Organic Process Research & Development

Technical Note

pubs.acs.org/OPRD

Catalytic Hydrogenation of Esters. Development of an Efficient Catalyst and Processes for Synthesising (*R*)-1,2-Propanediol and 2-(*l*-Menthoxy)ethanol

Wataru Kuriyama,* Takaji Matsumoto, Osamu Ogata, Yasunori Ino, Kunimori Aoki, Shigeru Tanaka, Kenya Ishida, Tohru Kobayashi, Noboru Sayo, and Takao Saito

Takasago International Corporation, Corporate Research and Development Division, 4-11, Nishiyawata 1-chome, Hiratsuka City, Kanagawa 254-0073, Japan

Supporting Information

ABSTRACT: A ruthenium catalyst for the reduction of esters by hydrogenation has been developed. Processes for the hydrogenation of esters have also been developed for (*R*)-1,2-propanediol and 2-(*l*-menthoxy)ethanol. The catalyst shows good catalytic activity for the hydrogenation of esters in methanol. Methyl lactate was reduced at 30 °C and gave turnover numbers (TON) up to 4000. The optical purity of the (*R*)-1,2-propanediol made by the hydrogenation of methyl (*R*)-lactate was higher than that via the asymmetric hydrogenation of hydroxyacetone. A hydrogenation process to replace the lithium aluminum hydride (LAH) reduction used in the production of 2-(*l*-menthoxy)ethanol was developed.

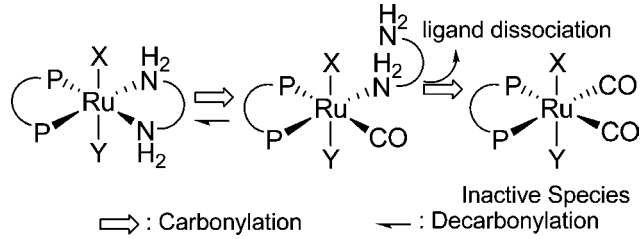
INTRODUCTION

Hydrogenation and hydride reduction are used for industrial scale ester reductions.[1] Hydrogenation reductions, employing a heterogeneous catalyst at high temperature and high pressure are used in the manufacture of structurally simple chemicals such as fatty alcohols.[1a,b] On the other hand, hydride reductions are used in pharmaceutical processes that form more structurally complex compounds.[1c] While hydride reagents are versatile,[2] their hazardous nature, complex postreaction workup procedures, and high level of residual waste are matters of concern in industrial operations.[1c] Replacing hydride reductions with hydrogenations enables companies involved in pharmaceutical intermediate production, which have expertise in hydrogenation reactions, to implement simple and convenient processes. For this purpose, catalysts which work under mild conditions would have significant industrial advantages. Herein we describe a catalyst for the hydrogenation of esters and its use in the production of (*R*)-1,2-propanediol and 2-(*l*-menthoxy)ethanol.

RESULT AND DISCUSSION

Ru-MACHO: A Catalyst for the Hydrogenation of Esters. Catalytic hydrogenation reductions of esters under relatively mild conditions have been reported by many research groups in recent decades.[3] Among them, catalytic $[RuCl_2(H_2NCH_2CH_2PPh_2)_2]$ with NaOMe showed excellent activity in THF.[3i] We have also reported that $[RuX^1X^2(dppp)(dpen)]$ (dppp: diphenylphosphinopropane, dpen: 1,2-diphenylethylenediamine, $X^1 = X^2 = Cl$, or $X^1 = H$, $X^2 = BH_4$), which possesses similar Ru/NH biofunctionality.[4] These complexes catalyze the hydrogenation of benzoic acid esters and optically active esters without loss of optical purity, however they have only moderate activities (TON ≈ 100 to 500). Therefore, we have focused our efforts toward the development of a more effective catalyst for industrial applications. We hypothesized that catalyst deactivation was caused by irreversible ligand dissociation and carbonylation (Scheme 1). $[RuCl_2(H_2NCH_2CH_2PPh_2)_2]$ was reported to catalyze the reduction of isopropyl benzoate more efficiently than methyl benzoate. The authors of that report reasoned that the methanol produced during the reduction of methyl benzoate deactivated the catalyst through carbonylation[3i]. Therefore, carbonylation resistant catalysts should show higher performance.

