derivative has been determined. The decomposition of these complexes suggests rate-limiting loss of nitrous oxide leads to unusual and reactive late-transition-metal terminal oxo intermediates.

Experimental Section

3a: [Ni(dppf)Cl_2],[27] (268 mg) dissolved in CH_2Cl_2 (15 mL) was treated in one addition with **1**[22] (2 equivalents, 249 mg) suspended in methanol (60 mL). Rapidly a deep orange color developed and the solution volume was immediately reduced to ca 10 mL by evaporation at ambient temperatures. The resulting bright orange crystals were isolated by filtration and washed with portions of cold methanol (4×10 mL) or until the filtrate was colorless. Recrystallization of this product from dichloromethane/ethanol at room temperature returns 243 mg (93 % yield) of **3a**. Elemental analysis calcd (%) $C_{34}H_{28}FeN_2NiO_2P_2 \cdot \frac{1}{2}CH_2Cl_2$: C 59.26, H 4.05, N 3.88; found: C 59.43, H 4.28, N 3.64; IR (KBr,): $\tilde{\nu} = 1480$ m, 1449 s, 1436 s, 1307 m, 1194 w, 1182 w, 1168 m, 1096 s, 1036 m, 1028 m, 999 w, 983 m, 917 m, 827 w, 799 m, 744.3 s, 692 s, 638 w, 625 m, 556 m, 510, s, 494 s, 471 cm^{-1} m; ^1H NMR (400 MHz, CD_2Cl_2): $\delta = 7.84$ (m, 8H), 7.52 (m, 4H), 7.42 (t, $J = 7.3$ Hz, 8H), 4.42 (m, 4H), 4.26 ppm (m, 4H); ^3P NMR (162 MHz, CD_2Cl_2): $\delta =$ 25.0 ppm (s) (UV/Vis: λ_{max}, (ε_{max}, $M^{-1}cm^{-1}$) in CH_2Cl_2: 406 nm (655); differential scanning calorimetry (DSC): $\Delta H = -802$ kcal mol^{-1} $T_{onset} =$ 75 °C. Crystals suitable for X-ray diffraction were grown from CH_2Cl_2/Et_2O at −15 °C.

Crystal data for **3a**: $C_{35}H_{28}Cl_2FeN_2NiP_2O_2$, $M = 755.99$, 143 K, triclinic space group $P\bar{1}$, $a = 10.6210(8)$, $b = 11.3831(9)$, $c = 15.515(2)$ Å, $\alpha =$ 84.021(2), $\beta = 72.745(2)$, $\gamma = 69.790(1)°$, $V = 1681.0(3)$ $Å^3$, $Z = 2$, $\rho_{calcd} =$ 1.494 $Mg\,m^{-3}$, $F(000) = 772$, 426 parameters; R_1 (wR_2) [$I > 2\sigma(I)$] = 0.064 (0.15), s(GOF) = 0.98. Crystals of **3a** were mounted on glass fibers with epoxy resin and diffraction data was collected on a Bruker Smart CCD diffractometer equipped with a sealed molybdenum tube which was monochromated to give $\lambda = 0.71073$ Å. The structure was solved using direct methods and refined using full-matrix least-squares on F^2 with SHELXTL. With the exception of the disordered dichloromethane solvate, all non-hydrogen atoms were refined anisotropically with element assignments as described in the text. CCDC-176081 (**3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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Aminocyclopentadienyl Ruthenium Chloride: Catalytic Racemization and Dynamic Kinetic Resolution of Alcohols at Ambient Temperature**

