Intramolecular, Nucleophile-Catalyzed Aldol-Lactonization (NCAL) Reactions: Catalytic, Asymmetric Synthesis of Bicyclic β-Lactones†

Guillermo S. Cortez, Reginald L. Tennyson, and Daniel Romo*

Department of Chemistry, Texas A&M University, P. O. Box 30012, College Station, TX 77843-3012

Supporting Information Available. General procedures for the intramolecular NCAL reactions and characterization data (including \(^1\)H and \(^{13}\)C NMR spectra) for bicyclic β-lactones 10a-10h and cyclopentenes 18 and 19. This material is available free of charge via the Internet at http://pubs.acs.org

† Dedicated to my mentor and friend Prof. A. I. Meyers, a father of asymmetric synthesis, on the occasion of his retirement
**General.** All reactions were carried out under N\(_2\) in oven-dried or flame-dried glassware. Mukaiyama’s reagent (2-chloro-1-methylpyridinium iodide) and keto-acid 8f were purchased from Acros and used as received. Triethylamine, diisopropylethyl amine, and acetonitrile were distilled from CaH\(_2\). All other commercially available reagents were purchased from Acros or Aldrich and were used as received. O-Acetylquinidine\(^1\), O-benzoylquinidine\(^2\), and O-acetylquinine\(^2\) were prepared according to literature procedures. Aldehyde acid substrates were obtained by NaIO\(_4\) cleavage of \(\alpha\)-hydroxy cyclic ketones (8a)\(^3\) or by ozonolysis of the corresponding trimethylsilylenol ethers (8b, 8c, 8e, 8f)\(^4\) or alkene acids (8d, 8g)\(^5\). Chiral GC analyses were performed using a 30 m Chiraldex \(\beta\)-DA column or a 2,3-di-OAc-6-TBS \(\beta\)-cyclodextrin column at the indicated oven temperatures and \(H_2\) carrier pressures. All NMR spectra were obtained in CDCl\(_3\) using tetramethylsilane (TMS) as internal standard, unless noted otherwise. Elemental analyses were conducted by Atlantic Micro Labs, Inc. In some cases, satisfactory HRMS or elemental analysis could not be obtained on the bicyclic-\(\beta\)-lactones (10a, 10c, 10e, 10f, and 13) due to apparent instability and/or volatility and therefore HRMS were obtained after \(\beta\)-lactone ring opening with 
\(N\)-benzyloxy amine to provide the corresponding benzyl hydroxamic acids.

**General Procedure for the Racemic NCAL Reaction as Described for Bicyclic \(\beta\)-lactone (+/−)-10a.**

![Chemical structure](https://example.com/structure.png)

To a solution of 2.95 g of Mukaiyama's reagent (11.53 mmol, 3.0 equiv) and 2.15 mL of triethylamine (15.37 mmol, 4.0 equiv) in 45.0 mL of acetonitrile at 25 °C was added via syringe pump a solution of aldehyde-acid 8a (500 mg, 3.84 mmol) in 31.9 mL of acetonitrile over 10 h (final concentration: 0.05 M). The resulting dark red solution was stirred for another 12 h, at which point the volatiles were removed under reduced pressure to give a brown residue. The crude reaction mixture was then partitioned between diethyl ether and water (100 mL each). The phases were separated, and the aqueous layer was extracted with diethyl ether (2 x 100 mL). The combined organic phases were washed with saturated NH₄Cl (3 x 200 mL), and then brine (100 mL), dried over MgSO₄, filtered, and concentrated to afford a faint-orange residue that was purified by flash chromatography on SiO₂ (1:1 → 1:0, Et₂O/hexanes) to afford β-lactone 10a (240 mg, 55%) as a light yellow oil: Rf 0.57 (Et₂O); IR (thin film)νmax 1818 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.00 (app t, J = 3.9 Hz, 1H), 3.90 (dd, J = 3.9, 7.8 Hz, 1H), 2.20 (dd, J = 6.3, 14.4 Hz, 1H), 2.13 (dd, J = 7.2, 12.6 Hz, 1H), 1.89-1.98 (m, 1H), 1.69-1.85 (m, 1H), 1.45-1.65 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 171.3, 77.4, 55.5, 30.5, 26.1, 22.0.

