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Synthesis of Stable Ruthenium Olefin Metathesis Catalysts with Mixed Anionic Ligands

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A series of ruthenium carboxylate complexes that contain two different anionic ligands was prepared. The complexes that bear iodide ligands exhibit remarkable chemical stability. Such complexes have a diminished tendency to undergo anionic ligand exchange and can be activated by various acids to form catalysts, which are active in olefin metathesis reactions.

Introduction

Olefin metathesis has become a standard tool in organic synthesis.[1a,1b] Since ruthenium complex **1a** was developed by Grubbs, modifications of the parent core have improved its catalytic activity.[1c] The real breakthrough came with the introduction of *N*-heterocyclic carbene ligands[1d] and discovery of Hoveyda-type catalysts **2**, which possess better stability and activity profiles (Figure 1).[1e]

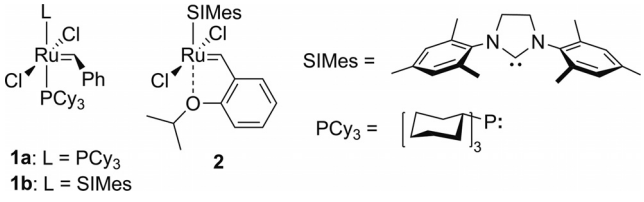
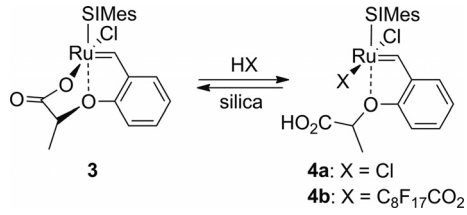


Figure 1. Ruthenium olefin-metathesis catalysts.

One of the platforms for the modification of catalyst properties are anionic ligands. A lot of research has been devoted to replace the parent chloride ligands with other halides, carboxylic, sulfonic, phosphonic, and nitric acids, etc.[2] Some of these modifications have been used to immobilize catalysts,[3] whereas others changed their reactivity and selectivity in olefin metathesis reactions.[4] Although examples of catalysts with two different anionic ligands have been reported,[4,5] halides and pseudohalides are generally labile, and the synthesis of catalysts with mixed anionic ligands seems to be problematic.[6] We have previously developed **3** with a chelating carboxylate ligand (Scheme 1).[7a] Although **3** is inactive in olefin metathesis, the cyclic ruthenium carboxylate can be cleaved by a broad selection of organic and inorganic acids[7b] to give highly active catalysts (e.g. **4a** and **4b**, Scheme 1).



Scheme 1. Complex **3** and catalytically active **4a** and **4b**.[7a]

The method to introduce an acid to the ruthenium coordination sphere is straightforward and does not require the use of silver or thallium salts.[2] We used this method to obtain a surfactant-decorated catalyst for metathesis in water emulsions,[8] whereas Lee and coworkers used **3** for metathesis in an ionic liquid.[9] Although **3** was used in some interesting applications, we observed that carboxylate complexes that bear two different anionic ligands (e.g. **4b**) undergo disproportionation to give a mixture of complexes. Our present work is focused on the inhibition of this process.

Results and Discussion

We have reported that different acids can be used to activate **3** to form active catalysts, which include complexes with mixed anionic ligands (e.g. **4b**).[7a] We observed that these complexes undergo disproportionation through anionic ligand exchange.[6] For example, when 1 equiv. of perfluorononanoic acid was added to a solution of **3** in $CDCl_3$, **4b** was formed immediately, however, ^1H NMR spectroscopic inspection of the reaction mixture has shown the presence of minor amounts of **5** and **4a** (Scheme 2).[10]

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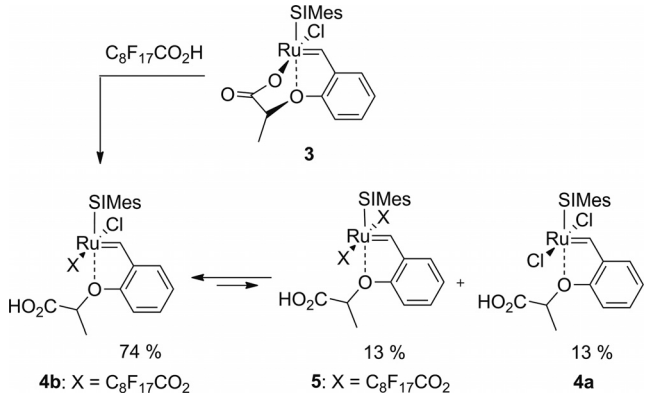
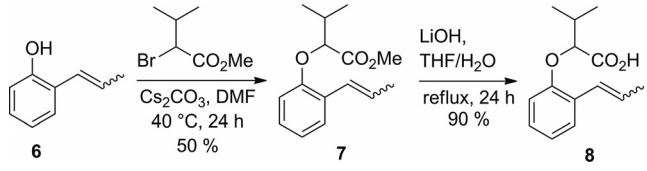


Scheme 2. Formation and disproportionation of **4b**.

