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Study of the Efficiency of Amino-Functionalized Ruthenium and Ruthenacycle Complexes as Racemization Catalysts in the Dynamic Kinetic Resolution of 1-Phenylethanol

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Dedicated to Prof. J. E. Bäckvall on the occasion of his 60th birthday.

Abstract: The ruthenium-amino structural motif in ruthenacycles and aminomethylpyridine ruthenium complexes turned out to be a useful basis for the design of readily accessible and active catalysts for the racemization of alcohols. Inspired by the proven ligand acceleration of 2-aminomethylpyridine (ampy) ligands in ruthenium-catalyzed hydrogen transfer, the readily accessible ampy-based oxazolines **8a** and **8b** were tested and led to novel and active ruthenium racemization catalysts. The highly active *ortho*-metalated-ampy Ru complex **7** was demonstrated to be a fast racemization catalyst (100% racemization of 1-phenylethanol at 70°C within 10 min). When used in the dynamic kinetic resolution of 1-phenylethanol towards 1-phenylethyl acetate, the cycloruthenated amine **5** was most active, leading to 86% of the (*R*)-1-phenylethylacetate with >99% *ee*.

Keywords: chiral alcohols; dynamic kinetic resolution; ligand assistance; racemization; ruthenium; transfer hydrogenation

Introduction

Optically active secondary alcohols are valuable intermediates and chiral auxiliaries in the fine chemical industry.[1] They can be prepared starting from prochiral ketones either by asymmetric hydrogenation,[2] hydrosilylation[3] or transfer hydrogenation (TH).[4] However, the resolution of racemic mixtures is still the most convenient way to prepare enantiomerically pure compounds on an industrial scale.[5] The kinetic resolution (KR) of racemic secondary alcohols by hydrolytic enzymes such as lipases and esterases is widely used to obtain a range of enantiomerically enriched alcohols or their esters.[6] However, the theoretical maximum 50% yield and the laborious separation of product from the remaining substrate are major drawbacks of the KR procedure. Dynamic kinetic resolution (DKR),[7] in which *in situ* racemization of unwanted enantiomers is coupled with KR, is an attractive method to overcome these drawbacks. Among a number of transition metals, including palladium, iridium and rhodium, known to catalyze rapid racemization of alcohols, ruthenium complexes have been shown to be the most effective catalysts (**1**–**3**, Figure 1).[8] Several groups have reported Ru racemization catalysts that are compatible with the enzymatic systems for the DKR.[9–11] Furthermore also heterogeneous ruthenium-based,[12] acidic zeolite catalysts[13] and ionic liquid[14] based systems have been reported

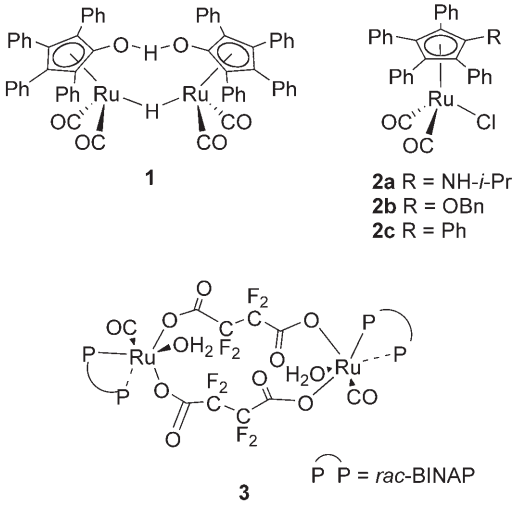
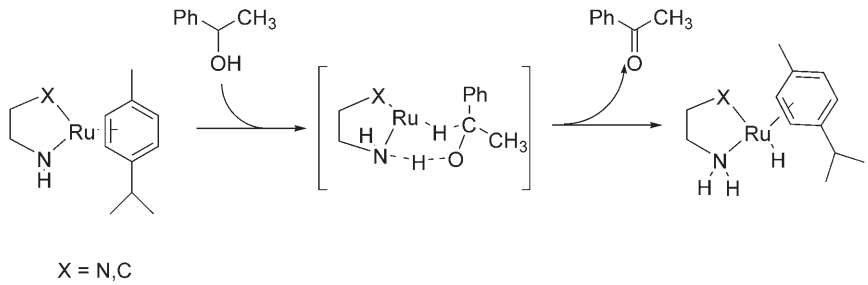


Figure 1. Ru catalysts developed for the racemization of alcohols.



