, 55%) as a viscous oil after flash chromatography (70:30 hexane:EtOAc): HPLC analysis (E. Merck LiChrosorb Si 60, 80:20 hexane:EtOAc, 1.00 ml/min) 3.6 (4%), 5.6 (96%); TLC analysis (70:30, hexane:EtOAc) R_f=0.25; $[\alpha]_D$ +135.5 (c 0.54, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.41–7.22 (5H, m), 6.32 (1H, d, *J*=15.8 Hz), 5.73 (1H, s), 5.65–5.59 (2H, m), 4.77–4.70 (2H, m), 3.61 (1H, dd, *J*=3.6, 4.1 Hz), 3.17 (1H, s), 2.18–2.02 (4H, m), 1.76–1.45 (5H, m),

0.97 (3H, d, J=6.5 Hz), 0.91 (3H, d, J=6.8 Hz), 0.82 (3H, d, J=6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7 (s), 152.3 (s), 139.2 (d), 135.2 (s), 133.1 (s), 130.2 (d), 128.6 (d), 128.5 (d), 128.5 (d), 117.8 (d), 78.7 (d), 76.9 (d), 54.6 (d), 48.9 (d), 30.9 (d), 24.2 (two allylic resonances overlapping, t), 22.3 (t), 22.2 (t), 18.9 (q), 18.3 (q), 14.1 (q); FTIR (ATR) 3500 (br s, OH), 1777 (s, C=O), 1735 (s, C=O), 1696 (s, C=C), 1647 (s, C=C); HRMS analysis (FAB, $C_{24}H_{31}NO_4$+Li=404.2413) found 404.2414 *m/z*.

2.3.9. Preparation of **12d**

(4*R*,5*S*)-4-Methyl-5-phenyl-3((2*E*,4*E*)-1-oxo-2,4-octadienyl)-2-oxazolidin-one (**11d**, 500.0 mg, 1.67 mmol) was condensed with isobutyraldehyde (0.22 ml, 2.5 mmol) via the general procedure described earlier using Bu_2BOTf (0.51 ml, 2.0 mmol) and Et_3N (0.33 ml, 2.3 mmol) to afford a diastereomeric mixture of β-hydroxyoxazolidinones (520.2 mg, 84%) as an oil after flash chromatography (85:15 hexane:EtOAc): HPLC analysis (E. Merck LiChrosorb Si 60, 80:20 hexane:EtOAc, 1.0 ml/min) 5.6 (60%), 5.9 (40%); TLC analysis (3:1 hexane:EtOAc) R_f=0.40; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.25 (5H, m), 6.63 (0.5H, dd, J=11.3, 4.0 Hz), 6.33 (0.5H, dd, J=10.1, 5.2 Hz), 6.01 (0.5H, dd, J=13.7, 10.15 Hz), 5.94 (0.5H, t, J=10.5 Hz), 5.80–5.60 (3H, m), 4.80–4.70 (2H, m), 3.65–3.60 (1H, m), 3.10 (1H, br s), 2.20–2.10 (2H, m), 1.75–1.68 (1H, m), 1.00–0.80 (12H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5 (s), 174.3 (s), 152.3 (s), 137.1 (d), 136.2 (d), 134.5 (s), 133.1 (d), 131.1 (d), 128.7 (d), 128.6 (d), 125.6 (d), 125.5 (d), 125.3 (d), 123.0 (d), 78.7 (d), 76.9 (d), 54.7 (d), 53.3 (d), 49.1 (d), 48.8 (d), 31.1 (d), 31.0 (d), 25.4 (t), 21.0 (t), 18.9 (q), 18.3 (q), 18.2 (q), 14.1 (q), 14.0 (q), 13.2 (q); FTIR (ATR) 3500 (br s, OH), 1778 (s, C=O), 1694 (s, C=O); HRMS analysis (FAB, $C_{22}H_{29}NO_4$+H=372.2175) found 372.2185 *m/z*.

2.3.10. Preparation of **12e**

(4*R*,5*S*)-4-Methyl-5-phenyl-3-((2*E*,4*E*)-6-methyl-1-oxo-2,4-heptadienyl)-2-oxazolidinone (**11e**, 880.0 mg, 2.95 mmol) was condensed with isobutyraldehyde (0.40 ml, 4.4 mmol) via the general procedure described earlier using Bu_2BOTf (3.40 ml, 1.0 M in DCM, 3.40 mmol) and Et_3N (0.60 ml, 4.3 mmol) to afford the β-hydroxyoxazolidinone (920.0 mg, 82%) as a viscous oil after flash chromatography (70:30 hexane:EtOAc): HPLC analysis (E. Merck LiChrosorb Si 60, 80:20 hexane:EtOAc, 1.00 ml/min) 5.6 (99%), 7.2 (1%); TLC analysis (70:30, hexane:EtOAc) R_f=0.37; $[\alpha]_D$ +129.5 (c 0.61, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.23 (5H, m), 6.56 (1H, dd, J=10.9, 4.0 Hz), 5.82 (1H, d, J=10.9 Hz), 5.67–5.62 (2H, m), 4.79–4.71 (2H, m), 3.63 (1H, dd, J=3.6, 3.6 Hz), 3.2 (1H, s), 1.78–1.65 (7H, m), 0.98 (3H, d, J=6.9 Hz), 0.93 (3H, d, J=6.9 Hz), 0.83 (3H, d, J=6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5 (s), 152.3 (s), 136.1 (s), 133.1 (s), 132.4 (d), 128.7 (d), 128.6 (d), 128.5 (d), 125.5 (d), 124.5 (d), 122.5 (d), 78.7 (d), 76.8 (d), 54.6 (d), 49.1 (d), 31.0 (d), 25.8 (q), 18.9 (q), 18.3 (q), 14.0 (q); FTIR (ATR) 3500 (br s, OH), 1776 (s, C=O), 1693 (s, C=O); HRMS analysis (FAB, $C_{22}H_{29}NO_4$+Li=378.2257) found 378.2249 *m/z*.

