Enantioselective Synthesis of γ -Aryl- γ -Butyrolactones by Sequential Asymmetric Epoxidation, Ring Expansion, and Baeyer-Villiger Oxidation

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Supporting Information

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General methods. All glassware used for the epoxidation was carefully washed to be free from any trace metals which catalyze the decomposition of Oxone. Column chromatography was carried out with 60 Å 230-400 mesh Whatman and Iatrobeds 6RS-8060 silica gel. The NMR spectra were measured in CDCl₃. High resolution mass spectra were performed at the mass spectrometry facility of Colorado State University. Cyclopropylidene olefins were prepared from aldehydes or ketones and 3-bromopropyltriphenylphosphonium bromide using *t*-BuOK in THF in a manner similar to the reported procedure [(a) Utimoto, K.; Tamura, M.; Sisido, K.; *Tetrahedron* **1973**, 29, 1169. (b) Schweizer, E. E.; Berninger, C. J.; Thompson, J. G. *J. Org. Chem.* **1968**, 33, 336.]. 3-Bromopropyltriphenylphosphonium bromide was prepared by heating PPh₃ with 1,3-dibromopropane at 130 °C in xylene according to the reported procedure and used directly after washing with hexane.

Characterization data of lactones in Table 1 and cyclobutanones in Scheme 4

Entry 1

Colorless oil; $[\alpha]_D^{25} = -46.3$ (*c* 1.8, CHCl₃) (80% ee). IR (film) 1770 cm⁻¹; ¹H NMR (400 MHz) δ 7.40-7.20 (m, 4 H), 5.75-5.70 (m, 1 H), 2.74-2.64 (m, 3 H), 2.36 (s, 3 H), 2.18-2.10 (m, 1 H); ¹³C NMR (75 MHz) δ 177.1, 137.6, 134.3, 130.8, 128.2, 126.5, 124.3, 79.0, 29.8, 28.9, 19.3; Anal. Calcd. for C₁₁H₁₂O₂: C, 74.98; H, 6.86. Found: C, 74.76; H, 6.68.

Entry 2

White solid; mp 59-60 °C; $[\alpha]_D^{25} = -11.9$ (*c* 1.1, CHCl₃) (89% ee). IR (film) 1766 cm⁻¹; ¹H NMR (400 MHz) δ 7.30-7.24 (m, 2 H), 6.94-6.88 (m, 2 H), 5.48-5.44 (m, 1 H), 3.82 (s, 3 H), 2.68-2.58 (m, 3 H), 2.26-2.15 (m, 1 H); ¹³C NMR (75 MHz) 176.9, 159.7, 131.2, 127.0, 114.2, 81.5, 55.5, 31.1, 29.4; Anal. Calcd. for C₁₁H₁₂O₃: C, 68.74; H, 6.29. Found: C, 69.00; H, 6.20.

(a) Sudhir, T.; Patil, A. V. K. *Chirality* **2004**, *16*, 336.

(b) Pirkle, W. H.; Spence, P. L. *J. Chromatogr. A* **1997**, *775*, 81.

Entry 3

Colorless oil; $[\alpha]_D^{25} = -21.1$ (*c* 1.0, CHCl₃) (90% ee); IR (film) 1767 cm⁻¹; ¹H NMR (300 MHz) δ 7.28-7.18 (m, 4 H), 5.47 (dd, *J* = 8.0, 6.0 Hz 1H), 2.70-2.56 (m, 3 H), 2.36 (s, 3 H), 2.26-2.12 (m, 1 H); ¹³C NMR (75 MHz) δ 177.0, 138.3, 136.4, 129.4, 125.4, 81.5, 31.1, 29.3, 21.4; Anal. Calcd. for C₁₁H₁₂O₂: C, 74.98; H, 6.86. Found: C, 74.88; H, 7.05.

(a) Sudhir, T.; Patil, A. V. K. *Chirality* **2004**, *16*, 336.

(b) Pirkle, W. H.; Spence, P. L. *J. Chromatogr. A* **1997**, *775*, 81.