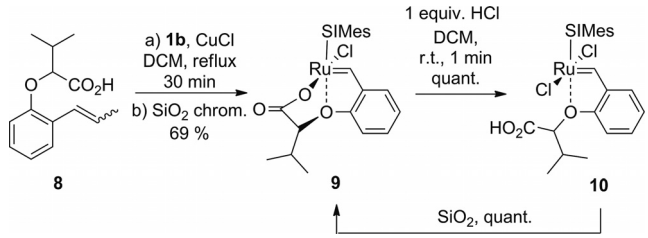
Although the desired complex **4b** was the major compound in this equilibrium (74%), the dichloride complex **4a** (13%) is much more active in metathesis and the overall reactivity of such a mixture is not well defined. This disproportionation may be irrelevant in many applications,[8,9] but could be a problem in some cases, such as immobilization. Moreover, the isolation of complexes with mixed anionic ligands in pure forms can be problematic due to the equilibrium mentioned. In one of our projects related to nanofiltration,[11] we became interested in well-defined complexes that show no tendency for anionic ligand exchange. We presumed that changing the chloride in **3** to another ligand may affect the equilibrium of the anionic ligand exchange. As the lability of anionic ligands in monoiodide ruthenium catalysts has not been investigated and the introduction of iodide is straightforward, we decided to prepare an iodide analogue of **3**. It is well known that changing a chloride ligand to iodide in ruthenium complexes can cause a serious decrease in the catalytic activity.[2r,12] To minimize this effect, we focused on the optimization of the parent structure of **3**. Our assumption was that the replacement of the methyl substituent in **3** with a bulkier isopropyl group would increase the activity of the resulting complex, which would compensate for the expected decrease in activity caused by the introduction of iodide.

Starting from commercially available 2-propenylphenol **6** and methyl 2-bromo-3-methylbutanoate, ester **7** was obtained. Mild hydrolysis afforded the carboxylic acid ligand precursor **8** in good yield (Scheme 3).



Scheme 3. Synthesis of **8**.

Precursor **8** was treated with Grubbs' second generation catalyst **1b** in the presence of CuCl as a phosphane scavenger to give **9** in good yield (Scheme 4). The initial product of this reaction was **10**, which underwent spontaneous cyclization to **9** during silica gel chromatography. Isolated **9** can be transformed back to the active **10** by the addition of 1 equiv. of HCl in diethyl ether, and **10** can be cyclized again to **9** using silica gel or a base.



Scheme 4. Synthesis of **9** and **10**.

During the cyclization of **10** to **9**, a new stereogenic center was created at the ruthenium centre. Because **8** also has a stereogenic center, one can expect the formation of a mixture of diastereoisomers. However, a careful inspection of the ^{1}H NMR spectrum of **9** shows that this product was formed as a single diastereoisomer.[13] Therefore, we think that the cyclization of carboxylate is stereospecific (the same is true for **3**). The activity of **10** was compared to the activity of **4a** and commercially available Hoveyda second generation catalyst **2** in the model ring closing metathesis (RCM) reaction of diethyl diallylmalonate (DEDAM, Figure 2).

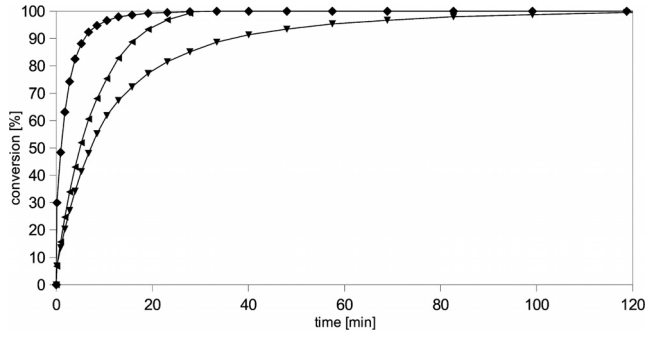
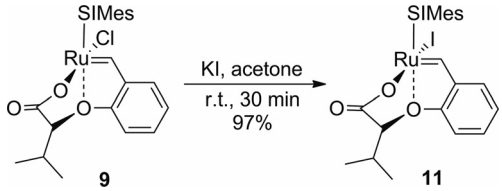


Figure 2. Comparison of the activity of **4a** (▼), **10** (◆), and **2** (◀) in the RCM of DEDAM. Conditions: catalyst loading 5 mol-%, T = 24 °C, c = 0.1 M, CD_2Cl_2. Conversion measured by ^{1}H NMR spectroscopy.

As expected, changing the methyl group in **4a** (obtained by acid activation of **3**) to a bulkier isopropyl group in **10** (obtained from **9**) greatly enhanced the catalytic activity in olefin metathesis. Interestingly, **10** was found to be slightly more active than **2** (Figure 2).

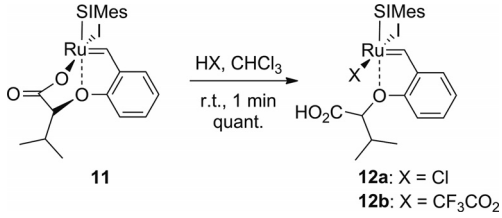
With the optimized structure of **9** in hand, we attempted to replace the chloride ligand to obtain the iodide analogue. A solution of **9** in acetone was treated with an excess of potassium iodide followed by filtration of the inorganic

salts. After triple repetition of this procedure, **11** was obtained in almost quantitative yield and high purity (Scheme 5).



Scheme 5. Synthesis of **11**.

Although chloride complexes **3** and **9** were found to be very stable (no decomposition in solution for days), to our surprise the iodide complex **11** was even more stable and could be stored as a stock solution for months, even in non-degassed solvents. Similar to **3** and **9**, **11** is not active in olefin metathesis and requires activation by acids. To test its susceptibility to anionic ligand exchange, we used HCl and trifluoroacetic acid to form mixed ligand complexes **12a**–**b** (Scheme 6).



Scheme 6. Activation of **11**.

When 1 equiv. of HCl in diethyl ether was added to a solution of **11** in $CDCl_3$ (0.02 M), the "opened" complex **12a** was formed immediately. We noted that the equilibration is significantly slower than for **4b**. Dichloride **10** and diiodide complexes were observed only in small amounts (< 5%).[14] Similarly, when 1 equiv. of trifluoroacetic acid was added to a solution of **11** in $CDCl_3$ (0.02 M), **12b** was obtained as the sole product without equilibration (cf. Scheme 2).[15] Moreover, after 2 h at 60 °C in [D_8]toluene or $CDCl_3$, no equilibration was observed. Complex **12b** was stable in solution for days without any sign of decomposition.