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Dynamic kinetic resolution (DKR) is an attractive method for the complete transformation of a racemic mixture into a single enantiomer.[1] The DKR of secondary alcohols is a prominent example, for which transition-metal-catalyzed racemization is coupled with enzymatic acylation.[2] In particular, Bäckvall and co-workers have introduced a notable catalyst system that provides a wide range of chiral acetates in good yields and excellent optical purities.[2b–f] However, the catalyst for the racemization of secondary alcohols is activated at high temperature, and needs the corresponding ketones as hydrogen mediators.[3] Thus, the catalyst system requires a thermally stable lipase; *p*-chlorophenyl acetate has been selected as an acyl donor,[2c] because oxidation of the starting alcohols occurs when the conventional alkenyl acetates are used as acyl donors.[4]

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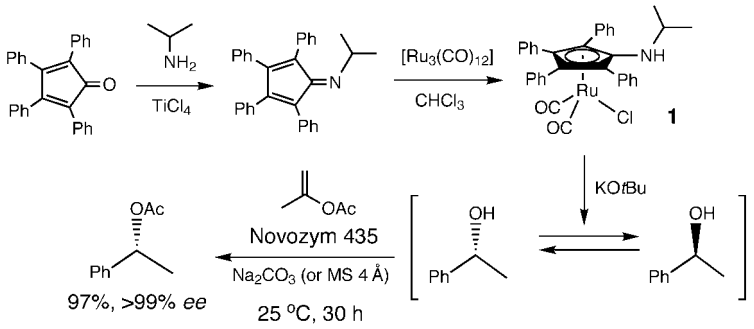
Herein we report a novel ruthenium catalyst that can racemize secondary alcohols efficiently at room temperature without the aid of hydrogen mediators.[5, 6] Furthermore, the catalytic racemization is compatible with the use of isopropenyl acetate for the DKR of secondary alcohols at room temperature (Scheme 1).



Scheme 1. Synthesis of **1** and DKR of 1-phenylethanol; MS = molecular sieve.

For the synthesis of aminocyclopentadienyl ruthenium chloride (**1**), it was fortunate to select chloroform as the solvent in the reaction of $[Ru_3(CO)_{12}]$ with the imine prepared from isopropylamine and 2,3,4,5-tetraphenylcyclopentadienone. Attempts at synthesizing the tricarbonyl analogue under various other reaction conditions failed. The molecular structure of **1** was confirmed by X-ray diffraction analysis (Figure 1).[7]

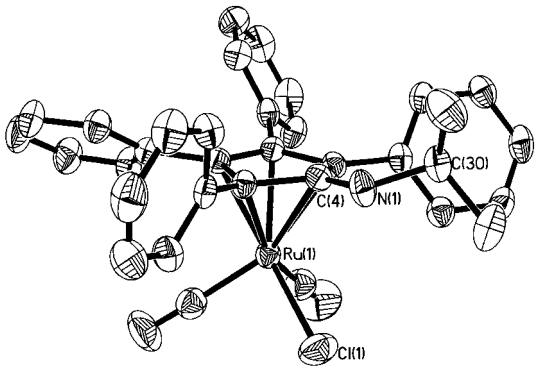


Figure 1. ORTEP plot (thermal ellipsoids set at 50% probability) of the molecular structure of **1**. All hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru(1)-Cl(1) 2.4137(8), Ru(1)-C(4) 2.430(3), N(1)-C(4) 1.339(3), N(1)-C(30) 1.467(3); Cl(1)-Ru(1)-C(4) 86.96(7), Ru(1)-C(4)-N(1) 131.6(2), C(4)-N(1)-C(30) 128.4(2).

We expected the generation of a coordinatively unsaturated and active species by the elimination of hydrogen chloride from **1** with a proper base.[8] Indeed, (*S*)-1-phenylethanol (> 99% *ee*) was racemized completely within 30 min at 25 °C by the catalytic species generated by the treatment of **1** with potassium *tert*-butoxide. The scope of the catalytic racemization was investigated under various conditions (Table 1): The racemization rate is not affected significantly by the polarity and the coordinating ability of solvents (entries 1 – 4, though it is slightly slower with acetone). Even without solvent, the racemization is practically completed in 12 h with only 0.3 mol% of **1** (entry 5). Notably, the catalytic species is still active in the presence of vinyl acetate in toluene (entry 6), although the racemization is almost prevented when vinyl acetate alone is employed as a solvent (entry 7).

