Supplemental Materials for:

The Palladium-Catalyzed Enantioselective Oxidation of Alcohols: A Dramatic Rate Acceleration by Cs_2CO_3/*t*-BuOH

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Material and Methods. Unless stated otherwise, reactions were performed in oven-dried glassware, under an atmosphere of oxygen, using freshly distilled solvents. Although we have never experienced an accident, all reactions must be performed with appropriate caution in a fume hood due to the flammable nature of mixtures of oxygen and organic solvents. All other commercially obtained reagents were used as received. Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm). ICN Silica gel (particle size 0.032-0.063 mm) was used for flash chromatography. Analytical chiral HPLC was performed on a Chiralcel OJ, AS, AD, OB-H or OD-H column (each is 4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. Analytical achiral GC was performed using an Agilent DB-WAX (30.0 m x 0.25 m) column. Analytical chiral GC was carried out using a Chiraldex B-DM column (30.0 m x 0.25 mm) purchased from Bodman Industries. Commercially available racemic alcohols in Table 3 (entries 1, 2, 3, 6, 7, 8, and 9) were purchased from the Sigma-Aldrich Chemical Company, Milwaukee, WI. Non-commercially available racemic alcohols used in Table 3 (corresponding to entries 4, 6, and 10) were prepared as previously described.[1] Commercially available samples of enantiopure alcohols for analytical comparison purposes (entries 1, 7, 8, and 9) were purchased from the Sigma-Aldrich Chemical Company, Milwaukee, WI. Non-commercially available enantiopure alcohols prepared by palladium-catalyzed oxidative kinetic resolution (Table 3 entries 2,[2] 3,[3] 6,[4] and 10[1,5]) were compared by optical rotation to known values. The previously unknown enantiopure alcohols (Table 3, entries 4 and 5) were assigned absolute stereochemisty by analogy to assigned resolution products.

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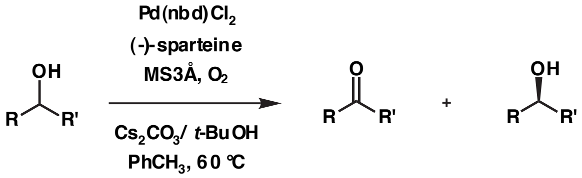
[1] (a) Ruble, J. C.; Latham, H. A.; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 1492. (b) Ruble, J. C., Tweddell, J.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 2794.

[2] Nakamura, K.; Inoue, Y.; Matsuda, T.; Misawa, I. *J. Chem. Soc., Perkin. Trans. 1* **1999**, 2397.

[3] Nieduzak, T. R.; Margolin, A. L. *Tetrahedron: Asymmetry* **1991**, *2*, 113.

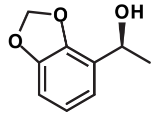
[4] Nakamura, K.; Matsuda, T. *J. Org. Chem.* **1998**, *63*, 8957.

[5] Argus, C. L.; Cort, L. A.; Howard, T. J.; Loc, L. B. *J. Chem. Soc.* **1960**, 1195.

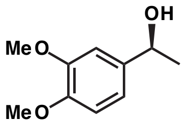


General Procedure for the Rate Accelerated Oxidative Kinetic Resolution of Secondary Alcohols. An oven dried reaction tube (outer diameter 16 mm, length 120 mm) equipped with a magnetic stir bar was charged with oven dried powdered molecular sieves (MS3Å, 0.5 g). After cooling, Pd(nbd)Cl_2 complex (0.05 mmol, 0.05 equiv) was added followed by toluene (2.0 mL), and (–)-sparteine (0.2 mmol, 0.20 equiv). The flask was cooled to -78 °C, then vacuum evacuated and filled with O_2 (3x, balloon), then heated to 60 °C for 15 min. Powdered anhydrous Cs_2CO_3 (0.5 mmol, 0.5 equiv.),[6] a toluene soultion (2.0 mL) of the alcohol (1.0 mmol, 1.0 equiv), and *t*-BuOH (1.5 mmol, 1.5 equiv.) was introduced and the reaction mixture was maintained at 60 °C. The reaction was monitored by standard analytical techniques (TLC, GC, ^{1}H-NMR, and HPLC) for % conversion and enantiomeric excess values. Aliquots of the reaction mixture (0.2 mL) were collected after 2 h, 4 h, 8 h, 12 h, 15 h, and 18 h depending on the course of the reaction (typically three aliquots per run). Each aliquot was filtered through a small plug of silica gel (Et_2O eluent), evaporated and analyzed.[7]

Optical rotations for new compounds:



$[\alpha]_D^{24}$ –26.8 (c 1.0, $CDCl_3$)*



$[\alpha]_D^{24}$ –39.3 (c 1.0, $CDCl_3$)*

*absolute stereochemistry of these molecules assigned by analogy.

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[6] For experiments that probed the effect of other addiives, the appropriate base/alcohol was used in the same general procedure.

[7] Percent conversions were measured by GC integration of the alcohol and the ketone peaks, correcting for response factors (for conditions see SM Table 2).

Table SM 1. Methods utilized for the determination of enantiomeric excess.

