Mechanistic Studies of Ruthenium-Catalyzed Anti-Markovnikov Hydroamination of Vinylarenes: Intermediates and Evidence for Catalysis through π-Arene Complexes

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Supporting Information

General. All operations were performed under an argon atmosphere by using standard Schlenk and drybox techniques. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on 500 or 400 MHz instruments in CD_2Cl_2 or acetone-d_6 (99.9% atom enriched), and ^{31}P NMR spectra were recorded on a 300 MHz instrument in protiated solvents. ^{1}H and ^{13}C NMR chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane and are referenced to residual solvents (δ_H 2.04 and δ_C 29.8 for acetone, δ_H 5.32 and δ_C 53.1 for dichloromethane,). ^{19}F and ^{31}P NMR chemical shifts were referenced to C_6F_6 and H_3PO_4 respectively. Vinylarenes, amines, DPPPent, triflic acid and dioxane were purchased from commercial sources and were used without further purification. Ether and tetrahydrofuran were distilled from sodium/benzophenone. Ru(COD)(2-methylallyl)$_2$ was synthesized according to the literature procedure.[1]

Synthesis of ruthenium(η^6-styrene) complex 1a. To the solution of Ru(COD)(2-methylallyl)$_2$ (388 mg, 1.21 mM) and DPPPent (740 mg, 1.68 mM) in THF (36 ml) were added TfOH (0.21 ml, 2.4 mM) and styrene (4.2 ml, 3.7 mM) successively at room temperature, and the reaction mixture was heated at 80 ˚C for 30 min. After evaporation of the solvent to one third of the original volume under reduced pressure, a yellow solid was generated. This solid was isolated by filtration and washing with THF to afford complex **1a** (655 mg, 0.809 mM) in 67% yield. IR (KBr) 3071, 2951, 2894, 2839, 1436, 1265 cm^{-1}; ^{1}H NMR (acetone-d_6, 500 MHz) δ = 1.98-2.13 (m, 2H), 2.20-2.32 (m, 4H), 2.45-2.54 (m, 2H), 4.74-4.80 (b, 1H), 5.45 (d, J = 6.0 Hz, 2H), 5.59 (t, J = 6.0 Hz, 2H), 5.77 (d, J = 10.9 Hz, 1H), 6.03 (d, J = 17.6 Hz, 1H), 6.52 (dd, J = 17.6, 10.9 Hz, 1H), 6.73 (t, J = 6.0 Hz, 1H), 7.13 (t, J = 6.6 Hz, 4H), 7.21-7.28 (m, 4H), 7.29-7.42 (m, 12H); ^{13}C NMR (acetone-d_6, 125 MHz) δ = 34.3 (t, J = 14.7 Hz), 40.2 (t, J = 5.7 Hz), 49.3 (t, J = 6.3 Hz), 92.1 (t, J = 3.1 Hz), 93.0, 97.0, 109.4, 122.4, 129.7 (t, J = 5.1 Hz), 129.8 (t, J = 4.9 Hz), 131.2 (t, J = 24.4 Hz), 131.3, 131.5, 131.9 (t, J = 4.5 Hz), 132.8, 133.3 (t, J = 4.6 Hz), 140.9 (t, J = 21.8 Hz); ^{31}P NMR (acetone-d_6, 122 MHz) δ = 67.3 (s); ^{19}F NMR (acetone-d_6, 376 MHz) δ = –79.3 (s); *Anal.* Calcd for $C_{39}H_{41}F_3O_3P_2RuS$: C, 57.84; H, 5.10. Found: C, 57.64; H, 4.88.

