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Phosphine−Amido Complexes of Ruthenium and Mechanistic Implications for Ketone Transfer Hydrogenation Catalysis

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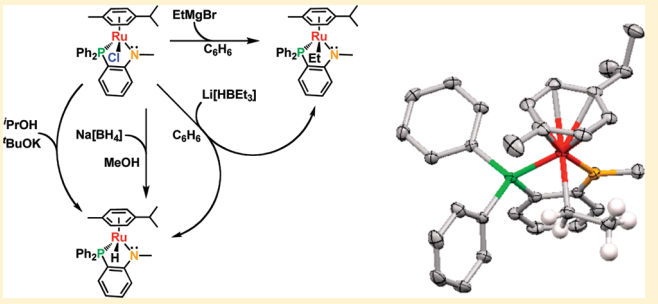
Supporting Information

ABSTRACT: The air-sensitive phosphine−anilido complexes [RuR(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (R = H, Et; Ar^- = *o*-$C_6H_4NMe^-$) have been prepared. While the precursor [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] is a moderately active ketone transfer hydrogenation catalyst under basic conditions, the hydrido derivative is much less active, ruling out the possibility of an inner-sphere mechanism during catalysis. The possibility of an alternate mechanism, related to the Meerwein−Ponndorf−Verley−Oppenauer (MPVO) pathway, is discussed. While attempts to isolate intermediate alkoxo derivatives demonstrate their propensity toward β-hydride elimination to afford the hydrido complex, the ethyl derivative is remarkably stable, even in refluxing benzene, providing an interesting contrast between the labilities of the Ru−O and Ru−C bonds.



The transfer hydrogenation of ketones represents a useful means of producing value-added alcohols under relatively benign conditions, and many effective catalyst systems involving phosphorus- and nitrogen-ligated ruthenium complexes have been developed for this purpose.[1−5] These metal-catalyzed reactions often rely on the inclusion of a strong base in reaction mixtures, either to activate the metal-containing precatalyst or to play a more direct role as a cocatalyst.[6]

The two mechanisms most commonly involved in the transfer hydrogenation of ketones are the inner-sphere and outer-sphere cycles. During an inner-sphere mechanism (Scheme 1, left cycle), the reagent ketone (acetophenone in the example shown) can be inserted into an M−H bond (generated by β-hydride elimination from the isopropoxo group) with concomitant elimination of acetone, to form a new alkoxide that is then protonated by the incoming reagent alcohol, releasing the product alcohol from the metal. In the outer-sphere mechanism, initially proposed by Noyori,[1] the inclusion of a strongly basic amido ligand within ruthenium-containing catalysts can allow for deprotonation of the alcohol (^{i}PrOH in this example) by the nucleophilic nitrogen donor with simultaneous hydride transfer to the adjacent metal atom via a highly ordered transition state (Scheme 1, right cycle). Transfer of the proton and hydride from the amine and metal, respectively, to the polar substrate (acetophenone) then generates the product alcohol (1-phenylethanol). In this case, the noninnocent amido ligand renders the catalyst exceptionally reactive without requiring the use of an external base in reaction media.[1]

A less common mechanism that has been proposed for aluminum- and tin-catalyzed processes but is rarely mentioned in the context of late-metal systems is the Meerwein−Ponndorf−Verley−Oppenauer (MPVO) mechanism (Scheme 2).[7,8] In this case the metal center can act as a scaffold, upon which the alkoxide (again, produced by adding base to the reaction mixture) can transfer its hydride directly to the electrophilic carbonyl functionality of a coordinated ketone, thereby avoiding the intermediacy of a hydrido complex.

Although most transfer hydrogenation reactions catalyzed by late-metal complexes can be rationalized on the basis of inner- or outer-sphere mechanisms, one possible exception is Stradiotto's highly active zwitterionic catalyst [RuCl(η^6-*p*-cymene)(*P*,*N*-1-P^iPr_2-2-NMe_2-$C_9H_5^-$)],[9] for which neither mechanism seems applicable. Previously, we showed that an *o*-phosphinoanilido complex of ruthenium, namely [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**1**; Ar^- = *o*-$C_6H_4NMe^-$), not unlike Stradiotto's catalyst, functions as a moderately active ketone transfer hydrogenation catalyst in the presence of base.[10] The necessity for base in conjunction with our amido catalyst appeared to rule out an outer-sphere mechanism, but at the time, we did not investigate this further. In the current work, we highlight new evidence that also discounts an inner-sphere process as the catalytically dominant pathway and discuss the possible operation of the less explored (MPVO) alternative.