Scheme 1. Outer-sphere mechanism for hydrogen transfer catalyzed by Ru-NH ligand complexes.

for the dynamic kinetic resolution, which offer the additional advantage of improved catalyst recycling.

In 1997, Bäckvall and co-workers pioneered ruthenium-catalyzed DKR of *sec*-alcohols with the Shvo precatalyst **1**.[9] Kim and Park reported afterwards the air-stable catalysts **2a** and **2b** which were found to be effective in the DKR of secondary alcohols at room temperature.[10] More recently, Bäckvall and co-workers reported the very effective catalyst **2c**, which is also active at room temperature. Application of this catalyst in the dynamic kinetic resolution, allowed for phenyl ethylacetate to be obtained in 98% yield with 99% *ee*.[9b,c] Very recently, van Nispen et al. reported a dinuclear ruthenium complex bearing tetrafluorosuccinate and (*rac*)-BINAP ligands as the racemization catalyst (Figure 1, structure **3**). Typically high yields were obtained in one day using as little as 0.1 mol% catalyst.[11a] However, the transition metal racemization catalysts reported require extensive synthesis (and are therefore costly) and are mostly air- and moisture-sensitive. We reasoned that simple and stable bifunctional amino ruthenium complexes which, upon treatment with base, lead to $(RNH_2)RuH(\eta^6\text{-arene})$ hydrido complexes hold promise because of their straightforward synthesis and their unique capabilities in hydrogen transfer between ketones and alcohols.

It is known that the NH_2 or NH moiety is essential in the catalytic cycle in hydrogen transfer hydrogenation of ketones.[15] This effect was designated by Noyori as bifunctional molecular catalysis, and is related to the interconversion of an amido Ru complex (16-electron) and an amine hydrido Ru complex (18-electron) as denoted in Scheme 1.

The reversibility of this reaction in the absence of other ketones, except the ketone derived from the starting alcohols, will allow for racemization activity. Indeed, in our earlier work[11c] on the chiral η^5-arene Ru complex $(TosNCH_2CH_2NH_2)RuCl(p\text{-cymene})$ (**4**) we were able to show that this ruthenium complex acted as a racemization catalyst. However, its stability and activity rapidly deteriorated in the presence of bases and acyl donors. We therefore embarked on a study to evaluate a series of $(RNH_2)Ru(\eta^6\text{-arene})$ complexes with higher stabilities for their potential in alcohol racemization under DKR conditions. We were thereby inspired by recent publications of the groups of Pfeffer and Baratta,[16,17] who reported stable and synthetically readily accessible transfer hydrogenation Ru catalysts. Pfeffer and co-workers showed that chiral cycloruthenated primary and secondary amines can be synthesized cleanly *in situ* in a single step.[16] From this class of compounds complex **5** (Figure 2) was included in this study. Another category of amine-containing ligands, are the 2-aminomethylpyridine (ampy) derivatives. Baratta and co-workers reported that several *ortho*-ruthenated complexes featuring an ampy motif show impressive TH catalytic activities towards ketones.[17] These complexes exhibited excellent thermal stability as well as impressive hydrogen transfer activity for various ketones (TOF's typically $>60{,}000\ h^{-1}$). From this category, compounds **6** and **7** were included in this study (Figure 2). Another class of stable and easy to prepare ligands containing the aminomethylene pyridine motif, are the 2-pyridyloxazolidines.[18] Ru complexes based

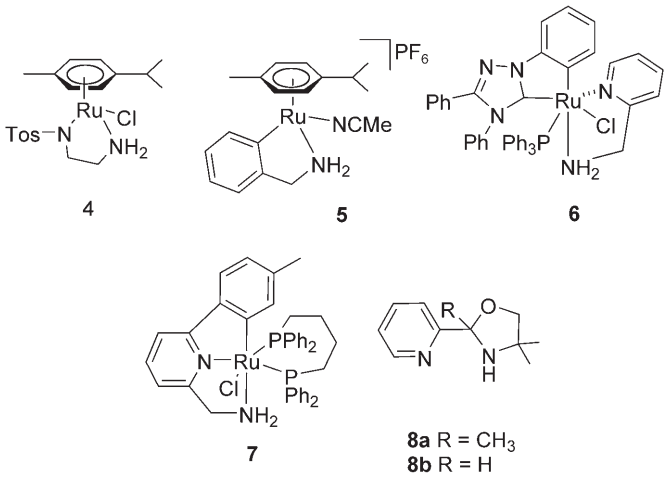


Figure 2. Ru-amino complexes and ligands used in this study.