These results show that iodide-bearing **12a** and especially **12b** have a greatly reduced tendency to disproportionation compared with **4b**. Careful analysis of the ^{1}H NMR spectra of **12a** and **12b** suggests that cleavage of the carboxylate is diastereoselective.[16]

Next, we compared **10**, **12a**, and **12b** in the RCM of DEDAM at room temperature (Figure 3).

As expected, **10** was the most active. Complex **12a** with mixed chloride–iodide ligands was only slightly less active, and **12b** with mixed iodide–trifluoroacetate ligands was far less active at room temperature. However, because of the excellent stability of **12b** in solution, after prolonged reaction times it was possible to reach higher conversions (15% after 8 h, 50% after 24 h, and 70% after 48 h) even at room temperature. Next, we examined **12b** under different reaction conditions (Figure 4).

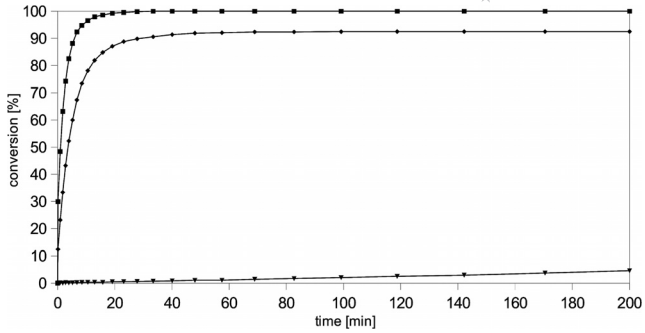


Figure 3. Comparison of activity of **10** (■), **12a** (♦), and **12b** (▼) in the RCM of DEDAM. Conditions: catalyst loading 5 mol-%, T = 24 °C, c = 0.1 M, CD_2Cl_2. Conversion measured by ^{1}H NMR spectroscopy.

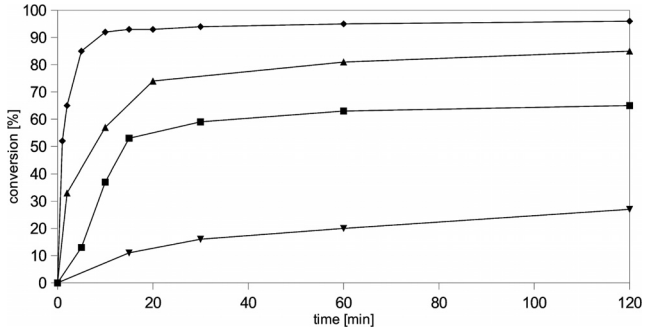


Figure 4. Activity of **12b** in the RCM of DEDAM. Conditions: catalyst loading 5 mol-%, c = 0.1 M; CH_2Cl_2, 40 °C (■); THF, 60 °C (▼); DCE, 60 °C (▲); toluene, 60 °C (♦). Conversion measured by ^{1}H NMR spectroscopy.

We noted that simply changing the reaction temperature from 24 to 40 °C gave better activity in CH_2Cl_2 (■). We decided to increase the temperature to 60 °C and test tetrahydrofuran (THF), 1,2-dichloroethane (DCE), and toluene as possible solvents. The reaction in THF at 60 °C (▼) was slower than that in CH_2Cl_2 at 40 °C. Although switching to DCE (▲) gave much better results, toluene (♦) was the best solvent (Figure 4).

Using 5 mol-% of catalyst in the RCM of a straightforward substrate such as DEDAM is far from the current state of the art of olefin metathesis. We decided to check the lower limit of catalyst loading in this reaction. We decreased the loading of **12b** to 0.1 mol-% and carried out the RCM of DEDAM in toluene at 80 and 100 °C (Table 1). Taking advantage of the excellent thermal stability of the iodide complex, the best results were obtained in toluene at 100 °C (Table 1, Entry 2). Thus, we decided to decrease the loading of **12b** to 0.05 mol-% and switch to boiling xylene as the solvent (Entry 3). It is surprising that even at 142 °C **12b** is stable for 2 h, and quite high conversion can be

Table 1. Low loading and high temperature application of **12b**.

Entry	Conditions	Loading of **12b**	2 h	24 h	48 h	72 h
1	toluene, 80 °C	0.1 mol-%	3%	55%	75%	84%
2	toluene, 100 °C	0.1 mol-%	32%	88%	93%	95%
3	xylene, 142 °C	0.05 mol-%	61%	70%	71%	71%

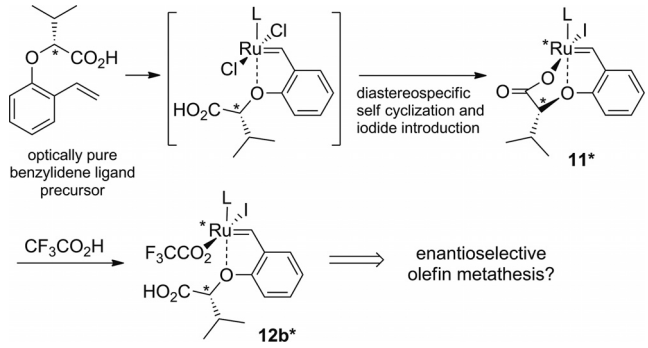
achieved for RCM under these conditions. At such a temperature, many commercially available catalysts decompose rapidly, even in the absence of a substrate.

In summary, the test reactions show that the introduction of iodide and trifluoroacetate ligands instead of chloride deactivates the complex, as the activity of **12b** at 60 °C is comparable to that of **12a** at 24 °C. However, the observed activity and thermal stability is high enough to make **12b** useful for a number of applications at higher temperatures.[17]

Encouraged by our observation that the self-cyclization of **10** to **9** is diastereospecific, we decided to check if the chiral information that originated from the optically pure benzylidene ligand and transferred to the metal center in **9** can be utilized in practical manner. We presumed that due to the stabilization of the anionic ligand sphere by iodide, the chiral information will be preserved at ruthenium, which would enable the use of chiral-at-metal iodide complexes, such as **12b***, in enantioselective metathesis (Scheme 7).