EXPERIMENTAL SECTION

General Comments. All solvents were deoxygenated, dried (using appropriate drying agents), distilled before use, and stored under nitrogen. All reactions were performed under an Ar atmosphere using standard Schlenk techniques. Isopropyl alcohol (^{i}PrOH; >99%, distilled over Mg turnings and stored under Ar) and acetophenone (99%, deoxygenated and stored under Ar over 5 Å molecular sieves), used

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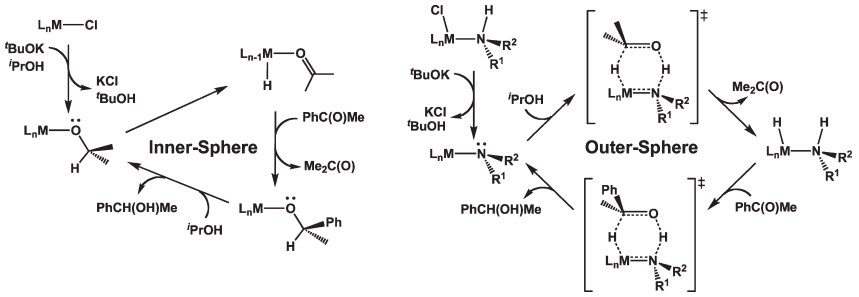
Scheme 1. Inner- (Left Cycle) and Outer-Sphere (Right Cycle) Mechanisms of Transfer Hydrogenation[a]



[a] The reaction of acetophenone with ^{i}PrOH occurs upon the addition of base (^{t}BuOK) to a metal halide precatalyst.

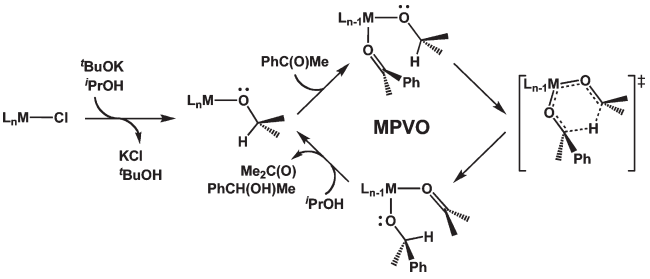
for transfer hydrogenation catalysis, as well as ethylmagnesium bromide (EtMgBr; 3.0 M in diethyl ether) and lithium triethylborohydride (Li[HBEt$_3$]; 1.0 M in tetrahydrofuran) were purchased from Aldrich. Sodium borohydride ($NaBH_4$; 98%) was purchased from Strem Chemicals. The complex [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**1**, Ar$^-$ = $C_6H_4NMe^-$), was prepared as previously reported.[10] NMR spectra were recorded on Varian Inova-400 and -500 and Varian Unity-500 spectrometers operating at 399.8, 498.1, and 499.8 MHz, respectively, for ^{1}H, at 161.8, 201.6, and 202.3 MHz, respectively, for ^{31}P and at 100.6, 125.3, and 125.7 MHz, respectively, for ^{13}C nuclei. *J* values are given in hertz (Hz). Overlapping or unresolved aromatic signals, observed in the typical 6−8 ppm range in the ^{1}H NMR spectrum and found between 80 and 120 ppm in the ^{13}C{^{1}H} NMR spectrum, are not reported. Spectroscopic data for complexes **2** and **3** are provided in Table 1. The elemental analysis of **3** was performed by the Microanalytical Laboratory within the Department.

Preparation of Metal Complexes. *(a). Reaction of [RuCl(η^6-p-cymene)(P,N-Ph$_2$PAr$^-$)] (**1**) with Li[HBEt$_3$].* An NMR tube was charged with **1** (22 mg, 39 μmol), sealed with a septum, and then evacuated and back-filled with Ar three times. The compound was dissolved in 0.7 mL of C_6D_6, producing a dark burgundy solution, and a 1.0 M solution of Li[HBEt$_3$] in tetrahydrofuran (42 μL, 42 μmol) was added via a microliter syringe, resulting in a red mixture that was left for several hours, allowing a white precipitate to settle from the bright red solution. The supernatant was transferred via cannula under Ar to a prepared NMR tube, and the sample was then analyzed by ^{1}H and ^{31}P{^{1}H} NMR spectroscopy. The resulting spectra indicated the formation of two products, [RuH(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**2**) and [RuEt(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**3**), in approximately equal proportions as judged by the intensities of the only two ^{31}P signals observed (at δ 70.1 and 68.7; see parts b and c for independent syntheses).

*(b). Hydrido(η^6-p-cymene)(P,N-diphenyl(o-N-methylanilido)phosphine)ruthenium(II), [RuH(η^6-p-cymene)(P,N-Ph$_2$PAr$^-$)] (**2**).* In a 25 mL Schlenk tube under anhydrous conditions and Ar atmosphere, [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**1**; 177 mg, 315 μmol) and sodium borohydride (26 mg, 687 μmol) were dissolved in 10 mL of methanol with stirring. The mixture, which initially turned blue-green, turned dark red after 10 min, and was stirred for a total of 30 min before removing the solvent in vacuo. Benzene (10 mL) was added to the remaining residue, and the resultant slurry was stirred for 10 min before allowing the precipitate to settle. The supernatant was filtered through a Celite plug and transferred to a prepared 50 mL Schlenk flask via cannula transfer under Ar. The solvent was removed in vacuo, resulting in an amorphous, red residue (156 mg). Although a satisfactory elemental analysis could not be obtained for this compound, its NMR spectra (^{1}H NMR spectrum provided as Supporting Information) leave no doubt about its formulation.

