Highly Efficient Chemoselective Hydrogenolysis of Epoxides Catalyzed by a (η^5-$C_5(CH_3)_5$)Ru Complex Bearing a 2-(Diphenylphosphino)ethylamine Ligand

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Received June 24, 2003

*Summary: Terminal epoxides are hydrogenolyzed to give secondary alcohols with high regioselectivity using the ternary catalyst system of Cp*RuCl(cod)−2-(diphenylphosphino)ethylamine (**1a**)−KOH (Cp* = η^5-$C_5(CH_3)_5$, cod = 1,5-cyclooctadiene) in 2-propanol under mild conditions.*

Recently much attention has been given to the design of transition-metal-based molecular catalysts with a “metal/NH bifunctionality”,[1,2] in which an amino proton and a metal hydride are concertedly transferred to C═O or C═N double bonds via pericyclic transition states.[3−5] The most striking aspect in these catalyses is that the Brønsted acidic amino proton and the Brønsted basic metal hydride are cooperatively activating the substrate, which is not necessarily bonded directly to the central metal. We have recently reported that a ternary catalyst system with a unique Brønsted acid−base function, Cp*RuCl(cod)−2-(dimethylamino)ethylamine (**1b**)−KOH, effects the hydrogenation of ketones in 2-propanol, in which 2-propanol participates in the heterolytic cleavage of H_2 possibly through the formation of a hydrogen-bonding network.[6] We now furtherextend this unique Brønsted acid−base catalyst system to the reductive opening reaction of epoxides with H_2, giving alcohols. Although hydrogenolysis of epoxides with heterogeneous catalysts such as modified Raney Ni or Pd/C has been extensively investigated as an industrial process,[7] there have been few reports on the selective hydrogenolysis of epoxides promoted by homogeneous catalysts.[8,9] We describe here that the Cp*Ru^{II}-based catalyst system including 2-(diphenylphosphino)ethylamine (**1a**) in place of **1b** as a primary amine ligand effects the selective hydrogenolysis of epoxides, leading to secondary alcohols.

Screening experiments using several amine ligands in the reaction of styrene oxide with H_2 revealed that the hydrogenolysis proceeds smoothly under 10 atm of H_2 at 30 °C in 2-propanol which contains a ternary catalyst system of Cp*RuCl(cod), **1a**, and KOH (epoxide: Ru:amine:KOH = 100:1:1.5:1) to give a mixture of branch and linear alcohols with an 89:11 molar ratio in 63% yield after 2 h (Scheme 1, entry 1 in Table 1). The reaction is delicately influenced by the ligand structures and the reaction conditions. When the primary amino group in **1a** was changed to a secondary (**1c**) or tertiary amino group (**1d**), a significant drop in the catalytic activity, but with a slight improvement in the regioselectivity, was observed (entries 3 and 4). 1,2-Bis(diphenylphosphino)ethane, in which the primary amino group in **1a** is replaced with a diphenylphosphino group, completely suppressed the reaction under the conditions described above. Furthermore, the use of an equimolar mixture of benzylamine and triphenylphosphine in place

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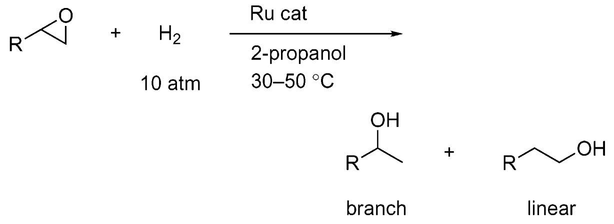
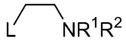
Scheme 1



R = Ph, $PhCH_2$, n-C_nH_{2n+1}, $CH_2{=}CH(CH_2)_2$, $CH_2{=}CHCH_2OCH_2$, $PhOCH_2$, i-$C_3H_7OCH_2$

Ru cat: Cp*RuCl(cod)−amine−KOH

amine ligand :



1a: L = Ph_2P, R^1,R^2 = H

1b: L = $(CH_3)_2N$, R^1,R^2 = H

1c: L = Ph_2P, R^1 = H, R^2 = CH_3

1d: L = Ph_2P, R^1,R^2 = CH_3

Table 1. Hydrogenolysis of Terminal Epoxides Catalyzed by Cp*RuCl(cod)−Amine Ligand−KOH under 10 atm of H_2 in 2-Propanol[a]

entry	R	amine ligand	temp, °C	time, h	yield, %	b:l[b]
1	Ph	**1a**	30	2	63	89:11
2	Ph	**1b**	30	2	<1	
3	Ph	**1c**	30	2	15	>99:1
4	Ph	**1d**	30	2	5	>99:1
5	Ph	**1a**	50	1	79	89:11
6	Ph	**1a**	50	18	>99	89:11
7	$PhCH_2$	**1a**	50	16	>99	>99:1
8	n-C_4H_9	**1a**	50	15	90	>99:1
9	n-C_6H_{13}	**1a**	50	18	93	>99:1
10	n-C_8H_{17}	**1a**	50	18	>99	>99:1
11	$CH_2{=}CH(CH_2)_2$	**1a**	50	16	98	>99:1
12	$CH_2{=}CHCH_2OCH_2$	**1a**	50	18	>99	>99:1
13	$PhOCH_2$	**1a**	50	17	99	>99:1
14	i-$C_3H_7OCH_2$	**1a**	50	18	>99	>99:1

