Supporting Information

Scope of Enantioselective Palladium(II)-Catalyzed Aerobic Alcohol Oxidations Using (-)-Sparteine

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General Information.

All reagents, unless specified, were bought from commercial sources and used without further purification. *tert*-Butanol was filtered through freshly activated alumina. (-)-Sparteine was prepared by dissolving the (-)-sparteine hydrosulfate pentahydrate salt in water, adding sodium hydroxide pellets until the pH > 10 and extracting the free-base product with ether (3 times). The extract was dried over sodium sulfate, filtered and solvent was removed *in vacuo*.

Results for non-benzylic alcohols from previous system (using previously published method):

Table S-1. Kinetic Resolution of non-benzylic alcohols.

$\begin{array}{c} \text{OH} \\ \\ \text{R}-\text{CH}-\text{R}^1 \\ \pm \end{array} \xrightarrow[\text{DCE, O}_2, 24\text{hrs}]{\begin{array}{c} 5 \text{ mol\% Pd(II)} \\ 20 \text{ mol\% (-)-sparteine} \end{array}} \begin{array}{c} \text{OH} \\ \\ \text{R}-\text{CH}-\text{R}^1 \\ \text{R}-\text{C}-\text{R}^1 \\ \parallel \\ \text{O} \end{array}$				
Entry	Substrate	Conditions ^a	%conv(%ee) ^{b,c}	Average ^d k_{rel}
1		A	58.5(77.8)	7.6
		B	65.6(87.0)	7.1
2 ^e		A	69.5(80.6)	4.7
		B	67.3(82.2)	5.5
3		A	68.2(89.0)	6.6
		B	67.5(89.6)	7.0
4		A	70.3(91.4)	6.5
		B	66.8(90.8)	7.6

^a Condition A, Pd(OAc)₂ at 60 °C and 0.25M alcohol; Condition B, Pd(MeCN)₂Cl₂ at 70 °C and 0.25M alcohol. ^bEnantioselectivity and conversion were determined by GC using commercial chiral columns and tetradecane as an internal standard. ^cData represents a single experiment. ^dThe k_{rel} value is an average of multiple experiments and measured at 20h. ^e measured at 12h.

OKR solvent screen for 3,3-dimethyl-2-butanol using

Pd(CH₃CN)₂Cl₂ or Pd(OAc)₂ : Basic experimental

procedure of screening solvents for above substrate is

same as described for *sec*-phenethyl alcohol. In a 5 ml round bottom flask equipped with a sidearm and stirbar, 0.5 ml of solvent, 3.3 mg (0.013 mmol, 0.05 equiv.) Pd(MeCN)₂Cl₂, or 2.8 mg (0.013 mmol, 0.05

equiv.) $\text{Pd}(\text{OAc})_2$ and 11.5 μl (0.05 mmol, 0.20 equiv.) of (-)-sparteine were combined. The flask was then attached to bottom of the screening apparatus (fig. 2). A balloon filled with oxygen gas was then attached to the top of the screening apparatus via a three way joint. The screening apparatus was then evacuated (water aspirator) and refilled with oxygen from the balloon three times. The reaction mixture was then allowed to stir for 30 minutes while heating in an oil bath at 65°C. To the flask 25.6 mg (0.25 mmol, 1.0 equiv.) of the alcohol in 0.5ml of solvent was added. Aliquots (0.1 ml) of the reaction were then periodically taken via syringe. The aliquot was quenched with 2% TFA/methanol. The sample was then analyzed using a GC equipped with a chiral column and referenced against a time zero sample (see table 1). Conversions were measured relative to tetradecane internal standard. The k_{rel} was then calculated.

Figure S-1. Results of solvent screen using $\text{Pd}(\text{CH}_3\text{CN})_2\text{Cl}_2$ and $\text{Pd}(\text{OAc})_2$

Preparation of *racemic*-(2-methoxyphenyl) phenyl methanol (1z):¹ To a solution of 2-methoxybenzaldehyde (1g, 7.35 mmol) in 20 mL THF, PhLi (4.5 mL, 8.08 mmol, 1.8M in cyclohexane/ether) was added dropwise while stirring at 0°C. It was allowed to come to room temperature and then stirred overnight. Reaction mixture was quenched with 10 mL methanol at 0°C and then treated with saturated brine followed by extraction with ether. The ether extract was dried with anhydrous sodium sulfate, evaporated and then purified by column chromatography (8% ethyl acetate/hexane). Yield 1.42 g (90%).