Isolated attempts to use optically active benzylidene ligands to obtain chiral ruthenium catalysts for enantioselective olefin metathesis have been reported without success.[18] The proposed explanation of the observed lack of asymmetric induction with these catalysts is that the optically active benzylidene ligand dissociates during the first catalytic cycle to leave achiral propagating species.[18a]

However, the reduced lability of the anionic ligands in **12a** and **12b** would, at least in theory, lead to stable chiral propagating species. Therefore, we decided to check if we could observe asymmetric induction in a model enantioselective olefin metathesis reaction promoted by acid-activated, optically active **11***.

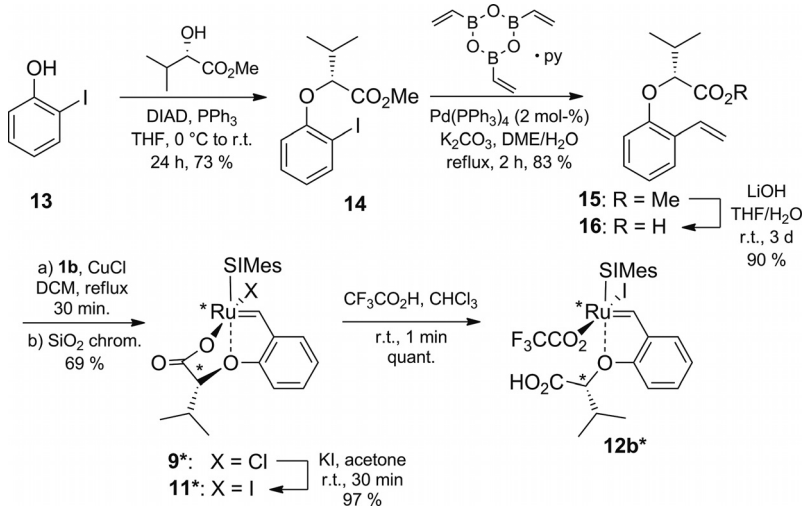


Scheme 7. Concept of chirality transfer from benzylidene to Ru.

To synthesize an optically pure version of **11**, we started from methyl (*S*)-2-hydroxy-3-methylbutanoate and 2-iodophenol **13** (Scheme 8). Compound **14** was prepared by a Mitsunobu reaction according to the described procedure.[19] To introduce a vinyl group, a Suzuki reaction was used to obtain styrene **15**. Mild hydrolysis afforded precursor **16** without the loss of optical purity.

Precursor **16** was used to obtain optically pure **9***. Next, we introduced the iodide ligand to obtain **11***. The optical purity of **9*** and **11*** was determined by HPLC (Figure 5).

In an analogous procedure to the formation of **12a** and **12b**, optically active **12a*** and **12b*** were obtained from **11***. Analysis of their ^{1}H NMR spectra showed the presence of only one diastereoisomer, which suggests no epimerization of the Ru center. Unfortunately, due to the reversible cyclization of **12a*** and **12b*** back to **11***, the activated complexes were not suitable for chiral HPLC measurements. Complexes **12a*** and **12b*** were tested in the model desymmetrization of triene **17** under conditions previously described in literature (Scheme 9).[20]



Scheme 8. Preparation of **9***, **11***, and **12b***.

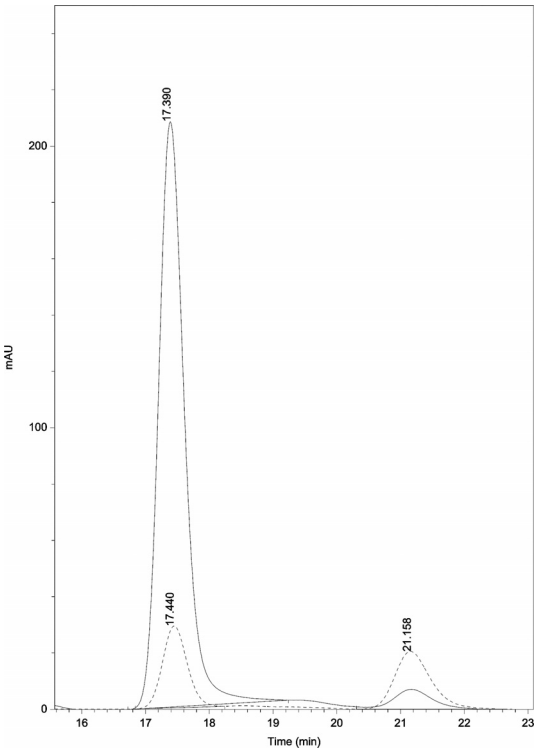
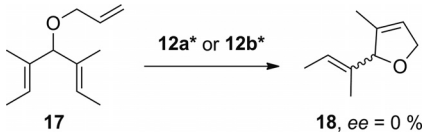
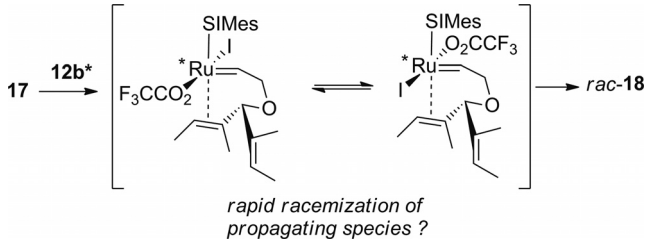


Figure 5. HPLC of **11*** (solid line) and racemic **11** (dashed line).



Scheme 9. Model desymmetrization of **17**.

