Nucleophilic Catalysis with π-Bound Nitrogen Heterocycles: Synthesis of the First Ruthenium Catalysts and Comparison of the Reactivity and the Enantioselectivity of Ruthenium and Iron Complexes

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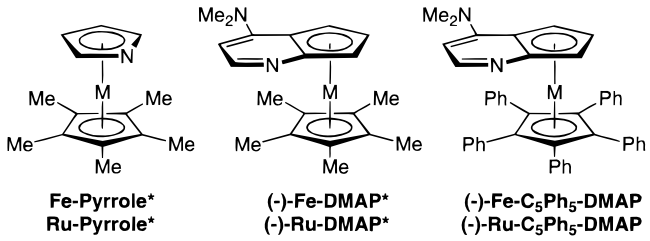
Received March 30, 1998

Abstract: Three ruthenium complexes that bear π-bound nitrogen heterocycles have been synthesized. It is established that these complexes serve as effective nucleophilic catalysts for a range of processes, including the acylation of alcohols with diketene, the ring opening of azlactones, and the addition of alcohols to ketenes; their activity is comparable to or somewhat greater than the corresponding iron catalysts. The relative efficiency of the ruthenium complexes as asymmetric catalysts is also evaluated: in the kinetic resolution of secondary alcohols, ruthenium is markedly less effective than iron, but in the deracemization/ring opening of azlactones, ruthenium is slightly more enantioselective. This study documents for the first time the impact of the metal on the reactivity and on the enantioselectivity of nucleophilic catalysts based on π-bound nitrogen heterocycles.

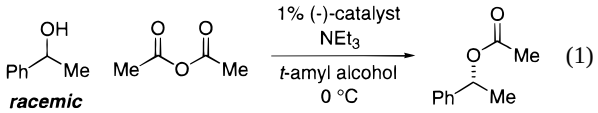
Introduction

In view of the wide array of reactions that are subject to catalysis by nucleophiles, there have been surprisingly few reports of effective asymmetric variants of these processes.[1] Consequently, we have recently initiated a program directed at the design and development of enantioselective nucleophilic catalysts.[2,3] We have focused our efforts on chiral derivatives of planar nitrogen heterocycles (e.g., DMAP[4] and imidazole), in part because these catalysts exhibit both high activity and broad applicability.

In our initial studies, we established that nitrogen heterocycles that are π-complexed to iron comprise a versatile new family of nucleophilic catalysts.[2a] In subsequent work, we demonstrated that enantiopure planar−chiral π-bound heterocycles catalyze both the deracemization/ring opening of azlactones (Fe-DMAP*)[3] and the asymmetric acylation of unsaturated secondary alcohols (Fe-C_5Ph_5-DMAP),[2b,c] providing the best enantioselectivity reported to date for either process with a nonenzymatic catalyst.



An appealing design feature of these planar−chiral nucleophilic catalysts is the potential to tune their reactivity and their enantioselectivity through appropriate choice of metal fragment (MCp^x above, where Cp^x = a cyclopentadienyl-derived ligand). In earlier work, we examined the effect of a change in Cp^x, and we determined that in the case of the asymmetric acylation of secondary alcohols, the proper choice of Cp^x is critical to achieving high selectivity (eq 1; selectivity factor = (rate of fast-reacting enantiomer)/(rate of slow-reacting enantiomer)).[5]



(1)

catalyst	selectivity factor
Fe-DMAP*	2
Fe-C_5Ph_5-DMAP	43

We have now begun to explore the effect that a change in M has on the reactivity and the enantioselectivity of these π-bound

(1) For example, see: (a) Acylation of alcohols: Vedejs, E.; Daugulis, O.; Diver, S. T. *J. Org. Chem.* **1996**, *61*, 430−431. Kawabata, T.; Nagato, M.; Takasu, K.; Fuji, K. *J. Am. Chem. Soc.* **1997**, *119*, 3169−3170. (b) Aldol: Denmark, S. E.; Winter, S. B. D.; Su, X.; Wong, K.-T. *J. Am. Chem. Soc*. **1996**, *118*, 7404−7405. (c) Allylation of aldehydes: Iseki, K.; Kuroki, Y.; Takahashi, M.; Kobayashi, Y. *Tetrahedron Lett.* **1996**, *37*, 5149−5150. Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161−6163. (d) Reduction of ketones: Schiffers, R.; Kagan, H. B. *Synlett* **1997**, 1175−1178. (e) [2+2] Cycloaddition: Wynberg, H.; Staring, E. G. J. *J. Am. Chem. Soc.* **1982**, *104*, 166−168. Wynberg, H. *Top. Stereochem.* **1986**, *16*, 87−129. Calter, M. A. *J. Org. Chem.* **1996**, *61*, 8006−8007. (f) [3+2] Cycloaddition: Zhu, G.; Chen, Z.; Jiang, Q.; Xiao, D.; Cao, P.; Zhang, X. *J. Am. Chem. Soc.* **1997**, *119*, 3836−3837.