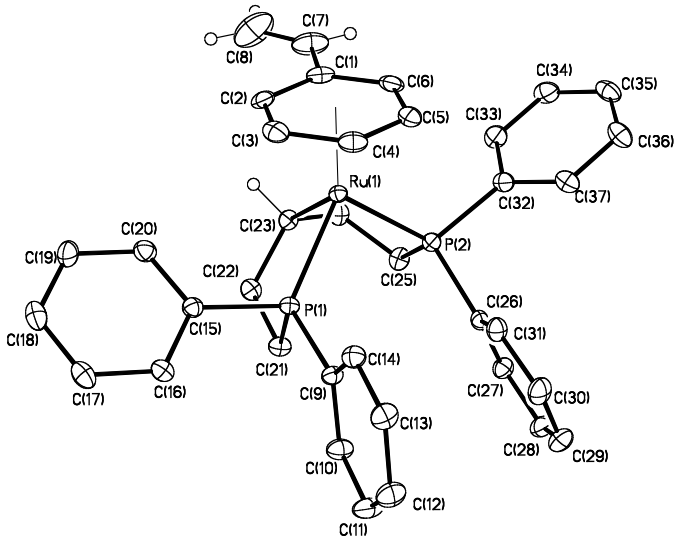

Figure S1. ORTEP plot of **1a** (hydrogen atoms and triflate anion are omitted for clarity). Selected bond lengths and angles: Ru-P(1) = 2.3007(8) Å; Ru-P(2) = 2.3068(8) Å; Ru-C(23) = 2.198(3) Å; Ru-$C_{styrene}$ = 2.253(3)-2.289(3) Å; P(1)-Ru-(P2) = 93.40(3) °. Full tables of data are provided in the .cif files.

Synthesis of Ruthenium(η^6-cymene) complex 2. Complex **2** was synthesized in 65% yield from 125 mg of Ru(COD)(2-methylallyl)$_2$ according to the procedure described above with cymen substituted for styrene. This complex was crystallized by layering an acetone solution with ether. IR (KBr) 3061, 2958, 2819, 1484, 1435, 1265 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 500 MHz) δ = 1.24 (d, J = 6.9 Hz, 6H), 1.97-2.14 (m, 4H), 2.15-2.30 (m, 2H), 2.40-2.49 (m, 2H), 2.41 (s, 3H), 2.94 (sept, J = 6.9 Hz, 1H), 4.55 (t, J = 6.8 Hz, 1H), 4.94-5.02 (m, 4H), 7.03-7.11 (m, 8H), 7.13 (t, J = 7.1 Hz, 4H), 7.32-7.40 (m, 8H); ^{13}C NMR (CD_2Cl_2, 125 MHz) δ = 22.5, 25.3, 31.2, 33.5 (t, J = 14.7 Hz), 39.5 (t, J = 5.8 Hz), 47.4 (t, J = 6.0 Hz), 90.9, 93.7, 110.3, 128.3 (t, J = 4.8 Hz), 129.9 (t, J = 23.8 Hz), 129.9 (t, J = 4.5 Hz), 130.0, 130.2, 131.4 (t, J = 4.4 Hz), 139.2 (t, J = 20.5 Hz); ^{31}P NMR (CD_2Cl_2, 122 MHz) δ = 65.5 (s); ^{19}F NMR (CD_2Cl_2, 376 MHz) δ = –81.2 (s); *Anal.* Calcd for $C_{41}H_{47}F_3O_3P_2RuS$: C, 58.63; H, 5.64. Found: C, 58.64; H, 5.55.

Synthesis of Ruthenium(η^6-(2-morpholinoethyl)benzene) complex 3a. An excess amount of morpholine (0.45 ml, 5.2 mM) in THF (3.0 ml) was added to the ruthenium(η^6-styrene) complex **1a** (56 mg, 0.069 mM) at room temperature. After 5 min, the reaction mixture became clear and was stirred for 1 h. Evaporation of the solvent under reduced pressure and washing with ether afforded **3a** (62 mg, 0.069 mM) in quantitative yield. IR (KBr) 3061, 2952, 2921, 2888, 2844, 1435, 1269 cm^{-1}; ^{1}H NMR (acetone-d_6, 500 MHz) δ = 2.10-2.34 (m, 6H), 2.35-2.41 (b, 4H), 2.45-2.53 (m, 2H), 2.59 (t, J = 6.6 Hz, 2H), 2.69 (d, J = 6.6 Hz, 2H), 3.52 (d, J = 4.6 Hz, 4H), 4.93 (t, J = 6.6 Hz, 1H), 5.27 (d, J = 5.9 Hz, 2H), 5.50 (t, J = 5.9 Hz, 2H), 6.65 (t, J