On the basis of the racemization results, the DKR of 1-phenylethanol was investigated with varying conditions (Table 2): Unexpectedly, the DKR is unsuccessful under the racemization conditions of the entry 6 in Table 1 despite the fact that the lipase itself does not interfere with the catalytic racemization. A breakthrough is the use of sodium carbonate or 4-Å molecular sieve as an additive (Table 2 entries 2 and 3). Isopropenyl acetate is a better acyl donor than vinyl acetate it gives faster and more productive DKR. Increasing temperature makes the DKR faster, but the production of acetophenone increases: 1.6% at 25 °C, 2.5% at 40 °C, and 10.4% at 70 °C (entries 4 – 6). In the

Table 1. Catalytic racemization of (*S*)-1-phenylethanol at 25 °C after activating **1** with potassium *tert*-butoxide.[a]

Entry	Solvent	*t* [h]	*ee*[b] [%]
1	toluene	0.5	0.0
2	CH_2Cl_2	0.5	0.0
3	THF	0.5	0.0
4	acetone	0.5	24.7
5	no solvent[c]	12	1.8
6	toluene + vinyl acetate[d]	1.0	6.8
7	vinyl acetate	5.0	96.4

[a] (*S*)-1-Phenylethanol (> 99% *ee*, 0.25 mmol) dissolved in a solvent (0.80 mL) was added to a flask containing **1** (6.2 mg, 4.0 mol%) and potassium *tert*-butoxide (0.013 mmol, 5.2 mol%). [b] Measured by HPLC equipped with a chiral column (Chiralcel OD, Daicel). [c] (*S*)-1-Phenylethanol (> 99% *ee*, 0.40 mL, 3.3 mmol) was added to a flask containing **1** (6.2 mg, 0.30 mol%) and potassium *tert*-butoxide (0.013 mmol, 0.40 mol%). [d] Toluene (0.80 mL) was mixed with vinyl acetate (0.38 mmol, 1.5 equiv).

Table 2. Dynamic kinetic resolution of 1-phenylethanol.[a]

Entry	Acyl donor[b]	Lipase[c] [mg]	Additive[d]	T [°C]	*t* [h]	Acetate [%][e]	*ee*[f] [%]
1	$CH_2{=}CHOCOCH_3$	0.7		25	96	55	98.6
2	$CH_2{=}CHOCOCH_3$	0.7	Na_2CO_3	25	96	89	97.0
3	$CH_2{=}C(CH_3)OCOCH_3$	0.7	molecular sieve 4 Å	25	40	98	98.5
4	$CH_2{=}C(CH_3)OCOCH_3$	0.7	Na_2CO_3	25	30	97	> 99
5	$CH_2{=}C(CH_3)OCOCH_3$	0.7	Na_2CO_3	40	24	95	> 99
6	$CH_2{=}C(CH_3)OCOCH_3$	0.7	Na_2CO_3	70	12	90	> 99
7	*p*-$ClC_6H_4OCOCH_3$[g]	7	Na_2CO_3	25	42	95	> 99

[a] The reactions were carried out with 0.25 mmol of 1-phenylethanol and 4 mol% of **1**, which was activated with 5 mol% of potassium *tert*-butoxide, in dry toluene (0.80 mL) under argon atmosphere. [b] 1.5 equiv of alkenyl acetate [c] Novozym 435. [d] Sodium carbonate (1.0 equiv) or molecular sieve 4 Å (60 mg) was used. [e] The yields were determined by GC. [f] The % *ee* values were determined by HPLC equipped with a chiral column ((*R*,*R*) Whelk-01, Merck). [g] 3 equiv.

