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Aminocyclopentadienyl Ruthenium Complexes as Racemization Catalysts for Dynamic Kinetic Resolution of Secondary Alcohols at Ambient Temperature

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Aminocyclopentadienyl ruthenium complexes, which can be used as room-temperature racemization catalysts with lipases in the dynamic kinetic resolution (DKR) of secondary alcohols, were synthesized from cyclopenta-2,4-dienimines, $Ru_3(CO)_{12}$, and $CHCl_3$: [2,3,4,5-Ph_4(η^5-C_4CNHR)]Ru-$(CO)_2Cl$ (**4**: R = *i*-Pr; **5**: R = *n*-Pr; **6**: R = *t*-Bu), [2,5-Me_2-3,4-Ph_2(η^5-C_4CNHR)]$Ru(CO)_2Cl$ (**7**: R = *i*-Pr; **8**: R = Ph), and [2,3,4,5-Ph_4(η^5-C_4CNHAr)]$Ru(CO)_2Cl$ (**9**: Ar = *p*-$NO_2C_6H_4$; **10**: Ar = *p*-ClC_6H_4; **11**: Ar = Ph; **12**: Ar = *p*-$OMeC_6H_4$; **13**: Ar = *p*-$NMe_2C_6H_4$). The tests in the racemization of (*S*)-4-phenyl-2-butanol showed that **7** is the most active catalyst, although the difference decreased in the DKR. Complex **4** was used in the DKR of various alcohols; at room temperature, not only simple alcohols but also functionalized ones such as allylic alcohols, alkynyl alcohols, diols, hydroxyl esters, and chlorohydrins were successfully transformed to chiral acetates. In mechanistic studies for the catalytic racemization, ruthenium hydride **14** appeared to be a key species. It was the major organometallic species in the racemization of (*S*)-1-phenylethanol with **4** and potassium *tert*-butoxide. In a separate experiment, (*S*)-1-phenylethanol was racemized catalytically by **14** in the presence of acetophenone.

Introduction

Developing efficient methods for asymmetric synthesis is essential to meet the increasing demand for enantiomerically pure compounds in pharmaceutical and agricultural industry. Asymmetric and catalytic transformations by chiral transition-metal complexes[1] or enzymes[2−4] have been developed for the efficient preparation of enantiomerically pure compounds. However, the resolution of racemic mixtures is still the most common way to prepare enantiomerically pure compounds on industrial scales.[2a,3] In particular, the kinetic resolution (KR) by enzyme catalysis has a long history that dates back to Pasteur's discovery; many enzymatic processes have been developed for hydrolysis of esters and for acylation of alcohols.[2,4] Rapidly developing biotechnologies, including direct evolution[5] and enzyme immobilization,[2b,6] will strengthen the potential of the enzymatic processes. The intrinsic nature of KR, however, limits the yield only to 50%; laborious separation of the product from the remaining substrate is needed.[7]

Thus, in situ racemization of the remaining substrate during KR, which is called dynamic kinetic resolution (DKR), is an attractive process to overcome the limitation of KR.[8] The substrates of DKR have been racemized thermally,[9] chemically,[10] biocatalytically,[11] or spontaneously.[12] Recently, the racemization catalyzed by metal

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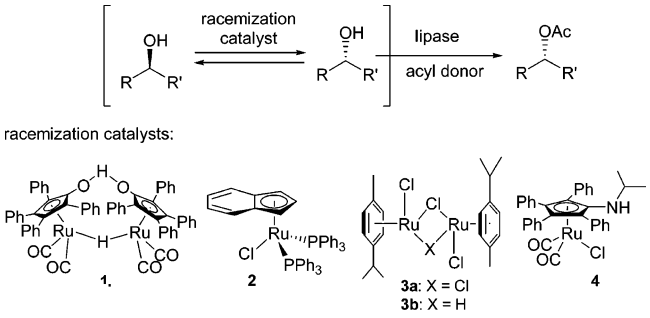
SCHEME 1



complexes has increased the potential of DKR.[13] Enzymatic acylation or hydrolysis has been successfully combined with the metal-catalyzed racemization for the DKR of alcohols,[14] allylic acetates,[15] and amines.[16] In the first example of the metal−enzyme combinations for DKR of alcohols, Williams et al. used a rhodium complex to transform racemic 1-phenylethanol into (*R*)-1-phenylethyl acetate in a moderate yield.[14n] Subsequently, Bäckvall et al. reported the use of a diruthenium complex (**1**),[14l] which greatly increased the yield and the optical purity of the product (Scheme 1). Soon after, we found that other ruthenium complexes,[14h,j] **2** and **3**, are also effective in the DKR of secondary alcohols.

