

Reduction of Imines by Hydroxycyclopentadienyl Ruthenium Hydride: Intramolecular Trapping Evidence for Hydride and Proton Transfer Outside the Coordination Sphere of the Metal

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Abstract: Reduction of imines by $[2,5-Ph_2-3,4-Tol_2(\eta^5-C_4COH)]Ru(CO)_2H$ (2) produces kinetically stable ruthenium amine complexes. Reduction of an imine by 2 in the presence of an external amine trap gives only the complex of the newly generated amine. Reaction of 2 with H₂N-*p*-C₆H₄N=CHPh (11), which contains an intramolecular amine trap, gave a 1:1 mixture of $[2,5-Ph_2-3,4-Tol_2(\eta^4-C_4CO)](CO)_2RuNH(CH_2Ph)(C_6H_4-p-NH_2)$ (8), formed by coordination of the newly generated amine to the ruthenium center, and $[2,5-Ph_2-3,4-Tol_2(\eta^4-C_4CO)](CO)_2RuNH_2C_6H_4-p-NHCH_2Ph$ (9), formed by coordination of the amine already present in the substrate. These results require transfer of hydrogen to the imine outside the coordination sphere of the metal to give a coordinatively unsaturated intermediate that can be trapped inside the initial solvent cage. Amine diffusion from the solvent cage must be much slower than coordination to the metal center. Mechanisms requiring prior coordination of the substrate to ruthenium would have led only to 8 and can be eliminated.

Introduction

Several years ago, Shvo discovered that diruthenium hydride complex {[2,3,4,5-Ph₄(η^{5} -C₄CO)]₂H}Ru₂(CO)₄(μ -H) (**1-S**) is an efficient catalyst for the hydrogenation of aldehydes and ketones¹ and is also very useful in the transfer hydrogenation of ketones using alcohols as the reducing agent.^{2,3} In the reduction of ketones to alcohols, the mononuclear [2,3,4,5-Ph₄(η^{5} -C₄COH)Ru](CO)₂H (**2-S**) was proposed to be the active reducing agent and has been shown to reduce aldehydes and ketones (Scheme 1).^{1b,c}

On the basis of detailed mechanistic studies on the related tolyl analogue [2,5-Ph₂-3,4-Tol₂(η^{5} -C₄COH)]Ru(CO)₂H (**2**), including observation of primary deuterium isotope effects for transfer of both OH and RuH, we proposed a mechanism involving concerted transfer of proton and hydride to aldehyde outside the coordination sphere of the metal (Scheme 2).⁴ Related mechanisms for aldehyde reduction have been proposed by Noyori for his very active ruthenium–diamine–diphosphine hydride catalysts.⁵

Density functional theory (DFT) calculations at the B3LYP/ LANL2DZ level of theory on the simplified model reaction of $(C_5H_4OH)Ru(CO)_2H$ (**2-H**) with formaldehyde support a concerted mechanism (Figure 1).⁶ We have found a concerted pathway with an early transition state in which the Ru–H bond has lengthened by 0.11 Å and the C–H distance is 1.42 Å; the CpO–H bond has lengthened by 0.11 Å, and the forming H–OMe distance is 1.35 Å. The calculated activation barrier of 13.8 kcal mol⁻¹ is similar to the experimental ΔH^{\ddagger} of 12 kcal mol⁻¹ found for the reaction of **2** with benzaldehyde. Details of the calculations of both H₂C=O and H₂C=NCH₃ reduction are presented in Supporting Information. Noyori has provided theoretical support for concerted hydrogen transfer from his ruthenium(diamine)(arene) catalysts to carbonyl compounds.⁷

Bäckvall has proposed an alternative mechanism involving Cp ring slippage and aldehyde coordination prior to concerted transfer of the hydrogens (Scheme 3).⁸ In this mechanism, an alcohol complex is the initial product of reduction. In contrast, in our proposed mechanism, an alcohol is formed outside the

 ⁽a) Shvo, Y.; Czarkie, D.; Rahamim, Y. J. Am. Chem. Soc. 1986, 108, 7400. (b) Menashe, N.; Shvo, Y. Organometallics 1991, 10, 3885. (c) Menashe, N.; Salant, E.; Shvo, Y. J. Organomet. Chem. 1996, 514, 97.
 (a) Almeida, M. L. S.; Beller, M.; Wang, G.-Z.; Bickvall, J. E. Chem.– Eur. J. 1996, 2, 1533. (b) Larsson, A. L. E.; Persson, B. A.; Bäckvall, J.

^{(2) (}a) Almeida, M. L. S.; Beller, M.; Wang, G.-Z.; Bäckvall, J. E. Chem.-Eur. J. 1996, 2, 1533. (b) Larsson, A. L. E.; Persson, B. A.; Bäckvall, J. E. Angew. Chem., Int. Ed. Engl. 1997, 36, 1211. (c) Persson, B. A.; Larsson, A. L. E.; Le Ray, M.; Bäckvall, J. E. J. Am. Chem. Soc. 1999, 121, 1645. (d) Persson, B. A.; Huerta, F. F.; Bäckvall, J. E. J. Org. Chem. 1999, 64, 5237. (e) Huerta, F. F.; Laxmi, Y. R. S.; Bäckvall, J. E. Org. Lett. 2000, 2, 1037. (f) Laxmi, Y. R. S.; Bäckvall, J. E. Chem. Commun. 2000, 611.

⁽³⁾ For excellent reviews of ligand-metal bifunctional catalysis, see: (a) Noyori, R.; Kitamura, M.; Ohkuma, T. *Proc. Natl. Acad. Sci. U.S.A.* 2004, 101, 5356. (b) Clapham, S. E.; Hadzovic, A.; Morris, R. H. *Coord. Chem. Rev.* 2004, 248, 2201.