= 5.9 Hz, 1H), 7.13 (t, J = 6.8 Hz, 4H), 7.27-7.42 (m, 16H); ^{13}C NMR (acetone-d_6, 125 MHz) δ = 31.1, 34.3 (t, J = 14.6 Hz), 40.6 (t, J = 5.8 Hz), 46.5 (t, J = 6.4 Hz), 54.7, 60.2, 67.7, 91.4, 93.9 (t, J = 3.1 Hz), 98.1, 116.3 129.70 (t, J = 5.3 Hz), 129.74 (t, J = 5.0 Hz), 131.2, 131.3 (t, J = 23.7 Hz), 131.4, 132.0 (t, J = 4.4 Hz), 133.3 (t, J = 4.5 Hz), 141.0 (t, J = 20.3 Hz); ^{31}P NMR (acetone-d_6, 122 MHz) δ = 68.0 (s); ^{19}F NMR (acetone-d_6, 376 MHz) δ = –79.3 (s); *Anal.* Calcd for $C_{43}H_{50}F_3NO_4P_2RuS$: C, 57.58; H, 5.62; N, 1.56. Found: C, 57.31; H, 5.38; N, 1.51.

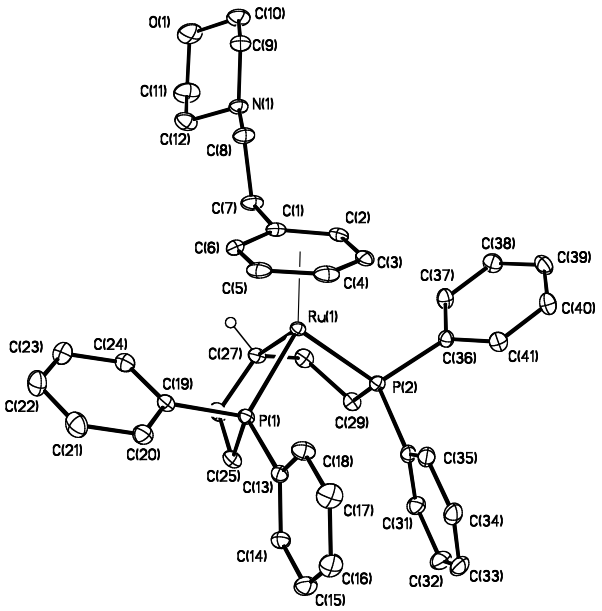

Figure S2. ORTEP plot of **3a** (hydrogen atoms and triflate anion are omitted for clarity). Selected bond lengths and angles: Ru-P(1) = 2.2842(10) Å; Ru-P(2) = 2.3109(9) Å; Ru-C(27) = 2.193(2) Å; Ru-C_{phenyl}= 2.235(2)-2.294 Å; P(1)-Ru-(P2) = 93.38(4) °. Full tables of data are provided in the .cif files.

Synthesis of Ru(η^6-styrene) complex with DPPPent analogue

Bis(3,5-dimethoxyphenyl)chlorophosphine.[2] To a stirred solution of dimethylphosphoramidous dichloride (2.8 ml, 24 mM) in THF (25 ml) was added 50 ml of a 1.0 M solution of 3,5-dimethoxyphenylmagnesium chloride in THF (50 mM) at 0 ˚C. After 2.5 h, the solvent was removed, and the residue was extracted with pentane to afford a solution of bis(3,5-dimethoxyphenyl)(dimethylamino)phosphine. To this solution was added 50 ml of a 1.0 M solution of HCl in Et_2O (50 mM), and the resulting solution was stirred for 1 h at room temperature. After filtration, the volatile materials were removed under reduced pressure to afford bis(3,5-dimethoxyphenyl)chlorophosphine. This crude product was used in the next step without further purification. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ = 3.78 (s, 12H), 6.46-6.49 (m,2H), 6.74 (dd, J = 8.8, 2.3 Hz, 4H); ^{31}P NMR (acetone-d_6,122 MHz) δ = 85.3 (s).