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DKR with *p*-chlorophenyl acetate, the reaction proceeds more slowly even with ten times more lipase (entry 7). This result clearly shows the advantage of isopropenyl acetate over *p*-chlorophenyl acetate as the acyl donor. Furthermore, the use of isopropenyl acetate makes the isolation of the acylated product much easier than with *p*-chlorophenyl acetate.[9]

Our catalyst system was effective also for the DKR of other aromatic alcohols and aliphatic alcohols (Table 3): Substituent effects are insignificant in the DKR of aromatic alcohols while the DKR of aromatic alcohols is somewhat faster than that of aliphatic alcohols.

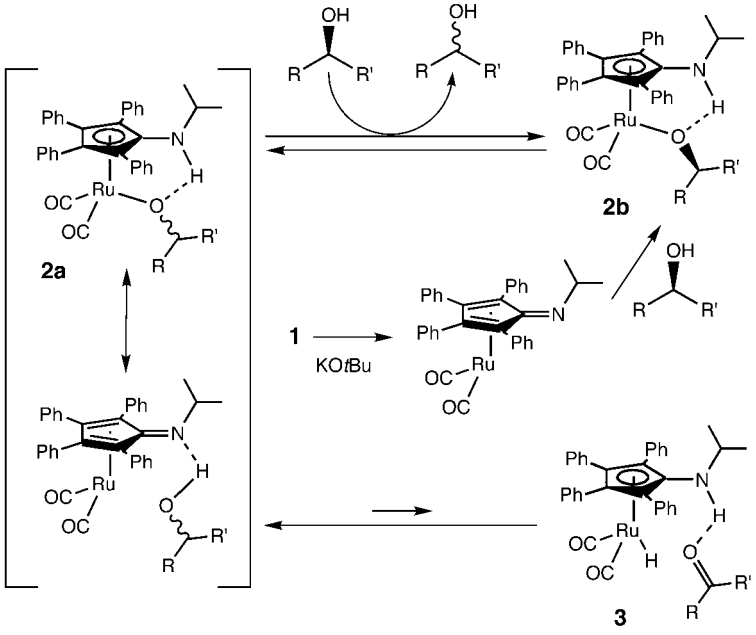
Table 3. Dynamic kinetic resolution of various alcohols.[a]

Entry	Alcohol[b]	*t* [h]	Acetate[b]	*ee* [%]
1	1-(*p*-chlorophenyl)ethanol	48	94%	>99[c]
2	1-(*p*-methoxyphenyl)ethanol	48	90%	>99[c]
3	1-indanol	48	89%	95.0[d]
4	1-cyclohexylethanol	72	86%	>99[e]
5	2-octanol	72	89%	90.5[e]

[a] The reactions were carried out with 1.00 mmol of an alcohol under the conditions of the entry 4 in Table 2. [b] Yields of isolated product. [c] By HPLC ((*R*,*R*) Whelk-01, Merck). [d] By HPLC after hydrolysis to 1-indanol (Chiralcel OD, Daicel). [e] By GC (Chiraldex B-PH, Alltech).

The observations recorded in Table 1 require a mechanism different from those involving simple hydrogen-transfer reactions for the catalytic racemization. In particular, the slow down of the racemization in acetone cannot be explained by the mechanisms involving ketones as hydrogen mediators. It is also notable that acetophenone was produced in only about 7% during the racemization in acetone. Thus, it is proposed that the racemization occurs during the reversible transformation between a ruthenium–alcohol complex (**2**) and a ruthenium–ketone complex (**3**; Scheme 2). The equilibrium would shift towards **2**, which exchanges alcohols rapidly at room temperature. The low yield of acetophenone during the racemization in acetone is explained by the slow exchange of ketones in **3**. Meanwhile, it is not clear yet why the racemization is inhibited significantly during the DKR without sodium carbonate or molecular sieves. A possible cause for the inhibition is the formation of acetic acid from the reaction of the acetylated lipase and water during the DKR. In a separate experiment, we observed that the racemization of 1-phenylethanol was inhibited by the addition of acetic acid and then recovered slowly by the subsequent addition of sodium carbonate.[10, 11]

