

New enantioselective heterogeneous catalysts

Gerard V. Smith^{a,b}, Jianjun Cheng^a and Ruozhi Song^a

^a Department of Chemistry and Biochemistry, Southern Illinois University at Carbondale, Carbondale, IL 62901-4409, USA

^b Department of Chemical Engineering, Research Center for Catalytic Technology, Pohang University of Science and Technology, Pohang, Republic of Korea

Received 11 July 1996; accepted 5 February 1997

A new enantioselective heterogeneous catalytic system has been made by partly decomposing (hydrogenolyzing) chiral silyl ethers in hydrogen over Pd black and differently dispersed Pd/SiO₂. Preliminary hydrogenations of two prochiral C=C's have demonstrated the feasibility of the method which produced catalysts attaining ee's up to 22%. The chiral silyl ethers appear to hydrolyze off the surface, but in the absence of water, the new catalysts catalyze reproducible ee's.

Keywords: chiral heterogeneous catalysts, chiral hydrogenations, enantioselective hydrogenations, prochiral C=C hydrogenation, silicon modified catalysts, enantioselective heterogeneous catalysts, α -methylcinnamic acid hydrogenation, trans-2-methyl-2-pentenoic acid hydrogenation

Enantioselective heterogeneous catalysts have long been sought for their ease of recycle, high turnover frequencies, and low costs. However, they have shown high enantioselectivities for only certain substrates. Thus modified Raney nickel is virtually 100% specific for hydrogenating β -keto esters, while cinchona-modified platinum is highly specific for hydrogenating α -keto acids. Although these successes in the hydrogenation of prochiral ketones have been impressive, recently reaching 96% ee [1], heterogeneous enantioselective hydrogenations of prochiral C=C double bonds have not been impressive [2]. Until recently, the highest optical yield from a heterogeneously catalyzed hydrogenation of a prochiral C=C π -bond was 66%. This was accomplished using a Pd-on-silk catalyst [3]; however, this catalyst turned out not to be reproducible. Similarly, the modified Ni and Pt catalysts mentioned above typically exhibit only low enantioselectivities for hydrogenating C=C double bonds, producing a high over Raney nickel of 17% [4], and a high over cinchona alkaloid-modified Pt of 30% [2]. Recently, however, an ee of 72% has been reported over a cinchona modified Pd/TiO₂ catalyst system in which the solvent, pressure and temperature are optimized [5].

These relatively low enantioselectivities compare unfavorably with those from homogeneous catalysts, which convert prochiral C=C bonds virtually 100% enantioselectively [6]. So an important problem exists: how do we attain the high enantioselectivities of homogeneous catalysts and retain the advantages of heterogeneous systems? Clearly, our poor understanding of the differences between the mechanisms of homogeneous and heterogeneous catalysis impedes progress, but also, new and innovative ways of preparing enantioselective heterogeneous catalysts have been slow in coming.

Important breakthroughs are needed in understanding the mechanisms of enantioselectivities on metal surfaces and in preparing enantioselective metal surfaces in new ways.

Enantioselective metal surfaces may be prepared in three basic methods: (I) deposit the metal onto a chiral support, (II) rearrange the metal surface atoms into a chiral arrangement, and (III) deposit a chiral moiety onto the metal surface. No enantioselective metal catalyst of method II is known, but several from I and III have been prepared by either depositing metals on chiral matrices (quartz, silk fibroin, polypeptide, polysaccharide, or cyclodextrin) or by physisorbing or chemisorbing chiral moieties (cinchona alkaloids, camphor, amino acids, hydroxy acids) on metal surfaces [3]. We would like to report preliminary experiments showing a new way of preparing enantioselective heterogeneous metal catalysts by method III. Our new catalyst system is synthesized by directly attaching chiral silyl ether modifiers to Pd surfaces through Si-metal bonds [7].

