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

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Received December 28, 2002

Abstract: Evaluation of the substrate scope for Pd(II)/(−)-sparteine catalyzed aerobic oxidative kinetic resolution of secondary alcohols is disclosed. An improved system is found with use of *tert*-butyl alcohol solvent in which benzylic and aliphatic alcohols as well as alcohols containing olefins are effectively oxidatively resolved. For substrates that successfully undergo oxidative kinetic resolution, k_{rel} values are generally between 10 and 20. Successful scale-up of various substrates to 10-mmol scale is described. Extension to oxidative desymmetrization of 1,3-*meso*-diols is successful with enantiomeric excesses ranging from 78 to 85%.

Chiral alcohols are ubiquitous in both natural products and pharmaceuticals. For this reason, access to enantiomerically enriched chiral alcohols is an important problem in organic synthesis. Of the many methods to synthesize enantiomerically enriched alcohols, kinetic resolutions are particularly attractive since racemic alcohols are often readily available and inexpensive. Kinetic resolution strategies of alcohols range from epoxidation of allylic alcohols,[1] to oxidative methods,[2] to resolution via acylation either by designed catalysts[3] or enzymes,[4] to Mitsunobu strategies.[5] As an alternate to existing kinetic resolutions of alcohols, we discovered the combination of a Pd(II) salt and (−)-sparteine effectively catalyzes the oxidative kinetic resolution of secondary benzylic alcohols with molecular oxygen as the terminal oxidant.[6−10] Aerobic oxidative kinetic resolution has recently been applied to the synthesis of various pharmaceuticals.[11] A noteworthy limitation of this methodology is the low selectivity (k_{rel} values <8) for the oxidation of saturated aliphatic alcohols and allylic alcohols.[12] Herein we wish to disclose an improved Pd(II)-catalyzed aerobic oxidative kinetic resolution of secondary alcohols, which circumvents this limitation, as well as the substrate scope and application of the Pd(II)/(−)-sparteine catalyst system in the oxidative desymmetrization of *meso*-diols.

With the selection of *sec*-phenethyl alcohol as the substrate to standardize the initial reaction conditions, it is possible that optimal conditions for other substrate classes may have been overlooked. Accordingly, several reaction parameters were reevaluated with use of the aliphatic alcohol, 3,3-dimethyl-2-butanol, as the standard substrate. As a first step in this process, several solvents were assessed for the oxidative kinetic resolution, using 5 mol % of $Pd(CH_3CN)_2Cl_2$ in combination with 20 mol % of (−)-sparteine at 65 °C. In this evaluation, *tert*-butyl alcohol, which was the second best in our original solvent evaluation for *sec*-phenethyl alcohol,[6] gave the highest selectivity and conversions followed by 1,2-dichloroethane (Figure 1). $Pd(OAc)_2$ was also evaluated with several solvents under similar conditions. The use of $Pd(OAc)_2$ in all solvents, except acetonitrile, gave poorer oxidative kinetic resolutions than $PdCl_2$ and the best results were found by using 1,2-dichloroethane to give 70.4% ee at 60.2% conversion, a k_{rel} value of 5.5. From the initial screens, *tert*-butyl alcohol in combination with $Pd(CH_3CN)_2Cl_2$ and (−)-sparteine is clearly the best system for oxidative kinetic resolution of this aliphatic

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[1] Epoxidation: Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

[2] Recent oxidative approaches: (a) Sun, W.; Wang, H.; Xia, C.; Li, J.; Zhao, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 1042. (b) Masutani, K.; Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron Lett.* **2000**, *41*, 5119. (c) Nishibayashi, I.; Takei, I.; Uemura, S.; Hidai, M. *Organometallics* **1999**, *18*, 2291. (d) Gross, Z.; Ini, S. *Org. Lett.* **1999**, *1*, 2077 (e) Hashiguchi, S.; Fujii, A.; Haack, K.-J.; Matsumura, K.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 288. (f) Rychnovsky, S. D.; McLernon, T. L.; Rajapakse, H. *J. Org. Chem.* **1996**, *61*, 1194.

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[4] (a) Wong, C.-H.; Whitesides, G. M. *Enzymes in Synthetic Organic Chemistry*; Pergamon: Oxford, UK, 1994; Chapter 2. (b) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129. (c) Burgess, K.; Jennings, L. D. *J. Org. Chem.* **1990**, *55*, 1138. (d) Burgess, K.; Cassidy, J.; Henderson, I. *J. Org. Chem.* **1991**, *56*, 2050.