*(c). Ethyl(η^6-p-cymene)(P,N-diphenyl(o-N-methylanilido)phosphine)ruthenium(II), [RuEt(η^6-p-cymene)(P,N-Ph$_2$PAr$^-$)] (**3**).* In a 50 mL Schlenk flask under anhydrous conditions and Ar atmosphere, **1** (84 mg, 149 μmol) was dissolved in 5 mL of benzene at ambient temperature and the solution was stirred for 5 min. Ethylmagnesium bromide (3.0 M in diethyl ether, 60 μL, 180 μmol) was added to the dark burgundy solution via syringe to produce a cloudy, red mixture, which was stirred for 5 min before removing the solvents in vacuo. While the mixture was stirred, 10 mL of benzene was added to produce a cloudy, orange-red mixture that was then filtered through a Celite plug in a glass pipet (via Ar overpressure through a cannula) into a prepared 25 mL Schlenk tube. The solvent volume was reduced to approximately 5 mL in vacuo, and the red solution was layered with 10 mL of *n*-pentane and left undisturbed for 18 h. The supernatant was then removed via cannula, and the red crystalline product was dried in vacuo (50 mg, 60% yield). Anal. Found: C, 66.73; H, 6.68; N, 2.66. Calcd for [$C_{31}H_{36}NPRu$]: C, 67.13; H, 6.54; N, 2.53%.

Scheme 2. MPVO Mechanism of Transfer Hydrogenation



*(d). Reactions of [RuCl(η^6-p-cymene)(P,N-Ph$_2$PAr$^-$)] (**1**) with Alkoxides.* In a 50 mL Schlenk flask under anhydrous conditions and Ar atmosphere, **1** (50 mg, 89 μmol) was dissolved in 5 mL of benzene at ambient temperature with stirring. In a 25 mL Schlenk flask, KOH (5 mg, 90 μmol) was dissolved in 5 mL of alcohol (either methanol or isopropyl alcohol) at ambient temperature with stirring, and this solution was then transferred (via Ar overpressure through a cannula) to the solution of **1** and the mixture was stirred for 10 min at ambient temperature before removing the solvents in vacuo. Benzene (10 mL) was then added to the resulting dark red residue, and the mixture was filtered through a Celite plug in a glass pipet (via Ar overpressure through a cannula) into a prepared 50 mL Schlenk flask. The solvent was removed in vacuo, and the residue was dissolved in 1 mL of C_6D_6 and the solution transferred to a prepared NMR tube via cannula. NMR spectra showed the exclusive formation of [RuH(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**2**), when either alcohol (methanol or isopropyl alcohol) was used. Similar reactions performed using ^{t}BuOK rather than KOH as the base yielded identical spectroscopic observations.

Ketone Transfer Hydrogenation Assay with [RuH(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (2). In a 50 mL Schlenk flask under anhydrous conditions and Ar atmosphere, [RuCl(η^6-*p*-cymene)-(*P*,*N*-Ph$_2$PAr$^-$)] (**1**; 50.0 mg, 89.0 μmol) and $NaBH_4$ (5.1 mg, 130 μmol)

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Table 1. $^{31}P\{^1H\}$, ^1H, and $^{13}C\{^1H\}$ NMR Data for Ruthenium Compounds[a]

$\delta(^{31}P\{^1H\})$/ppm[b]	$\delta(^1H)$/ppm[c]	$\delta(^{13}C\{^1H\})$/ppm[c]
	[RuH(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**2**)	
70.1 (s)	NCH_3: 3.30 (s, 3H)	NCH_3: 48.9 (s)
	$CH(CH_3)_2$: 2.15 (sept, $^3J_{HH}$ = 6.8 Hz, 1H)	$CH(CH_3)_2$: 32.3 (s)
	$ArCH_3$: 1.56 (s, 3H)	$CH(CH_3)_2$: 24.1 (s), 23.6 (s)
	$CH(CH_3)_2$: 1.06 (d, $^3J_{HH}$ = 6.8 Hz, 3H), 1.04 (d, $^3J_{HH}$ = 6.8 Hz, 3H)	$ArCH_3$: 19.0 (s)
	Ru*H*: −7.96 (d, $^2J_{PH}$ = 46.5 Hz, 1H)	
	[RuEt(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**3**)	
68.7 (s)	NCH_3: 3.26 (s, 3H)	NCH_3: 48.3 (s)
	$CH(CH_3)_2$: 2.13 (sept, $^3J_{HH}$ = 6.8 Hz, 1H)	$CH(CH_3)_2$: 31.6 (s)
	$ArCH_3$: 1.68 (s, 3H)	$CH(CH_3)_2$: 24.2 (s), 22.6 (s)
	CH_2CH_3: 1.38 (pt, $^3J_{HH}$ = 7.5 Hz, 3H)	CH_2CH_3: 23.4 (d, $^3J_{PC}$ = 4 Hz)
	CH_2CH_3: 1.10 (m, 1H), 0.80 (m, 1H)	$ArCH_3$: 17.5 (s)
	$CH(CH_3)_2$: 0.96 (d, $^3J_{HH}$ = 6.8 Hz, 3H), 0.94 (d, $^3J_{HH}$ = 6.8 Hz, 3H)	CH_2CH_3: 14.0 (d, $^2J_{PC}$ = 14 Hz)

[a] NMR abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet, sept = septet, p = pseudo. NMR data were recorded at 27 °C in C_6D_6. [b] ^{31}P chemical shifts are referenced to external 85% H_3PO_4. [c] ^1H and ^{13}C chemical shifts are referenced to external tetramethylsilane. Chemical shifts for aryl groups are not given.