(2) Kinetic resolution of secondary alcohols: (a) Ruble, J. C.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 7230−7231. (b) Ruble, J. C.; Latham, H. A.; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 1492−1493. (c) Ruble, J. C.; Tweddell, J.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 2794−2795.

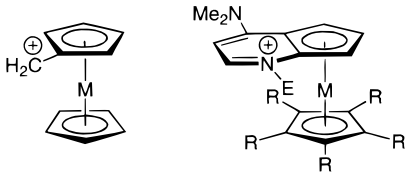
(3) Dynamic kinetic resolution of azlactones: Liang, J.; Ruble, J. C.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 3154−3155.

(4) (a) Scriven, E. F. V. *Chem. Soc. Rev.* **1983**, *12*, 129−161. (b) Hassner, A.; Krepski, L. R.; Alexanian, V. *Tetrahedron* **1978**, *34*, 2069−2076. (c) Höfle, G.; Steglich, W.; Vorbrüggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569−583.

(5) Reference 2c and unpublished results (J. C. Ruble).

S0002-7863(98)01061-0 CCC: $15.00
Published on Web 07/18/1998

heterocycles. In our initial studies, we have chosen to evaluate the impact of substituting Fe with Ru.[6] A qualitative analysis based on steric effects suggests that, due to longer metal−ligand bond distances, the Ru complexes might exhibit lower enantioselectivity ("less chiral") and greater reactivity (less sterically hindered) than the corresponding Fe complexes. Consideration of electronic effects also points to the possibility of enhanced reactivity in the case of ruthenium catalysts—for example, it is established that a ruthenocenyl group better stabilizes an adjacent cation than does a ferrocenyl group (**A**),[7] which suggests that the nitrogen of pyrindinylruthenium complexes might be more nucleophilic than that of pyrindinyliron complexes (cf. **A** and **B**). In this report, we synthesize the first Ru-based nucleophilic catalysts, and we compare their reactivity and their enantioselectivity with the corresponding Fe catalysts.



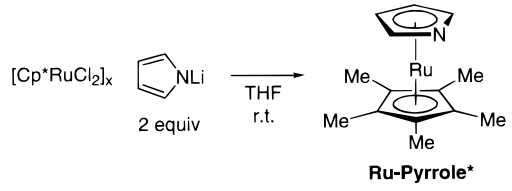
A **B**

Stability: Ru > Fe

Results and Discussion

Synthesis of Catalysts. To evaluate the consequences of substitution of Fe with Ru, we chose to investigate the ruthenium analogues of three of the azaferrocene and pyrindinyliron complexes that we had explored earlier, specifically, Ru-Pyrrole*, Ru-DMAP*, and Ru-C_5Ph_5-DMAP. None of these complexes had previously been synthesized.

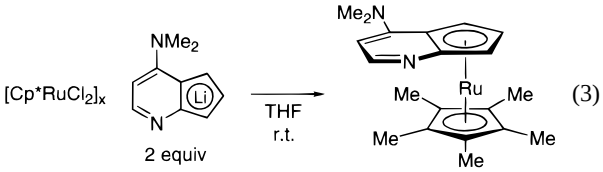
In 1988, Gassman reported that an array of mixed-sandwich ruthenocenes Cp*RuCp^x can be generated through treatment of $[Cp^*RuCl_2]_x$ with Cp^x anion.[8] Kelly subsequently applied this strategy to the first (and only) synthesis of an azaruthenocene, Cp*Ru(η^5-C_4Me_4N).[9] We have established that azaruthenocene Ru-Pyrrole* can also be produced through this procedure. Thus, reaction of commercially available $[Cp^*RuCl_2]_x$ with lithium pyrrolide in THF at room temperature affords Ru-Pyrrole* in good yield after purification by flash chromatography (51%; eq 2).