These new catalysts arise from our studies of the effects of siliconation on the catalytic activities and selectivities of dispersed, supported Pd and Pt [8–12]. The results from these and other studies [13,14] point to a process in which stepwise hydrogenolyses of trialkylsilanes occur over Pd and Pt. This process suggested a possible route for attaching chiral species to metal surfaces by incorporating a chiral moiety in the silyl fragment. If alkyl groups are hydrogenolyzed off one at a time, perhaps a chiral silyl ether can be partly hydrogenolyzed such that the chiral moiety will become attached to the metal surface. Indeed, in preliminary experiments we find that chiral alkoxytrimethylsilanes do appear to undergo partial hydrogenolysis on Pd and as a result,

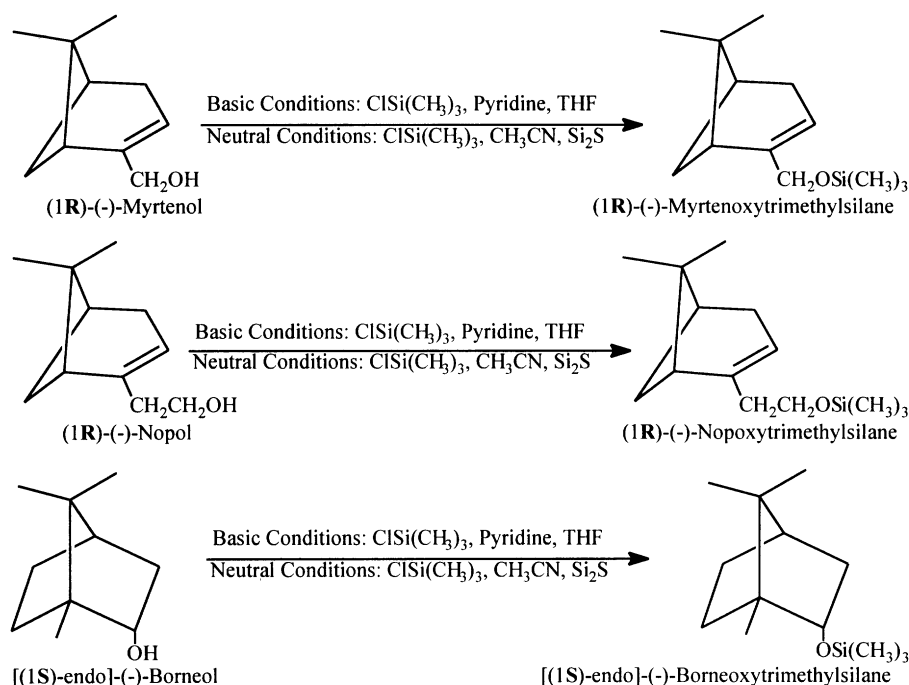


Figure 1. Preparation of the chiral silyl ethers. *Basic conditions:* Chiral alcohols (0.02 mol) were stirred in THF (20 ml) under N_2 at room temperature for 2 h; pyridine or Et_3N (0.05 mol) was added, then chlorotrimethylsilane (0.02 mol) dropwise, followed by stirring overnight. The alkoxytrimethylsilyl ethers were separated from the resulting pyridine hydrochloride in ether (50 ml), washed twice in H_2O (50 ml), once in sat. $NaCl$ (50 ml), and dried over anhyd. Na_2SO_4 . The ether was evaporated, and the silyl ethers were vacuum distilled (15–85% yields) and analyzed by 1H NMR (300 MHz). *Neutral conditions:* Freshly distilled $(CH_3)_3SiH$ (0.05 mol) was added to a well stirred suspension of Li_2S (0.02 mol) in dry acetonitrile (25 ml) under N_2 . To this mixture was added a chiral alcohol (0.02 mol) in acetonitrile (15 ml) and stirred overnight. Workup was the same as for basic conditions. Yields ranged from 5–72%.

form residues which impart enantioselectivities to the catalytic surfaces. We describe these results below.

First, three chiral silyl ethers were prepared three different ways from (1R)-(-)-nopol, (1R)-(-)-myrtenol, and [(1S)-endo]-(-)-borneol as shown in figure 1; their purities, and optical rotations are shown in table 1.