The racemization catalysts have pros and cons. The complex **1** is commercially available and easy to handle.[17] However, it needs hydrogen mediators for the racemization that proceeds through transfer−hydrogenation reactions.[18] Without adding ketones as hydrogen mediators, the racemization can proceed, but the yield of DKR decreases significantly due to the formation of ketones through the dehydrogenation of alcohols.[14l] The use of **1** with alkenyl acetates as acyl donors also decreases the yield of DKR. Bäckvall et al. solved this problem by using *p*-chlorophenyl acetate as the acyl donor.[14l] Unreacted *p*-chlorophenyl acetate, however, frequently makes the separation of the DKR product difficult in the purification step. The indenyl ruthenium complex **2** and the η^6-arene ruthenium complexes **3** do not catalyze the dehydrogenation of alcohols to produce molecular hydrogen in significant amount;[14h,j] only catalytic amounts of ketones are produced. However, **2** and **3** need weak bases as additives.

To develop new processes to circumvent the formation of ketones as side products in the DKR with **1**, we used, instead of racemic alcohols, ketones and enol acetates as substrates with hydrogen donors under the conditions for the DKR with **1**.[19] Ketones were hydrogenated with 2,6-dimethylheptan-4-ol or molecular hydrogen and then the resulting alcohols successfully transformed into chiral esters. Meanwhile, enol acetates acted as acyl donors and as the precursors of ketones; thus, the separation problem caused by *p*-chlorophenyl acetate was solved.

Although the DKR with metal−enzyme combinations has shown attractive potentials for asymmetric synthesis, it is desirable to develop racemization catalysts that are active at the temperature low enough for the DKR with thermally labile enzymes.[20] Recently in a preliminary communication,[21] we have reported the synthesis of a new ruthenium complex (**4**) and its catalytic activity in the racemization of secondary alcohols at room temperature. The catalytic activity is compatible with isopropenyl acetate and the enzymatic acylation of alcohols to make possible the room-temperature DKR of secondary alcohols. Herein, we present a full account of this work, including the synthesis of the derivatives of **4**, the scope of our catalyst system, and mechanistic studies for the catalytic racemization.

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(20) Usually, the complex **1** is heated over 60 °C to provide a reasonable activity. The high activity of **4** at room temperature has been applied to the DKR of secondary alcohols with subtilisin, which is a thermally labile lipase, to produce (*S*)-acetates: Kim, M.-J.; Chung, Y.; Choi, Y. K.; Lee, H. K.; Kim, D.; Park, J. *J. Am. Chem. Soc.* **2003**, *125*, 11494.

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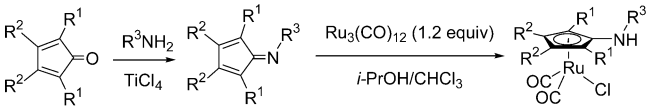
SCHEME 2. Synthesis of Aminocyclopentadienylruthenium Chloride Complexes



4: R^1= Ph, R^2= Ph, R^3= *i*-Pr
5: R^1= Ph, R^2= Ph, R^3= *n*-Pr
6: R^1= Ph, R^2= Ph, R^3= *t*-Bu
7: R^1= Me, R^2= Ph, R^3= *i*-Pr
8: R^1= Me, R^2= Ph, R^3= Ph
9: R^1= Ph, R^2= Ph, R^3= 4-nitrophenyl
10: R^1= Ph, R^2= Ph, R^3= 4-chlorophenyl
11: R^1= Ph, R^2= Ph, R^3= phenyl
12: R^1= Ph, R^2= Ph, R^3= 4-methoxyphenyl
13: R^1= Ph, R^2= Ph, R^3= 4-dimethylaminophenyl

TABLE 1. Catalytic Racemization of (*S*)-4-Phenyl-2-butanol under Various Conditions[a]

entry	catalyst	catalyst (mol %)	base (mol %)	ee[b] (%)
1	**4**	4.0	5.0	1.2
2	**4**	2.0	5.0	2.0
3	**4**	1.0	5.0	4.0
4	**4**	0.5	5.0	49.4
5	**4**	1.0	2.5	3.4
6	**4**	1.0	2.0	12.4
7	**4**	1.0	1.5	88.6
8	**4**	1.0	1.0	96.4

[a] (*S*)-4-Phenyl-2-butanol (>99% ee, 0.50 mmol) was added to a flask containing catalyst and potassium *tert*-butoxide dissolved in toluene (1.6 mL). [b] The % ee values were measured after 30 min by chiral HPLC (Chiralcel OD, Daicel).