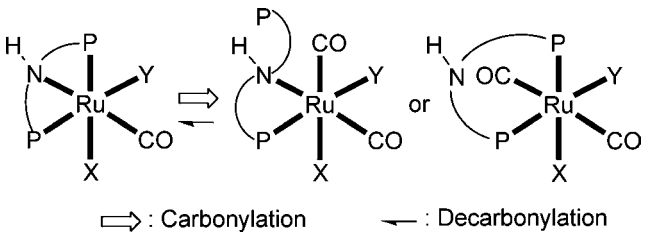
Scheme 1. Possible deactivation pathway



The lability of the second carbonyl ligand on ruthenium has also been reported.[5] In the example used, one of two carbonyl ligands on a ruthenium with a potentially tridentate ligand dissociated to form a monocarbonyl complex. Thus $[Ru(CO)(triphos\text{-}\kappa^3P)Cl_2]$ was synthesized from $[Ru(CO)_2(triphos\text{-}\kappa^2P)Cl_2]$ via decarbonylation. This result encouraged our synthesis of new [Ru(CO)(P^NH^P)] complexes. Carbonylation and decarbonylation of the complex should be reversible and any dicarbonyl species produced during reaction should be converted back into the original monocarbonyl species (Scheme 2). $[RuHCl(CO)(HN(CH_2CH_2PPh_2)_2)]$[6] was therefore synthesized to catalyze the hydrogenation of esters[7] more efficiently.

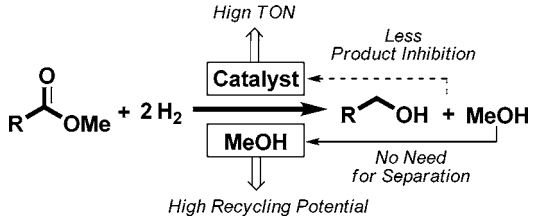
Received: August 26, 2011
Published: November 29, 2011

Scheme 2. Possible equilibrium between monocarbonyl and dicarbonyl species



The primary merit of the catalyst is that it shows good catalytic activity even in methanol, while $[RuCl_2(H_2NCH_2CH_2PPh_2)_2]$ gives almost no reaction in the solvent.[3i] This means that the catalyst is not deactivated by methanol[8a] and is less prone to alcohol inhibition in general.[8b] This property is advantageous for the reduction of methyl esters, because methanol is necessarily produced during methyl ester reduction. In addition, solvent recycling is much easier as it is unnecessary to separate byproduct methanol from the solvent (Scheme 3). In pharmaceutical processes, the use of solvents

Scheme 3. Advantages of $[RuHCl(CO)(HN(CH_2CH_2PPh_2)_2)]$



has high environmental impacts, and hence, improving solvent recycling is important.[9]

The complex is readily synthesized from $[RuHCl(CO)(PPh_3)_3]$ and $HN(CH_2CH_2PPh_2)_2$ and has been named Ru-MACHO because of its structure, which resembles a brawny athlete holding the ruthenium (Figure 1).

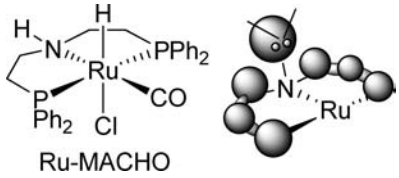
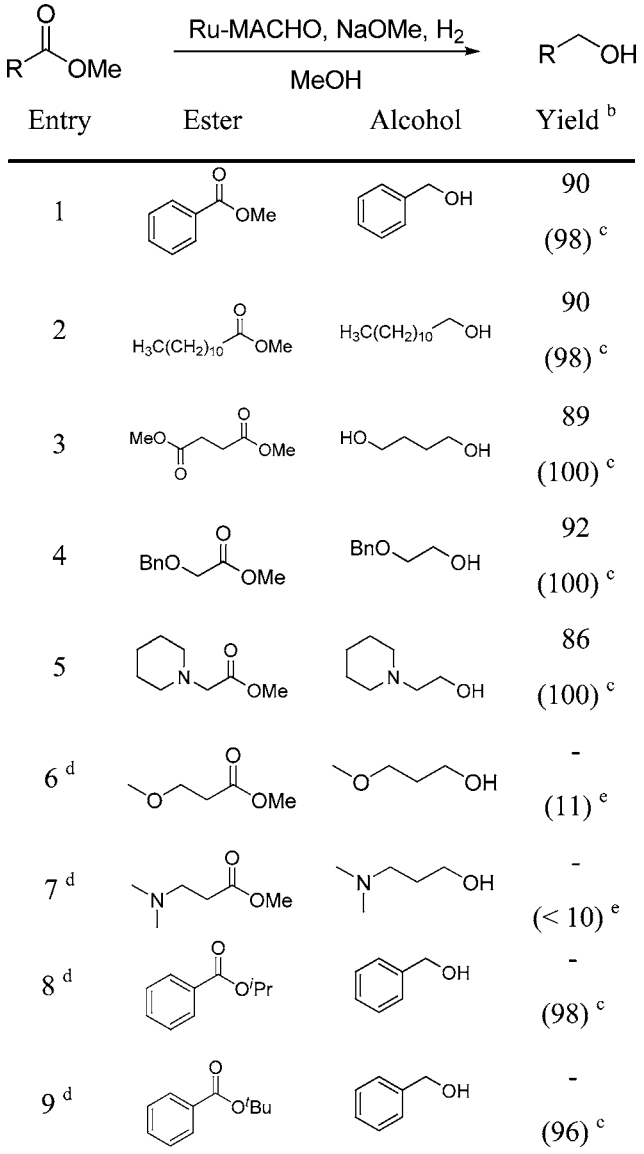


Figure 1. Ru-MACHO.