Second, 20 mg of the five different Pd catalysts [15] (see table 2) were each heated in a “U” tube reactor at $300^\circ C$ for 2 h and cooled to between 100 and $193^\circ C$ (cleavage of the C–Si bond has been shown to occur above $127^\circ C$ [14]) all under H_2 flowing at between 30 and 42 ml/min; then each was treated with one or more injections of 5 μl of silyl ether every 30 min to produce the catalysts labeled BOS-Pd (borneoxysilyl), MOS-Pd (myrtenoxysilyl), and NOS-Pd (nopoxysilyl). Following silyl ether injections, residual catalytic activities were assessed by hydrogenations of cyclohexene to establish

whether activity remained. Always, activities were greatly reduced after modification. The differently modified catalysts and conditions of their modifications are shown in table 3.

Third, the modified catalysts were tested for enantioselectivities during hydrogenations of prochiral molecules in a liquid phase hydrogenation apparatus previously described [16]. Hydrogenations in this apparatus were conducted in a Pyrex 1.5×10.0 cm reactor, the walls of which are lined with double-helical Vigreux indentations. Vortex mixing at 1900 revolutions per minute was shown to eliminate mass transfer problems in this system [17]. Additional assurance of the absence of mass transfer problems is the low activities of these

Table 1
Specific rotations of silyl ethers

Silyl ether ^a	Specific rotation ^b
(1R)-(-)-myrtenoxytrimethylsilane	–35.8
(1R)-(-)-nopoxytrimethylsilane	–25.8
[(1S)-endo]-(-)-borneoxytrimethylsilane	–38.7

^a GC analyses showed each > 99% one enantiomer.

^b $25^\circ C$, D line of Na.

Table 2
Characteristics of Pd catalysts [15]

%Pd	% D_{chem} ^a	% D_{em} ^b	Avg. particle size (nm)	Particle size range (nm)
100	0.5	–	–	–
1	4.4	2.08	55.64 ± 10.83	1.5–144.4
1	36.0	35.8	3.24 ± 0.64	1.8–5.4
1	77.8	69.8	1.66 ± 0.47	0.5–3.0
1	93.6	83.8	1.38 ± 0.34	0.5–2.6

^a Hydrogen chemisorption.

^b Electron microscopy.

Table 3
Catalyst modification conditions and parameters

Modified catalyst identifier	μl silyl ether injected	1% Pd/SiO ₂ ^a modified (% D)	Modification temp. (°C)	H ₂ flow (ml/min)
BOS-Pd(a)	1 × 5	77.8	127–129	30
BOS-Pd(b)	4 × 5	77.8	128–129	30
BOS-Pd(c)	6 × 5	77.8	128–129	30
BOS-Pd(d)	8 × 5	77.8	128–129	30
BOS-Pd(e)	20 × 5	77.8	134–135	30
BOS-Pd(f)	50 × 5	77.8	133–135	30
BOS-Pd(g)	6 × 5	77.8	100–103	40
BOS-Pd(h)	10 × 5	77.8	100–102	42
BOS-Pd(i)	2 × 5	77.8	190–193	30
BOS-Pd(j)	6 × 5	77.8	190–193	30
BOS-Pd(k)	2 × 5	77.8	165	30
BOS-Pd(l)	4 × 5	77.8	165	30
BOS-Pd(m)	4 × 5	4.4	130	30
BOS-Pd(n)	4 × 5	36.0	130	30
BOS-Pd(o)	4 × 5	93.6	130	30
BOS-Pd-black(a)	10 × 5	0.5 ^b	130	30
BOS-Pd-black(b)	20 × 5	0.5 ^b	130	30
MOS-Pd(a)	8 × 5	77.8	129–131	30
MOS-Pd(b)	16 × 5	77.8	130–131	30
MOS-Pd(c)	24 × 5	77.8	130–132	30
MOS-Pd(d)	160 × 5	77.8	130–132	30
MOS-Pd-black(a)	20 × 5	0.5 ^b	129–130	30
NOS-Pd(a)	2 × 5	77.8	129–131	30
NOS-Pd(b)	4 × 5	77.8	130–131	30
NOS-Pd(c)	8 × 5	77.8	130–132	30
NOS-Pd(d)	10 × 5	77.8	129	30
NOS-Pd-black(a)	4 × 5	0.5 ^b	130–132	30
NOS-Pd-black(b)	10 × 5	0.5 ^b	129–131	30
NOS-Pd-black(c)	20 × 5	0.5 ^b	129–131	30

^a 20 mg.