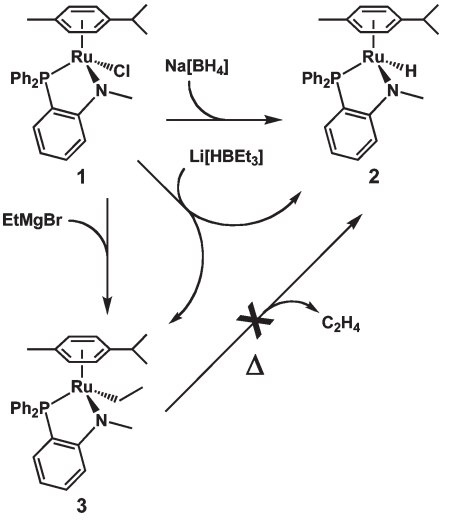
were dissolved in 7.0 mL of MeOH at ambient temperature and stirred for 15 min. The solvent was removed in vacuo, acetophenone (10.4 mL, 89.0 mmol) was added to the residue, and the cloudy, red mixture was stirred for 15 min. The precipitate (NaCl) was allowed to settle from the red solution, and a 2.08 mL aliquot (17.8 μmol of **2** dissolved in 17.8 mmol of acetophenone) was withdrawn via Gastight syringe and transferred to a prepared 50 mL three-necked, round-bottom flask equipped with a 0.5 in. stir bar and attached reflux condenser through which an Ar overpressure was applied. While it was stirred, the solution was heated to 90 °C for 10 min. A solution of ^{t}BuOK (8.0 mg, 71.3 μmol) in ^{i}PrOH (13.6 mL, 178 mmol) was then added via cannula transfer under Ar. A 1.0 mL aliquot of the reaction mixture was immediately withdrawn and passed through a column containing 2 cm of acidic alumina atop 2 cm of Florisil and collected in a vial so that less than 30 s elapsed between removal of the sample from the mixture and removal of catalyst from the sample. The vial was then capped and stored at 0 °C until the mixture could be analyzed by NMR spectroscopy and GC-EI-MS. Aliquots were withdrawn and treated as described above at 5, 60, and 120 min relative to the addition of ^{i}PrOH and ^{t}BuOK.

X-ray Structure Determination. Data were collected using Mo Kα radiation (λ = 0.710 73 Å) on a Bruker APEX-II CCD detector/D8 diffractometer[11] with the crystal of **3** cooled to −100 °C. The data were corrected for absorption through Gaussian integration from indexing of the crystal faces. The structure was solved using direct methods (SHELXS-97).[11] Refinements were completed using the program SHELXL-97.[12] Hydrogen atoms were assigned positions based on the sp^2 or sp^3 hybridization geometries of their attached carbon atoms and were given thermal parameters 20% greater than those of their parent atoms. A summary of the crystallographic experimental details for [RuEt(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**3**) is provided as Supporting Information.

RESULTS AND DISCUSSION

In earlier work, we reported that the phosphine−amido complex [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**1**; Ar^- = *o*-$C_6H_4NMe^-$) functions as a ketone transfer hydrogenation catalyst and found that the reaction occurred only in the presence of ^{t}BuOK.[10] This observation appeared to eliminate the possibility of an outer-sphere hydrogenation mechanism that should

Scheme 3. Synthesis of Hydrido (2) and Ethyl (3) Compounds



operate in the absence of base by catalytic involvement of the amido donor.[1] We speculated that the active catalyst may form by β-hydride elimination from a coordinated alkoxide to produce the hydrido complex [RuH(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**2**, Scheme 3), which could operate by an inner-sphere mechanism. In the present study, we have attempted to determine the role of base in the transfer hydrogenation reaction and to establish whether or not **2** is a catalytically relevant intermediate.

Attempts to prepare the hydride species by reacting compound **1** with 1 equiv of Li[$HBEt_3$] under ambient conditions in C_6D_6 led to the formation of two compounds in approximately equimolar quantities; in addition to the targeted hydride (**2**), the ethyl product [RuEt(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**3**) was also obtained. Ethyl group transfer from superhydride to ruthenium has previously been demonstrated in similar systems.[13,14] Each compound can be prepared independently as the sole product by reaction of **1** with either $NaBH_4$ in methanol to give the hydride