Hydrogenation of Esters with Ru-MACHO. The reduction of esters in methanol using Ru-MACHO is summarized in Table 1. Various kinds of esters were reduced with good conversion and selectivity in the presence of NaOMe (entries 1−5, 8, and 9). Aromatic and alkanoic acid methyl esters were successfully reduced (entries 1 and 2). The reduction of a diester (entry 3) using 0.1 mol % of the complex (0.05 mol % per ester group) was also completed with the diol produced in good yield. Oxygen- and nitrogen-containing functional groups at the α-position of ester groups did not impact the activity (entries 4 and 5), however substrates with those groups at β-position gave low yield with decomposition of substrates

Table 1. Hydrogenation of esters in methanol [a]



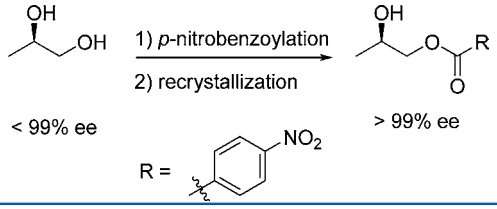
[a]Standard reaction conditions: substrate (200 mmol), Ru-MACHO (0.2 mmol), NaOMe (28% in MeOH, 20.0 mmol), MeOH (160 mL), H_2 (5 MPa), 100 °C, 16 h. [b]Isolated yield after distillation. [c]GC area %. [d]Substrate (10 mmol), Ru-MACHO (0.01 mmol), NaOMe (28% in MeOH, 1.0 mmol), MeOH (8 mL), H_2 (5 MPa), 100 °C, 16 h. [e]Yield based on ^{1}H NMR (internal standard; 2-methoxynaphthalene)

(entries 6 and 7). ^{i}Pr and ^{t}Bu esters also gave the corresponding alcohol in good yield (entries 8 and 9).

(*R*)-1,2-Propanediol Production with Ru-MACHO. To assess potential industrial applications of the catalyst, we first focused on the reduction of methyl lactate. Nonracemic 1,2-propanediol is a useful chiral building block for pharmaceuticals,[10] and has been produced via the asymmetric hydrogenation of hydroxyacetone since 1992 at Takasago.[11] Ru-SEGPHOS complex is a good catalyst for this reaction. The TON is up to 10,000, and the optical purity of the product is 98.5% ee. However, products with an ee greater than 99% can be required as pharmaceutical intermediates. The optical purity can be improved by recrystallization after *p*-nitrobenzoylation (Scheme 4).[11a] In this process, additional steps (*p*-nitorobenzoylation,

dx.doi.org/10.1021/op200234j | Org. ProcessRes. Dev. 2012, 16, 166−171

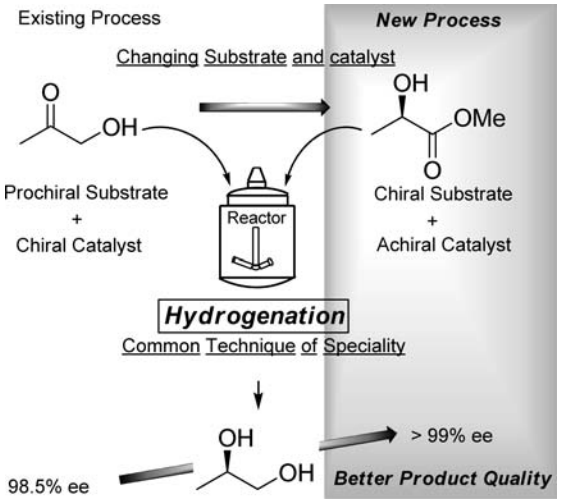
Scheme 4. Process for increasing optical purity of 1,2-propanediol



recrystallization) are required to obtain 1,2-propanediol with the required ee.

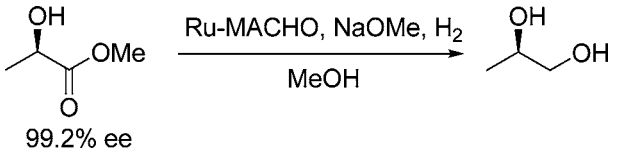
A better solution for us would be to catalyze the hydrogenation of methyl lactate, which starts at >99% ee, without the decrease in optical purity (Scheme 5). The shorter process could reduce energy, lead-time, and cost.