Unfortunately, despite many trials, which included variation of solvents, concentration, temperature, etc., no traces of asymmetric induction were observed with **12a*** and **12b***. This result can be explained by the fast racemization of the chiral 14-electron X–Ru*–I center after dissociation of the benzylidene ligand (Scheme 10).[21]



Scheme 10. Racemization of chiral propagating species: possible reason for the observed lack of asymmetric induction.

Conclusions

We have reported the preparation of stable ruthenium carboxylate complexes that contain different anionic ligands. Complex **11**, which bears an iodide ligand, exhibits remarkable stability and can be stored as a stock solution for months with no sign of decomposition. Upon activation of **11** by HCl and trifluoroacetic acid, **12a** and **12b** were obtained and their activity was investigated in the model RCM reaction of DEDAM.

We also found that the replacement of the methyl group with a more sterically demanding isopropyl group led to a significant increase of activity of the corresponding dichloride complex **10**. Finally, optically pure **9*** and **11*** were obtained and their purity was proven by HPLC. Despite the inhibition of anionic ligand exchange by the introduction of iodide, no asymmetric induction was observed when **12a*** and **12b*** were used in a model triene desymmetrization reaction.

It is important to note that **12a** and **12b** have a diminished tendency to undergo anionic ligand exchange. This property can be used to tag or immobilize a metathesis catalyst on various supports. Research in this direction is now underway in our laboratories.[22]

Experimental Section

General: The preparation of **9**, **10**, **12a**, and **12b** was carried out under Ar in predried glassware using Schlenk techniques. The preparation of **7** and **8** was carried out in air. CH_2Cl_2 (Aldrich) and DCE (Aldrich), were dried by distillation with CaH_2 under argon and were stored under argon. THF, toluene, and xylene were dried by distillation with Na/K alloy. The preparation of **11** was carried out in air in reagent-grade acetone. Column chromatography was performed using Merck silica gel 60 (230–400 mesh). NMR spectra were recorded in $CDCl_3$ or CD_2Cl_2 with Varian Gemini 200 MHz, Varian Mercury 400 MHz, Varian VNMRS 500 MHz, and Varian VNMRS 600 MHz spectrometers. MS (FD/FAB) were recorded with a GCT Premier spectrometer from Waters. MS (EI) spectra were recorded with a AMD 604 Intectra GmbH spectrometer. HPLC analysis was performed with a Daicel Chiralpak® AD-H column (254 nm). Optical rotations were measured with a Jasco P-2000 polarimeter, and the concentration (*c*) is given as g/100 mL. Compounds **1b** and **14** were prepared according to published procedures.[19] All other commercially available chemicals were used as received.

Methyl 3-Methyl-2-(2-propenylphenoxy)butanoate (7): Cs_2CO_3 (3.26 g, 10 mmol) was added to a solution of an *E*/*Z* mixture of 2-propenylphenol (671 mg, 5 mmol) in *N*,*N*-dimethylformamide (DMF, 20 mL). After stirring for 30 min at room temperature, methyl 2-bromo-3-methylbutanoate (1.07 g, 5.5 mmol) was added, and the reaction mixture was stirred for 24 h at 40 °C. The reaction mixture was poured onto water (100 mL) and extracted with diethyl ether (3 × 25 mL). The combined extracts were washed with brine and water and dried (Na_2SO_4). The solvent was evaporated to give the crude product as a yellow oil. Purification by silica gel chromatography (AcOEt/*c*-hexane, 97:3, v/v) afforded **7** as a colorless oil (615 mg, 50%). Mixture of isomers: *E*/*Z* = 4.5:1. IR (CH_2Cl_2): $\tilde{\nu}$ = 2966, 1757, 1486, 1235, 749 cm^{-1}. $C_{15}H_{20}O_3$ (248.32): calcd. C 72.55, H 8.12; found C 72.45, H 8.14. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.43 (dd, J = 7.6, 1.5 Hz, 0.8 × 1 H), 7.30–7.27 (m, 0.2 × 1 H), 7.17–7.12 (m, 0.2 × 1 H), 7.12–7.07 (m, 0.8 × 1 H), 6.96–6.88 (m, 1 H), 6.84–6.78 (m, 0.8 × 1 H), 6.69 (br. d, 0.2 × 1 H), 6.68–6.61 (m, 0.8 × 1 H + 0.2 × 1 H), 6.23 (dq, J = 15.9, 6.7 Hz, 0.8 × 1 H), 5.82 (dq, J = 11.6, 7.1 Hz, 0.2 × 1 H), 4.41 (d, J =

5.3 Hz, 1 H), 3.73 (s, 3 H), 2.37–2.26 (m, 1 H) 1.91 (dd, J = 6.7, 1.8 Hz, 0.8 × 3 H), 1.84 (dd, J = 7.1, 2.0 Hz, 0.2 × 3 H) 1.12 (d, J = 6.8 Hz, 0.8 × 3 H), 1.08 (d, J = 6.8 Hz, 0.8 × 3 H + 0.2 × 3 H), 1.06 (d, J = 6.8 Hz, 0.2 × 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.9, 155.6 (*Z*), 154.6 (*E*), 130.4, 127.7, 127.6, 126.4, 125.4 (*E*), 125.1 (*Z*), 121.4 (*E*), 120.7 (*Z*), 112.2 (*E*), 112.1 (*Z*), 81.8 (*E*), 81.7 (*Z*), 51.9 (*E*), 51.9 (*Z*), 31.8, 18.9 (*E*), 18.8 (*E*), 18.7 (*Z*), 17.9 (*E*), 17.8 (*Z*), 14.7 (*Z*) ppm. HRMS (EI): calcd. for $C_{15}H_{20}O_3$ [M]$^+$ 248.1412; found 248.1419.