In summary, we have demonstrated highly efficient racemization and DKR of secondary alcohols by the use of a novel ruthenium catalyst compatible with enzymatic resolution. The new mode of our catalytic racemization allows the use of more reactive isopropenyl acetate as an acyl donor and thus much less lipase. Furthermore, the simple method for the preparation of the catalyst can be applied for the development of more practical catalysts.



Scheme 2. Proposed mechanism for the catalytic racemization of secondary alcohols.

Experimental Section

1: In a 100-mL flask equipped with a grease-free high-vacuum stopcock, $[Ru_3(CO)_{12}]$ (1.0 g, 1.6 mmol) and the imine (1.0 g, 2.4 mmol) prepared from isopropylamine and 2,3,4,5-tetraphenylcyclopentadienone were dissolved in dry, degassed chloroform (30 mL).[12] After the flask was filled with Ar and closed, the solution was stirred at 90 °C for 5 days. The reaction mixture was concentrated and purified by chromatography on a silica-gel column to give yellow solid **1** (691 mg, 47% yield). The solid was recrystallized from CH_2Cl_2/Et_2O. m.p. 197 °C (dec.); ^{1}H NMR ($CDCl_3$; 300 MHz): $\delta = 7.57-6.91$ (m, 20H), 4.20 (d, $J = 4.1$ Hz, 1H), 3.3–3.23 (m, 1H), 0.86 ppm (d, $J = 3.2$ Hz, 6H); ^{13}C NMR ($CDCl_3$; 75 MHz): $\delta = 198.4$, 144.8, 133.7, 131.9, 130.6, 128.9, 128.7, 128.2, 127.7, 101.4, 81.7, 45.6, 25.2 ppm; IR (KBr, cm^{-1}): $\tilde{\nu}$(CO) = 2017 (S), 1963 (s); MS (FAB, *m*/*z*): 619.6(M^+); elemental analysis (%) calcd for $C_{34}H_{28}NO_2ClRu$: C 65.96, H 4.56, N 2.26; found: C 65.77, H 4.60, N 2.11.

Dynamic kinetic resolution of 1-phenylethanol: A solution of potassium *tert*-butoxide (1M in THF; 52 μL, 0.050 mmol) was added to a 50-mL flask equipped with a grease-free high-vacuum stopcock. The THF was removed under vacuum, and the flask was filled with argon. Then, **1** (24.8 mg, 0.04 mmol), Novozym 435 (2.8 mg; Novo Nordisk), Na_2CO_3 (104 mg, 1.00 mmol), a solution of 1-phenylethanol (120 μL, 1.00 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/hexane 1:8) to give (*R*)-1-phenylethyl acetate (156 mg, 95% yield, >99% *ee*).

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[7] Crystal data for **1**: $C_{34}H_{28}ClNO_2Ru$. $M_r = 619.09\ g\,mol^{-1}$. Orange crystal: size $0.50 \times 0.20 \times 0.20\ mm^3$, orthorhombic, $a = 20.1560(13)$, $b = 13.2405(9)$, $c = 21.1819(14)$ Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90°$, space group *Pbca*, $V = 5652.9(6)$ Å^3, $Z = 8$, $T = 223(2)$ K, $\rho_{calcd} = 1.455\ g\,cm^{-3}$, absorption coefficient $= 0.681\ mm^{-1}$. Siemens SMART diffractometer, $\lambda = 0.71073$ Å, scan mode-ω (ω-scan width: 1.92 to 23.33°). 22982 reflections were measured, giving 4077 unique data with $I > 2\sigma(I)$. $R = 0.0252$, $R_w = 0.0592$, GOF = 1.004. CCDC-179224 (**1**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit @ccdc.cam.ac.uk).