Scheme 5. Comparison of 1,2-propanediol processes



Our research indicated that reaction temperature is important in the optical purity (Table 2). The optical purity

Table 2. Hydrogenation of methyl (*R*)-lactate



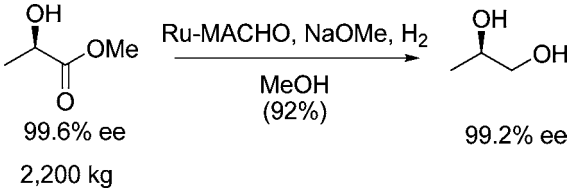
entry	S/C	temp.	ester[c]	diol[c] (yield)[d]	ee
1[a]	1000	80	<1	99 (−)	35.9
2[a]	1000	40	2	98 (−)	98.6
3[b]	4000	30	−	− (87)	98.6

[a]Reaction conditions: Substrate (10 mmol), Ru-MACHO (0.01 mmol), NaOMe (2 M in MeOH, 0.5 mmol), MeOH (5.5 mL), H_2 (5 MPa), 16 h. [b]Reaction conditions: Substrate (48 mmol), Ru-MACHO (0.012 mmol), NaOMe (2 M in MeOH, 0.96 mmol), MeOH (5 mL), H_2 (4 to 6 MPa), 24 h. [c]GC area %. [d]Isolated yield after silica gel column chromatography.

decreased from 99.2% ee to 35.9% ee at 80 °C (entry 1), but the loss of optical purity was less than 1% ee at 40 °C (entry 2). Even at a substrate/catalyst molar ratio (S/C) of 4000 at 30 °C, Ru-MACHO afforded a good yield of 1,2-propanediol with a loss of less than 1% ee (entry 3).

A large-scale methyl lactate hydrogenation was carried out with 0.05 mol % of Ru-MACHO on a multiton scale per batch (Scheme 6). After distillation, 1477 kg of (*R*)-1,2-propanediol was

Scheme 6. Large-scale hydrogenation of methyl (*R*)-lactate [a]

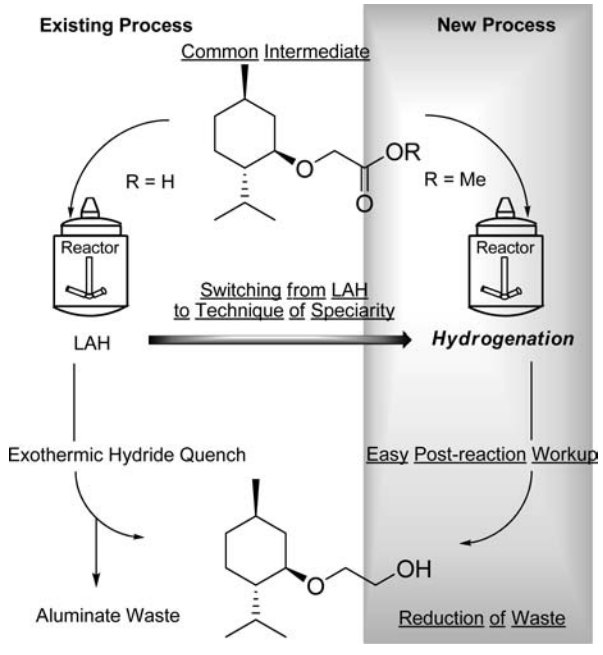


[a]Reaction conditions: substrate (2200 kg, 21,133 mol), Ru-MACHO (6.4 kg, 10.6 mol), NaOMe (28% in MeOH, 51.0 kg, 256.2 mol), MeOH (6369.2 kg), H_2 (4.0 to 4.2 MPa), 26 to 28 °C, 12 h.

produced with 99.2% ee from 2200 kg of methyl (*R*)-lactate with 99.6% ee.

2-(*l*-Menthoxy)ethanol Production with Ru-MACHO. 2-(*l*-Menthoxy)ethanol is a cooling agent.[12] It has a mild odor and a longer-lasting cooling action than menthol. The reduction of *l*-menthoxyacetic acid with LAH to produce 2-(*l*-menthoxy)-ethanol has been reported by Takasago.[13] However, large-scale LAH reductions are troublesome, particularly because of the exothermic postreaction hydride quench step. Using a Ru-MACHO-catalyzed hydrogenation reduction would eliminate these issues. The reaction would allow the use of a common intermediate, *l*-menthoxyacetic acid (after methyl esterification), and would have the additional benefits of employing this hydrogenation technique with its simple methodology and reduction of waste (Scheme 7).

Scheme 7. Comparison of 2-(*l*-menthoxy)ethanol processes

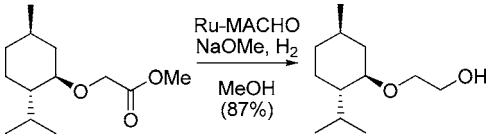


Ru-MACHO showed good catalytic activity for the reduction of methyl menthoxyacetate. The reaction was completed in 5 h at 80 °C with a S/C ratio of 2000. 2-(*l*-Menthoxy)ethanol was

dx.doi.org/10.1021/op200234j | Org. ProcessRes. Dev. 2012, 16, 166−171

obtained in 87% yield after distillation without exothermic postreaction hydride quench (Scheme 8).