Bis(di(3,5-dimethoxyphenyl)phosphino)pentane. A THF solution of pentamethylenebis(magnesium

bromide), which was prepared by mixing 1,5-dibromopentane (0.53 ml, 3.9 mM) and magnesium (220 mg, 8.9 mM) in THF (7.0 ml), was added to a solution of bis(3,5-dimethoxyphenyl)chlorophosphine (4.0 g of crude product obtained above) in THF (10 ml) at room temperature. After 1 h, water and EtOH were added to the reaction mixture. The resulting oily precipitate was separated and extracted with THF to give bis(di(4-methoxyphenyl)phosphino)pentane (950 mg, 1.4 mM) in 6% yield based on dimethylphosphoramidous dichloride. This product was used to prepare the ruthenium complex **1b** without further purification. ^{1}H-NMR (acetone-d_6, 400 MHz) δ = 1.39-1.51 (m, 4H), 1.56-1.68 (m, 2H), 1.75-1.81 (m, 4H), 3.73 (s, 24H), 6.32 (s, 4H), 6.56 (d, J = 7.4 Hz, 8H); ^{31}P NMR (acetone-d_6, 122 MHz) δ = –10.9 (s).

Ruthenium(η^6-styrene)(3,5-dimethoxy-DPPPent) complex 1b. **1b** was synthesized according to the procedure for **1a** and crystallized from THF-Et_2O in 15% based on Ru(COD)(2-methylallyl)$_2$. IR (KBr) 2938, 2837, 1590, 1461, 1414, 1263 cm^{-1}; ^{1}H NMR (acetone-d_6, 500 MHz) δ = 1.96-2.13 (m, 2H), 2.20-2.31 (m, 2H), 2.31-2.47 (m, 4H), 3.76 (s, 24H), 4.73-4.80 (b, 1H), 5.55 (d, J = 5.8 Hz, 2H), 5.73-5.79 (m, 3H), 5.97 (d, J = 17.5 Hz, 1H), 6.32-6.49 (m, 8H), 6.53-6.62 (m, 5H), 6.67 (t, J = 5.6 Hz, 1H); ^{13}C NMR (acetone-d_6, 125 MHz) δ = 34.6 (t, J = 14.3 Hz), 40.7 (t, J = 5.7 Hz), 48.6 (t, J = 6.2 Hz), 56.1, 56.2, 92.5, 93.6, 97.0, 102.1 102.7, 108.8, 110.3 (t, J = 4.9 Hz), 111.4 (t, J = 4.8 Hz), 122.1, 132.8, 133.2 (t, J = 24.4 Hz), 142.4 (t, J = 20.0 Hz), 161.8 (t, J = 7.1 Hz), 162.0 (t, J = 6.9 Hz); ^{31}P NMR (acetone-d_6, 122 MHz) δ = 70.1 (s); ^{19}F NMR (acetone-d_6, 376 MHz) δ = –81.2 (s); *Anal.* Calcd for $C_{48}H_{61}F_3O_{11}P_2RuS$: C, 54.08; H, 5.77. Found: C, 54.09; H, 5.47.

General procedure for catalytic reactions with isolated complexes (Schemes 2 and 6). The ruthenium catalyst (0.010 mM) was suspended in solvent (dioxane or THF, 0.2 ml) and styrene (0.41 mM). Morpholine (0.21 mM) and tetradecane (internal standard, 0.077 mM) were added at room temperature. This reaction mixture was heated at 100 ˚C (in dioxane) or 80 ˚C (in THF) in an oil bath. The yield at each time was determined by GC analysis of an aliquot removed by syringe through the septum in the cap of the vial.