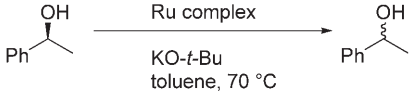
upon ligands **8a** and **8b** were therefore included in our study (Figure 2).

Results and Discussion

Racemization with *ortho*-Ruthenated $L_nRu(\eta^2$-ampy) Complexes

Complexes **6** and **7** (Figure 2) were synthesized[17b,c] and tested in the racemization of (*S*)-1-phenylethanol. As shown in Table 1, complexes **6** and **7** alone are inactive for the racemization of (*S*)-1-phenylethanol (entries 1 and 3). However, in the presence of potassium *tert*-butoxide, complexes **6** and **7** catalyze very efficiently the racemization of (*S*)-1-phenylethanol. The role of potassium *tert*-butoxide, as already well-documented, is to generate a ruthenium hydride species presumably *via* consecutive displacement of the chloride ligand, metathesis of alkoxides and β-elimination of acetophenone.[19] The complexes are among the fastest reported for racemization of secondary alcohols: At 70 °C in 30 min using 2 mol% of **6** (entry 2) and only 10 min using 1 mol% of **7** (entry 4) full racemization occurred.

Table 1. Racemization of (*S*)-1-phenylethanol at 70 °C in toluene with ruthenium complexes and base.[a]



Entry	**Ru complex** (mol %)	KO-*t*-Bu (mol %)	Time	*ee* [%]
1	**6** (2)		0.5 h	>99
2	**6** (2)	4	0.5 h	0
3	**7** (1)		10 min	>99
4	**7** (1)	1	1 min	50
			5 min	4
			10 min	0
5	**9** (2)	2.5	20 h	45
6	**9** (2) + **8a** (2.4)[b]		20 h	57
7	**9** (2) + **8a** (2.4)[b,c]	2.5	22 h	0
8	**9** (2) + **8b** (2.1)[d]	3.5	15 h	0
			0.5 h	58
9	**5** (5)	5	1 h	38
			18 h	0

[a] *Conditions:* Addition of KO-*t*-Bu to the Ru complex at 70 °C in toluene immediately followed by introduction of (*S*)-1-phenylethanol.
[b] Pre-treatment of the catalytic solution: **9**, **8** and KO-*t*-Bu stirred at 20 °C for 2 h prior to introduction of alcohol at 70 °C.
[c] Pretreatment at 70 °C as below resulted in only 42% *ee* after 20 h.
[d] Pre-treatment of catalyst solution: **9**, **8** and KO-*t*-Bu stirred in toluene at 70 °C for 2 h prior to introduction of the alcohol.

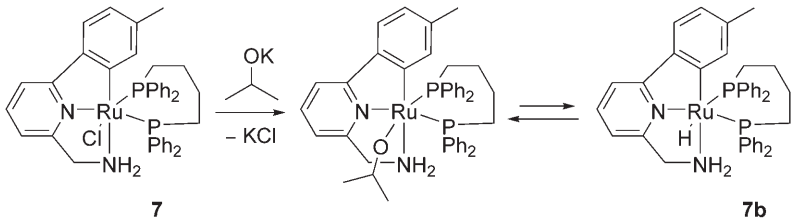
Table 2. Racemization of (*S*)-1-phenylethanol in the presence of additives.

Entry	Ru complex (mol %)[a]	Additives[b]	Time	*ee* [%]	TOF (h^{-1})[c]
1[d]	**6** (2)	-	30 min	0	100
2	**6** (1)	*i*-PrOAc	30 min	47	3
3	**6** (1)	CAL B/K_2CO_3	30 min	31	19
4	**7** (1)	-	10 min	0	300
5	**7** (1)	CAL B/K_2CO_3	20 min	49	76
6	**7** (0.5)	*i*-PrOAc	10 min	0	300
7[e]	**7b** (2)/*i*-PrOAc	-	60 min	>99	0

[a] Conditions KO-*t*-Bu (1 equiv.) was added to the Ru complex in toluene at 70 °C with stirring for 5 min and then addition of the alcohol (0.2 M) and the additives.
[b] *i*-PrOAc = 8 equivs. *vs.* (*S*)-1-phenylethanol; CAL B (20 mg); 1 equiv K_2CO_3 *vs.* (*S*)-1-phenylethanol.
[c] TOF mean values at different conversions; entries 1 and 4: TOFs may be underestimated as the reaction completion may be under 30 min and 10 min, respectively.
[d] Ru (2 mol%), KO-*t*-Bu (4 mol%).
[e] (*S*)-1-phenylethanol (1 M), *i*-PrOAc (10 equivs.), T = 70 °C; Ru (2 mol%) based on quantitative conversion to a single species.