(2)

Ru-Pyrrole*

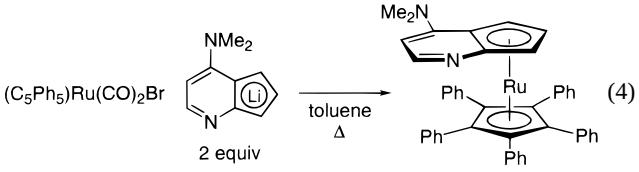
Pyrindinylruthenium complex Ru-DMAP* can be synthesized analogously, albeit in more modest yield (24%; eq 3).



(3)

Ru-DMAP*

The synthesis of the η^5-C_5Ph_5 analogue, Ru-η^5-C_5Ph_5-DMAP, obviously requires a different approach. The only method that has been described for the generation of mixed-sandwich ruthenocenes that bear an η^5-C_5Ph_5 group involves treatment of (η^5-C_5Ph_5)Ru(CO)$_2$X with a Cp^x anion.[10] We have found that this strategy can be extended to the synthesis of Ru-C_5Ph_5-DMAP (17%; eq 4).[11]



(4)

Ru-C_5Ph_5-DMAP

Worth noting from a practical standpoint is that these ruthenium complexes (Ru-Pyrrole*, Ru-DMAP*, and Ru-C_5Ph_5-DMAP) are reasonably stable to air and to moisture, even in solution (e.g., they may be purified by flash chromatography).

Resolution of Ru-DMAP* and Ru-C_5Ph_5-DMAP; Structural Characterization and Determination of the Absolute Configuration of (+)-Ru-DMAP*. As is the case for their iron analogues, the enantiomers of Ru-DMAP* and Ru-C_5Ph_5-DMAP can be separated through chiral HPLC (semipreparative Daicel Chiralcel columns). In the case of Ru-DMAP*, the (+) enantiomer elutes first; in the case of Ru-C_5Ph_5-DMAP, the (−) enantiomer elutes first. This elution behavior is identical to that observed for the corresponding iron complexes.[2b]

We were able to obtain X-ray quality crystals of enantiopure (+)-Ru-DMAP*, thereby confirming our structural assignment and allowing determination of absolute configuration (Figure 1). Interestingly, the (+) enantiomers of Ru-DMAP* and Fe-DMAP* have the same stereochemistry.[2b] Structurally, the primary difference between Ru-DMAP* and Fe-DMAP*[12] is the distance between the cyclopentadienyl planes (3.64 and 3.32 Å, respectively).[13]

Relative Reactivity of Fe and Ru Complexes. Our initial reactivity studies focused on Ru-Pyrrole*. We had established earlier that Fe-Pyrrole* serves as a nucleophilic catalyst for an array of processes, including the addition of benzyl alcohol to phenylethylketene and the acylation of 1-phenylethanol with diketene.[2a,14] We have determined that Ru-Pyrrole* also catalyzes each of these reactions. In the case of the acylation of 1-phenylethanol with diketene, Ru-Pyrrole* is somewhat less

(6) For studies comparing ferrocene- and ruthenocene-derived ligands, see: (a) Hayashi, T.; Ohno, A.; Lu, S.-j.; Matsumoto, Y.; Fukuyo, E.; Yanagi, K. *J. Am. Chem. Soc*. **1994**, *116*, 4221−4226. (b) Abbenhuis, H. C. L.; Burckhardt, U.; Gramlich, V.; Martelletti, A.; Spencer, J.; Steiner, I.; Togni, A. *Organometallics* **1996**, *15*, 1614−1621. (c) Li, S.; Wei, B.; Low, P. M. N.; Lee, H. K.; Hor, T. S. A.; Xue, F.; Mak, T. C. W. *J. Chem. Soc., Dalton Trans*. **1997**, 1289−1293.

(7) (a) Turbitt, T. D.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 2* **1974**, 185−189. (b) Hill, E. A.; Richards, J. H. *J. Am. Chem. Soc*. **1961**, *83*, 3840−3846.

(8) Gassman, P. G.; Winter, C. H. *J. Am. Chem. Soc*. **1988**, *110*, 6130−6135.

(9) Kelly, W. J.; Parthun, W. E. *Organometallics* **1992**, *11*, 4348−4350.

(10) Slocum, D. W.; Duraj, S.; Matusz, M.; Cmarik, J. L.; Simpson, K. M.; Owen, D. A. In *Metal-Containing Polymeric Systems*; Plenum: New York, 1985.

(11) We have confirmed the structural assignment for Ru-C_5Ph_5-DMAP through a low-resolution X-ray crystal structure (M. M.-C. Lo).

(12) Ruble, J. C., Hoic, D. A. Unpublished results.