FAB HRMS Calcd for C₁₃H₁₇O₃N: 236.1287. Found: 236.1277 (for the corresponding benzyl hydroxamic acid derivative).

β-Lactone 10b. This β-lactone was prepared from aldehyde-acid 8b (200.0 mg, 1.06 mmol). Purification by flash chromatography (3:7 → 2:3, EtOAc/hexanes) gave β-lactone 10b as a faint-yellow solid (118 mg, 66%): Rf 0.62 (4:1, EtOAc/hexanes); IR

6) This compound has been prepared as a racemate from cis-hydroxycyclopentanecarboxylic acid upon treatment with cold tosyl chloride-pyridine, see: Philp, R. P.; Robertson, A. V. *Aust. J. Chem.* 1977, 30, 123-130.
$\text{(CHCl}_3\text{)}\nu_{\text{max}} 1832 \text{ cm}^{-1}$; $^1$H NMR (300 MHz, benzene-$d_6$) $\delta$ 3.98 (app t, $J = 4.7$ Hz, 1H), 3.23-3.34 (m, 2H), 3.16-3.21 (m, 2H), 3.02 (dd, $J = 4.3, 8.5$ Hz, 1H), 1.98 (dd, $J = 1.2, 14.9$ Hz, 1H), 1.96 (ddd, $J = 1.5, 2.3, 14.0$ Hz, 1H), 1.37-1.41 (m, 1H), 1.31-1.36 (m, 1H); $^{13}$C NMR (75 MHz, benzene-$d_6$) $\delta$ 169.8, 115.6, 73.4, 64.7, 64.5, 53.9, 39.5, 36.4.


$\beta$-Lactone 10c. This $\beta$-lactone was prepared from aldehyde-acid 8c (160.0 mg, 1.01 mmol). Purification by flash chromatography (1.5:8.5, Et$_2$O/hexanes) afforded $\beta$-lactone 10c (100 mg, 68%) as a faint-yellow oil: $R_f$ 0.60 (2:3, EtOAc/hexanes); IR (CHCl$_3$)$\nu_{\text{max}}$ 1815 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.02 (app t, $J = 4.6$ Hz, 1H), 3.90 (ddd, $J = 1.2, 4.4, 9.5$ Hz, 1H), 2.07 (app t, $J = 15.6$ Hz, 2H), 1.67 (dd, $J = 9.2, 13.9$ Hz, 1H), 1.64 (dd, $J = 5.0, 15.4$ Hz, 1H), 1.21 (s, 3H), 1.11 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 172.8, 79.7, 56.6, 44.4, 40.6, 40.4, 31.3, 29.2.

FAB HRMS Calcd for C$_{13}$H$_{17}$O$_3$N: 264.1599. Found: 264.1594 (for the corresponding benzyl hydroxamic acid derivative).

$\beta$-Lactone 10d. This $\beta$-lactone was prepared from aldehyde-acid 8d (250 mg, 1.01 mmol). Purification by flash chromatography (3:7, EtOAc/hexanes) afforded $\beta$-lactone 10d (144 mg, 62%) as a white solid: $R_f$ 0.64 (3:2, EtOAc/hexanes); IR (CHCl$_3$)$\nu_{\text{max}}$ 1831, 1737 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.09 (app t, $J = 3.9$ Hz, 1H), 4.44 (dd, $J = 1.2, 3.9$ Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 2.65 (ddd, $J = 6.9, 14.0, 14.0$ Hz, 1H), 2.39
(dd, \( J = 7.3, 14.3 \) Hz, 1H), 2.27 (dd, \( J = 6.7, 15.1 \) Hz, 1H), 1.76 (dddd, \( J = 3.9, 7.2, 13.6, 19.0 \) Hz, 1H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 169.8, 167.5, 166.9, 77.3, 60.6, 60.2, 53.4, 53.1, 29.9, 28.8. Anal. Calcd for C\(_{10}\)H\(_{12}\)O\(_6\): C, 52.63; H, 5.30. Found: C, 52.64; H, 5.36.