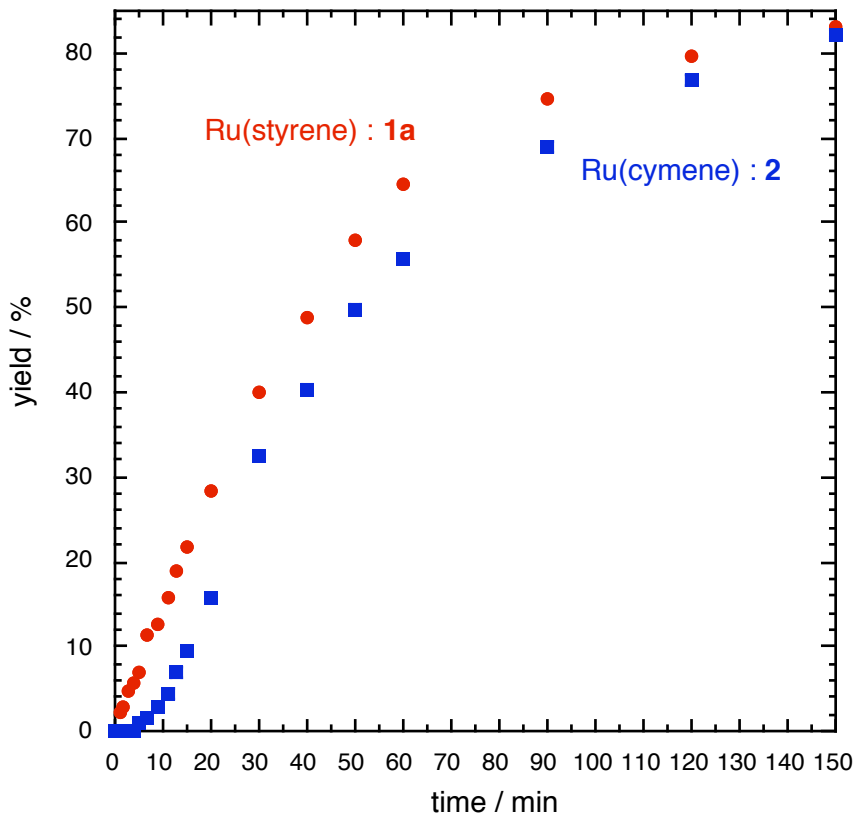

Figure S3. Appearance of aminoethylbenzene from the reaction of styrene with morpholine catalyzed by styrene complex **1 a** and cymene complex **2**.

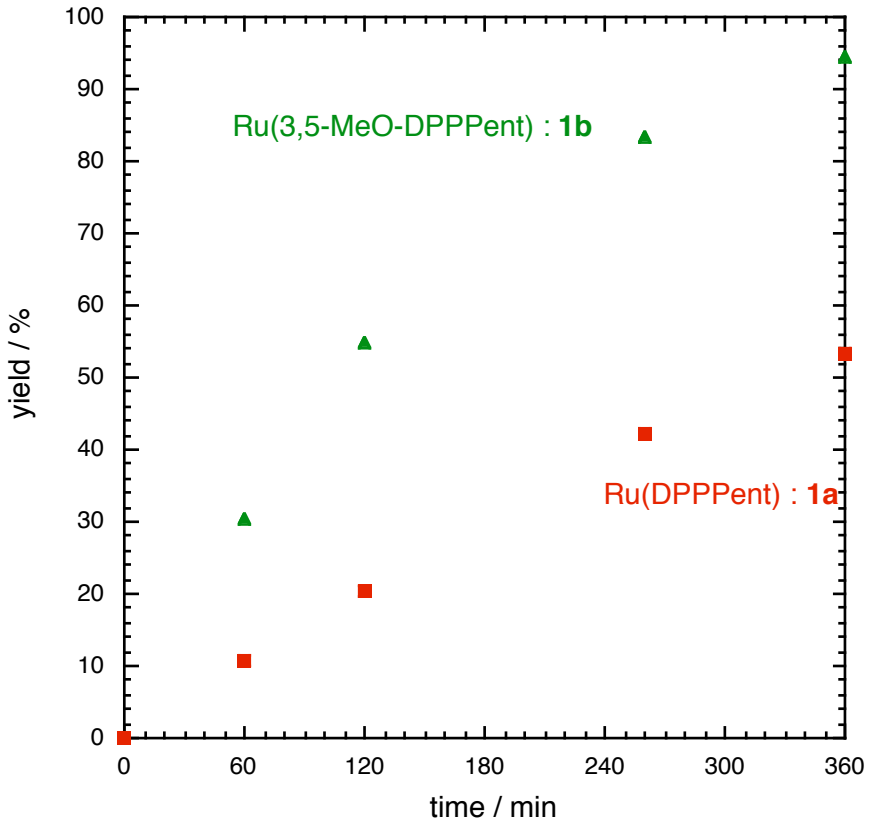

Figure S4. Appearance of aminoethylbenzene from the reaction of styrene with morpholine catalyzed by Ru(DPPPent) complex **1a** and Ru(3,5-dimethoxy-DPPPent) complex **1b**.