The next step is to investigate the stability of these complexes under dynamic kinetic resolution conditions, when lipase and acyl donors are present. As shown in Table 2, the true catalytic species derived from precatalyst **6** was deactivated in the presence of both isopropyl acetate and the combination of CAL B/K_2CO_3 (entries 1–3). The catalytically active species corresponding to precatalyst **7** deactivated quickly in the presence of the same combination CAL B/K_2CO_3 (entries 4 and 5) but appeared inert towards isopropyl acetate over the time monitored. However, a complementary experiment suggested a slow deactivation in the presence of isopropyl acetate. In an attempt to unravel the mechanism of deactivation of the generated ruthenium hydride species **7b** presumably formed during the catalytic reaction,[20] we monitored its evolution by ^{1}H and ^{31}P NMR. Complex **7b** was isolated from the equilibrium arising from the reaction of **7** with potassium isopropoxide in isopropyl alcohol at 60 °C on evaporation of the medium (Scheme 2).

Upon extended reaction with a ten-fold excess of isopropyl acetate, **7b**, showing two doublets at 65.7 and 34.6 ppm ($^2J_{P,P}$ = 17.2 Hz) on ^{31}P NMR slowly evolves at 60 °C over a period of 19 h to a single species showing two coupled signals on ^{31}P NMR at 59.5 and 44.0 ppm ($^2J_{P,P}$ = 38.1 Hz) in C_6D_6 and no characteristic ^{1}H shift for a hydride was detected upon reaction completion. This formed species was proven to be inactive towards racemization of (*S*)-1-phenylethanol under similar conditions, disappointingly rendering **7** as such unsuitable for DKR (Table 2, entry 7).



Scheme 2. Isolation of Ru-H species **7b**.

Racemization with Ru(η^6-arene)(ampy) Complexes

Dimeric $[RuCl_2(\eta^6\text{-cymene})]_2$ **9** is a common ruthenium precursor and displays itself significant catalytic activity in the aerobic oxidation of benzylic and allylic alcohols.[21] We decided to use this precatalyst in combination with the featured amine-functionalized ligands in order to generate *in situ* the actual ruthenium-hydrido-amino catalysts. One class of ligands that contains the proposed structural motif is the group of 2-pyridyloxazolidines **8** (Figure 2). They were readily prepared from 2-amino-2-methylpropanol and 2-acetylpyridine (for **8a**) or 2-pyridinecarboxaldehyde (for **8b**).[18] The combinations of **9**/**8** with potassium *tert*-butoxide were found to be active in the racemization of *(S)*-1-phenylethanol at 70 °C in toluene (Table 1). As the results in Table 1 show, the combinations **9**/KO-*t*-Bu and **9**/**8a** (without base) are slightly active (entries 5 and 6), whereas the *in situ* complexes obtained from **9** and **8** in the presence of base indeed showed the highest activity: full racemization could be obtained within a day, and the 1,3-oxazolidine ligand without the methyl substituent turned out to be slightly more active.[22]

Racemization with Aminocycloruthenated Ru Complex

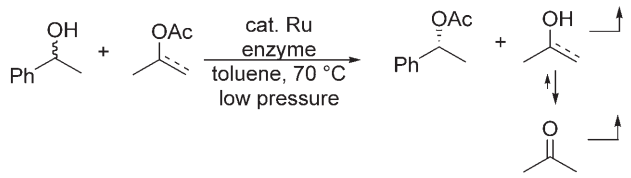
Pfeffer and co-workers recently showed that a variety of chiral cycloruthenated primary and secondary amines can be synthesized cleanly *in situ* upon reaction with dimeric $[RuCl_2(\eta^6\text{-cymene})]_2$ **9** and feature good activities in transfer hydrogenation of ketones.[16] Complex **5** was accordingly synthesized *in situ* upon reaction of dimer **9** with benzylamine, sodium hydroxide and potassium hexafluorophosphate in acetonitrile at room temperature in 65–70% yield. Aminocycloruthenated complex **5** displays a reasonable activity in the presence of potassium *tert*-butoxide (Table 1): the combination **5**/KO-*t*-Bu (5 mol%/5 mol%) catalyzed full racemization of (*S*)-1-phenylethanol in 18 h at 70 °C. Although not extremely active, the stability of the complex warranted further use under DKR conditions.