**β-Lactone 10e.** This β-lactone was prepared from aldehyde-acid 8e\(^7\) (150 mg, 0.95 mmol). Purification by flash chromatography (1:1 → 1:0, Et\(_2\)O/hexanes) gave β-lactone 10e (82.8 mg, 62%) as a light yellow oil: \( R_f \) 0.73 (Et\(_2\)O); IR (thin film)\( \nu_{max} \) 1824 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 4.36 (app d, \( J = 3.6 \), 1H), 3.86 (dd, \( J = 3.9, 7.7 \) Hz, 1H), 2.04 (dd, \( J = 6.6, 13.2 \) Hz, 1H), 1.85 (ddd, \( J = 7.5, 12.6, 14.9 \) Hz, 1H), 1.72 (dd, \( J = 6.9, 12.3 \) Hz, 1H), 1.60 (dd, \( J = 6.3, 12.0 \) Hz, 1H), 1.17 (s, 3H), 0.90 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 171.8, 83.7, 55.1, 40.3, 35.5, 24.2, 22.6, 21.9. 

FAB HRMS Calcd for C\(_{15}\)H\(_{21}\)O\(_3\)N: 264.1560. Found: 264.1608 (for the corresponding benzyl hydroxamic acid derivative).

**β-Lactone 10f.** This β-lactone was prepared from aldehyde-acid 8f (180 mg, 1.25 mmol). Purification by flash chromatography (1.5:8.5, Et\(_2\)O/hexanes) afforded β-lactone 10f (56.4 mg, 36%) as a faint-yellow oil: \( R_f \) 0.49 (1:1, Et\(_2\)O/hexanes); IR (CHCl\(_3\))\( \nu_{max} \) 1813 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 4.71 (ddd, \( J = 2.8, 4.4, 7.3 \) Hz, 1H), 3.67 (ddd, \( J = 3.4, 6.6, 9.8 \) Hz, 1H), 2.09 (dddd, \( J = 2.9, 4.9, 7.8, 14.7 \) Hz, 1H) 1.46-1.98 (m, 7H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 172.8, 70.8, 47.0, 25.7, 19.6, 19.3, 16.7.

---

FAB HRMS Calcd for C\textsubscript{14}H\textsubscript{20}O\textsubscript{3}N: 250.1443. Found: 250.1454 (for the corresponding benzyl hydroxamic acid derivative).

\[ \text{\textbeta-Lactone 10g.} \] This \textbeta-lactone was prepared from aldehyde-acid 8g (360 mg, 1.38 mmol). Purification by flash chromatography (1:1 \rightarrow 1:0, Et\textsubscript{2}O/hexanes) gave \textbeta-lactone 10g (190 mg, 57%) as a clear oil: R\textsub{f} 0.67 (Et\textsub{2}O); IR (thin film)\nu\textsub{max} 1829, 1737 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \delta 4.96-5.02 (m, 1H), 4.43 (m, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 2.24-2.38 (m, 1H), 1.98-2.20 (m, 2H), 1.75-1.96 (m, 2H), 1.44-1.60 (m, 1H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) \delta 170.6, 168.4, 168.2, 70.9, 53.2, 52.9, 51.9, 51.3, 25.7, 24.2, 14.6. Anal. Calcd for C\textsubscript{11}H\textsubscript{14}O\textsubscript{6}: C, 54.54; H, 5.83. Found: C, 54.81; H, 5.93.