^b Unsupported Pd.

modified catalysts. Because of these low activities, some reactions were run only to a small percentage completion. When run to high percentages completion, reaction times were several hours. Calculations of turnover frequencies and turnover numbers were impossible because surface coverages of the modifiers were unknown.

Hydrogenations were run at 27°C and 16.7 psi in the reactor, which had been charged with catalyst (20 mg), purged with H₂, and injected with 2 ml of a 0.10 M solution of one of two prochiral acids, α -methyl cinnamic acid (MCA) or trans-2-methyl-2-pentenoic acid (MPA) in methanol (other solvents where noted). After filtration, the products were analyzed by chiral GC (Shimadzu, GC-9A, capillary β -cyclodextrin column, BETA-DEX 120, 30 m × 0.25 mm, from Supelco). Experimental error was estimated at 12% through experiments under identical conditions in the apparent absence of the influence of traces of water (exps. 177, 181, 191, and 184, table 5; 9.1 ± 1.1 ee). An apparent larger overall maximum of 22% can be found (exps. 191–

193, table 5), but these experiments were not conducted under identical conditions.

Hydrogenations of MPA were used to estimate the effects of different conditions of modification (table 4). Initial experiments on MOS-Pd produced erratic results (exps. 146–149), which were later shown by experiments on BOS-Pd(b) likely due to traces of water (see below and table 5). Therefore the MOS-Pd system was abandoned. Likewise, the NOS-Pd catalysts produced only low ee's, and they were abandoned too. Consequently, the bulk of these preliminary experiments were performed over BOS-Pd(b).

Use of BOS-Pd(b) was determined in a series of 30 min hydrogenations over the BOS-Pd catalysts in which increasing amounts of [(1S)-endo]-(-)-borneoxytrimethylsilane {BOS-Pd(b)} (exps. 153–160, table 4 and figure 2) exhibited a maximum ee at 20 μl of modifier. Whether this was influenced by extent of conversion was not thoroughly examined; however, the existence of the maximum makes it seem unlikely. Moreover, for

Table 4
Hydrogenations of trans-2-methyl-2-pentenoic acid over B(M, N)OS-Pd/SiO₂

Exp.	Catalyst	Conversion (%)	ee (%)
146	MOS-Pd(d)	100	11.6
147 ^a	MOS-Pd(d) ^a	100 ^a	4.3 ^a
148 ^b	MOS-Pd(d) ^b	100 ^b	0.6 ^b
149 ^c	MOS-Pd(d) ^c	100 ^c	1.7 ^c
150	NOS-Pd(a)	11	0.7
151	NOS-Pd(b)	10	2.6
152	NOS-Pd(c)	8	3.1
153	BOS-Pd(a)	27 ^d	0.0
154	BOS-Pd(b)	8.5 ^d	9.0
155	BOS-Pd(b)	8.5 ^d	3.5
156	BOS-Pd(b)	8.5 ^d	3.8
157	BOS-Pd(c)	5 ^d	0.9
158	BOS-Pd(d)	1.5 ^d	0.0
159	BOS-Pd(e)	0.4 ^d	0.0
160	BOS-Pd(f)	0.4 ^d	0.0

^a Catalyst MOS-Pd/SiO₂(d) was washed with methanol after reaction (exp. 146) and then put back to the reactor for the hydrogenation of TMPA for the second time (exp. 147).

^b Catalyst MOS-Pd/SiO₂(d) was washed with methanol again after reaction (exp. 147) and then put back to the reactor for the hydrogenation of TMPA for the third time (exp. 148).