Dynamic Kinetic Resolution

Amino-ruthenium complex **4**, ampy-derived *in situ* catalytic systems obtained from **9**/**8a** and cycloruthenated amine **5** were subjected to DKR in combination with CAL B enzyme and potassium *tert*-butoxide in toluene at 70 °C. As acyl donors isopropenyl and isopropyl acetate were chosen.[23] The catalytic acylation is in principle reversible and hampered by its equilibrium (Scheme 3). However, in both cases the equilibrium towards the DKR product could be favoured by removal of the alcoholic product (either as acetone or isopropyl alcohol). To this end the reaction was conducted under reduced pressure. In all cases 1 equivalent of K_2CO_3 relative to alcohol was added. This base serves to absorb traces of water which originate from the CAL B sample, and which inhibit the acylation reaction.

As the results in Table 3 show, the use of 1 mol% of the reference Noyori-type $(TosNCH_2CH_2NH_2)$-RuCl(*p*-cymene) precatalyst **4** activated by 1 mol% of potassium *tert*-butoxide when combined with immobilized CAL B and isopropenyl acetate as the acylating agent shows after 48 h a conversion of 1-phenylethanol of 71%, affording 63% of the (*R*)-1-phenylethyl acetate with a satisfactory 97% *ee* (entry 1). The comparison of the simple *in situ* catalyst formed with **9**/**8a**/KO-*t*-Bu (1 mol% Ru) with the Noyori-type precatalyst shows a slightly better activity (77% conversion, entry 2) and a better selectivity towards the acylation (71% yield). Nevertheless, a satisfactory albeit lower 95% enantioselectivity was observed in that case.

Cycloruthenated amine **5** of the formula $[(\eta^2\text{-}C_6H_4\text{-}o\text{-}CH_2NH_2)Ru(NCMe)(\eta^6\text{-}p\text{-cymene})]PF_6$ gives the best result. After 48 h, 96% of *rac*-1-phenylethanol is converted (the only by-product is acetophenone) and



Scheme 3. Ru/enzyme combo DKR of 1-phenylethanol in the presence of isoprop(en)yl acetate.

Table 3. DKR of 1-phenylethanol catalyzed by Ru catalysts and CAL B.[a]

Entry	Ru catalysts (mol %)	Acyl donor	Conversion [%]	(*R*)-1-phenylethyl acetate Yield [%]	*ee* [%]
1	**4** (1)	isopropenyl acetate	71	63	97
2[b]	**9/8a** (1)	isopropenyl acetate	77	71	95
3[c]	**5** (5)	isopropyl acetate	96	86	>99

[a] Conditions: *rac*-1-phenylethanol (1.5 mmol), isopropenyl acetate (3 mmol), Ru catalyst (15 mmol), KO-*t*-Bu (30 mmol),CAL B (20 mg), toluene (20 mL), cumene or *n*-dodecane (370 mmol), Ar atmosphere, $T = 70\,^{\circ}C$, $P =$ 280 mbar, 48 h.

[b] **9** (7.5 mmol), **8a** (15 mmol), in a suspension of KO-*t*-Bu in toluene at 70 °C, 1 h under nitrogen.

[c] Ru catalyst (75 mmol), KO-*t*-Bu (75 mmol), isopropyl acetate (12 mmol).

86 % of enantiopure (*R*)-1-phenylethyl acetate (>99 % *ee*, entry 3) was obtained albeit using 5 mol % of potassium *tert*-butoxide and **5**.

Conclusions

In summary, we have shown that the use of certain amino chelating ligands afforded active to highly active Ru catalysts for the racemization of secondary alcohols. Especially the *ortho*-metalated ruthenium complex containing the 2-aminomethylpyridine motif, which was previously shown to be highly active in transfer hydrogenation, led to rapid racemization of 2-phenylethanol. However the stability of these complexes towards the immobilized lipase and the acyl donor under DKR conditions is rather unpredictable. Further studies on the deactivation pathway of these very active *ortho*-metalated ampy-based catalysts are required to ensure full compatibility with the immobilized enzyme and the acyl donor for very effective DKR.