(13) The corresponding distances for ruthenocene and ferrocene are 3.68 and 3.32 Å, respectively (Hardgrove, G. L.; Templeton, D. H. *Acta. Crystallogr*. **1959**, *12*, 28−32; Dunitz, J. D.; Orgel, L. E.; Rich, A. *Acta. Crystallogr*. **1956**, *9*, 373−375).

(14) For other catalysts, see: (a) Addition of alcohols to ketenes: Tidwell, T. T. *Ketenes*; Wiley: New York, 1995. (b) Acylation of alcohols with diketene: Wilson, S. R.; Price, M. F. *J. Org. Chem*. **1984**, *49*, 722−725.

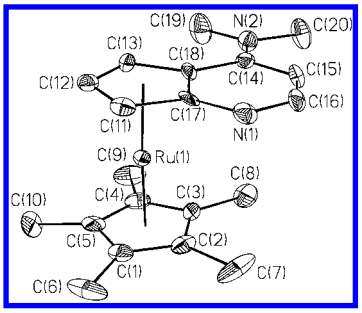
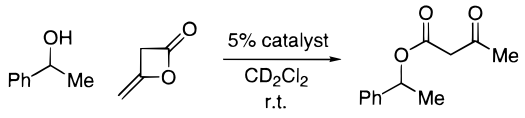


Figure 1. ORTEP illustration, with thermal ellipsoids drawn at the 35% probability level, of (+)-Ru-DMAP*.

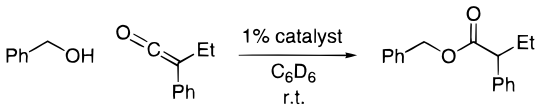
effective than Fe-Pyrrole* (eq 5).



(5)

catalyst	half-life (min)
Fe-Pyrrole*	27
Ru-Pyrrole*	39
none	no reaction

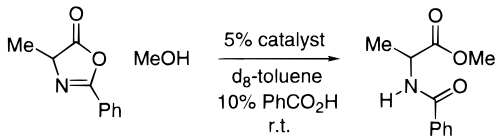
On the other hand, Ru-Pyrrole* is significantly more effective than its Fe analogue in catalyzing the addition of benzyl alcohol to phenylethylketene. In side-by-side reactions, under otherwise identical conditions, the ester forms more than twice as quickly in the presence of the Ru complex (eq 6).



(6)

catalyst	half-life (min)
Fe-Pyrrole*	9.6
Ru-Pyrrole*	3.8
none	450

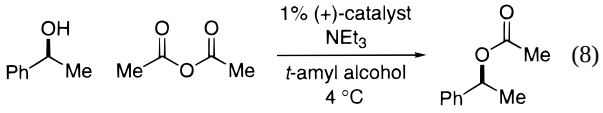
Turning to the chiral DMAP derivatives, we chose to explore the reactivity of Ru-C_5Ph_5-DMAP and Ru-DMAP* in the two reactions for which their Fe analogues are particularly effective asymmetric catalysts—the acylation of secondary alcohols[2] and the ring opening of azlactones by alcohols,[3] respectively. In the case of the ring opening of azlactones, we have determined that Ru-DMAP* is a somewhat more active catalyst than is Fe-DMAP* (eq 7).[15]



(7)

catalyst	half-life (h)
Fe-DMAP*	4.8
Ru-DMAP*	3.5
none	>400

For the acylation of secondary alcohols, Ru-C_5Ph_5-DMAP is more than twice as effective as Fe-C_5Ph_5-DMAP (eq 8). Thus, in the presence of 1% of the Ru complex, formation of the ester requires 1.3 h to proceed to 50% completion, whereas with the Fe complex, 3.5 h are necessary.[16]

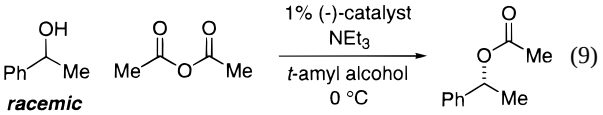


(8)

catalyst	half-life (h)
Fe-C_5Ph_5-DMAP	3.5
Ru-C_5Ph_5-DMAP	1.3
none	>800

In conclusion, a study of a cross-section of reactions reveals that the choice of metal has a measurable impact on the activity of nucleophilic catalysts based on π-bound heterocycles, with ruthenium complexes generally displaying greater reactivity than the corresponding iron complexes.