[5] (a) Chandrasekhar, S.; Kulkarni, G. *Tetrahedron*: *Asymmetry* **2002**, *13*, 615. (b) Li, Z.; Zhou, Z.; Wang, L.; Zhou, Q.; Tang, C. *Tetrahedron*: *Asymmetry* **2002**, *13*, 145. (c) Hulst, R.; Basten, A.; Fitzpatrick, K.; Kellog, R. M. *J. Chem. Soc., Perkin. Trans. 1* **1995**, 2961.

[6] Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Am. Chem. Soc.* **2001**, *123*, 7475.

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[9] For examples of Pd(II)-catalyzed aerobic oxidations, see: (a) Schultz, M. J.; Park, C.; Sigman, M. S. *Chem. Commun.* **2002**, 3034−3035. (b) Ten Brink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Adv. Synth. Catal.* **2002**, *344*, 355−369. (c) Kakiuchi, N.; Maeda, Y.; Nishimura, T.; Uemura S. *J. Org. Chem.* **2001**, *66*, 6620. (d) ten Brink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636. (e) Peterson, K. P.; Larock, R. C. *J. Org. Chem.* **1998**, *62*, 3185. (f) Kaneda, K.; Fujii, M.; Morioka, K. *J. Org. Chem.* **1996**, *61*, 4502. (g) Gomez-Bengoa, E.; Noheda, P.; Echavarren, A. M. *Tetrahedron Lett.* **1994**, *35*, 7097. (h) Blackburn, T. F.; Schwartz, J. *J. Chem. Soc., Chem. Commun.* **1977**, 157.

[10] (a) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 6750. (b) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **1998**, *39*, 6011.

[11] Sudalai, A.; Ali, I. S. *Tetrahedron Lett.* **2002**, *43*, 5435.

[12] See Supporting Information for details.

10.1021/jo0269161 CCC: $25.00

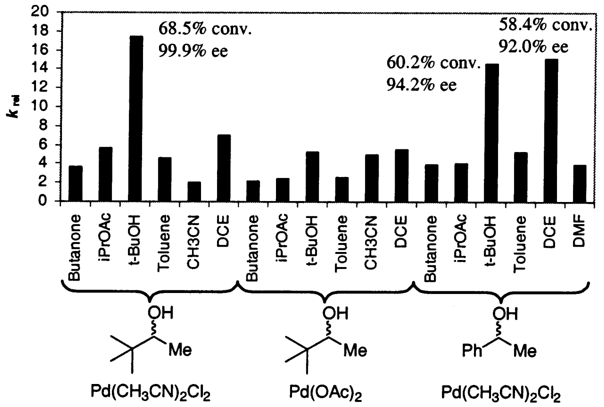


FIGURE 1. Comparison of k_{rel} values with use of $Pd(OAc)_2$ and $Pd(CH_3CN)_2Cl_2$ in different solvents.

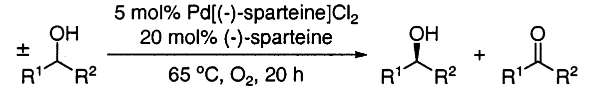
substrate giving an enantiomeric excess of 99.9% at 68.5% conversion, a k_{rel} value of 17.4.

Of particular interest, the oxidative kinetic resolution of *sec*-phenethyl alcohol with $Pd(CH_3CN)_2Cl_2$ as the metal source in various solvents showed effective kinetic resolutions can be obtained in both *tert*-butyl alcohol and 1,2-dichloroethane solvent. These observations showcase the need for continued re-optimization throughout the catalyst development process even when subtle changes are made to the system.

Since both an aliphatic and aromatic substrate successfully undergo oxidative kinetic resolutions in *tert*-butyl alcohol solvent, this system could lead to a more general solution for the oxidative kinetic resolution. However, wide variations in the k_{rel} values were observed when reproducing the initial results for 3,3-dimethyl-2-butanol. Suspecting that the poor solubility of Pd(II) salts in *tert*-butyl alcohol could lead to inconsistent formation of the active catalyst species, the addition of 20% 1,2-dichloroethane or toluene as a cosolvent was attempted to potentially eliminate this issue but led to no improvement. To circumvent the issue of inconsistent formation of the Pd[(−)-sparteine)]Cl_2 complex in situ, isolated Pd[(−)-sparteine)]Cl_2 was used to provide for consistent results. Additionally, the use of activated 3 Å molecular sieves further improved the reliability of the reaction.[13]