Results and Discussion

Synthesis of the Ruthenium Complexes. The ruthenium complex **4** was synthesized from 2,3,4,5-tetraphenylcyclopentadienone through the imination with isopropylamine, followed by the complexation of the resulting imine with $Ru_3(CO)_{12}$ in the presence of chloroform.[21] We, then, improved the procedure simply by adding 2-propanol as an additive (Scheme 2). This simple modification gave several advantages over the original one, including saving $Ru_3(CO)_{12}$, shorter reaction times, and better yields. The modified method provided the derivatives **5**−**13** from the corresponding cyclopentadienones and amines. Notably, when 2-propanol was used as the solvent in the presence of ∼3−5 equiv of chloroform, **4** was precipitated as analytically pure microcrystals from the reaction mixture.

Catalytic Racemization. The ruthenium complexes **4**−**13** were tested on the catalytic racemization of (*S*)-1-phenylethanol. The activities of **4**−**13**, however, were not distinguishable with this substrate. Then, we selected less reactive (*S*)-4-phenyl-2-butanol as the substrate to find proper conditions for the racemization (Table 1).[22] With complex **4**, the racemization rate did not decrease significantly until the amount of the catalyst was reduced to 1 mol %. However, the racemization slowed significantly when less than 2 mol % of base was used. The conditions of entry 3 in Table 1 were applied to comparing the activities of **5**−**13** (Table 2). The racemization rate was affected by the substituent of the amino group. Generally, alkyl substituents were better than aryl ones. The effect of alkyl substituents, however, was not simply correlated with the steric bulkiness; **4** having an isopropyl substituent was better than **5** as well as **6** (Table 2, entries 1−3). The replacement of phenyl groups with methyl ones at C(2) and C(5) of the cyclopentadienyl ring increased the racemization rate (entry 7). The activities of **4**, **7**, and **9** were almost the same at the dose of 1 mol %, but the racemization with **7** was about 4 times faster than that with **4** or **9** when the dose was cut down to 0.5 mol % (Table 2, entries 1, 4, and 6).[23] Electron-withdrawing aryl substituents increased the racemization rate; **9** having a *p*-nitrophenyl substituent was the best among **9**−**13** and similar to **4** (Table 2, entries 6−10).

TABLE 2. Catalytic Racemization of (*S*)-4-Phenyl-2-butanol with Complexes 4−13 at 25 °C[a]

entry	catalyst	% ee[b]
1	**4**	0.4 (49.4)[c]
2	**5**	8.4
3	**6**	25.4
4	**7**	0.2 (7.8)[c]
5	**8**	23.2
6	**9**	0.0 (57.2)[c]
7	**10**	32.8
8	**11**	26.0
9	**12**	78.0
10	**13**	86.8

[a] (*S*)-4-Phenyl-2-butanol (>99% ee, 0.50 mmol) was added to a flask containing catalyst (1.0 mol %) and potassium *tert*-butoxide (5.0 mol %) in toluene (1.6 mL). [b] The % ee values were measured by chiral HPLC (Chiralcel OD, Daicel) after 60 min. [c] The % ee value in parentheses were obtained after 30 min in the racemization with 0.5 mol % of the ruthenium complex.