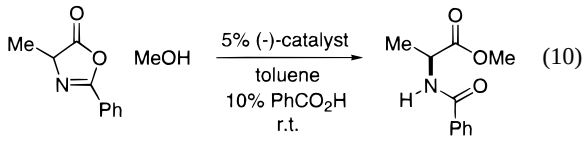
Relative Enantioselectivity of Fe and Ru Complexes. Planar−chiral Fe-C_5Ph_5-DMAP is the most enantioselective nonenzymatic catalyst reported to date for the acylation (kinetic resolution) of aryl−alkyl carbinols.[1a,2,17] We had demonstrated earlier that the stereoselectivity of this process is sensitive to the choice of Cp^x (eq 1), and comparison of the selectivity factor for the reaction catalyzed by Fe-C_5Ph_5-DMAP with that for Ru-C_5Ph_5-DMAP establishes that it is also sensitive to the choice of M (eq 9).[18,19]



(9)

catalyst	selectivity factor
Fe-C_5Ph_5-DMAP	43
Ru-C_5Ph_5-DMAP	10

Correspondingly, Fe-DMAP* is the most enantioselective nonenzymatic catalyst reported to date for the deracemization/ring opening (dynamic kinetic resolution) of azlactones.[3,20] Under otherwise identical conditions, Ru-DMAP* displays slightly enhanced stereoselectivity, thereby establishing a new benchmark for this process (eq 10).[21]



(10)

catalyst	% ee
Fe-DMAP*	54
Ru-DMAP*	57

Summary and Conclusions

The study of nucleophilic catalysis by π-complexed heterocycles is still in its infancy. While one investigation has described a dramatic difference in enantioselectivity due to a change in the structure of a remote cyclopentadienyl group

(15) The half-life for the corresponding reaction in the presence of 4-dimethylaminoquinoline (5%) is 70 h.

(16) The half-life for the corresponding reaction in the presence of 4-dimethylaminoquinoline (1%) is 80 h.

(17) Oriyama, T.; Hori, Y.; Imai, K.; Sasaki, R. *Tetrahedron Lett.* **1996**, *37*, 8543−8546.

(18) The (−) enantiomers of Fe-C_5Ph_5-DMAP and Ru-C_5Ph_5-DMAP preferentially acylate the same enantiomer of 1-phenylethanol (R), and based on this and other data, we have *tentatively* assigned the absolute configuration of (−)-Ru-C_5Ph_5-DMAP. Unfortunately, we have not yet been able to obtain an X-ray crystal structure of enantiopure Ru-C_5Ph_5-DMAP that is of sufficient quality to permit a definitive assignment.

(Cp^x), no report has yet explored the effect of a change in the transition metal (M) on either the reactivity or the enantioselectivity of this new family of catalysts. We therefore undertook a study of the Ru analogues of three Fe complexes known to be active (and in two cases enantioselective) nucleophilic catalysts. Based on steric and electronic considerations, we anticipated that the Ru systems might exhibit higher reactivity and lower enantioselectivity than the corresponding Fe systems.

In this paper, we have described the synthesis and resolution of the target Ru complexes, which are the first non-Fe-based π-bound heterocycles to be explored as nucleophilic catalysts. With respect to reactivity, the Ru analogues serve as effective catalysts for an array of processes, providing acceleration comparable to or somewhat greater than the corresponding Fe complexes.

With respect to enantioselectivity, we have evaluated the Ru catalysts in the two reactions for which the planar−chiral Fe compounds define the nonenzymatic state of the art. In the case of the kinetic resolution of aryl−alkyl carbinols, a process known to be sensitive to the choice of Cp^x, we have found that the selectivity is also sensitive to the choice of M: Ru-C_5Ph_5-DMAP is significantly less enantioselective than is Fe-C_5Ph_5-DMAP. In contrast, in the case of the deracemization/ring-opening of azlactones, Ru-DMAP* is *superior* to Fe-DMAP*, providing a modestly improved benchmark for this reaction.

We have thus documented for the first time the impact that the choice of metal has on the reactivity and on the enantioselectivity of nucleophilic catalysts based on π-bound heterocycles. Other approaches to tuning these systems are under investigation, and these studies will be reported in due course.

Experimental Section

General. ^1H and ^{13}C nuclear magnetic resonance spectra were recorded on a Varian XL-300 or a VXR-500 NMR spectrometer at ambient temperature. ^1H data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling constant (Hz), and integration. ^{13}C chemical shifts are reported in ppm downfield from tetramethylsilane (δ scale). All ^{13}C spectra were determined with complete proton decoupling.