To ensure the best conditions were selected, several other reaction variables were evaluated. Reducing the catalyst loading to 2.5 mol % led to an anticipated slower oxidation with only 40% conversion after 36 h. Varying the temperature of the reaction (55 and 70 °C) had little effect on the k_{rel} values. Overall, the optimal conditions for this oxidative kinetic resolution were 5 mol % of Pd[(−)-sparteine)]Cl_2,[12] 20 mol % of (−)-sparteine, 0.25 M alcohol in *tert*-butyl alcohol, and crushed activated molecular sieves (3 Å) at 65 °C under a balloon pressure of O_2. By re-optimizing for 3,3-dimethyl-2-butanol, a considerable improvement from a k_{rel} of 7.6 (77.8% ee at 58.5% conversion) to a k_{rel} of 17.3 (97.2% ee at 60.9% conversion) in *tert*-butyl alcohol was observed.

TABLE 1. Scope of Benzylic Alcohols in the Oxidative Kinetic Resolution



Entry	R^1	R^2	Solvent	%conv(%ee)[a,b]	k_{rel}[b]
1	4-MeC_6H_4	Me	^{t}BuOH	61.6(98.5)	19.0
2	4-MeC_6H_4	Me	DCE	57.0(94.3)[c]	17.1
3	4-FC_6H_4	Me	^{t}BuOH	63.5(96.3)	12.9
4	4-FC_6H_4	Me	DCE	52.9(80.7)[d]	12.2
5	2-naphthyl	Me	^{t}BuOH	55.9(90.2)	17.7
6	2-naphthyl	Me	DCE	65.7(95.9)[d]	10.1
7	7-MeO-2-naphthyl	Me	^{t}BuOH	69.0(98.8)	11.6
8	3,5-$CF_3C_6H_3$	Me	^{t}BuOH	55.0(70.2)	7.5
9	α-tetralol		^{t}BuOH	61.6(99.3)	21.9
10	α-tetralol		DCE	65.3(99.2)[c]	15.9
11	1-benzosuberol		^{t}BuOH	51.2(80.0)	17.8
12	1-benzosuberol		DCE	70.6(95.0)[c]	7.6
13	4-chromanol		^{t}BuOH	67.4(99.2)	13.6
14	4-chromanol		DCE	61.0(91.2)[c]	11.5
15	1-acenaphthol		^{t}BuOH	57.9(89.3)	13.5
16	1-acenaphthol		DCE	59.0(90.0)[c]	12.8
17	Ph	^{t}Bu	^{t}BuOH	21.2(6.0)	1.7
18	Ph	CH_2CO_2Et	^{t}BuOH	23.0(20.0)	6.1
19	Ph	COPh	^{t}BuOH	90.0(37.0)	1.4
20	Ph	2-$MeOC_6H_4$	^{t}BuOH	40.5(1.4)	1.1
21	Ph	≡—Me	^{t}BuOH	No oxidation	--
22	2-furyl	Me	^{t}BuOH	65.2(99.3)	16.3
23	2-furyl	Me	DCE	77.5(99.0)[c]	7.6
24	Ph	CF_3	^{t}BuOH	13.6(0.6)	1.1
25	2-pyridyl	Me	^{t}BuOH	No oxidation	--
26	ferrocenyl	Me	^{t}BuOH	66.6(99.8)	17.8
27	ferrocenyl	Me	DCE	66.2(94.0)[c]	9.3

[a] See Supporting Information for chiral separations. [b] Data represent a single experiment. [c] $Pd(MeCN)_2Cl_2$ at 70 °C and 0.25 M alcohol. [d] $Pd(OAc)_2$ at 60 °C and 0.25 M alcohol.

Substrate Scope. The benzylic substrate scope of the oxidative kinetic resolution with isolated Pd[(−)-sparteine)]Cl_2 and *tert*-butyl alcohol solvent was first examined. As was observed with the previous systems, simple benzylic alcohols (Table 1, entries 1−7) undergo an effective kinetic resolution with similar k_{rel} values observed with use of both 1,2-dichloroethane and *tert*-butyl alcohol as solvents. However, in all cases, the catalyst system performs better with *tert*-butyl alcohol as the solvent. A substrate with two trifluoromethyl groups gives a relatively low k_{rel} value (entry 8). Cyclic benzylic substrates (entries 9−16) are good substrates for the kinetic resolutions with k_{rel} values ranging from 13.5 to 21.0. Of particular note, both furyl- and ferrocene-substituted alcohols undergo effective kinetic resolutions (entries 22 and 26).