\[ \text{\textbeta-Lactone 10h.} \] This \textbeta-lactone was prepared from commercially available keto-acid 8h (500 mg, 3.47 mmol). Purification by flash chromatography (1.4:1 \rightarrow 1:0, Et\textsub{2}O/hexanes) gave \textbeta-lactone 10h (12.2 mg, 3%) as a light yellow oil: R\textsub{f} 0.73 (Et\textsub{2}O); IR (thin film)\nu\textsub{max} 1824 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \delta 3.43 (app d, J = 7.5 Hz, 1H), 2.17 (dd, J = 5.4, 14.4 Hz, 1H), 2.09 (dd, J = 4.5, 12.0 Hz, 1H), 1.71-1.95 (m, 2H), 1.68 (s, 3H), 1.44-1.64 (m, 2H); \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}) \delta 171.1, 87.3, 59.1, 40.3, 36.2, 27.2, 23.9, 21.5.
β-Lactone 13. This β-lactone was prepared from aldehyde-acid 12, derived from (R)-citronellic acid8 (100 mg, 0.64 mmol). Purification by flash chromatography (1:1 → 1:0, Et₂O/hexanes) gave β-lactone 13 (35.3 mg, 40%) as a faint-yellow oil: Rf 0.72 (Et₂O); \([\alpha]_{D}^{25} +30.2 (c 0.04,\text{ MeOH})\); IR (thin film)νmax 1813 cm⁻¹; \(^1^H\) NMR (300 MHz, CDCl₃) δ 5.02 (app t, J = 3.9 Hz, 1H), 3.57 (app d, J = 3.9 Hz, 1H), 2.59 (ddd, J = 7.2, 7.2, 14.1 Hz, 1H), 2.15 (dd, J = 6.9, 14.4 Hz, 1H), 2.04 (ddd, J = 6.0, 11.7, 17.9 Hz, 1H), 1.72-1.86 (m, 1H), 1.66 (dd, J = 7.5, 12.3 Hz, 1H), 0.93 (d, J = 7.2 Hz, 3H); \(^1^3^C\) NMR (75 MHz, CDCl₃) δ 171.0, 77.8, 62.6, 33.5, 29.3, 28.1, 18.9. FAB HRMS Calcd for C₁₄H₁₉O₃N: 250.1443. Found: 250.1455 (for the corresponding benzyl hydroxamic acid derivative).

General procedure for the Catalytic, Asymmetric NCAL Reaction as Described for Bicyclic β-lactone (+)-(1R, 2S)-10a.

\[ \text{CHO} \quad \text{CO₂H} \quad \text{CHO} \quad \text{CO₂H} \]

O-Acetyl quinidine1 (136 mg, 0.384 mmol), Mukaiyama’s reagent (2.95 g, 11.53 mmol), and 2.70 ml of Hunig’s base (15.4 mmol) were placed in a 100 mL round-bottomed flask and dissolved in 45 mL of CH₃CN. To this slurry was added a solution of aldehyde-acid 8a (500 mg, 3.84 mmol) in 32 mL of CH₃CN via syringe pump over 12 h. After the addition was complete, the reaction was stirred an additional 96 h at 25 °C. The solvent was removed in vacuo, and the orange residue was partitioned between Et₂O (100 mL) and water (100 mL). The phases were separated, and the aqueous layer was extracted

with Et₂O (2 x 100 mL). The combined organic phases were washed with saturated NH₄Cl solution (3 x 200 mL), and then brine (1 x 200 mL), dried over MgSO₄, and concentrated in vacuo. The residue was purified by flash chromatography on SiO₂ (1:1 → 1:0, Et₂O/hexanes) to give β-lactone (+)-10a (233 mg, 54%) as a light yellow oil: [α]D²⁵ +85.0 (c 0.02, MeOH). Enantiomeric excess was determined to be 92% by chiral GC analysis using a 2,3-di-OAc-6-TBS β-CD⁹ column (130 °C, 11 psi): t₁(1S,2R) = 20.68 min (minor), t₁(1R,2S) = 21.32 min (major). All other spectroscopic data matched that displayed by the same compound prepared using Et₃N as nucleophile.