TABLE 3. Dynamic Kinetic Resolution of 1-Phenylethanol with 4[a]

entry	acyl donor[b]	additive[c]	*t* (h)	acetate[d] (%)	% ee[e]
1	vinyl acetate	none	96	55	98.6
2	vinyl acetate	Na_2CO_3	96	89	97.0
3	isopropenyl acetate	Na_2CO_3	30	97	>99
4	isopropenyl acetate	MS 4 Å	40	98	98.5
5[f]	isopropenyl acetate	Na_2CO_3	84	96	98.6
6[g]	isopropenyl acetate	Na_2CO_3	144	77	>99
7	*p*-$ClC_6H_4OCOCH_3$[h]	Na_2CO_3	42	95	>99
8	$CH_3CO_2CH_2CF_3$[h]	Na_2CO_3	96	82	94.7
9	ethyl acetate[i]	Na_2CO_3	72	73	69.7

[a] The reactions were carried out with 1-phenylethanol (0.25 mmol), **4** (4 mol %), Novozym 435 (0.7 mg), and potassium *tert*-butoxide (5 mol %) in toluene (0.80 mL) at room temperature under argon atmosphere. [b] 1.5 equiv of alkenyl acetates. [c] Sodium carbonate (1.0 equiv) or 4-Å molecular sieves (60 mg) were used. [d] By GC. [e] By chiral HPLC ((*R*,*R*)-Whelk-01, Merck). [f] 2 mol % of **4**. [g] Without toluene, 0.40 mL of 1-phenylethanol (3.3 mmol) and 0.55 mL of isopropenyl acetate (5.0 mmol) were allowed to react with 0.3 mol % of **4**. [h] 3 equiv with 7.0 mg of Novozym 435 in 0.8 mL of toluene. [i] 0.8 mL.

DKR of 1-Phenylethanol under Various Conditions. The DKR of 1-phenylethanol with **4** was carried out with varying acyl donors and additives to find optimum conditions (Table 3). While the lipase and the acyl donors did not inhibit the racemization individually, the combined use in the DKR interfered with the racemization (Table 3, entry 1). In a separate experiment, acetic acid, which would be formed during the DKR, was

(22) The racemization of (*S*)-4-phenyl-2-butanol is slower than that of (*S*)-1-phenylethanol. See ref 10b.

(23) For a mathematical treatment of the kinetics of racemization, see: Ebbers, E. J.; Ariaans, G. J. A.; Houbiers, J. P. M.; Bruggink, A.; Zwanenburg, B. *Tetrahedron* **1997**, *53*, 9417. The rate constants (k_{rac}) for the racemization with **4**, **7**, and **9** are 0.012, 0.043, and 0.0093 min^{-1}, respectively.

TABLE 4. DKR of 4-Phenyl-2-butanol[a]

entry	catalyst	acetate[b] (%)	% ee[c]
1	**4**	62.6	91.7
2	**7**	70.3	91.8
3	**9**	64.0	91.9

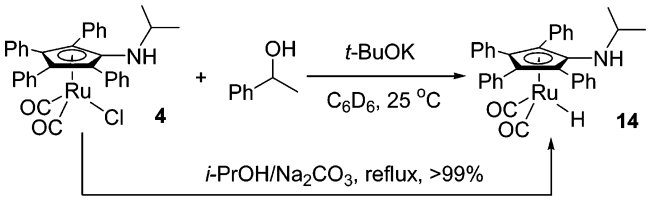
[a] The reactions were carried out with 0.25 mmol of 4-phenyl-2-butanol, isopropenyl acetate (1.5 equiv), Novozym 435 (0.7 mg), sodium carbonate (1.0 equiv), and the ruthenium complex (4 mol %) that was activated with potassium *tert*-butoxide (5 mol %) in toluene (0.8 mL) under argon atmosphere at 25 °C for 15 h. [b] By GC. [c] By chiral GC (Chiraldex B-PH, Alltech).

responsible for the interference.[24] The use of sodium carbonate or 4-Å molecular sieves solved the problem (Table 3, entries 2−4). Isopropenyl acetate was the best among five acyl donors tested. The DKR with isopropenyl acetate was much faster, even with 10 times less lipase, than those with *p*-chlorophenyl acetate and trifluoroethyl acetate (Table 3, entries 3, 7, and 8). It was still effective when the amount of catalyst **4** was cut down to a half although a longer reaction time was required (Table 3, entry 5). Furthermore, only with 0.3 mol % of **4**, the DKR without extra solvent produced (*R*)-acetate in 77% yield in 144 h (Table 3, entry 6). Replacing isopropenyl acetate with ethyl acetate, however, led to a poor result for the optical purity as well as for the yield (Table 3, entry 9).