Kinetic experiments

Nucleophilic addition of morpholine to 1a (Scheme 3). Ruthenium complex **1a** (8.1 mg, 0.010mM) was placed in screw-caped NMR-tube with a capillary glass tube that contained H_3PO_4 in dioxane as the external integration standard. NMP (0.10 ml) and dioxane (0.53 ml) were added at room temperature to dissolve complex **1a** completely. After establishing the temperature (20-50 ˚C) of the NMR spectrometer probe, morpholine (18.0 μl, 0.206 mM) was added through the septum in the cap of the sample tube. The sample was shaken and placed in the spectrometer. Data collection with as automated acquisition program was started immediately after placing sample into the probe. The intensity of the signal of **1a,** relative to that for the integration standard, was measured every 40-60 s. All experiments were fit to a first-order exponential. Values of k_{obs} are provided in Table S1, and Arrenius and Eyring plots are shown in figures S6 and S7.

Table S1. k_{obs} at various temperature

temp. / °C	kobs / s^{-1}
20	0.41×10^{-3}
30	0.62×10^{-3}
40	0.97×10^{-3}
50	1.3×10^{-3}
(100)	(6.2×10^{-3}/deduced from Arrhenius equation)

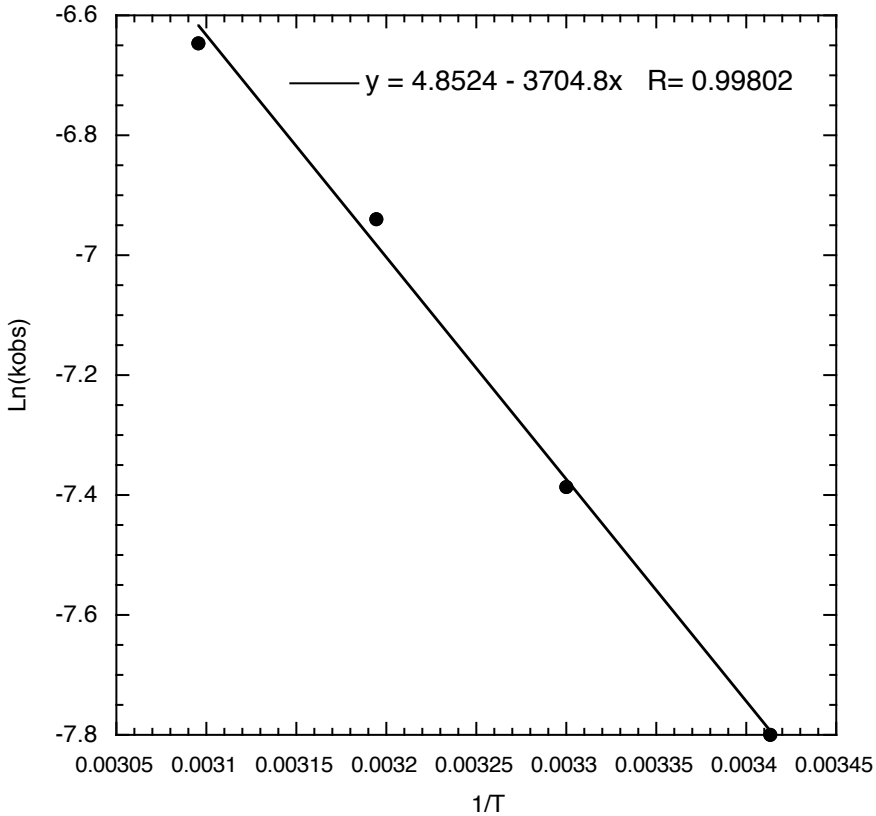

Figure S5. Arrhenius plot of the reaction of **1 a** with morpholine.