(--)-(1S, 2R)-β-lactone 10a. 51% yield; Prepared according to the general asymmetric NCAL procedure using Mukaiyama's reagent (1.53 g, 5.99 mmol), 1.40 mL of Hünig's base (7.99 mmol), and 73.2 mg of O-acetyl quinine (0.199 mmol) in 24.0 mL of CH₃CN, and 260.0 mg of aldehyde-acid 8a (1.98 mmol) in 16.6 mL of CH₃CN. This gave β-lactone 10a in 51% yield and 86% ee (chiral GC analysis using a 2,3-di-OAc-6-TBS β-CD column, 130 °C, 11 psi): t₁(1S,2R) = 20.49 min (major), t₁(1R,2S) = 22.40 min (major). [α]D²⁵ –48.1 (c 0.77, MeOH). All other spectroscopic data matched that displayed by the same compound prepared using Et₃N as nucleophile.

(+-)(3R, 4S)-β-lactone 10b. Prepared according to the general asymmetric NCAL procedure using Mukaiyama's reagent (2.03 g, 7.97 mmol), 1.80 mL of Hunig's base (4.03 mmol), and 97.0 mg of O-acetyl quinidine (0.100 mmol, 0.1 equiv.) in 32.0 mL of CH₃CN, and 500.0 mg of aldehyde-acid 8b (2.66 mmol) in 22.2 mL of CH₃CN. This gave β-lactone 10b in 37% yield and 92% ee (chiral GC analysis using a 30 m Chiraldex β–DA® column; 120 °C, 10 psi H₂); t₁(3S,4R) = 73.25 min (minor), t₁(3R,4S) = 73.59 min

---

9) We thank Prof. Vigh for providing this column for our studies. Shitangkoon, A.; Vigh, G. J. Chromatogr. A 1996, 31-42.
(major). \([\alpha]_D^{25} +62.6\ \text{(c 0.95, CHCl}_3\)). All other spectroscopic data matched that displayed by the same compound prepared using Et\(_3\)N as nucleophile.

\((+)-(1R, 2S)\)-\(\beta\)-lactone 10c. Prepared according to the general asymmetric NCAL procedure using Mukaiyama’s reagent (1.55 g, 6.07 mmol), 1.40 mL of Hunig’s base (8.08 mmol), and 74.0 mg of \(O\)-acetyl quinidine (0.202 mmol, 0.1 equiv.) in 24.4 mL of CH\(_3\)CN, and 320.0 mg of aldehyde-acid 8c (2.02 mmol) in 17.0 mL of CH\(_3\)CN. This gave \(\beta\)-lactone 10c in 45% yield and 90\% ee (chiral GC analysis using a 2,3-di-OAc-6-TBS \(\beta\)-CD\(^9\) column; 130 °C, 11 psi); \(t_{1R,2S} = 11.37\ \text{min, } t_{1S,2R} = 14.13\ \text{min}\). \([\alpha]_D^{25} +45\ \text{(c 0.6, CHCl}_3\)). All other spectroscopic data matched that displayed by the same compound prepared using Et\(_3\)N as nucleophile.

**Reduction of \((+)-\beta\)-Lactone 10a to \((-)\)-Diol 14.**

\[
(+)-10a \quad \rightarrow \quad (-)-14
\]