^c Exp. 149 was an attempt to reproduce exp. 146.

^d 30 min reaction time.

Table 5
Hydrogenations of α -methyl cinnamic acid over BOS-Pd/SiO₂(b) in methanol

Exp.	Conversion (%)	ee (%)
177	0.3	10.0
178 ^a	0.1 ^a	22.5 ^a
179 ^b	0.5 ^b	4.0 ^b
180 ^c	0.7 ^c	2.2 ^c
181	0.4	7.0
191	0.4	8.9
192 ^d	0.4 ^d	8.1 ^d
193 ^e	0.4 ^e	6.9 ^e
182 ^f	0.2 ^f	12.8 ^f
184	0.3	10.3

^a Modified catalyst from exp. 177 exposed to air 24 h then used for hydrogenation.

^b Catalyst washed with acetone twice after hydrogenation (exp. 178) then used for exp. 179.

^c Catalysts from exp. 179 washed again with acetone and used for exp. 180.

^d Catalyst from exp. 191 washed twice with 10 ml moisture-free methanol (99.5% methanol refluxed with Mg and I₂ 10 h, distilled, and stored with molecular sieves under N₂) then reused in exp. 192.

^e Catalyst from exp. 192 washed twice with 10 ml moisture-free methanol then reused in exp. 193.

^f Fresh modified catalyst exposed to air 24 h then used for hydrogenation.

those cases in which ee is reported to vary with conversion [18,19] a dynamic equilibrium is frequently invoked [20]. This seems not the case in our systems; however, traces of water tend to lower enantioselectivities as we suspect is the case for the sequence of experiments 154–156 in table 4.

Tests with MCA yielded higher ee's, probably because of the anchoring effect of the phenyl group [21]. So we used this probe molecule to examine effects of washing, oxidation, and dispersion. Using MCA we attempted to determine the stability of MOS-

Pd/SiO₂(d) by conducting a sequence of washings with methanol (exps. 146–148, table 4) in which ee's decreased considerably. A similar result occurred over BOS-Pd/SiO₂(b) (exps. 178–180, table 5); however, upon repeating the latter experiments with dry solvents (exps. 191–193), the ee's decreased much less, only 9% with the first washings and 15% with the second. Similarly, experiments with MPA in dry THF followed by washings in dry THF (exps. 194–196, table 6), produced first a 13% decrease in ee and next a 7.5% increase in ee. Since water was rigorously excluded from these last

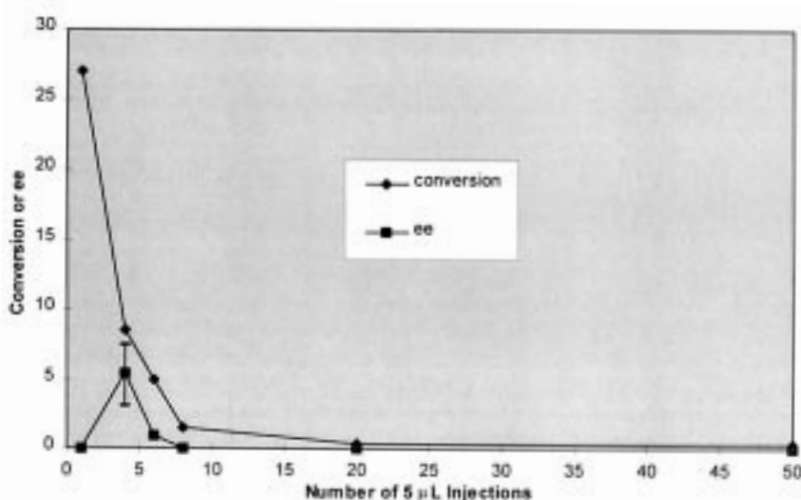


Figure 2. Effect of amount of borneoxytrimethylsilane on 30 min hydrogenations of trans-methyl-2-pentenoic acid.