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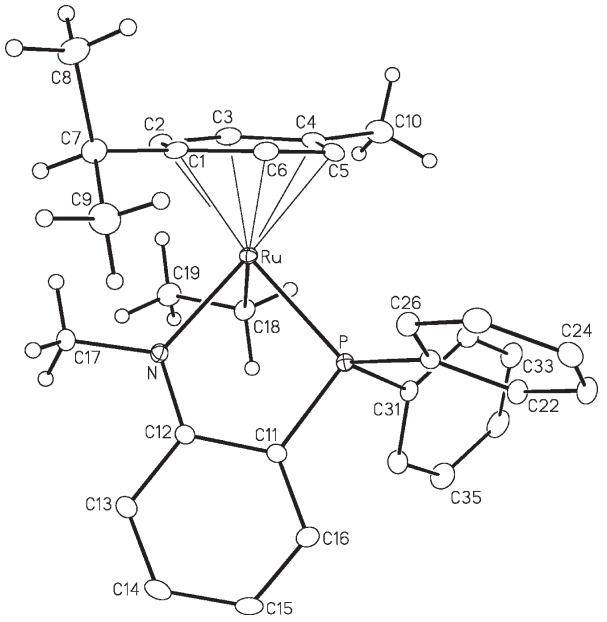

Figure 1. ORTEP diagram of [RuEt(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)] (**3**). Gaussian ellipsoids for all non-hydrogen atoms are depicted at the 20% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters for the methyl, methylene, and methine groups and are not shown for the aryl rings.

(**2**) or with EtMgBr in benzene to give the ethyl species (**3**), as outlined in Scheme 3.

Compound **2** is represented by a signal at δ 70.1 in the $^{31}P\{^1H\}$ NMR spectrum, while the hydride signal is found at δ −7.96 in the ^1H spectrum as a doublet with $^2J_{PH}$ = 46.5 Hz (see the Supporting Information). All other proton resonances (Table 1) are similar to those of the precursor chloro species (**1**)[10] and are fully consistent with the proposed geometry. Compound **3** shows a slightly more upfield chemical shift in the $^{31}P\{^1H\}$ NMR spectrum at δ 68.7, while the ^1H NMR spectrum shows three resonances for the ethyl ligand, with a pseudotriplet at δ 1.38 ($^3J_{HH}$ = 7.5 Hz), representing the methyl group, and two multiplets at δ 1.10 and 0.80, representing the diastereotopic protons of the methylene unit. Compound **2** decomposes in CD_2Cl_2, reverting predominantly to **1** (among other unidentified species) with concomitant production of CHD_2Cl (as made evident by a pentet signal at δ 3.06 in the ^1H NMR spectrum) equal to the amount of **1** regenerated.

Numerous attempts to purify and isolate **2** as an analytically pure solid were unsuccessful, since this product is quite unstable. For example, attempts to crystallize the complex from dark red (nearly black) benzene solutions using *n*-pentane, while employing our best efforts to provide completely inert conditions, produced a pale green (almost white) precipitate that was much less soluble in benzene, the NMR spectra for which reveal decomposition to numerous unidentified species. However, a benzene solution of **2** handled under strictly inert conditions could be concentrated in vacuo to a dark red amorphous residue, which was then quickly redissolved in anhydrous acetophenone and ^{i}PrOH, in which the compound is stable, allowing us to study its capabilities as a catalyst.

While attempts to crystallize complex **2** were unsuccessful, compound **3**, which is also highly air-sensitive, can be easily isolated as large red crystals by layering a saturated benzene solution with *n*-pentane. A crystallographic analysis of **3** (Figure 1) shows the chelating phosphine−amido ligand having the characteristic planar geometry of the amido group,[15] as demonstrated by the sum of the angles at nitrogen (359.7°). The ethyl group appears normal, and the lack of a β-agostic interaction, made evident by the expanded Ru−C(18)−C(19) angle (114.7(2)°, Table 2) and the Ru···H separation of greater than 3.2 Å, illustrates its κ^1 geometry in the solid state and is consistent with coordinative saturation of the complex. The length of the Ru−C(18) bond (2.154(2) Å) appears normal, being comparable to the Ru−C distances within [RuEt(η^6-C_6Me_6)(*S*,*S*′-N($P(^iPr)_2S)_2$] (2.133(3) Å)[13] and [$RuEt_2$((5,5′-^{t}Bu)$_2$-2,2′-Bipy)$_2$] (2.138(7) and 2.142(8) Å),[16] and the C(18)−C(19) distance (1.517(3) Å) is also characteristic of a C−C single bond. The Ru−N distance (2.102(2) Å) is longer than that within the coordinatively unsaturated anilido-containing complex [$RuH(PPh_3)$(*P*,*N*,*N*′-$Ph_2PCH_2P(Ph_2)$=N-(*o*)-$C_6H_4NH^-$)] (2.031(2) Å,)[17] suggesting that the presence of the larger *N*-methyl group within our hexacoordinate complex may hinder effective coordination of the amido nitrogen. This suggestion is supported by the structural parameters for **3**, which show that repulsion between the *p*-cymene isopropyl and amido methyl groups results not only in the somewhat elongated Ru−N bond but also in the unsymmetrical binding of the *p*-cymene ligand, in which the Ru−C(1) and Ru−C(6) distances (2.319(2) and 2.321(2) Å, respectively), adjacent to the isopropyl group, are elongated compared with the other Ru−C_{cymene} distances (2.186(2)−2.261(2) Å). Nevertheless, the Ru−N bond in **3** is still shorter than that within the related phosphine−amine complex [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr)]Cl (2.172(2) Å)[10] and those within a series of related amine species, [RuCl(η^6-*p*-cymene)(*P*,*N*-$Ph_2PC_6H_4NH_2$)]$^+$ (2.125−2.146 Å),[18] consistent with this anionic amido group functioning as a better donor than the amine and also possibly reflecting some degree of π-donor character to ruthenium by the amido lone pair. It is also noteworthy that the nitrogen−arene bond length within amido complex **3** (N−C(12) = 1.348(2) Å) is much shorter than those within the above amine compounds (1.458(4)[10] and 1.422−1.460 Å[18]), suggesting additional delocalization of the amido lone pair onto the aromatic ring. This proposed resonance delocalization of the lone pair in **3** is further illustrated by elongation of the aromatic C−C bonds involving the carbon