[a] Reaction conditions: epoxides:Ru:amine:KOH = 100:1:1.5:1; [epoxide] = 0.6 M in 2-propanol. [b] Branch/linear ratio determined by ^{1}H NMR.

of **1a** did not give any satisfactory result. 2-(Dimethylamino)ethylamine (**1b**), which is an effective ligand for the hydrogenation of ketones,[6] was almost inert in the present reaction (entry 2). These results clearly indicate that a P−N chelating ligand bearing an NH functionality is crucial for efficient hydrogenolysis of the epoxide. At higher temperature (50 °C), the reaction using **1a** rapidly proceeded to provide a satisfactory chemical yield without any change in the product distribution (entry 5).

A variety of terminal epoxides is efficiently convertible with the Cp*Ru^{II}-based catalyst bearing **1a** at 50 °C to the corresponding secondary alcohols preferentially in high yields, as listed in Table 1 (entries 6−14).[10,11] Alkenyl epoxides gave secondary alkenyl alcohols in quantitative yields without formation of saturated alcohols or epoxides (entries 11 and 12).[12] Terminal epoxides bearing another oxygen functionality on the side chain also undergo hydrogenolysis to afford the corresponding secondary alcohols in good yields (entries 12−14), indicating that groups next to the epoxide group do not interact with the metal center because of the coordinatively saturated nature of the Ru(II) complexes (vide infra). However, epoxides with more than one substituent are not susceptible to reductive ring opening under similar conditions.

2-Propanol is the solvent of choice for the present hydrogenolysis, as observed previously in the hydrogenation of ketones with the Cp*RuCl(cod)−**1b**−KOH catalyst system, in which 2-propanol may facilitate the heterolysis of molecular hydrogen via a hydrogen-bonding network.[6] The use of aprotic solvents such as acetonitrile, tetrahydrofuran, toluene, and CH_2Cl_2 resulted in low yields. It should be noted, however, that in the absence of H_2 styrene oxide was slowly converted in 2-propanol to the alcohols with concomitant formation of acetone (5% conversion after 2 h at 30 °C, branched (b):linear (l) = 89:11). These results suggest that 2-propanol serves not only as a promoter of the dihydrogen activation but also as a hydrogen source. Nevertheless, the pressurization of H_2 causes a significant improvement in the reaction rate. The isotope labeling experiments using D_2 and 2-propanol-d_8 provided a deeper insight into the reaction mechanism. The reaction of styrene oxide with D_2 (10 atm) in 2-propanol-d_8 at 50 °C for 16 h under otherwise identical conditions, as described in Table 1, gave a mixture of deuterated phenethyl alcohols quantitatively with a b:l ratio of 91:9. In these two isomeric products, the deuterium atoms were introduced at the hydroxy-bearing carbon (85−99% atom D) in addition to the β-carbon to the hydroxyl group (81−93% atom D). This result is consistent with rapid C−H bond activation at the hydroxy-bearing carbon of the product alcohols taking place after the hydrogenolysis of the C−O single bond of epoxides.[13]

Although the catalyst system based on Cp*RuCl(cod)−diamine **1b** provides excellent activity for H_2 activation with the aid of 2-propanol and for the reduction of carbonyl compounds but not of epoxides, Cp*RuCl(cod)−aminophosphine **1a** effects hydrogenation of both epoxides and carbonyls. The difference in the reactivity between **1a** and **1b** may be attributable to the electronic factor of these ligands. In fact, cationic Cp*Ru(CO) complexes **3a** and **3b**, which were readily

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(10) *Typical procedure for the hydrogenolysis of terminal epoxides:* a degassed solution of (2,3-epoxypropyl)benzene (427 mg, 3.18 mmol), **1a** (10.9 mg, 47.5 μmol), and KOH (1.8 mg 32.1 μmol) in 2-propanol (5.3 mL) was mixed with Cp*RuCl(cod) (12.1 mg, 31.8 μmol) that was placed in a 50 mL stainless steel autoclave. Hydrogen was introduced into the autoclave to 10 atm, and the reaction mixture was vigorously stirred at 50 °C for 16 h. After the hydrogen was carefully vented, the solvent was removed under reduced pressure, and the residue was distilled to give 1-phenyl-2-propanol (430 mg, >99% yield).

(11) Separate experiments showed that Cp*RuCl[$Ph_2P(CH_2)_2NH_2$] (**4a**) could be obtained from Cp*RuCl(isoprene) and **1a** on the basis of the procedure reported by Kirchner and co-workers[19] (see the Supporting Information). Since this preformed catalyst reduces the epoxide in 2-propanol containing KOH at an almost identical rate in comparison to the catalyst system, Cp*RuCl(cod)−**1a**−KOH, the ternary system was used here for experimental convenience. The details of the structures for a series of the aminophosphine complexes, including **4a**, will be reported separately.