Preparation of *racemic*-1-phenyl-but-2-yn-1-ol (1aa):² To a solution of benzaldehyde (1.06g, 0.01 mol) in 20 mL THF, propynylmagnesium bromide (22 mL, 0.011 mol, 0.5M in THF) was

added dropwise while stirring at 0°C. It was allowed to come to room temperature and then stirred overnight. Reaction mixture was quenched with 10 mL methanol at 0°C and then treated with saturated brine followed by extraction with ether. The ether extract was dried with anhydrous sodium sulfate, evaporated and then purified by column chromatography (10% ethyl acetate/hexane). Yield 1.24 g (86%).

Preparation *racemic*-1-(2-pyridyl)ethanol (1dd):³ To a solution of 2-acetyl pyridine (2.42 g, 0.02 mol) in 18 mL of 2:1 methanol/dichloroethane, sodium borohydride (0.83g, 0.022 mol) was

added portion wise. After stirring for 6h at room temperature, 10 mL of water was added slowly to quench the reaction. After addition of 200 mL of saturated brine, the reduced alcohol was extracted with ether. The ether extract was dried with anhydrous sodium sulfate, evaporated and then purified by column chromatography (12% ethyl acetate/hexane). Yield 1.69 g (69%).

Preparation *racemic*-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-ol (1t):⁴

To a solution of benzosuberone (3 g, 0.018 mol) in 18 mL of 2:1 methanol/dichloroethane, solid sodium borohydride (0.83g, 0.022 mol) was added portion wise. After stirring for 6h at room temperature, 10 mL of 1.0 M aqueous HCl was added slowly to quench the reaction. After addition of 200 mL of saturated brine, the reduced alcohol was extracted with ether. The ether extract was dried with anhydrous sodium sulfate, evaporated and then purified by column chromatography (5% ethyl acetate/hexane). Yield 3 g (98%).

Preparation of 1,3-*meso*-diols: The *racemic* β -hydroxy ketones were prepared following a reported procedure *via* aldol reaction of corresponding ketone and aldehyde using LDA as base.⁵ *Syn* reduction of aldol products using boron reagent yielded corresponding *syn*-diol with high selectivity.⁶

Table S-2. Synthesis of *meso*-diols.

$ \begin{array}{c} \text{R}-\text{C}(=\text{O})-\text{CH}_2\text{R}' + \text{R}-\text{C}(=\text{O})-\text{H} \xrightarrow[-78^\circ\text{C}]{\text{LDA}} \text{R}-\text{C}(=\text{O})-\text{CH}(\text{R}')-\text{CH}(\text{OH})-\text{R} \xrightarrow[\text{NaBH}_4]{\text{Et}_2\text{BOMe}} \text{R}-\text{CH}(\text{OH})-\text{CH}(\text{R}')-\text{CH}(\text{OH})-\text{R} \\ \text{3a'-e'} \qquad \qquad \qquad \text{2a-e} \end{array} $					
R	R'	β -hydroxy ketone	Yield	<i>meso</i> -diol	Yield
2-naphthyl	H	3a' ⁷	31	2a	73
phenyl	H	3b' ⁸	46	2b ⁸	67
t-butyl	H	3c' ⁸	79	2c ⁸	85
4-bromophenyl	H	3d' ⁹	80	2d	57
phenyl	Me	3e' ⁹	67	2e ⁹	45

superscripts indicate the reference, where compound is previously reported

1,3-Di-(2-naphthyl)-propane-1,3-meso-diol (2a): colorless solid, M.P.

122.8°C, IR (KBr): 3295, 1059, 1029, 860, 747, 479 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): 2.09-2.15 (m, 1H), 2.29-2.41 (m, 1H), 3.42 (brs, 2H), 5.21 (dd, 2H, $J = 2.7, 9.0$ Hz), 7.41-7.51 (m, 6H), 7.78-7.82 (m, 8H); ^{13}C NMR (75 MHz, CDCl_3): 47.50, 75.15, 94.11, 123.87, 124.38, 125.89, 126.18, 127.66, 127.95, 128.38, 132.98, 133.25, 141.44; HRMS calcd. 328.1463; obsd. 328.1464

1,3-Bis-(4-bromo-phenyl)-propane-meso-1,3-diol (2d): colorless solid, M.P.