Table 6
Hydrogenation of trans-2-methyl-2-pentenoic acid over BOS-Pd/
SiO₂(b) in different solvents

Exp.	Solvent	Conversion (%)	ee (%)
194	THF	5	7.7
195 ^a	THF ^a	5 ^a	6.7 ^a
196 ^b	THF ^b	5 ^b	7.2 ^b
171	pyridine	100	0.3
172	acetic acid	100	5.4
173	ethanol	100	0.2

^a Catalyst from exp. 194 washed twice with 10 ml moisture-free THF (refluxed 99.5% THF with Na 48 h, stored under N₂) then reused in exp. 195.

^b Catalyst from exp. 195 washed twice with 10 ml moisture-free THF then reused in exp. 196.

two sets of experiments, we conclude that traces of water lower enantioselectivities, presumably by hydrolyzing the silyl ethers off the Pd surface. Washing with dry methanol and dry THF does not appear to affect enantioselectivities outside experimental error.

During our earlier studies [9], we had found that oxidation of siliconated Pd catalysts increased subsequent hydrogenation activities, so we examined the possibility that oxidation might influence ee's resulting from hydrogenations over BOS-Pd(b). Simple exposure of BOS-Pd(b) to air for 24 h produced an ee of 12.8 (exp. 182, table 5); but doing the same to a previously used catalyst produced an even higher ee. In this latter experiment BOS-Pd(b) was recovered from exp. 177 and then exposed to air for 24 h, an ee of 22.5 was attained (exp. 178, table 5). Whether this latter ee is due to formation of a chiral carbonaceous layer from the prior hydrogenation [22] and the subsequent oxidation has not been explored.

Results from examination of the effect of dispersion on ee from α -methyl cinnamic acid are tabulated in table 7. All these experiments were carried out to virtually the same percent conversion under diffusion free conditions in methanol. A mild structure sensitivity exists with the lower dispersed catalysts producing lower ee's. Although carried out to higher conversion, the BOS-Pd-black fits this pattern with a very low enantioselectivity (exp. 189, table 8). In fact, each of the Pd-black modified catalysts exhibited high activities and

Table 7
Hydrogenations of α -methyl cinnamic acid over BOS-Pd/SiO₂ with
different dispersions in methanol

Exp.	Catalyst	1% Pd/SiO ₂ (%D)	Conversion (%)	ee (%)
185	BOS-Pd(m)	4.4	0.1	2.2
186	BOS-Pd(n)	36.0	0.2	3.5
177	BOS-Pd(b)	77.8	0.3	10.0
182	BOS-Pd(b)	77.8	0.2	12.8
184	BOS-Pd(b)	77.8	0.3	10.3
187	BOS-Pd(o)	93.6	0.5	11.7

Table 8
Hydrogenations of α -methyl cinnamic acid over palladium black cat-
alysts in methanol

Exp.	Catalyst	Conversion (%)	ee (%)
188	BOS-Pd black(a)	40	0.1
189	BOS-Pd black(b)	80	0.2
190	NOS-Pd black(b)	40	0.1

low enantioselectivities, even though large quantities of modifiers were deposited on them.

Although ee's reported here are not as high as those reported over the cinchona-modified Pd/SiO₂ system nor as high as other reports, we point out that these are preliminary results over a new unoptimized enantioselective heterogeneous catalyst system. Moreover, we report results of hydrogenation of C=C π -bonds in molecules containing minimal numbers of anchoring groups. The trans-2-methyl-2-pentenoic acid contains only one anchoring group (carboxyl) and α -methyl cinnamic acid contains only two (carboxyl and phenyl). These groups tend to increase enantioselectivities, presumably because they tend to anchor the molecules to the surface [21] and slow isomerization and flipping processes. All prochiral C=C double bond compounds yielding high ee's over enantioselective heterogeneous catalysts contain at least one of these [4] and typically three (two phenyl and one carboxyl) as in the case of (E)- α -phenylcinnamic acid [6,7]. Whether high enantioselectivities can be attained from prochiral C=C double bonds not containing such anchoring groups has yet to be determined.

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