Entry 4

Colorless oil; $[\alpha]_D^{25} = -16.7$ (*c* 1.2, CHCl₃) (91% ee); IR (film) 1761 cm⁻¹; ¹H NMR (300 MHz) δ 7.43-7.38 (m, 2 H), 7.29-7.24 (m, 2 H), 5.49 (dd, *J* = 8.1, 6.3 Hz, 1 H), 2.70-2.58 (m, 3 H),

2.29-2.16 (m, 1 H), 1.32 (s, 9 H); ^{13}C NMR (75 MHz) δ 177.0, 151.6, 136.3, 125.8, 125.3, 81.5, 34.9, 31.6, 31.1, 29.3; Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_2$: C, 77.03; H, 8.31. Found: C, 77.13; H, 8.19.

Entry 5

White solid; mp 98-100 °C; $[\alpha]_D^{25} = -19.0$ (*c* 1.1, CHCl_3) (91% ee); IR (film) 1771 cm^{-1} ; ^1H NMR (300 MHz) δ 7.89-7.81 (m, 4 H), 7.53-7.39 (m, 3 H), 5.70-5.66 (m, 1 H), 2.77-2.67 (m, 3 H), 2.34-2.25 (m, 1 H); ^{13}C NMR (75 MHz) δ 176.9, 136.7, 133.1, 133.0, 128.7, 128.0, 127.7, 126.5, 126.4, 124.3, 122.9, 81.3, 30.9, 29.0; Anal. Calcd. for $\text{C}_{14}\text{H}_{12}\text{O}_2$: C, 79.22; H, 5.70. Found: C, 79.46; H, 5.88.

Pirkle, W. H.; Spence, P. L. *J. Chromatogr. A* **1997**, 775, 81.

Entry 6

Colorless oil; $[\alpha]_D^{25} = -32.1$ (*c* 1.0, CHCl_3) (84% ee); IR (film) 1770 cm^{-1} ; ^1H NMR (400 MHz) δ 7.40-7.28 (m, 5H), 2.67-2.38 (m, 4 H), 1.71 (s, 3H); ^{13}C NMR δ (75 MHz) 176.5, 144.4, 128.7, 127.7, 124.2, 87.1, 36.4, 29.7, 29.2; Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{O}_2$: C, 74.98; H, 6.86. Found: C, 74.75; H 6.71.

Pirkle, W. H.; Spence, P. L. *J. Chromatogr. A* **1997**, 775, 81.

Entry 7

Colorless oil; $[\alpha]_D^{25} = -63.8$ (*c* 1.1, CHCl_3) (71% ee); IR (film) 1770 cm^{-1} ; ^1H NMR (400 MHz) δ 7.49-7.46 (m, 1 H), 7.31-7.26 (m, 1 H), 6.98-6.90 (m, 2 H), 3.86 (s, 3 H), 2.65-2.55 (m, 2 H), 2.51-2.41 (m, 2 H), 1.75 (s, 3 H); ^{13}C NMR (75 MHz) δ 176.9, 155.3, 132.1, 129.0, 125.3, 120.6, 111.3, 86.9, 55.3, 34.5, 29.1, 27.0; Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_3$: C, 69.88; H, 6.84. Found: C, 70.09; H, 6.90.

Entry 8

Colorless oil; $[\alpha]_D^{25} = -32.6$ (*c* 1.0, CHCl_3) (87% ee); IR (film) 1770 cm^{-1} ; ^1H NMR (400 MHz) δ 7.31-7.26 (m, 1H), 6.95-6.92 (m, 2 H), 6.85-6.82 (m, 1 H), 3.82 (s, 3 H), 2.68-2.28 (m, 4 H), 1.71 (s, 3 H); ^{13}C NMR (75 MHz) δ 176.5, 159.7, 146.0, 129.8, 116.5, 112.8, 110.3, 87.0, 55.5, 36.4, 29.6, 29.2; Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_3$: C, 69.88; H, 6.84. Found: C, 69.77; H, 6.66.

Molander, G. A.; Kollner, C. *J. Org. Chem.* **2000**, 65, 8333.

Entry 9

White solid; mp 35-36 °C; $[\alpha]_D^{25} = -35.3$ (*c* 1.0, CHCl₃) (82% ee). IR (film) 1774 cm⁻¹; ¹H NMR (400 MHz) δ 7.31-7.27 (m, 2 H), 6.91-6.87 (m, 2 H), 3.81 (s, 3 H), 2.69-2.35 (m, 4 H), 1.70 (s, 3 H); ¹³C NMR (75 MHz) δ 176.6, 159.0, 136.4, 125.5, 114.0, 87.1, 55.5, 36.4, 29.7, 29.3; Anal. Calcd. for C₁₂H₁₄O₃: C, 69.88; H, 6.84. Found: C, 69.85; H, 6.68.