 ⁽⁴⁾ Casey, C. P.; Singer, S. W.; Powell, D. R.; Hayashi, R. K.; Kavana, M. J. Am. Chem. Soc. 2001, 123, 1090.

 ^{(5) (}a) Noyori, R.; Ohkuma, T. Angew. Chem., Int. Ed. 2001, 40, 40, (b) Sandoval, C. A.; Ohkuma, T.; Muñiz, K.; Noyori, R. J. Am. Chem. Soc. 2003, 125, 13490.

⁽⁶⁾ The values were obtained with the B3LYP method associated with a double-ζ quality basis set (LANL2DZ) with an f polarization function added to Ru and 6-31++G(d,p) for the main group elements; Ru was treated with the effective core potential developed by Hay and Wadt. Single point energies were also calculated with Moller–Plesset (MP2) method at the B3LYP optimized geometries. To account for solvation effects, single point solvation free energies were estimated with a continuum model at the IEF-PCM level. For further details, see the Supporting Information.

⁽⁷⁾ Yamakawa, M.; Ito, H.; Noyori, R. J. Am. Chem. Soc. 2000, 122, 1466.
(8) Csjernyik, G.; Éll, A. H.; Fadini, L.; Pugin, B.; Bäckvall, J. E. J. Org. Chem. 2002, 67, 1657.



Scheme 2



coordination sphere of the metal, and an alcohol complex might or might not be formed following hydrogen transfer to a noncoordinated aldehyde (Scheme 2).

A clear distinction between our proposed concerted mechanism and Bäckvall's ring slip mechanism centers on whether the reduced species is initially coordinated to the metal. The question cannot be addressed for aldehyde reduction since Ru– alcohol complexes have never been observed and are expected to be extremely kinetically labile.⁹ In contrast, imine reduction produces kinetically stable ruthenium amine complexes and offers the possibility of determining whether the reduced amine is initially "born coordinated to the metal".

To distinguish between these two mechanisms, we set out to perform what we thought was a simple trapping experiment. Would reduction of an imine by 2 in the presence of an added amine trap give only the amine complex derived from the reduced imine, as suggested by Bäckvall, or would the added amine give rise to a second amine complex, as suggested by our proposed mechanism (Scheme 4)?

Here we describe the results of our trapping experiments using either an *inter*molecular amine trapping agent or an *intra*molecular amine trapping agent. These trapping experiments provide persuasive evidence that reductions proceed outside the coordination sphere of the metal to give an amine and a coordinatively unsaturated intermediate inside a solvent cage and that amine coordination occurs more rapidly than diffusion from the solvent cage.

Results

For a trapping experiment to be mechanistically significant, it is necessary that the trap form a kinetically stable product and that the trap be able to effectively compete for a reactive intermediate. Therefore, control experiments were performed to determine the exchange rates of the amine complexes and to determine the relative ability of the two amines to compete for an independently generated unsaturated intermediate A.

Amine complexes were synthesized by reaction of the amines with cyclopentadienone dimer 3, which serves as a synthetic source of unsaturated intermediate A (Scheme 5).

Kinetics of Isopropylamine Dissociation from 5. At the start, we knew that aliphatic amines dissociate slowly from Ru since we had found that PPh3 displacement of isopropylamine from ruthenium complex 5 required heating at 90 °C (Scheme 6).9 The kinetics of this ligand exchange reaction were measured by adding a >10-fold excess of PPh₃ to a toluene- d_8 solution of 5 and monitoring the disappearance of tolyl methyl resonances (δ 1.87) of **5** by ¹H NMR spectroscopy in a probe preheated to 90 °C. The disappearance of 5 followed first-order kinetics to over 80% conversion, indicating a first-order dependence on 5. No dependence of k_{obs} on PPh₃ concentration was observed: $k_{\rm obs} = 1.1 \times 10^{-3} \, {\rm s}^{-1}$ at 0.20 M PPh₃; 0.97 × 10^{-3} s^{-1} at 0.26 M; $1.3 \times 10^{-3} \text{ s}^{-1}$ at 0.39 M; $0.91 \times 10^{-3} \text{ s}^{-1}$ at 0.68 M. This establishes a dissociative mechanism for substitution reactions of ruthenium amine complexes. It also demonstrates that alkylamine complexes are very kinetically stable at room temperature and only undergo substitution upon heating.

Kinetics of *N*-Phenylbenzylamine Dissociation from 6. Aniline displacement of N-phenylbenzylamine from ruthenium complex 6 was more rapid and occurred at room temperature (Scheme 6). The kinetics of this ligand exchange reaction were measured by adding a >10-fold excess of aniline to a CD_2Cl_2 solution of 6 at low temperature and monitoring the disappearance of tolyl methyl resonances (δ 1.78 and 1.82) of **6** by ¹H NMR spectroscopy at 25 °C. The disappearance of 6 followed first-order kinetics to over 80% conversion, indicating a firstorder dependence on 6. No dependence of k_{obs} on aniline concentration was observed: $k_{\rm obs} = 1.5 \times 10^{-3} \, {\rm s}^{-1}$ at 0.20 M aniline; $1.8 \times 10^{-3} \text{ s}^{-1}$ at 0.26 M; $1.4 \times 10^{-3} \text{ s}^{-1}$ at 0.32 M; $1.4 \times 10^{-3} \text{ s}^{-1}$ at 0.40 M. Thus, while arylamine complexes are less kinetically stable than alkylamine complexes, they are kinetically stable below room temperature and undergo substitution at moderate rates at room temperature.

⁽⁹⁾ Casey, C. P.; Bikzhanova, G. A.; Bäckvall, J.-E.; Johansson, L.; Park, J.; Kim, Y. H. Organometallics 2002, 21, 1955–1959.



Figure 1. Calculated transition state for reaction of $(C_5H_4OH)Ru(CO)_2H$ (2-H) with formaldehyde supports a concerted mechanism with an early transition state.