Infrared spectra were obtained on a Perkin-Elmer Series 1600 FT-IR spectrophotometer. High-resolution mass spectra were recorded on a Finnegan MAT System 8200 spectrometer. Microanalyses were performed by E + R Microanalytical Laboratory, Inc. Gas chromatography analyses were accomplished on a Hewlett-Packard model 5890 Series 2 Plus gas chromatograph equipped with a flame ionization detector and a model 3392A integrator.

Analytical thin-layer chromatography was performed using EM Reagents 0.25 mm silica gel 60 plates. Flash chromatography was performed on EM Reagents silica gel 60 (230−400 mesh).

Solvents were distilled from the indicated drying agents: benzene (Na/benzophenone); pentane (Na/benzophenone); hexane (Na/benzophenone); THF (Na/benzophenone); Et_2O (Na/benzophenone); toluene (Na).

Pyrrole was distilled from CaH_2 and stored at −34 °C under nitrogen. Benzyl alcohol, 1-phenylethanol, diketene, MeOH, NEt_3 (from CaH_2), Ac_2O (from quinoline), and *tert*-amyl alcohol were distilled prior to use. C_6D_6 and toluene-d_8 were dried over alumina before use. *n*-BuLi (1.6 M in hexane) and $[Cp^*RuCl_2]_x$ (Strem) were used as received. Benzoic acid was recrystallized prior to use. Phenylethylketene[22] and 2-phenyl-4-methyloxazalone[23] were prepared according to literature methods.

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring.

Ru-Pyrrole* (eq 2).[8,9] *n*-BuLi (2.56 mL, 4.10 mmol) was added to a solution of pyrrole (274 μL, 4.08 mmol) in THF (10 mL), providing a light-yellow solution. After 1 h of stirring at room temperature, $[Cp^*RuCl_2]_x$ (504 mg, 1.64 mmol) was added, resulting in a red-brown solution. After stirring for 3 h at room temperature, the solution had turned bluish. After stirring for a total of 24 h, the reaction mixture was passed through a short plug of alumina, and a yellow band was collected (EtOAc as eluent), which provided a brown crystalline solid after evaporation of the solvent. Flash chromatography (silica; hexane → EtOAc) furnished a golden-yellow solid (255 mg, 51% yield; unoptimized).

^1H NMR (500 MHz, C_6D_6) δ 1.84 (s, 15H), 4.39 (s, 2H), 5.45 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.5, 76.5, 85.5, 94.9; IR (neat) 2969, 2901, 2854, 1472, 1378, 1348, 1269, 1191, 1105, 1067, 1034, 1004, 855, 844, 804, 740, 703, 637, 457 cm^{-1}; HRMS *m*/*z* 303.0561 [M^+], calcd for $C_{14}H_{19}NRu$: 303.0561. Anal. Calcd for $C_{14}H_{19}NRu$: C, 55.61; H, 6.33; N, 4.63. Found: C, 55.89; H, 6.42; N, 4.56; mp (under N_2): 150−152 °C; TLC (PMA positive) R_f = 0.60 (EtOAc).

Ru-DMAP* (eq 3).[8,9] *n*-BuLi (0.50 mL, 0.80 mmol) was added dropwise to a flask containing 4-dimethylaminopyridine[2a] (120 mg, 0.746 mmol) in THF (5 mL). The resulting reddish solution was stirred at room temperature for 1 h, and then $[Cp^*RuCl_2]_x$ (14.4 mg, 0.340 mmol) was added, providing a dark-brown solution. After stirring for 18 h at room temperature, the reaction mixture was filtered through silica (10% NEt_3/EtOAc as eluent), and a yellow-brown solution was collected and then concentrated. The resulting brown-green solid was chromatographed several times (hexane → EtOAc → 10% NEt_3/EtOAc), affording a green-yellow solid (32.2 mg, 24% yield; unoptimized).

^1H NMR (500 MHz, C_6D_6) δ 1.66 (s, 15H), 2.60 (s, 6H), 4.34 (t, J = 2.5, 1H), 4.59 (dd, J = 1.3, 2.8 Hz, 1H), 5.28 (dd, J = 1.3, 2.8 Hz, 1H), 5.43 (d, J = 5.0, 1H), 8.42 (d, J = 5.5, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.7, 41.4, 67.1, 69.9, 75.8, 77.3, 83.2, 93.7, 113.8, 151.0, 157.3; IR (neat) 2901, 1559, 1538, 1442, 1380, 1350, 1334, 1033, 1020, 903, 815, 787 cm^{-1}; HRMS *m*/*z* 396.1142 [M^+] calcd for $C_{20}H_{26}N_2Ru$: 396.1140. Anal. Calcd for $C_{20}H_{26}N_2Ru$: C, 60.74; H, 6.63; N, 7.08. Found: C, 60.94; H, 6.90; N, 6.89; mp (under N_2): 140−142 °C; TLC R_f = 0.55 (10% NEt_3/EtOAc).