Scheme 8. Hydrogenation of methyl *l*-menthoxyacetate [a]



[a]Reaction conditions: Substrate (160 mmol), Ru-MACHO (0.08 mmol), NaOMe (28% in MeOH, 1.55 g, 8 mmol), MeOH (73.2 mL), H_2 (4.5 MPa), 80 °C, 5 h.

CONCLUSIONS

This study describes a catalyst for the hydrogenation of esters, Ru-MACHO, and its utility in the production of (*R*)-1,2-propanediol and 2-(*l*-menthoxy)ethanol. The most notable feature of the catalyst is its high catalytic activity in methanol. For the production of (*R*)-1,2-propanediol, using Ru-MACHO results in a better quality product. The optical purity was 99.2% ee compared with less than 99% ee made via the asymmetric hydrogenation of hydroxyacetone. Ru-MACHO produced 2-(*l*-menthoxy)ethanol in satisfactory yield via hydrogenation without an undesirable exothermic, postreaction, hydride quench. The Ru-MACHO catalyst enables us to take advantage of existing hydrogenation expertise for the reduction of esters and develop alternative processes. Ru-MACHO is commercially available from Strem Chemicals and Sigma Aldrich.

EXPERIMENTAL SECTION

General Information. All reactions and manipulations were conducted under a nitrogen atmosphere in commercial solvents unless otherwise noted. NMR spectra were obtained on Varian Mercury Plus 300 spectrometer. NMR chemical shifts are reported in ppm relative to $CHCl_3$ (7.26 ppm for ^1H, and 77.0 ppm for ^{13}C), DMF (2.91 ppm for ^1H), and H_3PO_4 (0 ppm for ^{31}P as an external reference). Optical rotations were obtained on a JASCO P-1020 polarimeter. Mass spectra were recorded on a SHIMADZU LCMS-IT-TOF instrument.

Synthesis of Ru-MACHO. Under a N_2 atmosphere, toluene (183 kg), $HCl{\cdot}HN(CH_2CH_2PPh_2)_2$[14] (42 kg, 87.9 mol), water (42 kg), and NaOH (10.5 kg, 262.5 mol) were added to a stainless steel vessel. The mixture was stirred at 44 °C for 15 min. The two phases were separated, and the organic layer was washed with water (2 × 42 kg). The organic layer was concentrated to recover 74 kg of toluene. $[RuHCl(CO)(PPh_3)_3]$[15] (72 kg, 75.6 mol) in toluene (111 kg) was added to the solution. The mixture was stirred at reflux for 2 h, then cooled to 40 °C, and stirred for an additional 1.7 h. The resulting precipitate was filtered, washed with toluene (3 × 72 kg), and dried in vacuo to produce Ru-MACHO (38.8 kg, 63.9 mol, 85% based on $[RuHCl(CO)(PPh_3)_3]$) as a pale-yellow solid. Ru-MACHO was obtained as a mixture of the two possible isomers. ^1H NMR (300 MHz, DMF-d_7) δ: −15.01 (t, J = 19.8 Hz, 0.6H), −14.30 (t, J = 20.7 Hz, 0.4H), 2.20−3.78 (m, 8H), 4.39 (br, 0.6H), 5.58 (brt, J = 11.4 Hz, 0.4H), 7.08−7.60 (m, 12H), 7.65−8.20 (m, 8H); ^{31}P NMR (121 MHz, DMF-d_7) δ: 53.7 and 57.0. MS (ESI, m/z) calculated for $C_{29}H_{30}NOP_2Ru$ ($[M - Cl]^+$) 572.0846, found 572.0829; mp: 308 °C (dec).

General Procedure for Hydrogenation of Methyl Esters in Methanol Summarized in Table 1 (entries 1−5). Ru-MACHO (121.4 mg, 0.2 mmol) was placed in a 1000-mL stainless steel autoclave equipped with a mechanical stirrer. The atmosphere was replaced with nitrogen gas, and then MeOH (160 mL), substrate (200 mmol), and NaOMe (28% in MeOH, 3.86 mL, 20 mmol) were added. The vessel was purged three times with hydrogen gas (0.5 MPa) and pressurized with hydrogen (5 MPa). The mixture was stirred at 100 °C for 16 h, cooled to 25 °C, and then the hydrogen gas released. The mixture was analyzed by GC, concentrated in vacuo, and the residue was distilled.