Tol Tol

oc

OC

р

Α



These kinetic studies establish that both aryl- and alkylamine ruthenium complexes are kinetically stable at low temperature. Arylamine complexes are less kinetically stable than alkylamine complexes probably because of their lower basicity. If these amine complexes were generated during the reduction of imines well below room temperature, then they would be kinetically

H₂NR"

oċ

Additional Product From

Unsaturated Intermediate





stable and would give reliable information in trapping experiments.

Competition of Amines for Unsaturated Intermediate A. Control experiments were carried out prior to trapping experiments to determine whether the two amines can effectively compete for reactive coordinatively unsaturated intermediate **A** when it is generated independently. Cyclopentadienone dimer **3** was selected as a synthetic source of unsaturated intermediate **A** for these competition studies. In the first competition experiment, the reaction of dimer **3** with a mixture of *N*-methylbenzylamine and isopropylamine at room temperature in CD_2Cl_2 produced a 1:1 ratio of amine complexes **4** and **5** (Scheme 7). These two amine complexes are stable indefinitely in the presence of the other amine at room temperature. For example, isolated **4** showed no reaction with isopropylamine at

Scheme 7 To Tol Tol NHMe 00 oc 2 . CH₂Ph Me oc 00 ĊHMe₂ ĊH₀Ph NH_2 1:1 2 ĊHMe₂ NH_2 Tol To οċ 2 Tol Tol Ρ'n 3 Rυ OC. oc NHPh 00 00 2 ĊH₂Ph 1:3 Scheme 8 H₂NCHMe₂ 00 00 oc HN(Me)CH₂Ph οċ oč οċ 90 °C H₂NCHMe₂ . ℃HMe₂ 2 4 5 toluene-d₈ >95% below 0°C -60 °C H₂NC₆H₅ Tol Ph HN(Ph)CH₂Ph OC

OC

6

>95% below 0°C

Ph

Scheme 9

room temperature. At 90 °C, both 4 and 5 exchange amine ligands in the presence of the other amine. These competition experiments were carried out in CH2Cl2 because of the low solubility of 3 in toluene, the solvent employed for imine reduction.

2

H₂NC₆H₅

toluene-d₈ -60 °C

In a second competition experiment, the reaction of ruthenium cyclopentadienone dimer 3 with a mixture of N-phenylbenzylamine and aniline at 0 °C in CD₂Cl₂ produced a 1:3 ratio of amine complexes 6:7 (Scheme 7). The amine ratio remained the same upon warming up to room temperature. Arylamine complexes 6 and 7 are stable indefinitely below 0 °C and interconvert only slowly at room temperature.

These control experiments establish that the selected amine pairs could fairly compete for the reactive coordinatively unsaturated intermediate A, if it were generated in the proposed trapping experiments carried out well below room temperature.

MeN=CHPh Reduction in the Presence of Isopropylamine as a Possible Trapping Reagent. When a 1:1 mixture of MeN= CHPh and H_2NCHMe_2 was added to a toluene- d_8 solution of ruthenium hydride 2 at -60 °C, low temperature ¹H NMR spectroscopy showed that the only product was 4, the complex of the newly generated amine (Scheme 8). The ¹H NMR spectrum showed complete disappearance of the hydride (δ -9.76) and the hydroxyl (δ 8.60) resonances of 2 within 2 min at -60 °C.¹⁰ New resonances were observed at δ 1.80 and 1.82

corresponding to the inequivalent tolyl methyl groups of 4. Other peaks for the newly generated amine complex were too broad to assign. However, upon warming up to -20 °C, resonances due to the diastereotopic benzyl hydrogens of 4 at δ 3.58 (ABX, ${}^{3}J_{AB} = 13.1$ Hz, ${}^{3}J_{AX} = 11.3$ Hz, NHCHH), 3.77 (ABX, ${}^{2}J_{AB}$ = 13.1 Hz, ${}^{3}J_{\text{BX}}$ = 2.4 Hz, NHCHH), and to the N-methyl group of **4** at δ 2.38 (d, ${}^{3}J = 5.8$ Hz, NHCH₃) were observed. None of the isopropylamine complex 5 was seen, and 5% would have been easily detected. No change in the ¹H NMR spectrum was seen upon warming up to room temperature. However, upon heating at 90 °C for 1 h, resonances due to isopropylamine complex 5 were observed at δ 0.96 (d, ${}^{3}J = 6.5$ Hz) and 2.85 (nonet, ${}^{3}J = 6.5$ Hz). The final ratio of 4:5 was 1:1.

Рh

7

25 °C

slow

The initial exclusive formation of **4**, the complex of the newly generated amine, is in agreement with Bäckvall's ring slip mechanism involving prior coordination of the imine. This result is inconsistent with our mechanism involving hydrogen transfer to an imine outside the metal coordination sphere, unless coordination of the newly generated amine is faster than its diffusion from the solvent cage.

PhN=CHPh Reduction in the Presence of Aniline as a **Possible Trapping Reagent.** When a mixture of PhN=CHPh and H₂NPh (1:1) was added to a toluene- d_8 solution of 2 at -60 ° C, the only product was 6, the complex of the newly generated amine (Scheme 9). The ¹H NMR spectrum showed complete disappearance of 2 within 2 min at -60 °C and

⁽¹⁰⁾ In contrast, the reduction of the less basic N-aryl imine 11 by 2 is greatly retarded by isopropylamine (see below).

Scheme 10



Scheme 11

formation of $6^{.11}$ None of the aniline complex 7 was seen, and 5% would have been easily detected. Upon warming to room temperature, a single tolyl methyl resonance at δ 1.80 and a single NH₂ resonance at 3.87 due to aniline complex 7 slowly appeared. The final ratio of 6:7 was 1:5.