84.6°C, IR (KBr): 3269, 1487, 1062, 1010, 824, 647 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): 1.72-1.78 (m, 1H), 1.93-1.98 (m, 1H), 4.01 (brs, 2H), 4.80 (dd, 2H, $J = 2.7, 9.0$ Hz), 7.11 (d, 4H, $J = 9\text{Hz}$), 7.39 (d, 4H, $J = 9\text{Hz}$); ^{13}C NMR (75 MHz, CDCl_3): 47.14, 74.12, 121.40, 127.28, 131.50, 142.72; HRMS calcd. 383.9360; obsd. 383.9358

1,3-Bis-(4-bromo-phenyl)-3-hydroxy-propan-1-one (3d') light yellow solid, M.P.

98.4°C, IR (KBr): 3453, 1663, 1582, 1398, 1073, 1007, 827, 530 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): 3.18-3.35 (m, 2H), 3.67 (d, 1H, $J = 3\text{Hz}$), 5.27 (m, 1H), 7.27 (d, 2H, $J = 9\text{Hz}$), 7.47 (d, 2H, $J = 9\text{Hz}$), 7.58 (d, 2H, $J = 9\text{Hz}$), 7.76 (d, 2H, $J = 9\text{Hz}$); ^{13}C NMR (75 MHz, CDCl_3): 47.13, 69.20, 121.41, 127.39, 128.96, 129.54, 131.56, 131.97, 134.98, 141.77, 198.58; HRMS calcd. 381.9204; obsd. 381.9204

Preparation of [(-)-sparteine] PdCl_2 : In a 250 ml round bottom flask, 2.35 g of (-)-sparteine (10.0 mmol) and 2.59 g (9.99 mmol) of $\text{Pd}(\text{MeCN})_2\text{Cl}_2$ were added to 100 ml of 1,2-dichloroethane. The reaction was heated to 65 °C for one hour and then the solvent was removed *in vacuo*. The resulting red oil was taken up in CH_2Cl_2 and hexanes. Concentration and removal of the solvent *in vacuo* gave an orange-red powdery solid, which was rinsed with hexanes. Yield: 4.01 g, 97%. For analytical data, see: Mueller, J. A.; Jensen, D. R.; Sigman, M. S. *J. Am. Chem. Soc.* **2002**, *124*, 8202-8203.

General procedure for the oxidative kinetic resolution of secondary alcohols and desymmetrization of meso-diols using [(-)-sparteine] PdCl_2 in *t*-butanol: In a 5 ml round bottom flask equipped with a sidearm and stirbar, 1.0 ml of *t*-butanol, 5.6 mg (0.013 mmol, 0.05 equiv.) of [(-)-sparteine] PdCl_2 , 11.5 μl (0.05 mmol, 0.20 equiv.) of (-)-sparteine, 0.25 mmol (1.0 equiv.) of the alcohol or meso-diol and 25 mg powder molecular sieves(3Å) were combined. The flask was then attached to the bottom of the screening apparatus (fig. 2). A balloon filled with oxygen gas was then attached to the top of the screening apparatus via a three way joint. The screening apparatus was then evacuated (water aspirator) and refilled with oxygen from the balloon three times and then heated in an oil bath at 65°C. Aliquots (0.1 ml) of the reaction were then periodically taken via syringe. The aliquot was quenched with 2% TFA/methanol. The sample was then analyzed using a GC or HPLC equipped with a chiral column. Conversions were measured relative to tetradecane internal standard or by ^1H NMR.

General procedure for the gram scale oxidative kinetic resolution of alcohols and desymmetrization of

1,3-*meso*-diol: In a 100 ml two neck round bottom flask fitted with a reflux condenser, 10 mmol of the racemic alcohol (or *meso*-diol), 469 mg (2 mmol) of (-)-sparteine, 205 mg (0.5 mmol) of Pd[(-)-sparteine]Cl₂, 1.0 g molecular sieves, and 40 mL *tert*-butanol were combined. A balloon filled with oxygen gas was then attached to the top of the condenser via a three way joint. The apparatus was then evacuated (water aspirator) and refilled with oxygen from the balloon three times. The reaction mixture was then allowed to stir magnetically, while heating in an oil bath at 65°C. Reaction was monitored by GC or ¹H NMR as earlier. After 24 h, the mixture was cooled to room temperature and filtered through a pad of silica, washed with ether, concentrated under vacuum. Ketone by-product and optically active alcohol were then separated by column chromatography (5% ethyl acetate/hexane – 15% ethyl acetate/hexane). See Table 3 for isolated yields.