Entry 1: 19.5 g (180.3 mmol, 90%) of benzyl alcohol obtained as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.81 (br s, 1H), 4.67 (s, 2H), 7.20−7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 64.6, 126.8, 127.3, 128.3, 140.7. bp: 90 °C (14 mmHg)

Entry 2: 33.6 g (180.3 mmol, 90%) of dodecan-1-ol obtained as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.88 (t, J = 6.8 Hz, 3H), 1.20−1.40 (m, 18H), 1.50−1.60 (m, 2H), 3.64 (t, J = 6.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 22.6, 25.7, 29.3, 29.4, 29.6, 29.6, 31.9, 32.7, 62.8. bp: 108 °C (2.0 mmHg)

Entry 3: 16.0 g (177.5 mmol, 89%) of 1,4-butanediol obtained as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.60−1.76 (m, 4H), 2.40−2.60 (m, 2H), 3.60−3.80 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 29.7, 62.4. bp: 88 °C (1.0 mmHg)

Entry 4: 28.1 g (184.6 mmol, 92%) of 2-(benzyloxy)ethanol obtained as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.90 (br s, 1H), 3.56−3.61 (m, 2H), 3.72−3.77 (m, 2H), 4.55 (s, 2H), 7.28−7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 61.4, 71.3, 72.9, 127.4, 127.5, 128.1, 137.8. bp: 85 °C (0.3 mmHg)

Entry 5: 22.2 g (171.8 mmol, 86%) of piperidine ethanol obtained as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.36−1.52 (m, 2H), 1.52−1.70 (m, 4H), 2.32−2.58 (m, 6H), 2.58−3.20 (br, 1H), 3.59 (t, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 24.0, 25.6, 54.3, 57.7, 60.3. bp: 78 °C (8.0 mmHg)

General Procedure for Hydrogenation of Methyl Esters in Methanol Summarized in Table 1 (entries 6−9). Ru-MACHO (6.1 mg, 0.01 mmol) was placed in a 100-mL stainless steel autoclave equipped with a Teflon-coated stir bar. The atmosphere was replaced with nitrogen gas, and then MeOH (8 mL), substrate (10 mmol), and NaOMe (28% in MeOH, 193 μL, 1 mmol) were added. The vessel was purged three times with hydrogen gas (0.5 MPa) and pressurized with hydrogen (5 MPa). The mixture was stirred at 100 °C for 16 h and cooled to 25 °C, and the excess hydrogen gas was released. The mixture was analyzed by ^1H NMR or GC. See Supporting Information.

GC Conditions for Reactions in Table 1. Neutra Bond-1 (df = 0.40 μm, 0.25 mm i.d. × 30 m, GL-Sciences), Carrier gas: helium, Injection temp.: 200 °C, Detector temp.: 280 °C, Oven: 40 °C → 100 °C (5 °C/min)−100 °C (5 min hold) → 280 °C (10 °C/min)−280 °C (5 min hold).

General Procedure for Hydrogenation of Methyl (*R*)-Lactate Summarized in Table 2. Ru-MACHO was placed in a stainless steel autoclave equipped with a Teflon-coated stir bar. The atmosphere was replaced with nitrogen gas, followed by the addition of MeOH, methyl (*R*)-lactate (99.2% ee), and NaOMe (2 M in MeOH). The autoclave was purged three times with hydrogen gas (0.5 MPa) and pressurized with hydrogen (5 MPa). The mixture was stirred and cooled to 25 °C, and the excess hydrogen gas was released.

dx.doi.org/10.1021/op200234j | *Org. ProcessRes. Dev.* 2012, 16, 166−171

GC Conditions. For conversion: Inert Cap Pure-Wax (df = 0.25 μm, 0.25 mm i.d. × 30 m), Carrier gas: helium, Injection temperature: 250 °C, Detector temperature: 280 °C, Oven program: 60 to 250 °C (10 °C/min) to 250 °C (1 min hold). For product ee (analyzed after acetonization): CP-Chirasil-DEX CB (df = 0.25 μm, 0.25 mm i.d. × 25 m), Carrier gas: helium, Injection temperature: 250 °C, Detector temperature: 250 °C, Oven program: 60 °C (30 min). Acetonization procedure: Amberlyst-15 (~1 mg) was added to a solution of the diol (10 mg) in acetone (1 mL). The mixture was stirred at room temperature for 1 h. The reaction mixture was analyzed directly.

Entries 1 and 2. The reaction mixture was analyzed by GC.

Entry 3. The mixture was concentrated in vacuo. The residual oil was purified by silica gel column chromatography ($CHCl_3$/MeOH = 20/1 to 10/1). The diol was obtained as a colorless oil (3.19 g, 41.9 mmol, 87%, 98.6% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.16 (d, J = 6.3 Hz, 3H), 2.50−2.66 (br, 2H), 3.39 (dd, J = 7.8, 11.1 Hz, 1H), 3.62 (dd, J = 3.0, 11.1 Hz, 1H), 3.84−3.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.6, 67.8, 68.3.