Substrates with two large substituents are relatively poor for oxidation and kinetic resolution (entries 17 and 20). This finding fits with the interpretation that the differential in size of the substituents plays a significant role in the overall efficiency of the kinetic resolution. Additionally, the previous observation of a lower k_{rel} value as the size of R^1 increases fits this notion. When R^1 is

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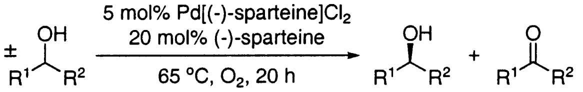
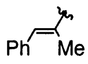
[13] Molecular sieves have been used by Uemura as a catalyst to disproportionate H_2O_2 formed in the reaction, see ref 10a. We also found that addition of a drop of water to the reaction mixture inhibits the reaction.

TABLE 2. Scope of Non-Benzylic Alcohols in the Oxidative Kinetic Resolution



Entry	R^1	R^2	Solvent	%conv(%ee)[a,b]	k_{rel}[b]
1	^{t}Bu	Me	^{t}BuOH	60.9(97.2)	17.3
2	^{t}Bu	Me	DCE	65.6(87.0)[c]	7.1
3	cyclopropyl	Me	^{t}BuOH	59.0(82.6)	9.1
4	cyclopropyl	Me	DCE	67.3(82.2)[c]	5.5
5	$(Ph)_2CH$	Me	^{t}BuOH	56.0(91.8)	19.6
6	cyclohexyl	Me	^{t}BuOH	53.0(61.0)	6.1
7	*endo*-borneol		^{t}BuOH	75.0(98.8)	8.3
8	1-cyclohexenyl	Me	^{t}BuOH	67.9(95.4)	9.0
9	1-cyclohexenyl	Me	DCE	67.5(89.6)[c]	7.0
10	 Ph Me	Me	^{t}BuOH	64.9(97.6)	13.1
11			DCE	66.8(90.8)[c]	7.6
12	2-cyclohexenol		^{t}BuOH	95.0(49.0)	1.4
13	*trans*-sobrerol		^{t}BuOH	72.8(99.3)	10.3
14	isopulegol		^{t}BuOH	55.0(84.3)	14.3

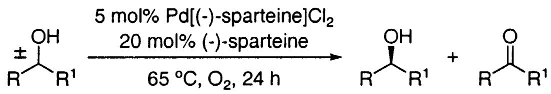
[a] See Supporting Information for chiral separations. [b] Data represent a single experiment. [c] $Pd(MeCN)_2Cl_2$ at 70 °C and 0.25 M alcohol.

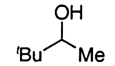
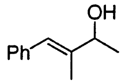
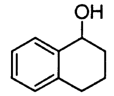
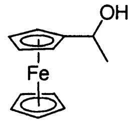
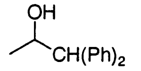
functionalized with either a ketone, ester, alkyne, or trifluoromethyl group, poor kinetic resolutions result. Very slow oxidation is observed with the ester and trifluoromethyl group (entries 18 and 24) while no apparent oxidation is observed for the propargylic alcohol (entry 21).[14] However, benzoin does undergo a rapid and clean oxidation but with an inefficient kinetic resolution (entry 19). These poor oxidation results are consistent with the observations of Uemura and co-workers in their related aerobic oxidation system and reflect either the ability to chelate the metal (ester or alkyne) or an overall difficult oxidation (trifluoromethyl).[10]

The assessment of scope continued by evaluation of several nonbenzylic substrates. Substrates with a large substituent (i.e. *tert*-butyl) perform very well (Table 2, entries 1 and 5). A substrate with a cyclopropyl substituent undergoes a reasonably effective kinetic resolution with a k_{rel} value of 9.1. Substrates containing olefins are viable substrates for oxidation. Kinetic resolutions of these substrates again rely on a significant difference in size to provide for an effective kinetic resolution. As an example, cyclohexenol undergoes a rapid oxidation but with a poor kinetic resolution. Of particular interest, racemic isopugelol, which contains a terminal homoallylic olefin, is an excellent substrate for oxidation and kinetic resolution with no observation of double bond isomerization. While an improved procedure would include the use of air in place of pure O_2, reactions run under an air atmosphere are not effective due to substantial decomposition of the catalyst.