Pirkle, W. H.; Spence, P. L. *J. Chromatogr. A* **1997**, 775, 81.

Entry 10

Colorless oil; $[\alpha]_D^{25} = -37.7$ (*c* 1.1, CHCl₃) (79% ee); IR (film) 1774 cm⁻¹; ¹H NMR (400 MHz) δ 7.29-7.23 (m, 2 H), 7.20-7.16 (m, 2 H), 2.66-2.58 (m, 1 H), 2.54-2.42 (m, 2 H), 2.40-2.34 (m, 1 H), 2.35 (s, 3 H), 1.71 (s, 3 H); ¹³C NMR (75 MHz) δ 176.6, 141.4, 137.4, 129.3, 124.1, 87.2, 36.4, 29.7, 29.2, 21.2; Anal. Calcd. for C₁₂H₁₄O₂: C, 75.76; H, 7.42. Found: C, 75.55; H, 7.20.

Pirkle, W. H.; Spence, P. L. *J. Chromatogr. A* **1997**, 775, 8.

Entry 11

Colorless oil; $[\alpha]_D^{25} = -39.3$ (*c* 1.0, CHCl₃) (84% ee); IR (film) 1771 cm⁻¹; ¹H NMR (300 MHz) δ 7.36-7.30 (m, 4 H), 2.70-2.38 (m, 4 H), 1.69 (s, 3 H); ¹³C NMR (75 MHz) δ 176.1, 142.9, 133.6, 128.8, 125.7, 86.6, 36.3, 29.6, 29.1; Anal. Calcd. for C₁₁H₁₁ClO₂: C, 62.72; H, 5.26. Found: C, 62.92; H, 5.10.

Sakurai, K.; Matsumoto, H.; Adachi, J. *Yakugaku Zasshi* **1968**, 88, 919.

Entry 12

White solid; mp 40-43 °C; $[\alpha]_D^{25} = -31.9$ (*c* 1.0, CHCl₃) (86% ee); IR (film) 1774 cm⁻¹; ¹H NMR (300 MHz) δ 7.50 (d, *J* = 8.4 Hz, 2 H), 7.25 (d, *J* = 8.4 Hz, 2 H), 2.70-2.37 (m, 4 H), 1.69 (s, 3 H); ¹³C NMR (75 MHz) δ 176.1, 143.4, 131.8, 126.0, 121.7, 86.6, 36.2, 29.5, 29.1; Anal. Calcd. for C₁₁H₁₁BrO₂: C, 51.79; H, 4.35. Found: C, 51.86; H 4.42.

Pirkle, W. H.; Spence, P. L. *J. Chromatogr. A* **1997**, 775, 81.

Entry 13

White solid; mp 79-80 °C; $[\alpha]_D^{25} = -28.6$ (*c* 0.8, CHCl₃) (87% ee); IR (film) 1774 cm⁻¹; ¹H NMR (300 MHz) δ 7.90-7.80 (m, 4 H), 7.52-7.40 (m, 3 H), 2.70-2.42 (m, 4 H), 1.80 (s, 3 H); ¹³C NMR (75 MHz) δ 176.6, 141.4, 132.9, 132.6, 128.7, 128.2, 127.6, 126.6, 126.4, 122.7, 122.5, 87.2, 36.2, 29.5, 29.2; Anal. Calcd. for C₁₅H₁₄O₂: C, 79.62; H, 6.24. Found: C, 79.49; H, 6.50.

Wolf, C.; Pirkle, W. H. *Tetrahedron* **2002**, 58, 3597.