Large-Scale Hydrogenation of Methyl (*R*)-Lactate in Scheme 6. Methyl (*R*)-lactate (2200.0 kg, 21,133 mol, 99.6% ee) and MeOH (2,384.6 kg) were added to a 14,000-L stainless steel autoclave equipped with a mechanical stirrer. NaOMe (28% in MeOH, 51.0 kg, 256.2 mol) was added to the mixture, and the input line was washed with MeOH (160 kg). A suspension of Ru-MACHO (6.4 kg, 10.6 mol) in MeOH (320 kg) was added to the mixture, and the input line was washed with MeOH (320 kg). The atmosphere was replaced with hydrogen gas. The vessel was pressurized with hydrogen (4 MPa) and stirred for 12 h at 27 °C, and the excess hydrogen gas was released. The mixture was transferred to a 10,000-L stainless steel vessel, and the transfer line was washed with MeOH (160 kg) and concentrated in vacuo. The residue was purified by distillation. The diol was obtained as a colorless oil (1477.0 kg, 19,410 mol, 92%, 99.2% ee). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.15 (d, J = 6.3 Hz, 3H), 2.75 (s, 2H), 3.38 (dd, J = 7.8, 11.1 Hz, 1H), 3.61 (dd, J = 3.0, 11.1 Hz, 1H), 3.83−3.96 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.5, 67.5, 68.1; bp: 45 °C (0.15 mmHg); $[\alpha]^{20.3}_D$ −30.3 (c 0.99, $CHCl_3$), [lit. $[\alpha]^{24.4}_D$ −28.6 ($CHCl_3$)].[16]

Reduction of Methyl *l*-Menthoxyacetate in Scheme 8. Ru-MACHO (48.6 mg, 0.08 mmol) was placed in a 200-mL stainless steel autoclave equipped with a mechanical stirrer. The atmosphere was replaced with nitrogen gas, followed by the addition of MeOH (73.2 mL), methyl *l*-menthoxyacetate[13,17] (36.6 g, 160 mmol), and NaOMe (28% in MeOH, 1.55 g, 8 mmol). The vessel was purged three times with hydrogen gas (0.5 MPa) and was pressurized with hydrogen (4.5 MPa). The mixture was stirred at 80 °C for 5 h and cooled to 25 °C, and the excess hydrogen gas was purged. The reaction mixture was concentrated in vacuo. Toluene (73 mL) was added to the residue, and the mixture was washed with water (3 × 74 mL) and concentrated in vacuo. The residue was purified by distillation to produce 2-(*l*-menthoxy)ethanol (27.9 g, 139.3 mmol, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.78 (d, J = 7.2 Hz, 3H), 0.80−1.10 (m, 9H), 1.18−1.30 (m, 1H), 1.30−1.45 (m, 1H), 1.57 −1.70 (m, 2H), 1.85 (br s, 1H), 2.04 −2.14 (m, 1H), 2.14 −2.28 (m, 1H), 3.38 (dt, J = 3.9, 10.5 Hz, 1H), 3.36 −3.48 (m, 1H), 3.63 −3.80 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.1, 20.8, 22.2, 23.2, 25.6, 31.4, 34.4, 40.3, 48.1, 62.1, 69.4, 79.5; bp: 85 °C (1.5 mmHg) ; $[\alpha]^{20.3}_D$ −91.1 (c 1.03, $CHCl_3$)

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR spectra, ^{13}C NMR spectra, and GC analytical data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Author for correspondence. E-mail: wataru_kuriyama@takasago.com. Telephone: +81-463-25-2187.

■ REFERENCES

(1) (a) Rieke, R. D.; Thakur, D. S.; Roberts, B. D.; White, G. T. *J. Am. Oil Chem. Soc.* **1997**, *74*, 333. (b) Rieke, R. D.; Thakur, D. S.; Roberts, B. D.; White, G. T. *J. Am. Oil Chem. Soc.* **1997**, *74*, 341. (c) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337.

(2) Seyden-Penne, J. *Reductions by the Alumino- and Borohydrides in Organic Synthesis*; VCH Publishers: New York, 1991.

(3) Examples of reactions below 5 MPa hydrogen pressure or 100 °C or both: (a) Grey, R. A.; Pez, G. P.; Wallo, A.; Corsi, J. *J. Chem. Soc., Chem. Commun.* **1980**, 783. (b) Grey, R. A.; Pez, G. P.; Wallo, A. *J. Am. Chem. Soc.* **1981**, *103*, 7536. (c) Teunissen, H. T.; Elsevier, C. J. *Chem. Commun.* **1997**, 667. (d) Teunissen, H. T.; Elsevier, C. J. *Chem. Commun.* **1998**, 1367. (e) Nomura, K.; Ogura, H.; Imanishi, Y. *J. Mol. Catal. A: Chem.* **2001**, *166*, 345. (f) Studer, M.; Burkhardt, S.; Blaser, H.-U. *Adv. Synth. Catal.* **2001**, *343*, 802. (g) Zhang, J.; Leitus, G.; Ben-David, Y.; Milstein, D. *Angew. Chem., Int. Ed.* **2006**, *45*, 1113. (h) Boardman, B.; Hanton, M. J.; van Rensburg, H.; Tooze, R. P. *Chem. Commun.* **2006**, 2289. (i) Saudan, L. A.; Saudan, C. M.; Debieux, C; Wyss, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 7473. (j) Clarke, M. L.; Díaz-Valenzuela, M. B.; Slawin, A. M. Z. *Organometallics* **2007**, *26*, 16. (k) Saudan, L.; Saudan, C. (Firmenich SA). PCT Int. Appl. WO/2008/065588 A1, 2008. (l) Ito, M.; Ikariya, T. *J. Synth. Org. Chem., Jpn.* **2008**, *66*, 1042. (m) Takebayashi, S.; Bergens, S. H. *Organometallics* **2009**, *28*, 2349. (n) Kuriyama, W.; Ino, Y.; Ogata, O.; Sayo, N.; Saito, T. *Adv. Synth. Catal.* **2010**, *352*, 92. (o) Fogler, E.; Balaraman, E.; Ben-David, Y.; Leitus, G.; Shimon, L. J. W.; Milstein, D. *Organometallics* **2011**, *30*, 3826.