3-Methyl-2-(2-propenylphenoxy)butanoic Acid (8): LiOH (479 mg, 20 mmol) was added to a solution of **7** (1241 mg, 5 mmol) in THF/H_2O (20 mL; 9:1 v/v). The mixture was heated to reflux with stirring for 24 h, cooled to room temperature, and acidified with diluted HCl. THF was removed in vacuo, and the residue was extracted with AcOEt (3 × 25 mL). The combined extracts were washed with brine and water and dried (Na_2SO_4). The solvent was evaporated to give the crude product as a yellow oil. Purification by silica gel chromatography (AcOEt/*c*-hexane = 2:1 v/v) afforded **8** as a white crystalline solid (1050 mg, 90%). Mixture of isomers: *E*/*Z* = 4.5:1. IR (CH_2Cl_2): $\tilde{\nu}$ = 3036, 2935, 1723, 1486, 1234, 749 cm^{-1}. $C_{14}H_{18}O_3$ (234.30): calcd. C 71.77, H 7.74; found C 71.87, H 7.65. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.74 (br. s, 1 H), 7.42 (dd, J = 7.7, 1.5 Hz, 0.8 × 1 H), 7.30–7.27 (m, 0.2 × 1 H), 7.19–7.14 (m, 0.2 × 1 H), 7.14–7.09 (m, 0.8 × 1 H), 6.99–6.90 (m, 1 H), 6.82–6.76 (m, 0.8 × 1 H), 6.75 (bd, 0.2 × 1 H), 6.70 (bd, 0.8 × 1 H), 6.64–6.58 (m, 0.2 × 1 H), 6.23 (dq, J = 15.9, 6.7 Hz, 0.8 × 1 H), 5.82 (dq, J = 11.6, 7.1 Hz, 0.2 × 1 H), 4.47 (d, J = 4.8 Hz, 1 H), 2.42–2.30 (m, 1 H) 1.90 (dd, J = 6.7, 1.7 Hz, 0.8 × 3 H), 1.83 (dd, J = 7.0, 1.9 Hz, 0.2 × 3 H) 1.15 (d, J = 6.8 Hz, 0.8 × 3 H), 1.12 (d, J = 6.8 Hz, 0.8*3 H + 0.2 × 3 H), 1.10 (m, 0.2 × 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8 (*E*), 176.5 (*Z*), 155.2 (*Z*), 154.3 (*E*), 130.5, 127.9, 127.7, 126.7, 125.3 (*E*), 125.0 (*Z*), 121.7 (*E*), 121.2 (*Z*), 112.4 (*Z*), 112.3 (*E*), 81.3 (*Z*), 81.1 (*E*), 31.7, 19.0 (*E*), 18.9 (*E*), 18.8 (*Z*), 17.6 (*E*), 17.5 (*Z*), 14.7 (*Z*) ppm. HRMS (EI): calcd. for $C_{14}H_{18}O_3$ [M]$^+$ 234.1256; found 234.1252.

Synthesis of 9: Compound **1b** (849 mg, 1 mmol) was dissolved in CH_2Cl_2 (10 mL), and **8** (234 mg, 1 mmol) was added under an argon atmosphere. The mixture was stirred for 5 min, CuCl (148 mg, 1.5 mmol) was added, and the mixture was heated to reflux for 30 min. The reaction mixture was allowed to cool to room temperature and concentrated in vacuo. From this point, all manipulations were carried out in air with reagent-grade solvents. The product was purified by silica gel chromatography (AcOEt/*c*-hexane = 1:3 v/v). The solvent was evaporated under vacuum, and the residue was dissolved in CH_2Cl_2 (2 mL). MeOH (5 mL) was added and CH_2Cl_2 was slowly removed under vacuum. The precipitated product was collected by filtration, washed with MeOH (5 mL), and dried in vacuo to afford **9**·MeOH as a green microcrystalline solid (471 mg, 69%). IR (CH_2Cl_2): $\tilde{\nu}$ = 2960, 1661, 1481, 1267 cm^{-1}. $C_{33}H_{39}ClN_2O_3Ru{\cdot}CH_4O$ (648.21 + 32.04): calcd. C 60.03, H 6.37, Cl 5.21, N 4.12; found C 60.12, H 6.38, Cl 5.33, N 4.02. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 16.47 (s, 1 H), 7.52–7.47 (m, 1 H), 7.11–7.06 (m, 4 H), 7.06–7.02 (m, 1 H), 6.94–6.89 (m, 2 H), 4.26 (d, J = 4.8 Hz, 1 H), 4.17 (br. s, 4 H), 2.6–2.3 (m, 18 H), 1.93–1.84 (m, 1 H), 1.07 (d, J = 6.8 Hz, 3 H), 0.70 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 291.8, 210.0, 180.9, 155.3, 146.6, 139.1, 129.9, 129.7, 129.5, 126.5, 122.1, 118.7, 93.1, 31.3, 21.1, 19.5, 18.5, 16.9 ppm.

Synthesis of 10: HCl (2 M in Et_2O, 50 μL, 0.1 mmol) was added to a solution of **9**·MeOH (68 mg, 0.1 mmol) in CH_2Cl_2 (0.5 mL). The product was precipitated by the addition of *n*-pentane (3 mL), collected by filtration, and dried in vacuo to give a green microcrystalline solid (68 mg, quant.). IR (CH_2Cl_2): $\tilde{\nu}$ = 3015, 2967, 1758, 1481, 1267, 1015, 749 cm^{-1}. $C_{33}H_{40}Cl_2N_2O_3Ru$ (684.67): calcd. C 57.89, H 5.89, Cl 10.36, N 4.09; found C 57.74, H 5.79, Cl 10.56, N 3.86. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 16.83 (s, 1 H), 10.62 (br., 1 H), 7.58–7.53 (m, 1 H), 7.16–7.04 (m, 4 H), 7.03–6.98 (m, 1 H), 6.96–6.92 (m, 1 H), 6.87–6.83 (m, 1 H), 4.67 (d, J = 5.3 Hz, 1 H), 4.18 (s, 4 H), 2.64–2.22 (m, 19 H), 1.06 (d, J = 6.8 Hz, 3 H), 0.78 (d, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 300.2, 207.4, 168.4, 151.6, 143.8, 139.2, 131.0, 129.7, 124.5, 123.4, 112.9, 86.9, 29.6, 21.1, 21.0, 17.9 ppm.