Again, the initial exclusive formation of 6, the complex of the newly generated amine, is in agreement with Bäckvall's ring slip mechanism involving prior coordination of the imine, and again, this result is consistent with our mechanism involving hydrogen transfer to an imine outside the metal coordination sphere only if coordination of the newly generated amine is faster than its diffusion from the solvent cage.

Intramolecular Amine Trapping Experiments. If coordination of the newly generated amine is faster than its diffusion from the solvent cage, then placing the imine and the amine trap within the same molecule should be able to trap the coordinatively unsaturated ruthenium intermediate **A** if it indeed was generated. We chose $H_2N-p-C_6H_4N=CHPh$ (11) for intramolecular trapping experiments.

Control experiments were performed to determine whether the two different amino groups of the trapping agent could fairly compete for the reactive coordinatively unsaturated intermediate **A** if it were generated and to determine whether the amine complexes were kinetically stable under their conditions of formation. Reaction of ruthenium cyclopentadienone dimer **3** with the diamine 4-(*N*-benzylamino)aniline **12** was performed at -60 °C in CD₂Cl₂ to determine the ratio of amine complexes formed when both amine groups compete for unsaturated intermediate **A** (Scheme 10). The reaction proceeded only after the temperature was increased to 0 °C. Secondary amine complex [2,5-Ph₂-3,4-Tol₂(η^4 -C₄CO)](CO)₂RuNH(CH₂Ph)-(C₆H₄-*p*-NH₂) (**8**) and primary amine complex [2,5-Ph₂-3,4-Tol₂(η^4 -C₄CO)](CO)₂RuNH₂C₆H₄-*p*-NHCH₂Ph (**9**) were formed in a 25:75 ratio at 0 °C (Scheme 10). Upon warming to room temperature, the ratio decreased to 20:80. This indicates that both amine centers can trap **A**, and that the product amine complexes **8** and **9** are stable below 0 °C.

Reduction of H₂N-*p*-C₆H₄N=CHPh (11). When a toluened₈ solution of H₂N-p-C₆H₄N=CHPh (11) was added to a toluene- d_8 solution of 2 at -60 °C, ¹H NMR spectroscopy showed resonances for a 1:1 mixture of secondary amine complex 8 and primary amine complex 9 (Scheme 11). The 1 H NMR spectrum showed complete disappearance of the hydride $(\delta - 9.76)$ and the hydroxyl ($\delta 8.60$) resonances of 2 within 2 min at -60 °C. New peaks corresponding to the inequivalent tolyl methyl groups of secondary amine complex 8 at δ 1.52 and 1.74 and to the single tolyl methyl group of primary amine complex 9 at δ 1.60 appeared. Other peaks for both 8 and 9 were too broad at -60 °C to assign. Nonetheless, upon warming to -20 °C, new resonances were observed at δ 3.95 (ABX, ${}^{2}J_{AB} = 12.0$ Hz, ${}^{3}J_{BX} = 2.0$ Hz, NHCHH) and 4.19 (ABX, ${}^{2}J_{AB}$ = 12.0 Hz, ${}^{3}J_{AX}$ = 10.0 Hz, NHCHH), corresponding to the diastereotopic benzyl hydrogens of 8. In addition, a new benzyl resonance at δ 3.68 and a new NH₂ resonance at δ 3.75 for 9 were also observed. The 1:1 ratio of 8:9 remained unchanged between -60 and -20 °C. Upon warming to 0 °C, secondary amine complex 8 slowly isomerized to primary amine complex **9** ($k_{\rm obs} = 5.2 \times 10^{-4} \text{ s}^{-1}$, $t_{1/2} = 22 \text{ min at } 0 \text{ °C}$). The slow isomerization of 8 at 0 °C establishes its kinetic stability at lower temperature. The final ratio of 8:9 was 6:94 in toluene- d_8 at room temperature. This is somewhat different from the 20:80 ratio seen in CD₂Cl₂.

The formation of both amine complexes 8 and 9 in this intramolecular trapping experiment requires the intervention of an intermediate, such as the coordinatively unsaturated species **A**. Either the newly formed secondary amine or the primary amine of the reduction product **12** can coordinate to the ruthenium of **A**. This is consistent with the mechanism we proposed earlier (Scheme 4). The fact that intermolecular amine traps are incapable of trapping coordinatively unsaturated intermediate **A**, therefore, suggests that the newly reduced amine

⁽¹¹⁾ New resonances were observed at -60 °C at δ 1.78 and 1.82 for the inequivalent tolyl methyl groups of **6**. Other peaks for **6** were too broad at -60 °C to assign. After warming up to -20 °C, new peaks corresponding to the diastereotopic benzyl hydrogens of **6** appeared at δ 4.02 (ABX, ${}^{2}J_{AB}$ = 13.5 Hz, ${}^{3}J_{AX}$ = 2.5 Hz, NHC*H*H), 4.24 (ABX, ${}^{2}J_{AB}$ = 13.5 Hz, ${}^{3}J_{BX}$ = 11.5 Hz, NHC*H*H).



and **A** are generated in a solvent cage, and that complexation is faster than diffusion from the cage. It should be noticed that more of the newly generated secondary amine complex **8** (50%) is formed in this imine reduction in toluene (Scheme 11) than from the trapping of intermediate **A** in the reaction of dienone dimer **3** in CH₂Cl₂ (25%) (Scheme 10). This may not be simply a solvent effect (see Discussion).

Mechanisms, including Bäckvall's ring slip mechanism (Scheme 3), which involve prior coordination of the substrate to ruthenium would have led only to **8**, in which the newly formed secondary amine is coordinated to ruthenium. Such mechanisms are inconsistent with the intramolecular trapping experiments leading to 1:1 mixtures of **8:9** and can be eliminated.