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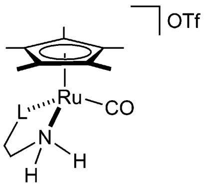
(13) A range of alcohols, labeled with deuterium at the hydroxy-bearing carbon, undergo rapid H−D scrambling in the presence of the same catalyst system: Ito, M.; Osaku, A.; Kitahara, S.; Hirakawa, M.; Ikariya, T. *Tetrahedron Lett.*, in press.



3a: L = Ph_2P
3b: L = $(CH_3)_2N$

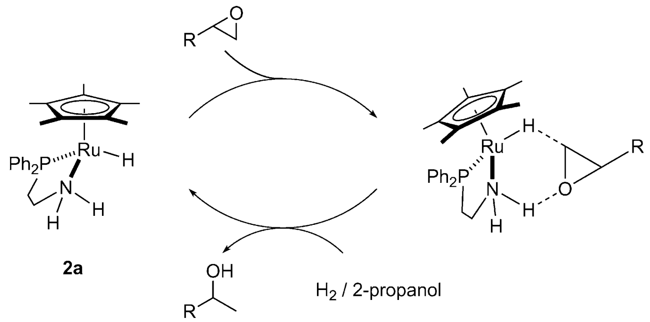


Figure 1. Conceivable catalytic cycle for the hydrogenolysis of terminal epoxides.

prepared from $[Cp^*Ru(CH_3CN)_3]OTf$ with **1a** and **1b** according to the procedure reported by Kirchner and coworkers,[14] show IR stretching vibrations at 1948 and 1931 cm^{-1}, respectively. These results may reflect the relatively electron deficient nature of the Ru center in a series of complexes with **1a**, compared to those with **1b**, due to the weaker σ-donating and stronger π-accepting abilities of the tertiary phosphino group.[15] Accordingly, the Brønsted acidity of the bonded NH_2 group of **1a** should be stronger than that of **1b**.[16] Therefore, epoxides may be smoothly reduced by $Cp^*RuH[Ph_2P(CH_2)_2NH_2]$ (**2a**) (Figure 1), which may be derived from Cp*RuCl(cod) and **1a** under the previously described reaction conditions.[17] It is conceivable that the hydride and proton of **2a** are transferred to the epoxides simultaneously via a six-membered transition state,[1,2] in which steric repulsion between the substituent of epoxides and **2a** becomes minimal, to produce secondary alcohols with a regeneration of **2a**. Recently, Morris and co-workers have clarified that an acidic amino proton and a basic hydride are involved in asymmetric hydrogenation of carbonyl compounds with Noyori-type hydrogenation catalysts.[2c−e]

In conclusion, we have found that the Cp*RuCl(cod)−**1a**−KOH combined system is an effective catalyst for hydrogenolysis of terminal epoxides. The present catalytic hydrogenolysis would provide a new alternative procedure for stoichiometric metal hydride reduction because of its unique chemoselectivity and regioselectivity. Our results may lead to the rational design of catalysts for the hydrogenation of a wide variety of other oxygen-containing polar functionalities, including ketals and carboxylic acid derivatives.[18]

Acknowledgment. We appreciate financial support from Taisho Pharmaceutical Co. Ltd. (M.I.) and from the Ministry of Education, Culture, Sports, Science and Technology of Japan (Nos. 12305057 and 14078209 “Reaction Control of Dynamic Complexes”). This work was partially supported by The 21 Century COE Program.

Supporting Information Available: Text giving experimental procedures for the preparation of the ligand **1c** and the complexes **3a**, **3b**, and **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM034006J

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(17) The reaction of **4a** with an equimolar amount of KOH in 2-propanol followed by evaporation of 2-propanol gave a brown-yellow powder. NMR analysis of this compound in THF-d_8 supported the formation of **2a**, although it could not be obtained in analytically pure form. ^1H NMR (THF-d_8): δ −10.6 (d, J = 40.3 Hz, 1H), 1.89 (d, J = 0.9 Hz, 15H), 2.25−2.33 (m, 2H), 3.00 (br s, 2H), 4.13 (br s, 2H), 7.02−7.53 (m, 8H), 8.13−8.18 (m, 2H). $^{13}C\{^1H\}$ NMR (THF-d_8): δ 11.2, 34.9 (d, J = 19.3 Hz), 45.5 (d, J = 9.7 Hz), 83.4 (d, J = 3.1 Hz), 126.7 (d, J = 9.2 Hz), 127.0 (d, J = 8.1 Hz), 128.3 (d, J = 10.7 Hz), 130.7 (d, J = 9.2 Hz), 131.0 (d, J = 11.2 Hz), 135.0 (d, J = 12.7 Hz), 142.5 (d, J = 21.3 Hz), 145.5 (d, J = 24.9 Hz). $^{31}P\{^1H\}$ NMR (THF-d_8): δ 79.4.

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