Table 2. Selected Structural Parameters for Compound 3

Bond Lengths (Å)			
Ru−P	2.2837(6)	P−C(21)	1.840(2)
Ru−N	2.102(2)	P−C(31)	1.833(2)
Ru−C(1)	2.319(2)	N−C(12)	1.348(2)
Ru−C(2)	2.261(2)	C(11)−C(12)	1.430(3)
Ru−C(3)	2.238(2)	C(12)−C(13)	1.430(3)
Ru−C(4)	2.228(2)	C(13)−C(14)	1.378(3)
Ru−C(5)	2.186(2)	C(14)−C(15)	1.394(3)
Ru−C(6)	2.321(2)	C(15)−C(16)	1.387(3)
Ru−C(18)	2.154(2)	C(11)−C(16)	1.397(3)
P−C(11)	1.795(2)	C(18)−C(19)	1.517(3)
Bond Angles (deg)			
P−Ru−N	81.30(5)	N−Ru−C(18)	82.52(8)
P−Ru−C(18)	82.97(6)	Ru−C(18)−C(19)	114.7(2)

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atom ipso to nitrogen (C(11)−C(12) and C(12)−C(13) = 1.430(3) Å) in comparison to other C−C bonds within the same group (ca. 1.39 Å) or adjacent phenyl groups (ca. 1.39 Å). The delocalization of the amido lone pair onto the aryl ring has been previously noted in a related series of phosphine−amido complexes of Rh and was proposed to rationalize the low basicity of the amido nitrogen in these species.[15] A comparison with the structure of **1**[10] shows a similar trend in the amido−aryl bond lengths in this species, and the corresponding amido lone-pair delocalization is presumably the reason this transfer hydrogenation catalyst does not operate via an outer-sphere mechanism. Also consistent with the electron-withdrawing character of the anilido ring in **3** is the significantly shorter P−C(11) bond (1.795(2) Å) compared to the two P−phenyl distances (1.840(2), 1.833(2) Å), indicating some resonance contribution from a phosphonium ylide structure, as previously discussed.[15] The electron-withdrawing arene also enhances the imine character of the adjacent nitrogen atom, making it a less effective donor to the metal and possibly contributing to the slightly longer Ru−N bond discussed above.

Under strictly inert conditions, compound **3** displays remarkable stability, even in refluxing benzene. This species' apparent resistance to β-hydride elimination inspired our attempts to prepare analogous alkoxo complexes, [Ru(OR)(η^6-*p*-cymene)-(*P*,*N*-Ph_2PAr^-)] (R = ^{i}Pr, Me), which should be generated upon the addition of a base to **1** in alcohols. However, numerous attempts to prepare such derivatives by reactions of **1** with KOH in MeOH or with 1 equiv or more of ^{t}BuOK or ^{i}PrONa in ^{i}PrOH consistently reveal the presence of **2**, due to its apparent formation from the putative, but spectroscopically unobserved, target alkoxide intermediates [Ru(OR)(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)]. Unfortunately, attempts to prepare an alkoxo complex, not having a β-hydride, by reaction of **1** with 1 equiv of ^{t}BuOK in C_6D_6 in the absence of alcohol resulted in a complex mixture of products, as made evident by $^{31}P\{^1H\}$ NMR analysis. Despite the stability of the ethyl derivative **3**, it appears that β-hydride elimination from alkoxo ligands of transient species, [Ru(OR)(η^6-*p*-cymene)(*P*,*N*-Ph_2PAr^-)], occurs (at least in the absence of reagent ketone) over the time it takes to carry out reactions and obtain NMR spectra. In this case, a classical β-hydride elimination from the coordinated alkoxide would require the generation of a vacant coordination site, either by ring slippage of the η^6-arene[19] or by dissociation of either the phosphorus or nitrogen donors. Although it may seem unlikely that dissociation of the anionic amido donor would occur, the presence of an electron-withdrawing arene seems to enhance the imine character of the adjacent nitrogen atom, as noted above, making it a less effective donor to the metal. Furthermore, amide dissociation from Ru could be promoted by potassium ion present.[20] Ring slippage also seems viable on the basis of the crystallographically observed distortions of the coordinated arene in **3** (discussed above). However, it is difficult to rationalize on these grounds why β-hydride elimination occurs so rapidly from alkoxides, while the ethyl substituent of **3** is so robust. Milstein et al. have offered another rationale for the apparent β-hydride elimination from a coordinatively saturated alkoxo complex.[21] This proposal, adapted to our system, involves dissociation of the alkoxide from the metal, allowing the substrate alcohol to form a C−H σ complex while the alkoxide anion is stabilized by exogenous alcohol. Subsequent deprotonation of the alcohol by the alkoxide, accompanied by hydride transfer from the alcohol to Ru, generates the Ru−H bond and either an aldehyde or a ketone. The involvement of such an elimination process could explain the stability of the ethyl complex, which contains a less polar and less labile Ru−C bond. The dissociation of alkoxide anion from ruthenium is consistent with our earlier inference that chloro complex **1** undergoes enantiomerization in dichloromethane solution via chloride ion dissociation to form a coordinatively unsaturated intermediate.[10]