H₂N-*p*-C₆H₄N=CHPh Reduction in the Presence of *p*-Isopropylaniline. We next investigated trapping experiments in which both an intramolecular and an intermolecular trap were available. When a solution of H₂N-*p*-C₆H₄N=CHPh (**11**) and *p*-isopropylaniline (1:1) in toluene-*d*₈ was added to a toluene*d*₈ solution of **2** at -60 °C, a 1:1 mixture of two amine complexes **8** and **9** was observed by ¹H NMR spectroscopy. No resonances for *p*-isopropylaniline complex **10** were seen. Reduction was complete within 2 min at -60 °C. Upon warming to -20 °C, resonances for the 1:1 mixture of the two amine complexes **8** and **9** became sharper, but their ratio did not change and no **10** was seen.

Upon warming to room temperature, isomerization of **8** to **9** occurred in less than 15 min to give a 6:94 equilibrium ratio of **8:9**. No *p*-isopropylaniline complex **10** was seen at this point. After 24 h at room temperature, ¹H NMR spectroscopy provided evidence for the formation of **10**: δ 1.12 (d, ³*J* = 7.0 Hz, CH-(CH₃)₂), 2.75 (septet, ³*J* = 7.0 Hz, CH(CH₃)₂), 4.39 (NH₂). The final ratio of **8:9:10** was 6:75:19.¹²

The reduction of H₂N-*p*-C₆H₄N=CHPh (11) in either the presence or absence of *p*-isopropylaniline was too fast to measure and was complete within 2 min at -60 °C.¹⁰

It is interesting that the external trapping agent *p*-isopropylaniline does not compete with intramolecular trapping. It is also intriguing that isomerization of **8** to **9** occurs without trapping of coordinatively unsaturated intermediate **A** by *p*-isopropylaniline. *Amine dissociation and recoordination from* **8** and **9** is apparently faster than diffusion from the solvent cage.

Reduction of H_2N -p- C_6H_4N =CHPh (11) in the Presence of Isopropylamine was dramatically slower than in its absence. When a solution of H_2N -p- C_6H_4N =CHPh (11) and isopropylamine (1:1) in toluene- d_8 was added to a toluene- d_8 solution of **2** at -60 °C, no reduction occurred. Reduction slowly proceeded only after increasing the temperature to -20 °C. ¹H NMR spectroscopy showed that the only products were a 1:1 mixture of amine complexes 8 and 9; no isopropylamine complex 5 was seen.

Upon warming to room temperature, isomerization of **8** to **9** occurred in less than 15 min without the appearance of isopropylamine complex **5**. After 24 h at room temperature, ¹H NMR spectroscopy showed the formation of **5**. The 60:40 ratio of **8:5** seen after 24 h shifted slowly to 20:80 after 7 days at room temperature.

Again, isomerization of 8 to 9 occurred without trapping by an external amine. This supports the view that amine dissociation and recoordination from 8 and 9 is faster than diffusion from the solvent cage. At longer times, trapping by the external amine occurs.

Rate Retardation by Isopropylamine. Unusually slow imine reduction by 2 was seen only with the combination of strongly basic isopropylamine with the weakly basic *N*-aryl imine **11**. Both the combination of weakly basic aniline with the weakly basic N-aryl imine 11, and the combination of strongly basic isopropylamine with the strongly basic N-alkyl imine, MeN= CHPh, led to rapid reactions with 2 at -60 °C. We hypothesized that the less basic N-aryl imine 11 cannot effectively compete with isopropylamine for hydrogen bonding to 2; this drastically decreases the amount of free 2 available for reaction with 11 and greatly decreases the rate of reaction of 2 with 11. In contrast, the more basic N-alkyl imine, MeN=CHPh, is better able to compete with isopropylamine for hydrogen bonding to 2 and reacts rapidly. Similarly, the less basic *N*-aryl imine 11 effectively competes with the less basic aniline for hydrogen bonding to 2; aniline does not hydrogen bond as strongly to 2 and is less effective at slowing the reaction with 11. Since the reaction of 2 with 11 is too fast to measure at -60 °C, we cannot determine whether the reaction is somewhat slower in the presence of aniline.

Interaction of Isopropylamine with Hydroxycyclopentadienyl Ruthenium Hydride 2. To explain why isopropylamine dramatically slows the reduction of H_2N -p- C_6H_4N =CHPh (11) by 2, we hypothesized that hydrogen bonding between isopropylamine and the hydroxyl group of the hydroxycyclopentadienyl ligand of 2 would reduce the concentration of 2 available for reaction with 11. To test this hypothesis, we investigated the interaction of 2 with isopropylamine by NMR and IR spectroscopy.

An inversion-saturation T_1 NMR experiment was performed in order to determine whether isopropylamine is hydrogen bonded to **2** (Scheme 12). T_1 is a measure of the spin-lattice relaxation rate and is dependent on the tumbling rate, which should be faster for free rather than hydrogen bonded isopropylamine.¹³ T_1 times are correlated between the isopropylamine and organometallic fragments and different from the T_1 of the free isopropylamine in solution.¹⁴ The T_1 for the isopropyl methyl resonance of **2-H₂NCHMe₂** was 0.4 s, while the T_1 time

⁽¹²⁾ The observed 6:75 (=7:93) ratio of **8:9** is within experimental error of the 6:94 equilibrium ratio reported above.



Figure 2. A molecular drawing of 9 shown with 30% probability ellipsoids.

for the free isopropylamine was 2.8 s at -60 °C. This provides compelling evidence for association between 2 and isopropylamine.