Table S-3. Optical rotation of isolated alcohols.

alcohol	%ee	specific rotation $[\alpha]_D^{20}$	alcohol	%ee	specific rotation $[\alpha]_D^{20}$
92.2	+7.71 (neat) ^a		90.0	-85.3 (c = 1.3, CHCl ₃) ^f
96.6	-5.92 (c = 2.5, CHCl ₃) ^b		90.0	-29.8 (c = 2.15, CHCl ₃) ^g
98.3	+3.22 (c = 0.5, CHCl ₃) ^c		95.0	-27.8 (c = 0.75, CHCl ₃) ^h
99.1	+31.70 (c = 2.56, CHCl ₃) ^d		89.0	-62.3 (c = 1.5, CHCl ₃) ⁱ
99.3	+ (c = 0.16, C ₆ H ₆) ^e		92.0	-26.9 (c = 1.0, CHCl ₃) ^h

(a) Configuration consistent with Newman, P.; Rutkin, P.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 465. (b) Configuration consistent with Cram, D. J.; Elhafez, F. A. A.; *J. Am. Chem. Soc.* **1954**, *76*, 28. (c) Configuration consistent with Fuganti, C.; Grasselli, P.; Spreafico, F.; Zirotti, C.; Casati, P. *J. Chem. Res. Synop.* **1985**, 22. (d) Configuration consistent with Palmer, M. J.; Kenny, J. A.; Walsgrove, T.; Kawamoto, A. M.; Wills, M.; *J. Chem. Soc. Perkin Trans. 1*; **2002**, 3, 416. (e) Locke, A. J.; Richards, C. J.; *Organometallics* **1999**, *18*, 3750. (f) Configuration consistent with Mashraqui, S. H.; Kellogg, R. M.; *J. Org. Chem.* **1984**, *49*, 2513. (g) Configuration consistent with Narasaka, K.; Miwa, T.; Hayashi, H.; Otha, M. *Chem. Lett.* **1984**; 1399. (h) Configuration assigned by analogy (i) Configuration consistent with Vicario, J. L.; Badia, D.; Dominguez, E.; Rodriguez, M.; Carrillo, L. *J. Org. Chem.* **2000**, *65*, 3754.

Table S-5. Aromatic Substrates.

Entry	Alcohol	Solvent	%conv(%ee)	k_{rel}	Entry	Alcohol	Solvent	%conv(%ee)	k_{rel}
1		^t BuOH	61.6(98.5)	19.0	17		^t BuOH	21.2(6.0)	1.7
2		DCE	57.0(94.3)	17.1	18		^t BuOH	23.0(20.0)	6.1
3		^t BuOH	63.5(96.3)	12.9	19		^t BuOH	90.0(37.0)	1.4
4		DCE	52.9(80.7)	12.2	20		^t BuOH	40.5(1.4)	1.1
5		^t BuOH	55.9(90.2)	17.7	21		^t BuOH	No Oxidation	NA
6		DCE	65.7(95.9)	10.1	22		^t BuOH	65.2(99.3)	16.3
7		^t BuOH	69.0(98.8)	11.6	23		DCE	77.5(99.0)	7.6
8		^t BuOH	55.0(70.2)	7.5	24		^t BuOH	13.6(0.6)	1.1
9		^t BuOH	61.6(99.3)	21.9	25		^t BuOH	No Oxidation	NA
10		DCE	65.3(99.2)	15.9	26		^t BuOH	66.6(99.8)	17.8
11		^t BuOH	51.2(80.0)	17.8	27		DCE	66.2(94.0)	9.3
12		DCE	70.6(95.0)	7.6					
13		^t BuOH	67.4(99.2)	13.6					
14		DCE	61.0(91.2)	11.5					
15		^t BuOH	57.9(89.3)	13.5					
16		DCE	59.0(90.0)	12.8					

Table S-5. Other Substrates.

Entry	Alcohol	Solvent	%conv(%ee)	k_{rel}	Entry	Alcohol	Solvent	%conv(%ee)	k_{rel}
1		^t BuOH	60.9(97.2)	17.3	8		^t BuOH	67.9(95.4)	9.0
2		DCE	65.6(87.0)	7.1	9		DCE	67.5(89.6)	7.0
3		^t BuOH	59.0(82.6)	9.1	10		^t BuOH	64.9(97.6)	13.1
4		DCE	67.3(82.2)	5.5	11		DCE	66.8(90.8)	7.6
5		^t BuOH	56.0(91.8)	19.6	12		^t BuOH	95.0(49.0)	1.4
6		^t BuOH	53.0(61.0)	6.1	13		^t BuOH	72.8(99.3)	10.3
7		^t BuOH	75.0(98.8)	8.3	14		^t BuOH	55.0(84.3)	14.3

Table S-6. GC and HPLC separation conditions.