(4) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40.

(5) Sarmah, B. J.; Dutta, D. K. *J. Organomet. Chem.* **2010**, *695*, 781.

(6) (a) Kuriyama, W.; Matsumoto, T.; Ino, Y.; Ogata, O. (Takasago International Corporation). PCT Int. Appl. WO/2011/048727 A1, 2011. (b) Similar [RuHCl(CO)[(HN($CH_2CH_2P^iPr_2$)$_2$] complex has been reported to catalyze dehydrogenation of alcohols: Bertoli, M.; Choualeb, A.; Lough, A. J.; Moore, B.; Spasyuk, D.; Gusev, D. G. *Organometallics* **2011**, *30*, 3479.

(7) Catalytic hydrogenation of esters with pincer ruthenium carbonyl complex has been reported by Milstein et al. See refs 3g and 3o.

(8) Negative effects of methanol and product alcohol on ester hydrogenation with Ru/NH bifunctional catalysts were reported. (a) Catalyst deactivation by methanol was proposed, and no reaction in methanol was reported in ref 3i for [$RuCl_2(H_2NCH_2CH_2PPh_2)_2$]. (b) Alcohol (product) inhibition for hydrogenation of methyl benzoate at room temperature under 4 atm of H_2 with *trans*-[Ru((*R*)-BINAP)(H_2)(en)] was reported in ref 3m.

(9) Butters, M.; Catterick, D.; Craig, A.; Curzons, A.; Dale, D.; Gillmore, A.; Green, S. P.; Marziano, I.; Sherlock, J.-P.; White, W. *Chem. Rev.* **2006**, *106*, 3002 and references cited therein.

(10) Examples of pharmaceutical processes using nonracemic 1,2-propanediol or its derivatives. (a) Levofloxacine : Fujiwara, T.; Ebata, T. (Daiichi Seiyaku Co., Ltd.). U.S. Pat. 5,312,999, 1994. (b) Tenofovir: Ripin, D. H. B.; Teager, D. S.; Fortunak, J.; Basha, S. M.; Bivins, N.; Boddy, C. N.; Byrn, S.; Catlin, K. K.; Houghton, S. R.;

Jagadeesh, S. T.; Kumar, K. A.; Melton, J.; Muneer, S.; Rao, L. N.; Rao, R. V.; Ray, P. C.; Reddy, N. G.; Reddy, R. M.; Shekar, K. C.; Silverton, T.; Smith, D. T.; Stringham, R. W.; Subbaraju., G. V.; Talley, F.; Williams, A. *Org. Process Res. Dev.* **2010**, *14*, 1194. (c) MK-0941: Yoshikawa, N.; Xu, F.; Arredondo, J. D.; Itoh, T. *Org. Process Res. Dev.* **2011**, *15*, 824.

(11) (a) Kumobayashi, H.; Sayo, N.; Akutagawa, S.; Sakaguchi, T.; Tsuruta, H. *J. Chem. Soc. Jpn., Chem. Ind. Chem.* **1997**, 835. (b) Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264. (c) Sumi, K.; Kumobayashi, H. *Top. Organomet. Chem.* **2004**, *6*, 63.

(12) For menthol and related cooling compounds see: Eccles, R. *J. Pharm. Pharmacol.* **1994**, *46*, 618.

(13) Green, C. B.; Nakatsu, T.; Ishizaki, T.; Lupo, A. T. (Takasago International Corporation). U.S. Pat. Appl. 2002/0198412 A1, 2002.

(14) Nuzzo, R. G.; Haynie, S. L.; Wilson, M. E.; Whitesides, G. M. *J. Org. Chem.* **1981**, *46*, 2861.

(15) Ahmad, N.; Levison, J. J.; Robinson, S. D.; Uttley, M. F. *Inorg. Synth.* **1974**, *15*, 45.

(16) Shieh, N; Price, C. C. *J. Org. Chem.* **1959**, *24*, 1169.

(17) Soper, Q. F.; Whitehead, C. W.; Behrens, O. K.; Corse, J. J.; Jones, R. G. *J. Am. Chem. Soc.* **1948**, *70*, 2849.