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[9] The separation of the product from unreacted *p*-chlorophenyl acetate is difficult in some cases.[2c]

[10] When 5 mol % of acetic acid was added to the mixture given in entry 1 in Table 1, the optical purity of 1-phenylethanol changed only to 69.0 % *ee* in 30 min. However, the racemization was completed in 5 h by the subsequent addition of sodium carbonate (1 equiv).

[11] 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$(CO)_2$}$_2$] and trifluoroacetic acid: C. P. Casey, S. W. Singer, D. R. Powell, R. K. Hayashi, M. Kavana, *J. Am. Chem. Soc.* **2001**, *123*, 1090.

[12] The imine was prepared in 90 % yield according to the procedure described by W. Dai, R. Strinivasan, J. A. Katzenellenbogen, *J. Org. Chem.* **1989**, *54*, 2204. Physical properties of the imine: m.p.: 223 °C; ^{1}H NMR ($CDCl_3$): $\delta = 7.25 - 6.75$ (m, 20H), 4.08 – 4.00 (m, 1H), 1.04 ppm (d, $J = 3$ Hz, 6H); ^{13}C NMR ($CDCl_3$): $\delta = 165.8$, 137.6, 131.9, 130.2, 129.8, 128.2, 127.8, 127.4, 127.2, 127.1, 126.5, 52.3, 24.6 ppm; MS (FAB, *m*/*z*): 425.27 (M^+); elemental analysis (%) calcd for $C_{32}H_{27}N$: C 90.31, H 6.39, N 3.29; found: C 90.26, H 6.62, N 3.14.

Chiral Epoxides by Desymmetrizing Deprotonation of *meso*-Epoxides**

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Epoxides are widely utilized as versatile synthetic intermediates, and the epoxide functional group is also found in a number of interesting natural products.[1] Therefore, the development of efficient (especially asymmetric) methods for the elaboration of epoxides is an important ongoing challenge.[2] In contrast to chemistry exploiting the electrophilic nature of epoxides, the utility of epoxides as nucleophiles (via oxiranyl anions, eg **1**-Li), first studied by Eisch and Galle,[3] is less developed.[4] A current requirement with this latter strategy is that the epoxide must possess an activating substituent (electron-withdrawing, trialkylsilyl, or trialkylstannyl group) attached to the epoxide ring. Electron-withdrawing and trialkylsilyl substituents facilitate the formation of oxiranyl anions by promoting deprotonation (usually lithiation) and prolonging the solution lifetime of these otherwise very labile intermediates. Trialkylstannyl- and sulfinyl-substituted epoxides react with organolithium species (by transmetalation and desulfinylation, respectively) rapidly enough at low temperatures, such that the resultant unstabilized oxiranyl anions can exhibit synthetically useful nucleophilic (rather than carbene-type) reactivity with a range of electrophiles.[5] Such reactions demonstrate the value of oxiranyl-lithium species as important intermediates in the elaboration of epoxides, but they also indicate the potential limitation of requiring an activated epoxide precursor to carry out the chemistry.

Recently, we showed that direct lithiation of terminal epoxides, followed by electrophile trapping of the nonstabilized oxiranyl anion intermediates, was possible in the presence of a diamine ligand.[6] However, the reaction was restricted to silylation (with TMSCl; TMS = trimethylsilyl) present during generation of the oxiranyl anion) and deuteration (MeOD as an external electrophile). Here we report the first examples of unactivated epoxides undergoing direct deprotonation to give destabilized (alkyl-substituted) oxiranyl anions, and their subsequent trapping with a range of electrophiles (including C–C-bond formation). Furthermore, a new enantioselective approach to substituted epoxides is demonstrated: symmetry breaking by asymmetric lithiation[7, 8] – electrophile trapping, at an epoxide functionality fused to eight- and seven-membered rings.

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