Finally, three of these easily accessible systems utilizing a hydrido-amino bifunctional Ru catalyst proved to be stable and efficient in the presence of CAL B and other additives, thus enabling their use in an efficient DKR reaction with good selectivities, enantiopurities and yields.

Experimental Section

All racemization and dynamic kinetic resolution reactions were carried out under an argon atmosphere. Complex **4** was previously described.[11c] Complexes **6**, **7** and **7b** were prepared as described by Baratta and co-workers[17b,c,20] and their identity verified by ^{1}H NMR and ^{31}P NMR. Anhydrous solvents, substrates and acylating agents were obtained commercially and used without further purification. *Candida antarctica* lipase B was the commercially available Novozym 435. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 300 MHz instrument or Bruker Avance 400 MHz instrument relative to TMS. ^{31}P Chemical shift was measured on the Varian Inova 300 MHz relative to 1 % H_3PO_4. Enantiomeric excesses were determined by chiral GC using a Shimadzu GC-17 A, equipped with a Chirasil-DEX CB column (25 m × 0.32 mm, df = 0.25 μm), He as carrier gas.

In situ Formation of [(η^2-C_6H_4-*o*-CH_2NH_2)Ru(NCMe)(η^6-*p*-cymene)]PF_6 5

Complex **5** is the non-chiral analogue of compound **2** in ref.[16] and was used as an *in situ* preparation from benzylamine and Ru dimer **9** as described; mixing of [$RuCl_2$(η^6-cymene)], the primary amine with base and KPF_6 in acetonitrile for 72 h was followed by filtration over alumina. *In situ* NMR was performed to check the formation of the compounds: ^{1}H NMR (300 MHz, CD_3CN, 25 °C, TMS): $\delta = 1.13$ [d, $^3J_{H,H} = 6.9$ Hz, 3 H, $CH(CH_3)_2$], 1.16 [d, $^3J_{H,H} = 6.9$ Hz, 3 H, $CH(CH_3)_2$], 2.00 (s, 3 H, CH_3CN), 2.36 (s, 3 H, CH_3), 2.64 [sept, $^3J_{H,H} = 6.9$ Hz, 1 H, $CH(CH_3)_2$], 3.63 (s, 1 H, NH), 3.68 (m, 1 H, CH), 3.96 (m, 1 H, CH), 4.80 (s, 1 H, NH), 5.12 (dd, $^2J_{H,H} = 1.2$ Hz, $^3J_{H,H} = 6.0$ Hz, 1 H, *p*-cymene), 5.28 (dd, $^2J_{H,H} = 1.2$ Hz, $^3J_{H,H} = 6.0$ Hz, 1 H, *p*-cymene), 5.48 (dd, $^2J_{H,H} = 1.2$ Hz, $^3J_{H,H} = 6.0$ Hz, 1 H, *p*-cymene), 5.80 (dd, $^2J_{H,H} = 1.2$ Hz, $^3J_{H,H} = 6.0$ Hz, 1 H, *p*-cymene), 6.75–7.05 (m, 3 H, aromatic CH from benzyl), 7.76 (dd, $^2J_{H,H} = 1.2$ Hz, $^3J_{H,H} = 7.5$ Hz, 1 H, aromatic CH *ortho* to Ru–C); ^{13}C NMR (100.10 MHz, $CDCl_3$, TMS): $\delta = 17.83$ (CH_3), 21.87 [CH(CH_3)$_2$], 22.27 [CH(CH_3)$_2$], 31.19 [CH(CH_3)$_2$], 54.73 (CH_2), 81.99 ($CH_{p\text{-cymene}}$), 82.87 ($CH_{p\text{-cymene}}$), 87.17 ($CH_{p\text{-cymene}}$), 89.31 ($CH_{p\text{-cymene}}$), 99.94 ($C_{p\text{-cymene}}$), 109.13 ($C_{p\text{-cymene}}$), 120.92 (CH_{ar}), 123.34 (CH_{ar}), 126.41 (CH_{ar}), 139.19 (CH_{ar}), 147.63 (C_{ar}), 168.49 [(C–Ru)$_{ar}$].