Synthesis of 11: Complex **9**·MeOH (136 mg; 0.2 mmol) was dissolved in reagent-grade acetone (10 mL) in air, and KI was added (1.66 g; 10 mmol). The mixture was stirred for 30 min and then filtered. The addition of KI and stirring for 30 min was repeated twice more. The mixture was filtered, and the solvent was evaporated in vacuo. The residue was redissolved in CH_2Cl_2 (2 mL), passed through a pad of silica, and washed with AcOEt (10 mL). The solvents were evaporated in vacuo, and the residue was dissolved in CH_2Cl_2 (1 mL). MeOH was added (3 mL), and CH_2Cl_2 was slowly removed under vacuum. The precipitated product was collected by filtration, washed with MeOH (1 mL), and dried in vacuo to afford **11**·MeOH as a dark green microcrystalline solid (150 mg, 97%). IR (CH_2Cl_2): $\tilde{\nu}$ = 2960, 1661, 1480, 1266, 752 cm^{-1}. $C_{33}H_{39}IN_2O_3Ru{\cdot}CH_4O$ (739.66 + 32.04): calcd. C 52.92, H 5.62, I 16.44, N 3.63; found C 52.27, H 5.66, I 16.58, N 3.59. ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 15.80 (s, 1 H), 7.62–7.57 (m, 1 H), 7.12–7.03 (m, 5 H), 7.03–7.00 (m, 1 H), 7.00–6.97 (m, 1 H), 4.29 (d, J = 5.5 Hz, 1 H), 4.25–4.05 (br., 4 H), 2.75–2.10 (br., 18 H), 1.84 (m, 1 H), 1.05 (d, J = 6.8 Hz, 3 H), 0.71 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, CD_2Cl_2): δ = 290.1, 211.3, 179.8, 155.1, 146.6, 139.1, 130.2, 129.6, 126.4, 122.1, 118.6, 93.1, 31.3, 20.8, 19.1, 18.9, 17.4 ppm.

Synthesis of 12a: HCl (2 M in Et_2O, 50 μL, 0.1 mmol) was added to a solution of **11**·MeOH (77 mg, 0.1 mmol) in $CHCl_3$ (0.5 mL). The product was precipitated by the addition of *n*-pentane (3 mL), collected by filtration, and dried in vacuo to give a green microcrystalline solid (77 mg, quant.). IR (CH_2Cl_2): $\tilde{\nu}$ = 3008, 2965, 1759, 1479, 1265, 749 cm^{-1}. $C_{33}H_{40}ClIN_2O_3Ru$ (776.13): calcd. C 51.07, H 5.19, I 16.35, N 3.61; found C 50.93, H 5.18, I 16.23, N 3.38. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 16.34 (s, 1 H), 10.75 (br., 1 H), 7.61–7.56 (m, 1 H), 7.17–7.11 (br., 1 H), 7.11–7.01 (br. m, 4 H), 4.77 (d, J = 4.5 Hz, 1 H), 2.69–2.60 (m, 1 H). 1.07 (d, J = 7.0 Hz, 3 H), 0.73 (d, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 301.0, 208.6, 168.3, 151.9, 143.5, 131.5, 129.8, 124.4, 123.7, 113.10, 86.8, 29.7, 21.2, 17.7 ppm.

Synthesis of 12b: Trifluoroacetic acid (8 μL, 0.1 mmol) was added to a solution of **11**·MeOH (77 mg, 0.1 mmol) in $CHCl_3$ (0.5 mL). The product was precipitated by the addition of *n*-pentane (3 mL), collected by filtration, and dried in vacuo to give a green microcrystalline solid (85 mg, quant.). IR (CH_2Cl_2): $\tilde{\nu}$ = 3397, 2963, 2917, 1776, 1657, 1482, 1267, 1173, 578 cm^{-1}. $C_{35}H_{40}F_3IN_2O_5Ru$ (853.69): calcd. C 49.24, H 4.72, F 6.68, I 14.87, N 3.28; found C 48.95, H 4.73, F 6.66, I 14.76, N 3.06. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 16.06 (s, 1 H), 8.45 (br., 1 H), 7.64–7.59 (m, 1 H), 7.12–7.02 (m, 4 H), 7.01–6.95 (m, 2 H), 4.48 (d, J = 5.4 Hz, 1 H), 4.35–4.00 (br., 4 H), 2.90–2.55 (br., 3 H), 2.55–2.00 (br., 15 H), 1.90–1.76 (m, 1 H), 1.06 (d, J = 6.8 Hz, 3 H), 0.73 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 295.6, 210.5, 184.4, 158.6 (q, J = 40 Hz), 154.7, 146.6, 131.0, 129.8, 126.9, 122.5, 118.7, 92.7, 31.4, 21.1, 19.2, 17.4 ppm.