A solution of DIBAl-H (238 \(\mu\)L in 0.78 mL of CH\(_2\)Cl\(_2\), 0.45 mmol) was added dropwise to a solution of \(\beta\)-lactone \((+)-10a\) (53 mg, 0.47 mmol) in 5.3 mL of CH\(_2\)Cl\(_2\) cooled to 0 °C. After stirring for 5 min, the solution was warmed to 25 °C and stirred for 1.0 h. The reaction mixture was then cooled to 0 °C, diluted with 2.4 mL of ethyl acetate and quenched with acetone (1.5 mL) and Rochelle’s salt (4.0 mL). The mixture was vigorously stirred at 25 °C for 10 h. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 x 4 mL). The combined organic layers were washed with brine (1 x 8 mL), dried over MgSO\(_4\), filtered, and concentrated to give diol 14 as a colorless oil (26.1 mg, 48% yield). Purification by flash chromatography on SiO\(_2\) (100%
EtOAc) gave an analytically pure sample: $[\alpha]_{D}^{25} = -33.0^\circ$ (c 0.02, MeOH; lit $[\alpha]_{D}^{25} = -37.7^\circ$ (c 0.68, MeOH.) All other spectroscopic data matched that previously reported.\(^{10}\)

**Conversion of (+)-β-lactone 10b to carbocyclic intermediate 20.**

![Conversion of (+)-β-lactone 10b to carbocyclic intermediate 20.](image)

A solution of (+)-β-lactone 10b (101.8 mg, 0.598 mmol) in 6.0 mL of anhydrous THF was cooled to 0 °C and treated with 850 μL of BH$_3$•DMS (15 equiv., 8.97 mmol). After stirring for 18 h at 25 °C, excess borane was quenched by careful addition of 5% Et$_3$N in anhydrous MeOH (8 mL). The volatiles were removed under reduced pressure to give a residue that was dissolved in 8 mL of 5% Et$_3$N/MeOH. The solvent was again removed, repeating this operation a total of five times. The crude diol was dissolved in 12.0 mL of THF and treated with 2.5 mL of 1.0 N aq. HCl. The yellow solution was stirred at 25 °C for 20 h, at which point the reaction mixture was poured onto 10 mL of brine and 20 mL of CH$_2$Cl$_2$. The phases were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (4 x 20 mL). The organic phases were combined, and then washed with brine, dried over MgSO$_4$, filtered, and concentrated to afford a light yellow residue that was purified by flash chromatography on SiO$_2$ (EtOAc) to afford cyclopentenol 18 (34.2 mg, 51% yield for the two steps) as a colorless oil: $R_f$ 0.45 (1:9, MeOH/EtOAc); $[\alpha]_{D}^{25} = -15.9^\circ$ (c 0.34, MeOH); IR (CHCl$_3$)$_{\nu_{max}}$ 3435 (broad), 1703, 1670 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.70 (dd, $J = 2.4$, 5.6 Hz, 1H), 6.22 (dd, $J = 2.0$, 5.6 Hz, 1H), AB of ABX ($\delta_A = 3.74$, $\delta_B = 3.69$, $J_{AB} = 10.5$ Hz, $J_{AX} = 6.1$ Hz, $J_{BX} = 5.9$ Hz, 2H), 3.12-3.22 (m, 1H), 2.47 (dd, $J = 6.6$, 18.9 Hz, 1H), 2.16 (dd, $J = 2.1$, 18.8 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 209.8, 165.5, 135.2, 64.4, 44.1, 37.6.