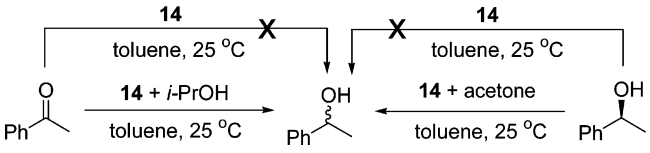
On the basis of the results in Table 2, complexes **4**, **7**, and **9** were tested on the DKR of 4-phenyl-2-butanol to select a racemization catalyst for the DKR of other alcohols (Table 4). The DKR with **7** gave a better yield than those with **4** and **9**, but the difference was not significant.

DKR of Various Secondary Alcohols. The complex **4** was selected for the DKR of various secondary alcohols to see the scope of our catalyst system, because of the easy preparation of **4** on a large scale (Table 5). In addition to the simple alcohols described in the previous communication (Table 5, entries 1−6),[21] a variety of functionalized alcohols were examined as the substrates to be resolved. In most cases, *Candida antarctica* lipase B (CALB) immobilized on acrylic resin (trade name: Novozym 435) was used as the resolving enzyme. Most of the allylic alcohols examined were efficiently resolved: 9 out of 10 were converted to the corresponding (*R*)-allylic acetates in good yields (83−94%) with high optical purities (>99% ee) (Table 5, entries 7−16). 1-Phenylpropanone was formed from phenyl vinyl carbinol in 38% yield through isomerization during the DKR.[18d,25] The alkynyl group of a propargyl alcohol remained intact during the DKR (Table 5, entry 17). The DKRs of 1,2- and 1,3-diols protected with a trityl group were highly efficient (Table 5, entries 18−20).[26] Secondary diols, existing as mixtures of *dl*- and *meso*-isomers, were transformed into the corresponding (*R*,*R*)-diacetates highly selectively: enantiomeric excess reached greater than

SCHEME 3



SCHEME 4



99%, and diastereomeric excess ranged from 97 to 98% (Table 5, entries 21 and 22).[14k,27] *β*-Hydroxy butyric acid *tert*-butyl ester was also a good substrate for DKR (Table 5, entry 23).[28] Chlorohydrins, in general, were not good substrates for CALB. In these cases, CALB was replaced by *Pseudomonas cepacia* lipase immobilized on ceramic (LPS-C) or on toyonite (LPS-T) to get improved results (Table 5, entries 24 and 25). In particular, slow enzymatic acylation limited the DKR of 3-chloro-1-phenylpropanol; the corresponding (*R*)-acetate was formed in only 31% yield after 7 days with LPS-T (entry 26).

Mechanistic Studies. To obtain clues to the active species in the catalytic racemization, a benzene-d_6 solution of **4**, 1-phenylethanol, and potassium *tert*-butoxide was analyzed by ^{1}H NMR at room temperature (Scheme 3). Instead of any organometallic species having an alcohol or an alkoxy ligand,[29] a ruthenium hydride (**14**) was observed as the major species. In fact, in a separate experiment, the hydride complex **14** was obtained in quantitative yield by refluxing a 2-propanol solution of **4** in the presence of sodium carbonate under argon.

Notably, the ruthenium hydride **14** required ketone for the racemization of alcohols (Scheme 4);[30] the racemization of (*S*)-1-phenylethanol was completed in 2 h at room temperature with 4 mol % of **14** and 10 mol % of acetone or acetophenone. The DKR of 1-phenylethanol was also successful with **14**; (*R*)-1-phenylethyl acetate was obtained in 95% yield and >99% ee after 3 days under the conditions similar to those of the entry 1 in Table 5. Because acetone was produced from isopropenyl acetate during the DKR, no extra ketones were needed for the DKR with **14**. During the racemization and the DKR, **14** appeared intact.[31] Another notable observation was that no reaction occurred between **14** and acetophenone until an alcohol was added. When 2-propanol was used as

(24) The racemization of (*S*)-1-phenylethanol was inhibited by the addition of acetic acid, and then recovered slowly by the subsequent addition of sodium carbonate. A related complex, [{2,5-Ph_2-3,4-tol_2(η^5-C_4COH)}Ru(CO)$_2$(O_2CCF_3)], is formed in the reaction of [{2,5-Ph_2-3,4-tol_2(η^4-C_4CO)Ru(CO)$_2$}$_2$] with trifluoroacetic acid: Casey, C. P.; Singer, S. W.; Powell, D. R.; Hayashi, P. K.; Kavana, M. *J. Am. Chem. Soc.* **2001**, *123*, 1090.