The enantiomers of Ru-DMAP* were separated through semi-preparative chiral HPLC (Daicel Chiralcel OD, 1 cm × 25 cm; 2-propanol/hexane/diethylamine 22/78/0.2; 3.0 mL/min). One enantiomer was collected from 8.25 to 11.00 min, and the other enantiomer was collected from 15.25 to 20.00 min.

A crystal suitable for X-ray analysis was grown of the fast-eluting enantiomer (evaporation of an Et_2O/pentane solution at 4 °C). $[\alpha]^{20}_D$ = +969.5° (c = 0.13, $CHCl_3$).

Ru-C_5Ph_5-DMAP (eq 4). *n*-BuLi (0.250 mL, 0.400 mmol) was added dropwise to a solution of 4-dimethylaminopyridine[2a] (64.1 mg, 0.400 mmol) in toluene (2 mL), resulting in a cloudy, tan reaction mixture. After stirring for 1 h at room temperature, a purple solution of $(C_5Ph_5)Ru(CO_2)Br$[24] (275.4 mg, 0.404 mmol) in toluene (3 mL) was added, providing a brown reaction mixture. The solution was transferred to a two-neck flask fitted with a reflux condenser, and it was then refluxed for 22 h. After cooling to room temperature, the reaction mixture was concentrated, and the resulting brown residue was extracted (Et_2O/H_2O). The organic layer was passed through alumina and then concentrated. Flash chromatography (silica; 50% EtOAc/hexane → 10% NEt_3/EtOAc) provided a yellow solid (46.8 mg, 17% yield; unoptimized).

(19) (−)-Ru-C_5Ph_5-DMAP can be recovered in essentially quantitative yield at the end of the reaction.

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(21) (−)-Ru-DMAP* can be recovered in essentially quantitative yield at the end of the reaction.

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^{1}H NMR (500 MHz, $CDCl_3$) δ 3.02 (s, 6H), 4.73 (t, $J = 2.8$, 1H), 5.27 (dd, $J = 1.0$, 1.5 Hz, 1H), 5.40 (d, $J = 2.0$, 1H), 5.74 (d, $J = 5.0$, 1H), 6.85 (d, $J = 7.5$, 10H), 7.00 (t, $J = 8.0$, 10H), 7.07 (m, 5H), 8.11 (d, $J = 5.0$ Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.7, 69.5, 72.9, 79.1, 81.5, 91.8, 97.3, 116.8, 126.2, 127.0, 132.3, 134.9, 153.0, 156.9; IR (neat) 3055, 2925, 1600, 1564, 1540, 1502, 1443, 1397, 1349, 1028, 784, 740, 699, 572, 556 cm^{-1}; HRMS *m*/*z* 706.1921 [M^+], calcd for $C_{45}H_{36}N_2Ru$: 706.1922. Anal. Calcd for $C_{45}H_{36}N_2Ru$: C, 76.57; H, 5.14; N, 3.97. Found: C, 76.36; H, 4.99; N, 4.13; mp: >250 °C; TLC $R_f = 0.60$ (10% NEt_3/EtOAc).

The enantiomers of Ru-C_5Ph_5-DMAP were separated through preparative HPLC (Daicel Chiralcel AD, 5 cm × 50 cm; ethanol/hexane/diethylamine 5/95/0.3; 50 mL/min). One enantiomer was collected starting at 62 min ($[\alpha]^{20}_D = +552.9°$ ($c = 0.14$, $CHCl_3$)), and the other enantiomer was collected starting at 103 min.

A crystal suitable for a low-resolution X-ray crystal structure was grown by slow diffusion at room temperature of hexane into an Et_2O solution of Ru-C_5Ph_5-DMAP, followed by cooling to −11 °C.

Acylation of (+)-1-Phenylethanol with Diketene (eq 5). A stock solution was prepared of (±)-1-phenylethanol (32 μL, 0.26 mmol) and diketene (24 μL, 0.31 mmol) in CD_2Cl_2 (4.0 mL). Fe-Pyrrole* and Ru-Pyrrole* (0.0050 mmol) were weighed into each of two vials, and stock solution (1.6 mL) was added to each vial. Each reaction solution was transferred to a screw-cap NMR tube, and the remaining stock solution was transferred to a third screw-cap NMR tube (control reaction). The reactions were monitored by ^{1}H NMR in order to determine the half-lives for reaction.