Table 3. Transfer Hydrogenation of Acetophenone with Catalysts 1 and 2

entry	complex	t_{rxn} (min)	conversion (%)[a]	TOF (h^{-1})[b]
1[c]	**1**	5	13	1560
2[c]	**1**	60	34	340
3[c]	**1**	120	46	230
4	**2**	5	1	120
5	**2**	60	7	70
6	**2**	120	9	45

[a] Determined by GC and ^{1}H NMR analyses. [b] Turnover frequency determined at the corresponding reaction time (t_{rxn}) in column 3. [c] Previously published results.[10] Reaction conditions: temperature 90 °C; Ru/^{t}BuOK/acetophenone/^{i}PrOH = 1/4/1000/10 000.

A catalytic study of **2** showed its significantly reduced activity relative to that of its precursor **1** for acetophenone transfer hydrogenation in the presence of catalytic 4 equiv of ^{t}BuOK (see Table 3), with turnover frequencies an order of magnitude less for the hydrido species **2** compared to the chloro precursor **1** in the presence of alkoxide ion.[10] Such an observation suggests that the hydrido complex **2** may represent a means of catalyst deactivation, rather than the active species in the cycle involving **1**. However, the fact that we do observe some (albeit significantly reduced) substrate conversion in the presence of **2** could indicate that partial decomposition of the unreactive hydrido species occurs during its preparation or under the forcing reaction conditions to generate small amounts of a more active species. Alternatively, the small amount of conversion that we observe using **2** as the catalyst could reflect the operation of a very slow inner-sphere process. Consistent with our observations, Stradiotto et al. have recently reported a catalyst system comprised of a zwitterionic indenyl species, [RuCl(η^6-*p*-cymene)(*P*,*N*-1-P^{i}Pr$_2$-2-NMe_2-$C_9H_5^-$)], that is catalytically active in the presence of base and have also ruled out the involvement of the related hydrido complex [RuH(η^6-*p*-cymene)(*P*,*N*-1-P^{i}Pr$_2$-2-NMe_2-$C_9H_5^-$)], in transfer hydrogenation reactions carried out under conditions similar to our own.[9] The fact that these hydrido complexes have low activity in both cases indicates that an inner-sphere mechanism (Scheme 1, left cycle) is not the catalytically dominant pathway for both **1** and Stradiotto's compound. The catalytic dependence on external base in our reaction also rules out the involvement of an outer-sphere mechanism for transfer hydrogenation,[10] which is certainly not possible for Stradiotto's system. Pelagatti et al. have also examined the related amine species [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph_2P-(*o*-$C_6H_4NH_2$)]Cl, as a ketone transfer hydrogenation catalyst, which is also dependent on an excess of external base.[18] However, in this case, base is required for conversion of the amine to the active amido complex. Although it is possible that protonation of the amido group in **1** occurs in alcohol and that base is required to regenerate the active amido group, we have ruled out this possibility, since compound **1** shows no evidence for conversion to an amine in alcohols.

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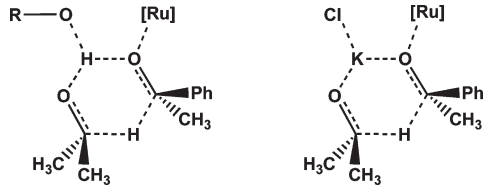

Figure 2. Possible variations of an MPVO transition state.

A remaining mechanistic possibility that deserves consideration is the Meerwein–Ponndorf–Verley–Oppenauer (MPVO)[2,7,8] pathway, in which an alkoxo ligand transfers its hydride directly to a coordinated ketone without the intermediacy of a metal-bound hydrogen atom (Scheme 2). In our case, an MPVO mechanism again requires either dissociation of the phosphorus or nitrogen donors from the (yet unobserved) coordinatively saturated isopropoxo complex [Ru(^{i}PrO)(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] or ring slippage[19] of the η^6-*p*-cymene group to generate a second vacant coordination site for complexation of substrate ketone. In the event of coordinative unsaturation at this complex, binding of the O-donor substrate acetophenone to Ru would give rise to mutually cis ketone and isopropoxo ligands, allowing direct hydride transfer from the isopropoxo ligand to the ketone. While the MPVO mechanism has been proposed to operate within transfer hydrogenation reactions catalyzed by tin[22] and aluminum[23] species, there is a lack of evidence supporting its involvement within processes catalyzed by transition metals (although this possibility has been suggested by Morris et al.).[2]