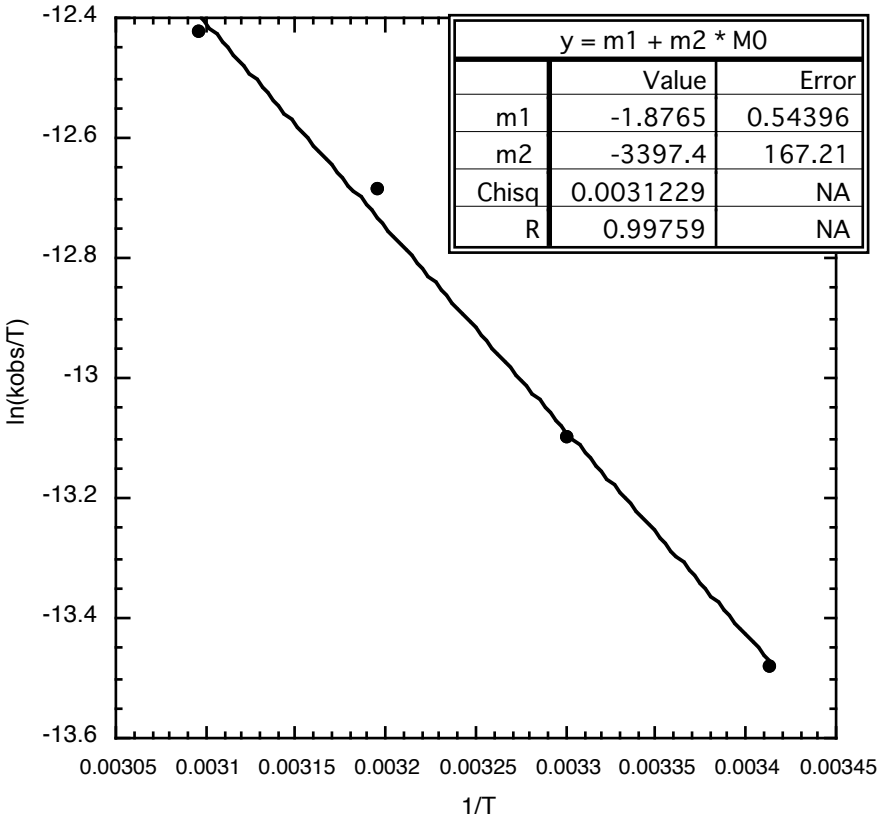

Figure S6. Eyring plot of the reaction of **1a** with morpholine.

Arene exchange reaction of 3 with styrene (Scheme 5). Ruthenium complex **3** (8.1 mg, 0.010mM) and styrene (46.0 ml, 0.40 mM) were placed into a screw-caped NMR tube containing a glass capillary tube that contains H_3PO_4 in dioxane as external integration standard. NMP (0.10 ml) and dioxane (0.50 ml) were added at room temperature to dissolve complex **1a** completely. After establishing the temperature of NMR spectrometer probe at 100 ˚C, the NMR sample tube was placed into the probe, and measurement of NMR spectra every 40 s by an automated data acquisition program was started immediately. Integration intensities, relative to those of the phosphoric acid standard, were fit to a first-order exponential.

References for synthetic procedure

1) Genet, J. P.; Pinel, C.; Ratovelomanana-Vidal, V.; Mallart, S.; Pfister, X.; Cano De Andrade, M. C.; Laffitte, J. A.; *Tetlahedron Asymmetry* **1994**, *5*, 665

2) Gambs, C.; Consiglio G.; Togni A.; *Inorg. Chim. Acta* **2001**, *84*, 3105.

Procedure for X-ray diffraction analysis of 1a.

A pale yellow blade crystal of $C_{38}H_{37}F_3O_3P_2RuS$ having approximate dimensions of 0.20 x 0.20 x 0.15 mm^3 was mounted with epoxy cement on the tip of a fine glass fiber. All measurements were made on a Nonius KappaCCD diffractometer with graphite monochromated Mo-Kα radiation.

Cell constants and an orientation matrix for data collection corresponded to a primitive monoclinic cell with dimensions:

$$a = 9.4151(19)\ \text{Å} \quad \alpha = 90°$$
$$b = 17.713(4)\ \text{Å} \quad \beta = 92.19(3)°$$
$$c = 10.369(2)\ \text{Å} \quad \gamma = 90°$$
$$V = 1727.9(6)\ \text{Å}^3$$

For Z = 2 and F.W. = 880.87, the calculated density is 1.526 g/cm^3. Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be $P2_1$ (#4).

The data were collected at a temperature of 173(2) K to a maximum 2θ value of 56.56°. Four omega scans consisting of 39, 31, 37, and 24 data frames, respectively, were collected with a frame width of 1.9° and a detector-to-crystal distance, Dx, of 35.0 mm. Each frame was exposed twice (for the purpose of de-zingering) for a total of 57 s. The data frames were processed and scaled using the DENZO software package.[1]

A total of 7226 reflections were collected of which 7226 were unique and observed (R_{int} = 0.000, Friedel pairs not merged). The linear absorption coefficient, μ, for Mo-Kα radiation is 6.60 cm^{-1}, and no absorption correction was applied. The data were corrected for Lorentz and polarization effects.

