Enantioselective β -Lactone Formation from Ketene and Aldehydes Catalyzed by a Chiral Oxazaborolidine

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Supplementary Materials

Materials and Methods. Unless stated otherwise, reactions were performed in flame-dried glassware under a positive pressure of nitrogen using freshly distilled dry solvents. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F₂₅₄ precoated plates (0.25 mm). Flash chromatography was performed using Baker silica gel (40 μ m particle size). NMR spectra were recorded on Varian Innova-500, or Mercury-400 instruments and calibrated using residual undeuterated solvent as an internal reference. IR spectra were recorded on Avatar 360 FT-IR spectrometer. Low-resolution and high-resolution mass spectral analyses were performed at the Harvard University Mass Spectrometry Center. Analytical high performance liquid chromatography (HPLC) was performed on Isco 2350 Series or Waters 626 HPLC using the indicated chiral column. Gas chromatography (GC) analyses were performed on Hewlett-Packard 6850 Series GC System equipped with flame ionization detector using indicated column (30 m x 0.25 mm). Commercial grade reagents and solvents were used without further purification except as indicated below. Dichloromethane and MeCN were distilled from calcium hydride.

(R)-4-(2-Phenylethyl)oxetane-2-one.¹ The general procedure was followed employing 66 μ l of 3-phenylpropanol (0.5 mmol). Purification by flash chromatography gave 64 mg (73%) of β -lactone. Analysis of enantiomers by chiral HPLC (Daicel Chiralcel OD-H column, flow rate 1 mL/min, 10% IPA, 90% hexane, T_r 15.9 (S) and 18.1(R) provided the enantiomeric ratio: 4(S):4(R) = 90:9 (81%ee). $[\alpha]_D^{25} +5.62$ (c 0.32, CHCl_3). Spectral data has been reported previously.¹ IR (film) 3029, 2933, 1821, 1740, 1455, 1412, 1133, 1113 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 2.06-2.12 (m, 1H), 2.18-2.24 (m, 1H), 2.72-2.77 (m, 1H), 2.82-2.87 (m, 1H), 3.05 (dd, $J = 4.2, 18$ Hz, 1H), 3.49 (dd, $J = 5.4, 16$ Hz, 1H), 4.50-4.53 (m, 1H), 7.22-7.35 (m, 5H).

(S)-4-Cyclohexyloxetane-2-one.¹ The general procedure was followed employing 60.5 μ l of cyclohexane carboxaldehyde (0.5 mmol). Purification by flash chromatography gave 60 mg (78%) of β -lactone. Analysis of the enantiomers by chiral GC (cyclosil B column, flow rate 1ml/min at 110 $^\circ\text{C}$, T_r 31.3 (major) and 32.7 (minor) min) provided the enantiomeric ratio: 4(S):4(R) = 85:15 (70%ee). $[\alpha]_D^{25} +2.12$ (c 0.33, CHCl_3 , 70% ee). Spectral data has been reported previously.¹ IR (film) 2968, 2881, 1818, 1760, 1470, 1125 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 0.95-1.06 (m, 2H), 1.10-1.34 (m, 4H), 1.57-1.87 (m, 4H), 1.93-1.94 (m, 1H), 3.10 (dd, $J = 4.8, 12$ Hz, 1H), 3.41 (dd, $J = 6, 16.8$ Hz, 1H), 4.17-4.19 (m, 1H).

(S)-4-Isopropyloxetane-2-one.¹ The general procedure was followed employing 45.5 μ l of isobutyraldehyde (0.5 mmol). Purification by flash chromatography gave 35.5 mg (62%) of β -lactone. Analysis of the enantiomers by chiral GC (Chiraldex γ -TA column, flow rate 0.5ml/min at 100 °C, T_r 27.4 (major) and 30.5 (minor) min) provided the enantiomeric ratio: 4(S):4(R) = 84:16 (68% ee). $[\alpha]_D^{25} +4.00$ (c 0.25, CHCl_3 , 68% ee). Spectral data has been reported previously.¹ IR (film) 2931, 2838, 1821, 1711, 1451, 1277, 1129 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 0.94 (d, J = 6.6 Hz, 3H), 1.03 (d, J = 6.6 Hz, 3H), 1.91-1.95 (m, 1H), 3.08 (dd, J = 4.2, 14.4 Hz, 1H), 3.42 (dd, J = 6, 22.2 Hz, 1H), 4.17-4.20 (m, 1H).

(S)-4-Pentyloxetane-2-one.² The general procedure was followed employing 60 μ l of hexanol (0.5 mmol). Purification by flash chromatography gave 55.5 mg (78%) of β -lactone. Analysis of the enantiomers by chiral GC (Chiraldex γ -TA column, flow rate 0.5ml/min at 100 °C, T_r 41.9 (major) and 44.2 (minor) min) provided the enantiomeric ratio: 4(S):4(R) = 92:8 (84% ee). $[\alpha]_D^{25} +3.04$ (c 0.23, CHCl_3 , 84% ee). Spectral data has been reported previously.² IR (film) 2964, 2935, 1864, 1821, 1708, 1239, 1129, 1011 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 0.82-0.85 (m, 3H), 1.12-1.39 (m, 6H), 1.66-1.71 (m, 1H), 1.76-1.80 (m, 1H), 2.99 (dd, J = 5.4, 19.8 Hz, 1H), 3.45 (dd, J = 6.6, 19.2 Hz, 1H), 4.43-4.46 (m, 1H).

(R)- 4-(2-Benzyloxyethyl)-oxetane-2-one.¹ The general procedure was followed employing 84 mg of 3-benzyloxypropionaldehyde (0.5 mmol). Purification by flash chromatography gave 60 mg (58%) of β -lactone. Analysis of the enantiomers by chiral HPLC (Chiralcel OD-H column, flow rate 0.9ml/min 15% IPA, 85% hexane, T_r 13.5 (minor) and 17.0 (major) min) provided the enantiomeric ratio: 4(S):4(R) = 17:82 (65% ee). $[\alpha]_D^{25} +9.75$ (c 0.80, CHCl_3 , 65% ee). Spectral data has been reported previously.¹ IR (film) 2925, 2860, 1823, 1725, 1455, 1362, 1117, 1102 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 2.11-2.17 (m, 2H), 3.24 (dd, J = 4.2, 16.8 Hz, 1H), 3.57 (dd, J = 5.4, 16.2 Hz, 1H), 3.5-3.68 (m, 2H), 4.54 (s, 2H), 4.74-4.76 (m, 1H).

(R)- 4-(2-Methylpropyl)-oxetane-2-one.¹ The general procedure was followed employing 53.6 μl of isovalaraldehyde (0.5 mmol). Purification by flash chromatography gave 46.3 mg (72%) of the β -lactone. Enantiomers were analyzed, after lactone opening with benzylamine to form the benzylamide, by chiral HPLC (Chiralcel OD-H column, flow rate 1ml/min 5% IPA, 95% hexane, T_r 8.4 (major) and 13.4 (minor) min) provided the enantiomeric ratio: 4(S):4(R) = 83:16 (67% ee). $[\alpha]_D^{25} +7.33$ (c 0.15, CHCl_3 , 67% ee). Spectral data has been reported previously.¹ IR (film) 2964, 1864, 1823, 1710, 1372, 11239, 1113 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 0.94 (d, J

= 6 Hz, 6H), 1.56-1.6 (m, 1H), 1.77-1.81 (m, 2H), 3.02 (dd, $J = 4.2, 10.2$ Hz, 1H), 3.52 (dd, $J = 6, 16.8$ Hz, 1H), 4.54-4.57 (m, 1H).

References.

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