As noted above for the alkoxide–hydride transformation, the requirement for coordinative unsaturation in the MPVO mechanism is somewhat troublesome in the context of the stability of the ethyl complex **3**. However, given the requirement for base in reaction mixtures and the possibility for stabilization of outer-sphere alkoxide by exogenous alcohol (or even potassium ions), as noted above, a variant of the classical MPVO mechanism might involve replacement of the dissociated isopropoxide anion by acetophenone and subsequent direct hydride transfer from alkoxide to ketone via a six-membered transition state without requiring a vacant coordination site at ruthenium, as shown in Figure 2. Adolfsson and co-workers have also proposed an MPVO-like transition state for a hydrido ruthenium complex in which a dianionic peptido/alkoxo ligand chelates at the metal while the ligand's oxygen atom also binds a lithium ion;[20] however, this mechanism operates by hydride transfer from the ruthenium center to the substrate ketone (rather than directly from alkoxide to ketone) and is perhaps more reminiscent of an outer-sphere transfer. When the process is viewed as an MPVO reaction, the O–Ru(L$_n$)–H moiety is analogous to an alkoxide, which binds to a lithium ion via oxygen, as does the substrate ketone, allowing hydride transfer from the ruthenium center to the ketone. When the reaction is considered as an outer-sphere process, hydride and lithium ion (rather than proton) are simultaneously transferred from ruthenium and ligand, respectively, to the ketone.

Noyori's diamido ruthenium catalyst [Ru(η^6-*p*-cymene)(*N*,*N*-(*S*,*S*)-TsDPEN^{2-})], which operates in the absence of base, cannot be rationalized by an MPVO pathway, on the basis of the observation that its enantioselectivity is not affected when a chiral hydrogen donor is used (during such a process, a chiral alkoxo ligand should promote enantioselective hydrogen transfer to an adjacent prochiral ketone).[1,24] One might suggest conducting a similar experiment with our catalyst **1** using enantiomerically pure 2-butanol as the hydrogen donor and probing for enantiomeric excess as additional support for an MPVO mechanism. However, we did not conduct the experiment, because it became apparent that this would fail to rule out an inner-sphere process (some degree of enantioselectivity should be expected for either pathway). Our chiral precatalyst **1** exists as a racemate; therefore, coordination of an enantiomerically pure alkoxide may favor one of two diastereoisomeric alkoxo complexes. In the case of an MPVO mechanism, the resulting stereochemical influence on a coordinated prochiral ketone is apparent. In the case of an inner-sphere mechanism, two energetically distinct β-hydride elimination pathways also exist, one of which may be more kinetically accessible, thereby favoring formation of one enantiomer of **2** over the other. The resulting stereochemical bias prevents us from discounting an inner-sphere mechanism on the basis of the observation of an enantiomeric excess. However, in the case of Noyori's complex, the fact that the enantioselectivity does not differ when either racemic or enantiomerically pure alcohols are used appears to rule out both inner-sphere and MPVO hydrogen transfer processes. A comparison of the catalytic features of complex **1** (containing a relatively inert amido functionality)[15] to those of Noyori's catalyst shows how differences in the basicity of amido groups can influence their involvement during catalysis, resulting in entirely different reaction mechanisms.

CONCLUSIONS

Hydrido and ethyl complexes of ruthenium, containing chelating phosphine–amido ligands, have been prepared and characterized. Although reaction of the chloro precursor [RuCl(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**1**) with Li[HBEt$_3$] does yield the targeted hydride species, [RuH(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**2**), the ethyl complex [RuEt(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**3**) is also obtained in approximately equimolar amounts, providing an interesting example of carbon–boron bond activation (a fundamental process in Suzuki–Miyaura coupling reactions).[25]

The instant generation of the hydride species **2** upon reaction of **1** with alkoxides is in contrast to the inertness of the ethyl complex **3** and suggests that β-hydride elimination from a putative, formally coordinatively saturated alkoxo intermediate is not the route to the hydride **2**. Instead, we suggest that alkoxide dissociation precedes hydride abstraction by the metal, much as proposed by Milstein et al.[21]

The hydrido complex [RuH(η^6-*p*-cymene)(*P*,*N*-Ph$_2$PAr$^-$)] (**2**) is found to be much less catalytically active than the analogous chloro species **1** for the transfer hydrogenation of acetophenone with ^{i}PrOH in the presence of base, suggesting that **2** is not a catalytically relevant intermediate and that the role of base in the catalysis by **1** is *not* for generation of this hydride. The catalytic dependence on an external base and the relatively poor activity of the hydride species allow us to rule out both traditional outer- and inner-sphere mechanisms, respectively, as the catalytically dominant pathway within our system. We instead suggest the possible role of an MPVO mechanism (or variant thereof), the involvement of which in late-metal systems could be more prominent than previously thought.

ASSOCIATED CONTENT

Supporting Information. A figure giving the ^{1}H NMR spectrum of **2** and a table and CIF file giving crystallographic data

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for **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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