Methyl (*R*)-3-Methyl-2-(2-vinylphenoxy)butanoate (15): Methyl (*R*)-2-(2-iodophenoxy)-3-methylbutanoate (**14**, 334 mg, 1 mmol) was

dissolved in DME (7 mL). Tetrakis(triphenylphosphane)palladium(0) (23 mg, 0.02 mmol) was added, and the mixture was stirred under an argon atmosphere for 30 min. Potassium carbonate (138 mg, 1 mmol), water (3 mL), and 2,4,6-trivinylcyclotriboroxane pyridine complex (241 mg, 1 mmol) were added, and the reaction mixture was heated to reflux under argon for 2 h. The reaction mixture was cooled to room temperature, diluted with water (50 mL), and extracted with diethyl ether (3 × 10 mL). The combined extracts were dried (Na_2SO_4), and the solvent was evaporated. The residue was dissolved in hexane (50 mL) and passed through a short aluminum oxide column. The solvent was evaporated to give the crude product as a yellow oil. Purification by silica gel chromatography (AcOEt/*c*-hexane = 2:98 v/v) afforded **15** as a colorless oil (194 mg, 83%). $[\alpha]_D^{rt}$ = +3.06 ($CHCl_3$, *c* = 0.97). IR (CH_2Cl_2): $\tilde{\nu}$ = 2967, 1756, 1485, 1235, 749 cm^{-1}. $C_{14}H_{18}O_3$ (234.30): calcd. C 71.77, H 7.74; found C 71.61, H 7.50. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.52 (dd, *J* = 7.7, 1.7 Hz, 1 H), 7.23–7.13 (m, 2 H), 6.99–6.91 (m, 1 H), 6.71–6.65 (m, 1 H), 5.75 (dd, *J* = 17.8, 1.5 Hz, 1 H), 5.28 (dd, *J* = 11.1, 1.4 Hz, 1 H), 4.44 (d, *J* = 5.2 Hz, 1 H), 3.73 (s, 3 H), 2.42–2.27 (m, 1 H), 1.12 (d, *J* = 6.8 Hz, 3 H), 1.09 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 155.3, 131.6, 129.0, 127.6, 126.7, 121.6, 114.6, 112.4, 81.9, 52.3, 32.0, 19.0, 18.1 ppm. HRMS (EI): calcd. for $C_{14}H_{18}O_3$ $[M]^+$ 234.1256; fouded 234.1248.

(*R*)-3-Methyl-2-(2-vinylphenoxy)butanoic Acid (16): LiOH (96 mg, 4 mmol) was added to a solution of **15** (234 mg, 1 mmol) in THF/H_2O (10 mL, 9:1 v/v). The mixture was stirred at room temperature for 3 d and acidified with diluted HCl. THF was removed in vacuo, and the residue was extracted with AcOEt (3 × 25 mL). The combined extracts were washed with brine and water and dried (Na_2SO_4). The solvent was evaporated to give the crude product as a yellow oil. Purification by silica gel chromatography (AcOEt/*c*-hexane = 2:1 v/v) afforded **16** as a colorless oil (198 mg, 90%). $[\alpha]_D^{rt}$ = +1.52 ($CHCl_3$, *c* = 1.11). IR (CH_2Cl_2): $\tilde{\nu}$ = 3068, 2968, 1722, 1485, 1234, 748 cm^{-1}. $C_{13}H_{16}O_3$ (220.27): calcd. C 70.89, H 7.32; found C 70.23, H 7.15. ^1H NMR (400 MHz, $CDCl_3$): δ = 10.02 (br., 1 H), 7.55–7.49 (m, 1 H), 7.23–7.11 (m, 2 H), 7.01–6.93 (m, 1 H), 6.75–6.69 (m, 1 H), 5.80–5.70 (m, 1 H), 5.32–5.25 (m, 1 H), 4.49 (d, *J* = 4.7 Hz, 1 H), 2.37 (m, 1 H), 1.18–1.09 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.9, 155.1, 131.5, 129.0, 127.6, 126.8, 121.7, 114.8, 112.4, 81.2, 31.9, 19.1, 17.7 ppm. HRMS (EI): calcd. for $C_{13}H_{16}O_3$ $[M]^+$ 220.1099; found 220.1092.

Synthesis of 9*: Complex **9*** was prepared from **1b** and **16** in a procedure analogous to the formation of **9**. Optical purity was confirmed by HPLC with a Daicel Chiralpak® AD-H column. 254 nm; *n*-hexane/2-propanol 9:1 v/v. 1 mL/min; *ee* = 96%.

Synthesis of 11*: Complex **11*** was prepared from **9*** in a procedure analogous to the formation of **11**. Optical purity was confirmed by HPLC with a Daicel Chiralpak® AD-H column. 254 nm; *n*-hexane/2-propanol 9:1 v/v. 1 mL/min; *ee* = 96%.

Synthesis of 12a* and 12b*: Complexes **12a*** and **12b*** were prepared in a procedure analogous to the formation of **12a** and **12b**. Due to their self-cyclization to **11***, HPLC analysis was not possible.

NMR spectroscopic data for **9***, **11***, **12a***, and **12b*** were identical to those recorded for racemic complexes. Due to the intense color of the catalyst solutions, we were unable to measure optical rotations for these compounds.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra of complexes **9**, **10**, **11**, **12a** and **12b**.

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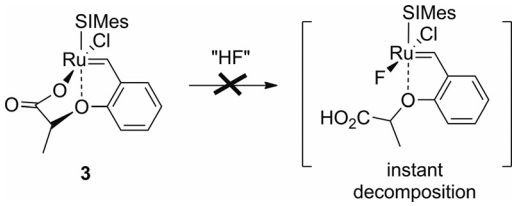
mation of a mixed ruthenium fluoride complex. In typical experiment, a solution of **3** in CD_2Cl_2 was mixed with small amount of aqueous HF or HF·py complex. A new benzylidene signal was observed in the ^1H NMR spectra, which was followed in seconds by complete decomposition of the newly formed complex.



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[14] Characteristic shifts of benzylidene proton in the ^1H NMR spectrum ($CDCl_3$): major **12a** (> 90%) at 16.34 ppm, minor **10** (< 5%) at 16.83 ppm, and diiodide complex (< 5%) at 15.84 ppm.
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