(25) For the ruthenium-catalyzed isomerization of allylic alcohols to saturated ketones, see: Trost, B. M.; Kulawiec, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 2027.

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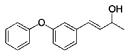
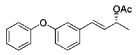
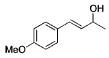
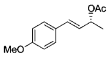
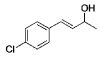
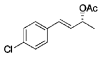
(30) (*S*)-1-Phenylethanol was not racemized without ketone at room temperature.

TABLE 5. DKR of Various Alcohols[a]

Entry	Substrate	Product	*t* (day)	Yield[b] (%)	ee[c] (%)	Entry	Substrate	Product	*t* (day)	Yield[b] (%)	ee[c] (%)
1			1.3	95	>99	14			4	90	>99[f]
2			2	94	>99	15			4	62[g]	80.6
3			2	90	>99	16			4	93	>99
4			2	89	95.0[d]	17			3	95	>99
5			3	86[e]	>99[f]	18[h,i]			6	97	99.0
6			3	89[e]	90.5[f]	19[h]			6	94	>99[j]
7			3	93	98.0	20[h]			6	91	>99[j]
8			4	92	>99	21[k,l]			3	95	>99 (97.6% *de*)
9			4	83	98.9	22[k,l]			3	94	>99 (96.7% *de*)
10			4	92	98.8	23[h,m]			5	94	>99
11			4	90	>99	24[h,n]			7	75	95.0
12			4	94	>99	25[o]			5	62[p]	87.0[j]
13			4	90	>99	26[n]			7	31[p]	>99

[a] The reactions were performed on a 1.0 mmol scale with isopropenyl acetate (1.5 equiv), Novozym 435 (3 mg), Na_2CO_3 (1.0 equiv), **4** (4 mol %), and potassium *tert*-butoxide (5 mol %) in toluene (3.2 mL) at 25 °C. [b] Isolated yields. [c] By chiral HPLC ((*R*,*R*)-Whelk-O1, Merck). [d] By chiral HPLC (Chiralcel OD, Daicel) after hydrolysis to 1-indanol. [e] By GC. [f] By chiral GC (Chiraldex B-PH, Alltech). [g] 1-Phenylpropanone was formed in 38% yield. [h] 0.6 M. [i] Novozym 435 (9.0 mg/mmol) was used. [j] By chiral HPLC (Chiralcel OD, Daicel).[k] At 40 °C. [l] Novozym 435 (6.0 mg/mmol) was used. [m] LPS-C (3.0 mg/mmol) was used. [n] LPS-T (3.0 mg/mmol) was used. [o] LPS-C (4.0 mg/mmol) was used. [p] By ^{1}H NMR.

solvent, **14** catalyzed the transfer hydrogenation of acetophenone. However, it was a slow reaction; only 59% of acetophenone transformed to 1-phenylethanol in 5 days at room temperature with 4 mol % of **14**. By heating at 70 °C, the hydrogenation was almost completed in 20 h.

The low reactivity of **14** toward acetophenone is parallel with that of an analogous hydride complex (**15**) reported recently by Casey et al.,[32] which does not react even with benzaldehyde at room temperature (Scheme 5). The low activity is ascribed to low acidity of the NHPh unit: pK_a > 25.[32] An ammonium complex (**16**), formed by the treatment of **15** with triflic acid at −80 °C, rapidly hydrogenates benzaldehyde to give benzyl alcohol and a ruthenium triflate (**17**). Meanwhile, above −25 °C, **16** is not stable and loses H_2 to form **17**.[32]

SCHEME 5

Our results imply that the ruthenium hydride **14** is a key species for the catalytic racemization of secondary alcohols. We propose a species integrated with **14**, an alcohol, and a ketone as shown in Scheme 6 to explain the racemization by ketone and **14** that alone cannot hydrogenate ketone. In the species, the alcohol donates a proton and a hydride to the nitrogen and the ruthenium of **14**, respectively, on hydrogenating the ketone. The donation of a proton facilitates the hydrogenation of the ketone outside the coordination sphere of the metal, as in the reaction of the ammonium complex **16** and benzaldehyde.[32] Then, the racemization proceeds through the exchange of alcohols. The fast and reversible hydrogen transfer in the integrated species would explain why the interconversion between two enantiomers of 1-phenyl-

(31) A toluene-d_8 solution of **14**, acetophenone, and 1-phenylethanol was monitored by ^{1}H NMR at −78 to +25 °C in the hope of finding a clue to the cooperative participation of acetophenone and 1-phenylethanol in the catalytic action of **14**. However, only **14** was observed with its initial amount maintained.