Norton's IR method for determination of the pK_a of metal carbonyl hydrides was adapted to study hydrogen bonding between **2** and H₂N(CHMe₂).¹⁵ When isopropylamine (1.3 equiv) was added to a toluene solution of **2** (0.022 M), IR bands due to **2** at 2015 and 1956 cm⁻¹ disappeared and new bands at 1999 and 1946 cm⁻¹ appeared and were assigned to **2-H₂NCHMe₂**. These shifts provide evidence for strong hydrogen bonding in toluene. Previously, in determining the pK_a of hydroxyl proton of **2** in acetonitrile, we observed IR bands at 1985 and 1920 cm⁻¹ for NEt₃H⁺[2,5-Ph₂-3,4-Tol₂(η^{5} -C₄CO)]-Ru(CO)₂H]^{-,4}

The inversion—saturation T_1 NMR and IR experiments provide strong evidence for hydrogen bonding between isopropylamine and the hydroxyl group of the hydroxycyclopentadienyl ligand of **2**. This supports the hypothesis that this interaction reduces the concentration of **2** available for reaction with **11** and is responsible for the much slower rates seen in the presence of isopropylamine.

The X-ray Structure of $9^{16,17}$ is similar to that of the isopropylamine complex (η^4 -C₄Ph₄CO)(CO)₂RuNH₂CHMe₂.⁹ The Ru metal center in **9** is formally five-coordinate with a bidentate (η^4 -Ph₂Tol₂C₄C=O) ligand, two carbonyls, and an amine (Figure 2). The short C(1)-O(1) distance of 1.264(8) Å is best described as a C=O unit. The Ru-C(1) bond in **9** is significantly shorter than the average corresponding distance of 2.58(7) Å in related complexes¹⁸⁻²⁰ due to a moderately strong O(1)···H-N(1) hydrogen bond between the cyclopen-

- (13) (a) Sanders, J. K. M.; Hunter, B. K. Modern NMR Spectroscopy, A Guide for Chemists; Oxford University Press: London, 1993. (b) Abragam, A. The Principles of Nuclear Magnetism; Oxford University Press: London, 1971.
- (14) Bakhmutov, V. I.; Vorontsov, E. V.; Antonov, D. Yu. Inorg. Chim. Acta 1998, 278, 122.
- (15) (a) Jordan, R. F.; Norton, J. R. J. Am. Chem. Soc. 1982, 104, 1255. (b) Moore, E. J.; Sullivan, J. M.; Norton, J. R. J. Am. Chem. Soc. 1986, 108, 2257.
- (16) X-ray crystal data for C₄₆H₃₈N₂O₃Ru (9): monoclinic, P2₁, a = 11.719(3) Å, b = 9.906(2) Å, c = 17.403(5) Å, β = 97.938(10)°, V = 2000.9(10) Å³, Z = 2, T = 100(2) K, D_{calcd} = 1.274 Mg/m³, R(F) = 0.0466 for 5737 independent reflections. All non-hydrogen atoms were refined with anisotropic displacement coefficients. All hydrogen atoms were included in the structure factor calculation at idealized positions and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients.
- (17) Bruker-AXS: SADABS V.2.05, SAINT V.6.22, SHELXTL V.6.10 and SMART 5.622 Software Reference Manuals, Madison, Wisconsin, USA, 2000–2003.
- (18) Allen, F. H. Acta Crystallogr. 2002, B58, 380-388.

tadienone oxygen atom and the H atom on the coordinated primary amine. The five-membered ring of the dienone ligand is not planar; the C(O) carbon atom is displaced from the plane defined by atoms C(2), C(3), C(4), and C(5) away from the Ru center by 0.139(10) Å. Thus, the Ru–C(1) distance of 2.407-(8) Å is longer than the Ru–C distances to C(2) and C(5) (av. 2.240(10) Å), which are adjacent to C(1), and then the Ru–C bond lengths to the other two cyclopentadienone carbon atoms C(3) and C(4) (av. 2.179(17) Å). The envelope flap angle in the cyclopentadienone ligand between the planes defined by atoms C(2)–C(3)–C(4)–C(5) and C(2)–C(1)–C(5) measured 9.1(9)°. O(1) is not coplanar with atoms C(2)–C(1)–C(5) and is displaced toward the amine ligand as a consequence of the hydrogen bonding interaction, with the angle between the C= O vector and the C(2)–C(1)–C(5) plane being 4.2(9)°.

Discussion

Two mechanisms have been proposed for the reduction of aldehydes by hydroxycyclopentadienyl ruthenium hydride **2**. We proposed a mechanism involving concerted transfer of proton and hydride to aldehyde outside the coordination sphere of the metal that generates the coordinatively unsaturated intermediate **A** (Scheme 2).⁴ Bäckvall proposed an alternative mechanism involving Cp ring slippage and aldehyde coordination prior to concerted transfer of the hydrogens (Scheme 3). These mechanisms are not readily distinguished in the case of aldehyde reduction because the alcohol complexes are too labile and undetected. Imine reduction offered the possibility of determining whether the reduced amine is initially "born coordinated to the metal" since Ru–amine complexes are kinetically stable.

Intermolecular Trapping Experiments were carried out that involved reaction of 2 with an imine in the presence of an added amine trap (Scheme 4). In both cases studied, only the amine complexes from the reduced imine were observed at low temperature (Schemes 8 and 9); amine complexes expected from trapping of an unsaturated intermediate, such as A, by the added amine were not seen. While these results are consistent with prior imine coordination proposed in Bäckvall's ring slip mechanism, they can also be explained by imine reduction outside the coordination sphere to give a new amine and coordinatively unsaturated species A inside a solvent cage followed by more rapid coordination of the amine to ruthenium than diffusion apart.

An Intramolecular Trapping Experiment was devised to distinguish these possibilities that involved reduction of H_2N - $p-C_6H_4N=CHPh$ (11) by 2 at -60 °C (Scheme 11). In this case, a 1:1 mixture of two amine complexes 8 and 9 was formed. 8 is the complex of the newly generated amine, while 9 is the complex of the intramolecular amine trap, and both are kinetically stable at low temperature. The formation of 9 requires the intervention of a coordinatively unsaturated intermediate A that can be trapped. Since Bäckvall's mechanism would have led to 8 as the exclusive kinetic product, this ring slippage mechanism can be ruled out.