The structure was solved by direct methods and expanded using Fourier techniques[2]. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were treated as idealized contributions. The final cycle of full-matrix least-squares refinement[3] on F was based on 7226 observed reflections (I > 2.00σ(I)) and 433 variable parameters and converged with unweighted and weighted agreement factors of:

$$R = \Sigma\ ||Fo| - |Fc|| \ / \ \Sigma\ |Fo| = 0.0299$$
$$R_W = \{\Sigma[w\ (F_o^2 - F_c^2)^2] \ / \ \Sigma[w(F_o^2)^2]\}^{1/2} = 0.0748$$

The maximum and minimum peaks on the final difference Fourier map corresponded to 0.489 and –0.681 e^-/$Å^3$ respectively.

Procedure for X-ray diffraction analysis of 3a.

A colorless blade crystal of $C_{42}H_{46}F_3NO_4P_2RuS$ having approximate dimensions of 0.20 x 0.10 x 0.10 mm^3 was mounted with epoxy cement on the tip of a fine glass fiber. All measurements were made on a Nonius KappaCCD diffractometer with graphite monochromated Mo-Kα radiation.

Cell constants and an orientation matrix for data collection corresponded to a triclinic cell with dimensions:

$a = 10.976(2)$ Å $\alpha = 96.64(3)°$
$b = 11.496(2)$ Å $\beta = 102.89(3)°$
$c = 16.223(3)$ Å $\gamma = 97.58(3)°$
$V = 1955.7(7)$ Å^3

For Z = 2 and F.W. = 880.87, the calculated density is 1.496 g/cm^3. Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be *P*-1 (#2).

The data were collected at a temperature of 173(2) K to a maximum 2θ value of 56.54°. Seven omega scans consisting of 37, 37, 34, 29, 24, 29, and 7 data frames, respectively, were collected with a frame width of 2.0 ° and a detector-to-crystal distance, Dx, of 35.0 mm. Each frame was exposed twice (for the purpose of de-zingering) for a total of 40 s. The data frames were processed and scaled using the DENZO software package.[1]

A total of 16375 reflections were collected of which 9648 were unique and observed ($R_{int} = 0.0347$). The linear absorption coefficient, μ, for Mo-Kα radiation is 5.94 cm^{-1}, and no absorption correction was applied. The data were corrected for Lorentz and polarization effects.

The structure was solved by direct methods and expanded using Fourier techniques[2]. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were treated as idealized contributions. The final cycle of full-matrix least-squares refinement[3] on F was based on 9648 observed reflections ($I > 2.00\sigma(I)$) and 520 variable parameters and converged with unweighted and weighted agreement factors of:

$$R = \Sigma \, ||Fo| - |Fc|| \, / \, \Sigma \, |Fo| = 0.0385$$

$$R_W = \{\Sigma[w \, (F_o^2 - F_c^2)^2] \, / \, \Sigma[w(F_o^2)^2]\}^{1/2} = 0.0975$$

The maximum and minimum peaks on the final difference Fourier map corresponded to 0.614 and –0.702 e$^-$/Å^3 respectively.

Refinement of the triflate counterion was made difficult by positional disorder. The asymmetric unit contains two half molecules of the counterion, both of which reside on crystallographic inversion centers. In the first component, S(1)-O(1-3)-C(42)-F(1-3), the inversion is centered on C(42). All atoms of this counterion were refined with 50% occupancy factors. The second component, S(1')-O(1'-3'), possesses an inversion center on the S(1')-S(1'A) vector. Without a unique CF_3 component, S(1') was modeled as an undersized sulfur atom to compensate for a superimposed carbon atom. Likewise, the O(1 '-3') were modeled as oversized oxygen atoms to compensate for the superimposed fluorine atoms.

References for crystallographic procedure

(1) Z. Otwinowski and W. Minor, "Processing of X-Ray Diffraction Data Collected in Oscillation Mode," Methods in Enzymology, vol. 276: Macromolecular Crystallography, part A, 307-326, 1997, C.W. Carter, Jr. & R.M. Sweet, Eds., Academic Press.

(2) *Acta Cryst.* **A46** (1990) 467-473

(3) Least Squares function minimized: $\Sigma w(F_o^2 - F_c^2)^2$