Scheme 4

Colorless oil; $[\alpha]_D^{25} = +38.1$ (*c* 1.1 CHCl_3) (90% ee); IR (film) 1784 cm^{-1} ; ^1H NMR (400 MHz) δ 7.38 (d, $J = 8.4\text{ Hz}$, 2 H), 7.20 (d, $J = 8.4\text{ Hz}$, 2 H), 4.56-4.50 (m, 1 H), 3.30-3.18 (m, 1 H), 3.10-2.98 (m, 1 H), 2.60-2.48 (m, 1 H), 2.31-2.19 (m, 1 H), 1.32 (s, 9 H); ^{13}C NMR (100 MHz) δ 208.5, 150.1, 133.7, 126.9, 125.8, 64.5, 45.0, 34.7, 31.5, 17.9; HRMS Calcd for $\text{C}_{14}\text{H}_{18}\text{O}$ (M^+) 202.1358; found: 202.1353.

Scheme 4

Colorless oil; $[\alpha]_D^{25} = -58.2$ (*c* 1.0, CHCl_3) (85% ee); IR (film) 1775 cm^{-1} ; ^1H NMR (300 MHz) δ 7.26 (d, $J = 8.1\text{ Hz}$, 2 H), 7.16 (d, $J = 8.1\text{ Hz}$, 2 H), 3.23-2.99 (m, 2 H), 2.56-2.46 (m, 1 H), 2.34 (s, 3 H), 2.19-2.10 (m, 1 H), 1.54 (s, 3 H); ^{13}C NMR (100 MHz) δ 212.7, 139.6, 136.6, 129.5, 125.7, 68.0, 42.8, 26.5, 25.7, 21.2; Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}$: C, 82.72; H, 8.10. Found: C, 82.88; H, 7.99.

Nemoto, H.; Ishibashi, H.; Nagamochi, M.; Fukumoto, K. *J. Org. Chem.* **1992**, *57*, 1707.

The spectral data for the determination of enantiomeric excess of the lactones

(Table 1, entry 1)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (90/10); **Flow rate:** 0.7mL/min; **detection:** UV 220nm

HPLC conditions: column: Chiralcel AD, Chiral Technologies Inc.

Eluent: Hexane/IPA (95/5); **Flow rate:** 1.0mL/min; **detection:** UV 254nm

(Table 1, entry 3)

HPLC conditions: column: Chiralcel OD, Chiral Technologies Inc.

Eluent: Hexane/IPA (95/5); **Flow rate:** 1.0mL/min; **detection:** UV 254nm

Racemate

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	21.167	49.7601	675461
2	22.952	50.2399	681973
		100.0000	1357434

Chiral lactone

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	22.014	4.9426	18191
2	23.226	95.0574	349849
		100.0000	368040

(Table 1, entry 4)

HPLC conditions: column: Chiralcel OD, Chiral Technologies Inc.

Eluent: Hexane/IPA (90/10); **Flow rate:** 1.0mL/min; **detection:** UV 220nm

Racemate

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	10.281	49.8193	16797036
2	11.373	50.1807	16918864
		100.0000	33715900

Chiral lactone

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	10.516	95.7095	25459446
2	11.941	4.2905	1141313
		100.0000	26600760

(Table 1, entry 5)

HPLC conditions: column: Chiralcel OD, Chiral Technologies Inc.

Eluent: Hexane/IPA (90/10); **Flow rate:** 1.0 mL/min; **detection:** UV 220nm

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	21.336	49.5584	17626918
2	25.999	50.4416	17941036
		100.0000	35567952

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	21.368	4.6392	455752
2	26.087	95.3608	9368224
		100.0000	9823976

(Table 1, entry 6)

GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Advanced Separation Technologies Inc.

Oven: 110 °C; **Carrier:** Helium, head pressure: 20 psi; **Detection:** FID 250 °C

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		76.584	50.2522	29891
2		80.952	49.7478	29591
	Totals		100.0000	59482

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		76.912	92.1460	29466
2		83.074	7.8540	2512
	Totals		100.0000	31978

(Table 1, entry 7)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (90/10); **Flow rate:** 1.0mL/min; **detection:** UV 220nm

Racemate

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	12.552	50.2166	22995436
2	21.343	49.7834	22797070
		100.0000	45792504

Chiral lactone

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	12.802	85.4523	5279133
2	21.794	14.5477	898740
		100.0000	6177873

(Table 1, entry 8)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (85/15); **Flow rate:** 0.7mL/min; **detection:** UV 254nm

Racemate

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		21.872	49.7983	1335810
2		23.622	50.2017	1346629
Totals			100.0000	2682439