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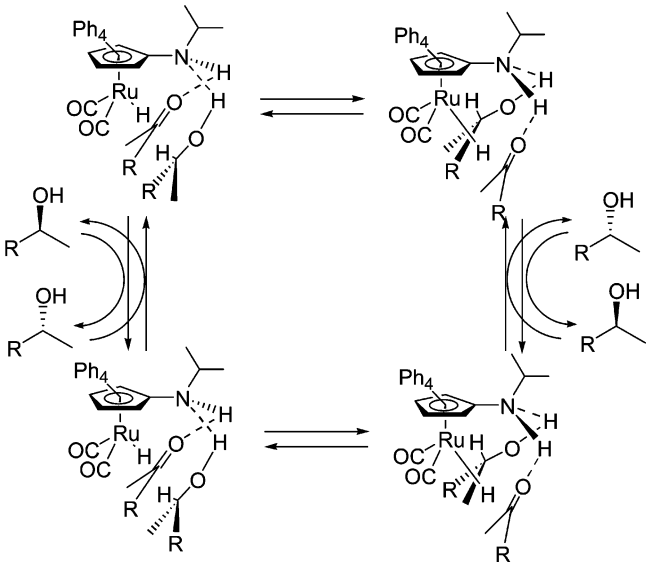
SCHEME 6



ethanol is much faster than the transfer hydrogenation of acetophenone in 2-propanol.

Conclusion

We have described a new class of ruthenium complexes that are excellent racemization catalysts for the dynamic kinetic resolution of a wide scope of secondary alcohols with lipases. Now the transformation of racemic secondary alcohols into chiral acetates is possible at room temperature with isopropenyl acetate more efficiently than before.

Experimental Section

General Methods. All reactions were performed under a dry argon atmosphere. 4-Chlorophenyl acetate was synthesized according to literature.[14l] LPS-T (*P. cepacia* lipase immobilized on toyonite) was prepared according to the literature.[33] 4-Phenyl-3-buten-2-ol, 4-(4-methylphenyl)-3-buten-2-ol,[34] 4-(4-methoxyphenyl)-3-buten-2-ol,[34] 4-(1-naphthalenyl)-3-buten-2-ol,[34] 4-(2,4,6-trimethylphenyl)-3-buten-2-ol,[34] 4-(1,1′-biphenyl)-4-yl-3-buten-2-ol,[34] 4-(3-phenoxyphenyl)-3-buten-2-ol,[34] 4-phenyl-3-butyn-2-ol,[35] 1-(trityloxy)-2-propanol,[26] 1-(trityloxy)-2-butanol,[26] 4-(trityloxy)-2-butanol,[26] α,α′-dimethyl-1,3-benzenedimethanol,[36] α,α′-dimethyl-1,4-benzenedimethanol,[36] *tert*-butyl-3-hydroxybutyrate,[28] 2-(chloro-1-phenyl-ethanol),[28] 1-cyclohexyl-2-propen-1-ol,[37] and 3-chloro-1-phenoxy-2-propanol[38] were prepared according to the literature.

Synthesis of [2,3,4,5-Ph$_4$(η^5-C$_4$CNH^{i}Pr)]Ru(CO)$_2$Cl (4). The original synthetic procedure[21] was modified by adding 2-propanol. In a 500-mL flask equipped with a grease-free high-vacuum stopcock, $Ru_3(CO)_{12}$ (2.4 g, 3.8 mmol) and the imine (4.0 g, 9.4 mmol) prepared from isopropylamine and 2,3,4,5-tetraphenylcyclopentadienone were dissolved in dry and degassed chloroform (117 mL) and 2-propanol (1.1 mL, 14.4 mmol). After the flask was filled with argon and closed, the solution was stirred at 90 °C for 55 h. The reaction mixture was concentrated and chromatographed on a silica gel column (ethyl acetate/*n*-hexane = 1/8, then CH_2Cl_2) to give **4** as a yellow solid. The solid was recrystallized from CH_2Cl_2/*n*-hexane (3.2 g; 56%).