Since this reaction involves the use of a reagent in the gas phase, it is imperative to show the reaction is amenable to common laboratory scale. For this purpose, oxidative kinetic resolution was performed on a 10-mmol scale for several substrates. Good overall mass recovery was observed of both the optically enriched alcohol and the prochiral ketone byproduct (Table 3). These larger scale reactions did require slightly increased reaction times of 24 h, compared to 20 h for smaller scale reactions, and showed a slight decrease in k_{rel} values (1.2−1.7). Overall, scale-up of the oxidative kinetic resolution of alcohols was effective for aliphatic, allylic, and benzylic alcohols.

TABLE 3. Oxidative Kinetic Resolution on 10 mmol Scale



Entry	Substrate	Scale	%conv(%ee)[a]	k_{rel}	yield(%)
1		1.00g	58.2(92.2)	15.7	37(55)[b]
2		1.58g	67.3(98.3)	11.9	30(63)[b]
3		1.45g	62.1(99.1)	20.2	35(61)[b]
4		2.25g	65.4(99.3)	16.1	33(65)[b]
5		2.07g	59.7(96.6)	18.3	38(57)[b]

[a] Data represent a single experiment. [b] Isolated yield of ketone.

Extension to *meso*-Diol Desymmetrization. A related enantioselective oxidation with significant potential in organic synthesis is the oxidative desymmetrization of a *meso*-diol.[15] A variety of diol substrates are potentially useful in such a desymmetrization reaction, including 1,2- and 1,3-diols. The enantioselective oxidation of 1,3-diols leads to enantiomerically enriched β-hydroxycarbonyl compounds (aldol-type products), and significant effort has been made to develop methodology for these reactions.[16,17] Therefore, the catalyst system developed for the oxidative kinetic resolution of alcohols was evaluated in the oxidative desymmetrization of 1,3-*meso*-diols. Generally good yields (69−79%) and good ee values (78−85%) of β-keto alcohols are obtained from various *meso*-1,3-diols (Table 4). Upon scaling up the reaction to

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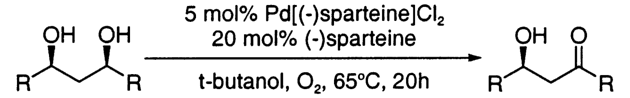
(14) For an example of Vanadium-catalyzed aerobic oxidations of propargylic alcohols, see: Maeda, Y.; Kakiuchi, N.; Matsumura, S.; Nishimura, T.; Kawamura, T.; Uemura, S. *J. Org. Chem.* **2002**, *67*, 6718−6724.

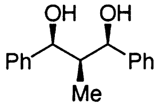
(15) For examples of nonenzymatic desymmetrization of *meso*-diols see: (a) Trost, B. M.; Mino, T. *J. Am. Chem. Soc.* **2003**, *125*, 2410. (b) Hodgson, R.; Majid, T.; Nelson, A. *J. Chem. Soc., Perkin Trans. 1* **2002**, *14*, 1631−1643. (c) Jiang, L.; Burke, S. D. *Org. Lett.* **2002**, *4*, 3411−3414. (d) Harada, T.; Sekiguchi, K.; Nakamura, T.; Suzuki, J.; Oku, A. *Org. Lett.* **2001**, *3*, 3309−3312. (e) Harada, T.; Yamanaka, H.; Oku, A. *Synlett* **2001**, *1*, 61−64. (f) Yamada, S.; Katsumata, H. *J. Org. Chem.* **1999**, *64*, 9365. (g) Oriyama, T.; Imai, K.; Hosoya, T.; Sano, T. *Tetrahedron Lett.* **1998**, *39*, 397. (h) Via acetal cleavage, see: Fujioka, H.; Nagatomi, Y.; Kotoku, N.; Kitagawa, H. *Tetrahedron* **2000**, *56*, 10141. (i) Kinugasa, M.; Harada, T.; Oku, A. *J. Am. Chem. Soc.* **1997**, *119*, 9067.

(16) For a recent review, see: Machajewski, T. D.; Wong, C.-H.; Lerner, R. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1352.

(17) For a review of catalytic asymmetric Mukaiyama aldol reactions, see: Carreira, E. M. *Comput. Asym. Catal.* **1999**, *I−III*, 997.

TABLE 4. Oxidative Desymmetrization of 1,3-*meso*-Diols



entry	R	yield(%)	ee(%)
1	2-naphthyl	79(63)[a]	85(92)[a]
2[b]	2-naphthyl	72	85
3	Ph	69(54)[a]	82(90)[a]
4	*tert*-Bu	69(55)[a]	78(90)[a]
5	4-BrC$_6$H$_4$	78(62)[a]	85(95)[a]
6		74(60)[a]	79(89)[a]

[a] Values after one recrystallization from dichloromethane (0.5 mL)/hexane (2.0 mL) at −20 °C for 24 h. [b] On 10 mmol scale (3.23 g).