Chiral lactone

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		22.122	6.6944	84134
2		23.628	93.3056	1172645
Totals			100.0000	1256779

(Table 1, entry 9)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (80/20); **Flow rate:** 1.0mL/min; **detection:** UV 254nm

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		15.159	50.1297	637066
2		21.201	49.8703	633770
Totals			100.0000	1270836

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		15.158	9.1240	193026
2		20.641	90.8760	1922555
Totals			100.0000	2115581

(Table 1, entry 10)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (90/10); **Flow rate:** 1.0mL/min; **detection:** UV 220nm

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	8.234	50.1156	19024342
2	12.129	49.8844	18936546
			100.0000
			37960888

Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	8.209	10.5990	1751974
2	11.858	89.4010	14777703
			100.0000
			16529677

(Table 1, entry 11)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (90/10); **Flow rate:** 1.0mL/min; **detection:** UV 220nm

Minutes				
Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		15.994	49.3174	0386610
2		18.701	50.6826	0674125
Totals			100.0000	1060736

Minutes				
Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		16.439	8.1763	931490
2		18.913	91.8237	0461128
Totals			100.0000	1392618

(Table 1, entry 12)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (90/10); **Flow rate:** 1.0mL/min; **detection:** UV 210nm

Minutes			
Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	18.067	49.5804	9297580
2	22.323	50.4196	9454948
		100.0000	18752528

Minutes			
Peak No	Ret Time (min)	Result ()	Peak Area (counts)
1	18.429	6.8714	1330072
2	22.104	93.1286	18026454
		100.0000	19356526

(Table 1, entry 13)

HPLC conditions: column: Chiralcel OJ, Chiral Technologies Inc.

Eluent: Hexane/IPA (80/20); **Flow rate:** 1.0mL/min; **detection:** UV 220nm

Racemate

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		20.401	49.7394	3849744
2		25.450	50.2606	4309256
Totals			100.0000	8159000

Chiral lactone

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		20.671	6.3397	587444
2		25.503	93.6603	8678678
Totals			100.0000	9266122

(Scheme 4)

GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Advanced Separation Technologies Inc.

Oven: 125 °C; **Carrier:** Helium, head pressure: 25 psi; **Detection:** FID 250 °C

Racemate

Peak No	Peak Name	Ret. Time (min)	Result ()	Area (counts)
1		55.056	50.2529	35736
2		57.507	49.7471	35376
Totals			100.0000	71112

Chiral

Peak No	Peak Name	Result ()	Ret. Time (min)	Area (counts)
1		95.1982	54.979	37332
2		4.8018	58.221	1883
Totals		100.0000		39215

(Scheme 4)

GC Conditions: Column: Chiraldex B-DM (Cat. No. 77023), Advanced Separation Technologies Inc.
Oven: 110 °C; Carrier: Helium, head pressure: 30 psi; Detection: FID 250 °C

Minutes					Minutes				
Peak No	Peak Name	Result ()	Ret. Time (min)	Area (counts)	Peak No	Peak Name	Result ()	Ret. Time (min)	Area (counts)
1		49.2249	19.761	3630	1		92.3220	19.634	20643
2		50.7751	20.417	3744	2		7.6780	20.396	1717
Totals		100.0000		7374	Totals		100.0000		22360


```
Pulse Sequence: s2p1
Solvent: CDCl3
Ambient temperature
File: b1117--p-H
INOVA-500 "epoxide"
```

```
Relax. delay 0.000 sec
Pulse 28.7 degrees
Acq. time 2.667 sec
Width 6000.0 Hz
6 repetitions
OBSERVE H1 300.1592179 MHz
DATA PROCESSING
Gauss apodization 0.896 sec
FT size 32768
Total time 0 min, 21 sec
```

13C OBSERVE

Pulse Sequence: szpul
Solvent: CDCl3
Ambient temperature
File: b117-p-C
INOVA-400 "narnia"

Relax. delay 1.700 sec
Pulse 44.5 degrees
Acq. time 0.533 sec
Width 30018.8 Hz
1136 repetitions
OBSERVE C13, 100.6067913 MHz
DECOUPLE H1, 400.1083268 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 32768
Total time 622730 hr, 10 min, 7 sec