Preparation of 4,4,2-Trimethyl-2-pyridin-2-yl-1,3-oxazolidine (8a)

To a solution of 2-amino-2-methyl-1-propanol (1.51 g, 17 mmol) and *p*-toluenesulfonic acid hydrate (28.5 mg, 0.15 mmol) in anhydrous toluene (50 mL) was added freshly distilled 2-acetylpyridine (1.82 g, 15 mmol). The mixture was refluxed overnight under nitrogen with azeotropic removal of water using a Dean–Stark set-up. After evaporation of the solvent under reduced pressure, a yellow residue was obtained (2.31 g, 80 %). Purification by kugelrohr distillation gave pure liquid **8a**. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): $\delta =$ 8.57 (1 H, m, NCH), 7.67 (1 H, m, NCHC*H*), 7.65 (1 H, m, NCC*H*), 7.16 (1 H, m, NCCC*H*), 3.70–3.39 (2 H, OCH_2), 3.10 (1 H, s, NH), 1.67 (3 H, s, CH_3), 1.33 (3 H, s, CH_3), 1.04 (3 H, s, CH_3); ^{13}C NMR (100.10 MHz, $CDCl_3$, TMS): $d =$ 164.1, 148.5, 136.5, 122.2, 119.4, 97.2, 77.5, 59.4, 29.7, 25.9, 23.8.

Preparation of 4,4-Dimethyl-2-pyridin-2-yl-1,3-oxazolidine (8b)

2-Pyridinecarboxaldehyde (0.89 g, 8.31 mmol) and 2-amino-2-methyl-1-propanol (0.75 g, 8.41 mmol) were added in 80 mL of absolute ethanol. The reaction mixture was stirred at room temperature for 3 h. After evaporation of the sol-

vent under reduced pressure a yellow crude oil was obtained. Purification by kugelrohr distillation gave yellow oil; yield: 1.39 g (94%). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 8.61 (1H, m, NCH), 8.45 (1H, OCH), 7.69 (1H, m, NCHC*H*), 7.42 (1H, m, NCC*H*), 7.22 (1H, m, NCCC*H*), 3.69–3.51 (2H, OCH_2), 3.14 (1H, s, NH), 1.38 (3H, s, CH_3), 1.32 (3H, s, CH_3); ^{13}C NMR (100.10 MHz, $CDCl_3$, TMS): δ = 157.1, 149.4, 136.7, 123.7, 122.4, 91.9, 76.8, 59.9, 26.0, 23.8

Typical Procedure for the Racemization of (*S*)-1-Phenylethanol

To a Schlenk-type flask containing 1–5 mol% of a ruthenium catalyst and 1–5 mol% of KO-*t*Bu (if required) was added in toluene (5 mL). The solution was stirred at 70°C under an argon atmosphere prior to the introduction of (*S*)-1-phenylethanol (0.5 mmol, 62 mg) at 70°C. The *ee*s were monitored over time by taking aliquots (0.5 mL) that were filtered through a short silica gel pad column and diluted to a suitable concentration in diethyl ether for chiral GC analysis. In case of *in situ* generated complexes ligand and Ru precursor **9** were stirred for 2 h at room temperature or 70°C (see Table 1). For calculation of TOF and $ee_{initial}$ = 100%, TOF [h^{-1}] = 50[1−(*ee*/100)]/(ct) where *ee*, c and t are the enantiomeric excess, the catalyst loading in mol% and the time in hour respectively. In some cases (*S*)-1-phenylethanol with $ee_{initial}$ = 50% was used (Table 2 entries 2,3 and 6) and TOF [h^{-1}] = 25[1−(*ee*/100)]/(ct).

Typical Procedure for Dynamic Kinetic Resolution of 1-Phenylethanol

In a round-bottom flask equipped with a distillation column were introduced potassium carbonate (207 mg, 1.5 mmol), CAL B (20 mg) and toluene (10 mL). The suspension was dried azeotropically at 70°C under reduced pressure for 1 h. A solution of Ru complex (75 μmol), KO-*t*-Bu (8.4 mg, 75 μmol), *rac*-1-phenylethanol (183 mg, 1.5 mmol) and *n*-dodecane (63 mg, 0.370 mmol) in toluene (5 mL) was stirred at 70°C for 1 h and cannulated to the CAL B suspension and isopropyl acetate (3 mmol) or isopropenyl acetate (12 mmol) was then introduced. The resulting suspension was stirred under reduced pressure (280 mbar) at 70°C and monitored in time by taking aliquots that were subjected to chiral GC analysis.

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