2.3.11. Preparation of **14**

(4*S*)-4-Isopropyl-3((2*E*,4*E*)-7-cyclohexyl-1-oxo-2,4,6-heptatrienoyl)-2-oxazolidinone (**13**, 482.6 mg, 1.59 mmol), was condensed with isobutyraldehyde (0.21 ml, 2.3 mmol) via the general procedure described earlier using Bu_2BOTf (0.48 ml, 1.9 mmol) and Et_3N (0.31 ml, 2.2 mmol) to afford the β-hydroxyoxazolidinone (474.7 mg, 79%) as a yellow solid after flash chromatography (85:15 hexane:EtOAc): HPLC analysis (E. Merck LiChrosorb Si 60, 80:20 hexane:EtOAc, 1.00 ml/min) 6.8 (100%); TLC analysis (3:1 hexane:EtOAc) R_f=0.40; m.p. 48–50°C; $[\alpha]_D$ −115.7 (c 0.51, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.42 (1H, dd, J=10.1, 5.2 Hz), 6.18 (1H, d, J=15.3 Hz), 6.09 (1H, dd, J=10.1, 5.2 Hz), 5.80–5.70 (2H, m), 4.80 (1H, dd, J=2.8, 6.4 Hz), 4.45–4.40 (1H, m), 4.30–4.20 (2H, m), 3.65–3.58 (1H,

m), 3.24 (1H, d, J=2.4 Hz), 2.40–2.00 (5H, m), 1.80–1.60 (5H, m), 1.00–0.85 (12H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6 (s), 153.1 (s), 136.7 (d), 136.4 (d), 135.4 (s), 130.4 (d), 124.4 (d), 124.3 (d), 76.4 (d), 62.8 (t), 57.9 (d), 48.3 (d), 30.8 (d), 27.8 (d), 25.7 (t), 24.1 (t), 22.1 (t), 22.0 (t), 18.7 (q), 18.1 (q), 17.5 (q), 14.3 (q); FTIR (ATR) 3500 (br s, OH), 1770 (s, C=O), 1680 (s, C=O); HRMS analysis (FAB, $C_{22}H_{33}NO_4$+Li=382.2570) found 382.2559 *m/z*.

Acknowledgements

Financial support of this work by the National Institutes of Health (GM34927) is gratefully acknowledged. We thank the NIH (SIG 1-S10-RR06301) for NMR instrumentation funding and the NSF (CHE-93000831) for GC–MS instrumentation funding.

References

1. Takacs, J. M.; Boito, S. C.; Myoung, Y.-C. *Current Org. Chem.* **1998**, *2*, 233–254.
2. Mehta, G.; Rao, H. S. P. In *The Chemistry of Functional Groups: The Chemistry of Polyenes and Dienes*; Rappoport, Z. Ed.; Wiley: New York, 1997; Vol. 1, pp. 359–480.
3. Takacs, J. M.; Weidner, J. J. *J. Org. Chem.* **1994**, *59*, 6480–6483.
4. Takacs, J. M.; Jaber, M. R.; Clement, F.; Walters, C. *J. Org. Chem.* **1998**, *63*, 6757–6760.
5. Evans, D. A.; Sjogren, E. B.; Bartroli, J.; Dow, R. L. *Tetrahedron Lett.* **1986**, *27*, 4957–4960.
6. Mead, K. T.; Park, M. *Tetrahedron Lett.* **1995**, *36*, 1205–1208.
7. Chattopadhyay, S. K.; Pattenden, G. *Tetrahedron Lett.* **1995**, *36*, 5271–5274.
8. We found that freshly prepared dibutylboron triflate often gave much more satisfactory results than the commercial samples we used. For the preparation of dibutylboron triflate, see: Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099–3111.
9. Roush, W. R. *Adv. Cycloaddit.* **1990**, *2*, 91–146.
10. Schneider, C.; Rehfeuter, M. *Tetrahedron* **1997**, *53*, 133–144.
11. Abarbi, M.; Parrin, J.-L.; Cintrat, J.-C.; Duchene, A. *Synthesis* **1996**, 82–86.
12. Dreiding, A. S.; Pratt, R. J. *J. Am. Chem. Soc.* **1953**, *75*, 3717.
13. Concepcion, A. B.; Maruoka, K.; Yamamoto, H. *Tetrahedron* **1995**, *51*, 4011–4020.
14. Piers, E.; Jung, G. L.; Ruediger, E. H. *Can. J. Chem.* **1987**, *65*, 670–682.
15. Bellasoued, M.; Salemkour, M. *Tetrahedron* **1996**, *52*, 4607–4624.
16. For other applications of the LiOH-promoted Horner–Wadsworth–Emmons reaction of phosphonocrotonates, see reference 4 and: Bonadies, F.; Cardilli, A.; Lattanzi, A.; Orelli, L. R.; Scettri, A. *Tetrahedron Lett.* **1994**, *35*, 3383–3386.
17. Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron: Asymmetry* **1994**, *5*, 961–974.
18. Lee, E.; Hur, C. U.; Park, J. H. *Tetrahedron Lett.* **1989**, *30*, 7219–7220.