When 2-propanol was used as solvent with 5 equiv of chloroform, **4** was precipitated from the reaction mixture. By heating a solution of $Ru_3(CO)_{12}$ (0.30 g, 0.5 mmol), the imine (0.50 g, 1.20 mmol), and chloroform (470 μL, 5.9 mmol) in dry 2-propanol (15 mL) at 90 °C for 24 h, **4** was obtained in 33% yield (236 mg).

[2,3,4,5-Ph$_4$(η^5-C$_4$CNH^{i}Pr)]Ru(CO)$_2$H (14). In a 100-mL flask equipped with a grease-free high-vacuum stopcock, **4** (372 mg, 0.6 mmol) and Na_2CO_3 (191 mg, 1.8 mmol) were suspended in 2-propanol (24 mL). After the flask was filled with argon, the mixture was stirred at 90 °C for 12 h. After Na_2CO_3 was filtered through a Celite pad under argon, the solvent was evaporated under vacuum to give **14** as a light brown solid (350 mg, >99% yield). Mp: 90 °C dec. ^{1}H NMR (300 MHz, C_6D_6): δ 7.57−6.73 (m, 20H), 3,00−2.93 (m, 1H), 2.57 (d, J = 9.0 Hz, 1H), 0.71 (d, J = 6.3 Hz, 6H), −9.14 (s, 1H). ^{13}C NMR (75 MHz, C_6D_6): δ 203.6, 134.1, 133.4, 132.9, 132.8, 130.2, 129.0, 127.8, 127.1, 106.3, 91.0, 50.1, 21.9. IR (KBr, cm^{-1}): ν(CO) = 2000, 1941. MS (FAB): *m*/*z* 586 (23) [M$^+$ + 1], 528 (80), 526 (100). Anal. Calcd for $C_{34}H_{29}NO_2Ru$: C, 69.85; H, 5.00; N, 2.40. Found: C, 69.40; H, 5.04; N, 2.36.

General Procedure for the Catalytic Racemization of (*S*)-Alcohols. A solution of potassium *tert*-butoxide (1.0 M in THF; 26 μL, 0.026 mmol) was added to a 25-mL flask equipped with a grease-free high-vacuum stopcock. THF was removed under vacuum, and the flask was filled with argon. Then, **4** (3.1 mg, 0.005 mmol) and (*S*)-4-phenyl-2-butanol (76 μL, 0.5 mmol) were added, and the mixture was dissolved in toluene (1.6 mL). After being stirred at 25 °C for 1 h, the reaction mixture was filtered through a short silica gel pad to measure the % ee value.

General Procedure for the Dynamic Kinetic Resolution of Secondary Alcohols. A solution of potassium *tert*-butoxide (1 M in THF; 52 μL, 0.050 mmol) was added to a 50-mL flask equipped with a grease-free high-vacuum stopcock. THF was removed under vacuum, and the flask was filled with argon. Then, **4** (24.8 mg, 0.04 mmol), Novozym 435 (2.8 mg), Na_2CO_3 (104 mg, 1.0 mmol), a solution of 1-phenylethanol (120 μL, 1.0 mmol) in toluene (3.2 mL), and isopropenyl acetate (168 μL, 1.5 mmol) were added sequentially under argon. After being stirred at 25 °C for 30 h, the reaction mixture was concentrated and purified by chromatography on a silica gel column (ethyl acetate/*n*-hexane = 1/8) to give (*R*)-1-phenylethyl acetate (156 mg, 95% yield, >99% ee).[14l] Spectral data of (*R*)-1-(*p*-chlorophenyl)ethyl acetate, (*R*)-1-(*p*-methoxyphenyl)ethyl acetate, (*R*)-1-indanyl acetate, (*R*)-1-cyclohexylethyl acetate, (*R*)-2-octyl acetate, and (*R*)-4-phenyl-2-butyl acetate were identical with those reported previously.[14j,l,19]

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Supporting Information Available: Experimental details and characterization data for the ruthenium complexes **5**−**13** and characterization data for the chiral acetates produced in the DKR of various alcohols. This material is available free of charge via the Internet at http://pubs.acs.org.

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