Alcohol	Retention Times (in minutes)	Method	Conditions ¹
16.23 major 23.55 minor	HPLC	1ml / min 95%hexanes/IPA Chiralcel OD column
9.16 minor 10.61 major	HPLC	1ml / min 98%hexanes/IPA Chiralcel OD column
50.35 major 50.65 minor	GC	50° C hold 2min, ramp 2°C/min to 160°C
32.58 minor 32.81 major	GC	50° C hold 2min, ramp 4°C/min to 160°C
20.71 major 24.23 minor	HPLC	1ml / min 98%hexanes/IPA Chiralcel OD column
19.28 major 21.90 minor	HPLC	1ml / min 96.5%hexanes/IPA Chiralcel OD column
27.00 minor 27.14 major	GC	50° C hold 2min, ramp 4°C/min to 160°C
21.38 major 25.12 minor	HPLC	1ml / min 90%hexanes/IPA Chiralcel OD column
11.8 minor 17.5 major	HPLC	1ml / min 90%hexanes/IPA Chiralpak AS column
43.35 major 50.21 minor	HPLC	1ml / min 99.5%hexanes/IPA Chiralpak AS column
27.35 (decomposed) 27.48 (decomposed)	GC	50° C hold 2min, ramp 4°C/min to 160°C
14.17 minor 14.40 major	GC	50° C hold 2min, ramp 4°C/min to 160°C
23.45 minor 23.82 major	GC	50° C hold 2min, ramp 4°C/min to 160°C

¹All GC separations were performed using an autosampling HP 6890 GC fitted with a Hewlett Packard HP Chiral 20% Permethyated β-cyclodextrin column (.25μm film thickness, 30m length, phase ratio 320) using a 2.0 mL/min carrier gas (H₂) flow rate

Table S-4. GC and HPLC separation conditions (cont.).

Alcohol	Retention Times (in minutes)	Method	Conditions ¹
30.42 (no oxidation) 30.82	GC	50° C hold 2min, ramp, 2°C/min to 160°C
7.60 major 14.15 minor	HPLC	1ml / min 90%hexanes/IPA Chiralpak AS column
6.13 minor 6.27 major	GC	50° C hold 2min, ramp 4°C/min to 160°C
10.18 minor 11.62 major	HPLC	1ml / min 99%hexanes/IPA Chiralcel OD column
43.97 minor 44.325 major	GC	50° C hold 2min, ramp 1°C/min to 160°C
23.33 minor 23.62 major	GC	50° C hold 2min, ramp 4°C/min to 160°C
47.81 major 48.31 minor	GC	50° C hold 2min, ramp 1°C/min to 160°C
10.63 minor 12.36 major	HPLC	1ml / min 96%hexanes/IPA Chiralcel OD column
17.71 minor 17.95 major	GC	50° C hold 2min, ramp 4°C/min to 160°C
16.61 major 16.73 minor	GC	50° C hold 2min, ramp 10°C/min to 200°C
19.53 minor 19.76 major	GC	50° C hold 2min, ramp 4°C/min to 160°C

¹All GC separations were performed using an autosampling HP 6890 GC fitted with a Hewlett Packard HP Chiral 20% Permethylated β -cyclodextrin column (.25 μ m film thickness, 30m length, phase ratio 320) using a 2.0 mL/min carrier gas (H₂) flow rate

Table S-4. GC and HPLC separation conditions (cont.).

Alcohol	Retention Times (in minutes)	Method	Conditions ¹
43.68 major 52.21 minor	HPLC	1ml / min 95%hexanes/IPA Chiralpak AS column
14.2 major 16.3 minor	HPLC	1ml / min 95%hexanes/IPA Chiralcel OD column
17.64 minor 17.78 major	GC	50° C hold 2min, ramp 5°C/min to 150°C
14.8 minor 25.6 major	HPLC	1ml / min 90%hexanes/IPA Chiralpak AS column
14.2 major 16.3 minor	HPLC	1ml / min 95%hexanes/IPA Chiralcel OD column
29.02 major 29.87 minor	GC	50° C hold 5min, ramp 2°C/min to 150°C
25.22 major 25.44 minor	GC	50° C hold 5min, ramp 2°C/min to 150°C

¹All GC separations were performed using an autosampling HP 6890 GC fitted with a Hewlett Packard HP Chiral 20% Permethylated β -cyclodextrin column (.25 μ m film thickness, 30m length, phase ratio 320) using a 2.0 mL/min carrier gas (H₂) flow rate

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