Addition of Benzyl Alcohol to Phenylethylketene (eq 6). A stock solution was prepared of benzyl alcohol (31 μL, 0.30 mmol) and phenylethylketene (40 μL, 0.27 mmol) in C_6D_6 (2.8 mL). A portion of this solution (0.7 mL) was added to each of three sealable NMR tubes. A stock solution of Fe−Pyrrole* and of Ru−Pyrrole* (0.0070 mmol catalyst in 1.0 mL of C_6D_6) was prepared. One of the catalyst stock solutions (0.1 mL) or C_6D_6 (0.1 mL; control reaction) was added to each of the three NMR tubes. The reactions were then monitored by ^{1}H NMR to determine the half-lives for reaction.

Ring Opening of an Azlactone with MeOH (eqs 7 and 10). A stock solution was prepared of azlactone (52.6 mg, 0.300 mmol), benzoic acid (3.8 mg, 0.031 mmol), and MeOH (18 μL, 0.44 mmol) in toluene-d_8 (3.0 mL). (−)-Fe-DMAP* and (−)-Ru-DMAP* (0.0050 mmol) were weighed into each of two vials, and stock solution (1.0 mL) was added to each vial. Each reaction solution was transferred to a sealable NMR tube, and the reactions were monitored by ^{1}H NMR in order to determine the half-lives for reaction. A separate control experiment (no catalyst) was also run. After the reactions were complete, the α-amino acid derivatives were isolated by flash chromatography and analyzed by chiral GC (Chiraldex GTA).

Acylation of 1-Phenylethanol with Ac_2O (eq 8). A stock solution was prepared of (*S*)-1-phenylethanol (109 mg, 0.903 mmol) and NEt_3 (141 μL, 1.01 mmol) in *tert*-amyl alcohol (1.5 mL). (+)-Fe-C_5Ph_5-DMAP and (+)-Ru-C_5Ph_5-DMAP (0.0028 mmol) were weighed into each of two vials, and stock solution (580 μL) was added to each vial. The solutions were warmed slightly in order to completely dissolve the catalysts, which are otherwise slow to dissolve. The solutions were then cooled to 4 °C, and Ac_2O (32 μL, 0.34 mmol) was added to each vial.

Aliquots were removed periodically from each reaction. The alcohol and acetate were separated from the catalyst by chromatography, and the conversion was assayed by GC.

Kinetic Resolution of 1-Phenylethanol (eq 9). A stock solution was prepared of (±)-1-phenylethanol (90 μL, 0.75 mmol) and NEt_3 (78 μL, 0.56 mmol) in *tert*-amyl alcohol (1.5 mL). (−)-Ru−C_5Ph_5-DMAP (1.9 mg, 0.0027 mmol) was weighed into a vial, and stock solution (0.56 mL) was added to the vial. The vial was warmed slightly in order to completely dissolve the catalyst. The solution was then cooled to 4 °C, and Ac_2O (18 μL, 0.19 mmol) was added.

After 4.5 h at 4 °C, an aliquot was removed. The alcohol and acetate were separated from the catalyst by flash chromatography (25% → 75% EtOAc/hexane), and they were then analyzed by chiral GC (Chiraldex BPH), which revealed a 71% ee of R acetate and a 54% ee of S alcohol at 43% conversion ($\Rightarrow s = 10$).

Acknowledgment. We thank Dr. Gregory A. Reichard (Schering-Plough), Diego A. Hoic, Jack Liang, Michael M.-C. Lo, J. Craig Ruble, and Jennifer Tweddell for assistance. Support has been provided by the Alfred P. Sloan Foundation, the American Cancer Society, the Camille and Henry Dreyfus Foundation, Eli Lilly, Firmenich, Glaxo Wellcome, the National Institutes of Health (National Institute of General Medical Sciences, R01-GM57034), the National Science Foundation (predoctoral fellowship to C.E.G.; Young Investigator Award, with funding from Merck, Pharmacia & Upjohn, Bristol-Myers Squibb, DuPont, Bayer, Rohm & Haas, and Novartis), Pfizer, Procter & Gamble, and the Research Corporation.

Supporting Information Available: Crystal structure data for Ru-DMAP* and Fe-DMAP* (11 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA981061O