The combination of the failure of intermolecular trapping with successful intramolecular trapping provides evidence for hydride

⁽¹⁹⁾ Bruno, I. J., Cole, J. C., Edgington, P. R., Kessler, M., Macrae, C. F., McCabe, P., Pearson, J., Taylor, R. Acta Crystallogr. 2002, B58, 389– 397.

⁽²⁰⁾ The distances from ruthenium to the cyclopentadienone carbon atoms were compared with the corresponding values in 29 related complexes reported to the Cambridge Structural Database (CSD).



and proton transfer to the imine outside the metal coordination sphere to produce the new amine and intermediate **A** inside a solvent cage; coordination of the new amine to ruthenium occurs before diffusion apart.

When the reduction of H_2N -p- C_6H_4N =CHPh (11) by 2 was performed in the presence of an external amine, such as p-isopropylaniline or isopropylamine, only intramolecular trapping products 8 and 9 were formed, confirming that only amines inside the initial solvent cage can compete for coordination to ruthenium. Interestingly, the isomerization of 8 to 9 in the presence of an external amine occurred intramolecularly without formation of complexes of the added amines. This is consistent with amine dissociation from 8 to give A and the diamine within a solvent cage. Again, coordination of the amine to A is more rapid than diffusion apart. At longer times and higher temperature, 8 and 9 do react with external amines to give new products. Escape from the solvent cage can occur, but it is slower than coordination.

Is it really believable that diffusion from the solvent cage can be slower than coordination of the newly produce imine to intermediate A? What might slow escape from the cage? We suggest that the newly reduced amine is initially hydrogen bonded to the dienone oxygen as **B** (Scheme 13). This is expected to be a weak hydrogen bond between a weakly acidic amine hydrogen and a weakly basic dienone oxygen. (The dienone oxygen acts as a base in hydrogen bonding to a proton on a complexed amine in all of the amine complexes reported here.) In a nonpolar solvent, such as toluene, hydrogen bonding between these two units has few competitors. The barrier for escape from the cage is the sum of the hydrogen bond energy and activation energy for diffusion. We suggest that the barrier for coordination of an amine to **B** is lower than this combined barrier. The intramolecular isomerization of 8 to 9 occurred without trapping by an external amine. This isomerization requires breaking the hydrogen bond between the diamine and

the dienone oxygen in **B** to give diamine and **A** within the solvent cage and re-formation of a different hydrogen bond and complexation before diffusion out of the solvent cage can occur. As pointed out earlier, more of the newly generated secondary amine complex **8** (50%) was formed in reduction of imine **11** in toluene than in the reaction of dienone dimer **3** with diamine **12** in CH₂Cl₂ (25%). This might be due to collapse of the initial hydrogen bonded intermediate **B** to **8** before breaking the hydrogen bond to give **A** and diamine **12** inside the solvent cage.

In other work on the mechanism of imine reduction by 2 in THF, a shift in the rate-determining step was seen as a function of imine basicity.²¹ For imines with electron-withdrawing substituents on nitrogen, significant kinetic isotope effects were observed for concerted transfer of hydride and proton from 2 to the imine. For imines with electron-donating alkyl substituents on nitrogen, we observed imine isomerization, deuterium exchange, and inverse equilibrium isotope effects that established a mechanism involving reversible hydrogen transfer to the imine followed by rate-determining coordination of the amine to ruthenium (Scheme 14).

Another very rapid process was uncovered in our unpublished studies of the stereochemistry of imine reduction by $2^{.22}$ When hydrogen is transferred to an imine, two stereocenters are formed, one at carbon and a second at nitrogen. We established that hydrogen is transferred via a stereospecific addition of deuterium from 2-RuDOD to PhN=CHPh and related imines, resulting in a trans addition of deuterium (Scheme 15). The observed stereospecificity requires that complexation of the stereospecifically formed amine to ruthenium be much faster than nitrogen inversion, which has a very low barrier (~7.5 kcal mol⁻¹).²³

⁽²¹⁾ Casey, C. P.; Johnson, J. B. J. Am. Chem. Soc. 2005, 127, 1883.

⁽²²⁾ Casey, C. P.; Bikzhanova, G. A. Unpublished results.



In summary, the combination of failed intermolecular and successful intramolecular trapping of a coordinatively unsaturated intermediate in the reduction of imines by hydroxycyclopentadienyl ruthenium hydride 2 provides convincing evidence for hydrogen transfer outside of the metal coordination sphere. In addition, we have uncovered a remarkable array of extremely fast reactions of the hydrogen bonded unsaturated species **B**. "Slow" reactions of **B** include breaking of the hydrogen bond and diffusion from the solvent cage and inversion of the nitrogen lone pair. These reactions are only slow in comparison with the even faster coordination of nitrogen to ruthenium and reversible dehydrogenation of the amine.

Experimental Section

[2,5-Ph₂-3,4-Tol₂(η^4 -C₄CO)](CO)₂RuNH(CH₃)(CH₂Ph) (4). Procedure A. A solution of *N*-benzylidenemethylamine (3.4 μ L, 0.02 mmol) was added to a solution of 2 (11.4 mg, 0.02 mmol) in toluened₈ (0.5 mL) at -78 °C. The solution was slowly warmed to room temperature, and solvent was evaporated under vacuum to give a green solid which was recrystallized from hexane at -10 °C to give pure 4 as a pale green precipitate (8 mg, 62% yield).