---

**4-Trityloxymethyl-cyclopent-2-enone (19).** A solution of alcohol 18 (34.0 mg, 0.303 mmol) in 3.40 mL of anhydrous CH$_2$Cl$_2$ at ambient temperature was treated with 126.0 mg of triphenylmethyl chloride (0.453 mmol), 60 µL of anhydrous pyridine (0.727 mmol) and a catalytic amount of DMAP. After 18 h, the clear mixture was partitioned between saturated NH$_4$Cl (20 mL) and EtOAc (20 mL). The phases were separated, and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over MgSO$_4$, filtered and concentrated to afford a cloudy residue that was purified by flash chromatography on SiO$_2$ (3:7, Et$_2$O/hexanes) to provide trityl ether 19 (96.6 mg, 90% yield) as a colorless residue that solidifies upon standing: R$_f$ 0.68 (1:1, EtOAc/hexanes); $[\alpha]_D^{25}$ $-$17° (c 0.5, MeOH); IR (CHCl$_3$)$_{\text{max}}$ 1709, 1601 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.74 (dd, $J$ = 2.4, 5.9 Hz, 1H), 7.38-7.42 (m, 7H), 7.28-7.33 (m, 8H), 6.22 (dd, $J$ = 2.0, 5.4 Hz, 1H), 3.27 (dd, $J$ = 5.9, 8.3 Hz, 1H), 3.20 (dddd, $J$ = 1.9, 4.4, 8.3, 10.7 Hz, 1H), 3.12 (dd, $J$ = 6.3, 8.3 Hz, 1H), 2.46 (dd, $J$ = 6.3, 18.6 Hz, 1H), 2.10 (dd, $J$ = 1.9, 18.6 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 209.5, 166.0, 143.7, 134.9, 128.6, 127.9, 127.1, 86.6, 65.2, 42.1, 38.0; FAB HRMS calcd for C$_{25}$H$_{24}$O$_2$ [M + Na] 379.1674, found 379.1670.

**4-Trityloxymethy-cyclopent-2-enol (20).** Enone 19 (80.0 mg, 0.225 mmol) was dissolved in 11.5 mL of anhydrous THF, cooled to $-78$ °C, and treated with 240 µL of DIBAL-H (1.0 M in PhCH$_3$, 1.04 equiv.). After 30 minutes, an additional 0.70 equiv. of DIBAL-H was added. The reaction mixture was quenched by addition of 100 µL of water.
and 600 mg of silica gel. The resulting slurry was allowed to warm to ambient temperature and was stirred vigorously for 1 h. The mixture was then filtered through a pad of anhydrous Na$_2$SO$_4$, washing with EtOAc. The solvent was removed under reduced pressure to give a residue (>19:1 dr, $^1$H NMR) that was purified by flash chromatography to afford the desired cis-hydroxypentenol 20 (70 mg, 87% yield) as a colorless residue that crystallizes upon standing: $R_f$ 0.63 (4:1, Et$_2$O/hexanes); $[\alpha]_{D}^{25}$ $-66.3^\circ$ (c 1.0, CHCl$_3$); literature $[\alpha]_{D}^{25}$ $-72.1^\circ$ (c 1.2, CHCl$_3$);$^{11}$ IR (CHCl$_3$)$\nu_{\text{max}}$ 3682, 3598, 3495, 1596, 1489 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.48-7.42 (m, 6H), 7.22-7.38 (m, 9H), 5.94-6.02 (m, 2H), 4.68-4.78 (m, 1H), 3.29 (dd, $J = 4.7$, 9.0 Hz, 1H), 3.07 (dd, $J = 5.0$, 9.0 Hz, 1H), 2.80-2.90 (m, 1H), 2.38 (ddd, $J = 7.5$, 8.6, 14.0 Hz, 1H), 2.12 (d, $J = 8.7$ Hz, 1H, OH), 1.44 (dt, $J = 3.3$, 14.0 Hz, 1H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 143.8, 135.7, 134.8, 128.8, 127.8, 127.0, 86.9, 76.6, 65.9, 44.8, 37.4; FAB HRMS calcd for C$_{25}$H$_{22}$O$_2$ [M + Na] 377.1517, found 377.1517.

Proof of absolute configuration of (+)-10c was obtained via x-ray analysis of a crystalline derivative prepared as shown below.

\[
\begin{align*}
\text{BBr}_3 \cdot \text{DMS, THF} \\
\text{0 °C, 24 hours} \\
\text{Ph}_3\text{CMe}_2\text{SiBr, AgNO}_3, \text{DMF}
\end{align*}
\]

The silicon atom was sufficient for anomalous dispersion techniques allowing assignment of the absolute configuration. The Chem3D representation of the x-ray structure is provided below.