10 mmol, the oxidative desymmetrization performs quite well (entry 2). Only a small difference in enantioselectivity is observed when a substituent at the 3-position is incorporated (entry 6). Additionally, activated C−Br bonds are tolerated in the oxidative desymmetrization. Very little over oxidation to the dione is observed. The enantiomeric excess of the products can be enhanced through recrystallization to 90−95% ee with only a small decrease of yields (~15%).

Unfortunately, 1,2-diols are not good substrates for oxidative desymmetrization. *meso*-Hydrobenzoin oxidized to benzoin with a maximum ee of 37%. *cis*-1,2-Cyclohexanediol and *cis*-1,2-cyclopentanediol oxidized to the corresponding α-hydroxy ketone with only 10% ee. In these cases, the yield of the α-hydroxy ketone was low due to over oxidation yielding the diketone as the major product.

Mechanistic Considerations. Considering the kinetic resolutions are generally better in *tert*-butyl alcohol than in DCE as solvent, some mechanistic experiments were performed.[18] In a study of the kinetics of oxidative kinetic resolutions, it was found the rate dependence on exogenous (−)-sparteine concentration fits the same model for both *tert*-butyl alcohol and DCE solvents. A possible explanation for the enhanced reactivity in *tert*-butyl alcohol is the Pd[(−)-sparteine]Cl$_2$ could react with *tert*-butyl alcohol in the presence of base to form a new species where the chloride ligands are replaced with alkoxide ligands. To test if this is thermodynamically favorable, Pd[(−)-sparteine]Cl$_2$ was heated in *tert*-butyl alcohol (65 °C, 20 h) in the presence of exogenous (−)-sparteine. ^{1}H NMR analysis of the resulting isolated complex showed only Pd[(−)-sparteine]Cl$_2$, with no incorporation of *tert*-butyl alcohol. This observation is consistent with the prediction, based on acid/base chemistry, that *tert*-butyl alcohol should not replace a chloride ligand in the resting state of the catalyst.[19] Consistent with these observations, we consider the simplest explanation of the improved kinetic resolutions in *tert*-butyl alcohol solvent to be its enhanced ability to support cationic intermediates due to its higher polarity.

In conclusion, the scope of Pd(II)/(−)-sparteine catalyzed enantioselective oxidations has been evaluated. Replacement of 1,2-dichloroethane with *tert*-butyl alcohol as solvent has provided for an improved catalyst system that is effective not only for benzylic alcohols but also for allylic and aliphatic alcohols. Applying this methodology to the desymmetrization of 1,3-*meso*-diols has also been accomplished to deliver chiral β-keto alcohols in good yield and enantioselectivity. While higher k_{rel} values have been obtained in other alcohol kinetic resolutions, the value of this kinetic resolution protocol is the simplicity in which it can be accomplished and the ability to isolate synthetically viable levels of the optically active alcohols. All reagents are commercially available and the consumed reagent is molecular oxygen. Alcohols are generally used without extensive purification.

A key limitation is the use of (−)-sparteine as the chiral element. While it is a relatively inexpensive reagent, access to (+)-sparteine is synthetically challenging[20] and the development of useful analogues is ongoing.[21] Significant effort in our laboratory has focused on the understanding of this process and the development of new catalyst systems with antipodal selectivity.[22] Future work will utilize the mechanistic information garnered to both eliminate the need for exogenous (−)-sparteine in the kinetic resolution and develop new catalysts that can utilize air instead of pure O$_2$ as the terminal oxidant.

Acknowledgment. This work was supported by the National Institutes of Health (NIGMS No. RO1 GM63540) and by a Research Innovation Award sponsored by Research Corporation. We would like to thank the University of Utah Research Foundation, Merck Research, Rohm and Haas Research, and Invenux Inc. for partial support of this research. We thank Johnson Matthey for palladium salts. S.K.M. would like to thank the University of Utah for sponsorship of a Faculty Intern position. D.R.J. is supported by an ACS Division of Organic Chemistry Graduate Fellowship sponsored by Schering-Plough Research Institute.

Supporting Information Available: Experimental procedures, characterization data, NMR spectra, and chiral chromatographic separation data. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0269161

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