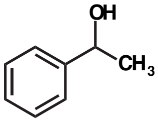
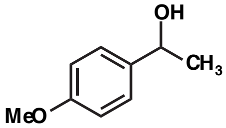
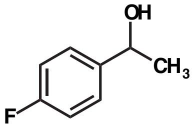
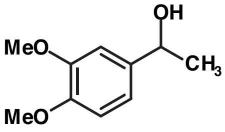
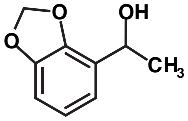
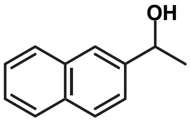
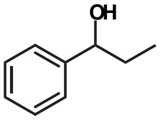
entry	Substrate	ee Assay	Conditions	Retention Time of (*R*) isomer (min)	Retention Time of (*S*) isomer (min)
1.		HPLC Chiralcel OD-H	2% EtOH/hexane 1.0 mL/min	19.72	29.04
2.		HPLC Chiralcel OD-H	4% EtOH/hexane 1.0 mL/min	16.88	18.66
3.		HPLC Chiraldex AS	2% EtOH/hexane	15.10	17.35
4.		HPLC Chiralcel OD-H	5% EtOH/hexane 1.0 mL/min	21.36	23.60
5.		HPLC Chiralcel OD-H	1% EtOH/hexane 1.0 mL/min	18.88	21.05
6.		HPLC Chiralcel AS	2% 2-propanol/hexane 1.0 mL/min	18.60	21.13
7.		HPLC Chiralcel OB-H	1% EtOH/hexane 1.0 mL/min	25.31	30.28

Table SM 1 (continued).

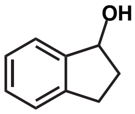
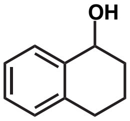
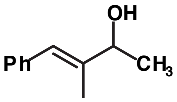
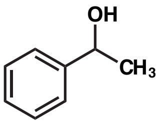
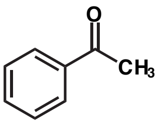
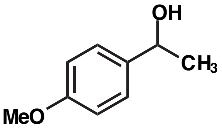
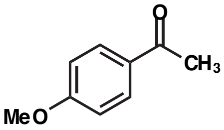
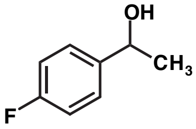
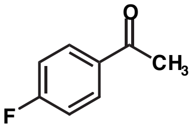
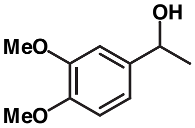
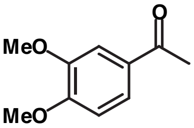
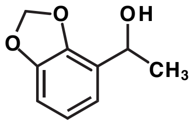
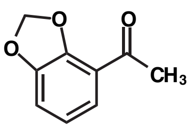
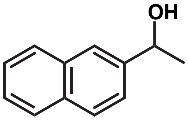
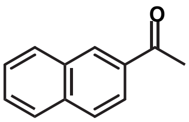
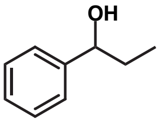
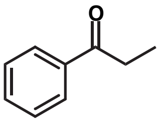
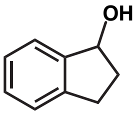
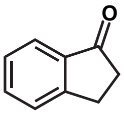
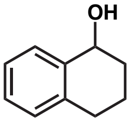
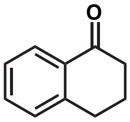
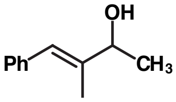
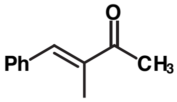
entry	Substrate	ee Assay	Conditions	Retention Time of (*R*) isomer (min)	Retention Time of (*S*) isomer (min)
8.		HPLC Chiralcel AS	2% 2-propanol/hexane 1.0 mL/min	15.84	20.10
9.		HPLC Chiralcel AS	2% EtOH/hexane 1.0 mL/min	12.21	16.48
10.		HPLC Chiralcel OD-H	2% EtOH/hexane 1.0 mL/min	17.58	20.88

Table SM 2. Methods utilized for the determination of % conversion.

entry	alcohol	ketone	GC Conditions[a]	Retention Time of alcohol (min)	Retention Time of ketone (min)
1.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	28.60	25.53
2.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	34.44	33.50
3.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	29.42	25.46
4.			70 °C, 0 min; 3.0 °C/min to 270 °C 1.0 mL/min carrier gas flow	38.52	37.60
5.			70 °C, 0 min; 3.0 °C/min to 270 °C 1.0 mL/min carrier gas flow	36.32	35.04
6.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	42.00	38.85
7.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	29.66	26.97

[a] All assays performed on Agilent DB-WAX column.

Table SM 2 (continued).

entry	alcohol	ketone	GC Conditions[a]	Retention Time of alcohol	Retention Time of ketone
8.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	32.70	31.76
9.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	32.95	34.47
10.			70 °C, 15 min; 7.0 °C/min to 220 °C 1.0 mL/min carrier gas flow	34.22	32.54

[a] All assays performed on Agilent DB-WAX column.