Procedure B. *N*-Methylbenzylamine (26 μ L, 0.2 mmol) was added via syringe to a CD₂Cl₂ suspension of ruthenium cyclopentadienone dimer (3) (114 mg, 0.1 mmol), and the mixture was stirred for 30 min, until all the material dissolved. Solvent was evaporated under vacuum to give a green solid which was recrystallized from hexane at -10 °C to give pure 4 as a pale green precipitate (109 mg, 79%), mp 174-177 °C (dec). IR (CH₂Cl₂): 2011 (s), 1952 (s) cm⁻¹. ¹H NMR (CD₂-Cl₂, 250 MHz): δ 1.66 (br m, NH), 2.22 (s, tolyl CH₃), 2.24 (s, tolyl CH₃), 2.40 (d, ${}^{3}J = 5.8$ Hz, NCH₃), 3.58 (ABX, ${}^{2}J_{AB} = 13.1$ Hz, ${}^{3}J_{AX}$ = 11.3 Hz, NHCHH), 3.77 (ABX, ${}^{2}J_{AB}$ = 13.1 Hz, ${}^{3}J_{BX}$ = 2.4 Hz, NHCHH), 6.95 (t, ${}^{3}J = 8.0$, 4 H, aromatic), 7.06–7.31 (m, 15 H, aromatic), 7.56 (m, 2 H, aromatic), 7.72 (m, 2 H, aromatic). ¹³C{¹H} NMR (CD₂Cl₂, 75 MHz): δ 21.1, 21.2 (tolyl CH₃); 45.1 (NCH₃); 66.2 (NCH₂Ph); 83.5, 84.2 (C 3, 4 of Cp); 103.7, 104.0 (C 2, 5 of Cp); 126.6-138.0 (20 resonances, aromatic); 163.8 (C1 of Cp); 200.9, 201.0 (CO). HRMS (EI) calcd for C41H35NO3102Ru, 691.1654; found, 691.1785.

[2,5-Ph₂-3,4-Tol₂(η^4 -C₄CO)](CO)₂RuNH(Ph)(CH₂Ph) (6). Procedure A. A solution of *N*-benzylideneaniline (3.6 mg, 0.02 mmol) was added to a solution of 2 (11.4 mg, 0.02 mmol) in toluene- d_8 (0.5 mL) at -78 °C. The solution was slowly warmed to room temperature, and solvent was evaporated under vacuum to give a green solid which was recrystallized from hexane at -10 °C to give pure 6 as a pale green precipitate (9 mg, 60% yield).

Procedure B. *N*-phenylbenzylamine (35 μ L, 0.20 mmol) was added via syringe to a CD₂Cl₂ suspension of ruthenium cyclopentadienone dimer (**3**) (114 mg, 0.10 mmol), and the mixture was stirred for 30 min, until all the material dissolved. Solvent was evaporated under vacuum to give a green solid which was recrystallized from hexane at -10 °C to give pure **6** as a dark green precipitate (112 mg, 75%), mp 191–193 °C (dec). IR (CH₂Cl₂): 2016 (s), 1957 (s) cm⁻¹. ¹H NMR (CD₂Cl₂, 500 MHz): δ 2.18 (s, tolyl CH₃), 2.24 (s, tolyl CH₃), 3.69 (br d, ${}^{3}J$ = 11.0 Hz, NH), 3.80 (ABX, ${}^{2}J_{AB}$ = 13.5 Hz, ${}^{3}J_{AX}$ = 2.5 Hz, NHC*H*H), 4.39 (ABX, ${}^{2}J_{AB}$ = 13.5 Hz, ${}^{3}J_{BX}$ = 11.5 Hz, NHC*HH*), 6.8–7.4 (m, 26 H, aromatic), 7.79 (dd, ${}^{3}J$ = 8.0, 1.0 Hz, 2 H, aromatic). ${}^{13}C{}^{1}H$ } NMR (CD₂Cl₂, 125 MHz): δ 21.1, 21.2 (tolyl CH₃); 63.3 (NCH₂Ph); 83.5, 85.1 (C 3, 4 of Cp); 103.8, 103.9 (C 2, 5 of Cp); 119.9, 125.1, 126.6, 126.8, 127.9, 128.2, 128.6, 128.8, 129.0, 129.1, 129.5, 130.5, 131.0, 132.2, 132.3, 132.8, 133.1, 137.2, 138.0, 138.3, 150.7 (aromatic); {}^{24}163.8 (C 1 of Cp); 199.1, 201.2 (CO). HRMS (ESI) (M + H)⁺ calcd for C₄₆H₃₇NO₃¹⁰²Ru, 754.1895; found, 754.1885.

[2,5-Ph₂-3,4-Tol₂(η⁴-C₄CO)](CO)₂RuNH(CH₂Ph)(C₆H₄-p-NH₂) (8) and [2,5-Ph₂-3,4-Tol₂(η⁴-C₄CO)](CO)₂RuNH₂C₆H₄-p-NHCH₂Ph (9). A solution of 4-amino-N-(benzylidene)aniline (4.0 mg, 0.02 mmol) was added to a solution of 2 (11.4 mg, 0.02 mmol) in toluene-d₈ (0.5 mL) at -78 °C. The solution was slowly warmed to -30 °C. Both 8 and 9 were formed in a 1:1 ratio at -30 °C. The amine complex 8 was not isolated since it isomerized to 9 upon warming to room temperature. ¹H and ¹³C{¹H} NMR spectra for 8 were obtained by subtracting resonances belonging to 9 from the ¹H and ¹³C{¹H} NMR spectra of the mixture of 8 and 9. For 8: ¹H NMR (CD₂Cl₂, 500 MHz, -30 °C) δ 2.16 (s, tolyl CH₃), 2.22 (s, tolyl CH₃), 3.47 (ABX, ³*J*_{AX} = 10.0 Hz, ${}^{3}J_{\text{BX}} = 2.0 \text{ Hz NHCHH}$, 3.52 (br s, NH₂), 3.63 (ABX, ${}^{2}J_{\text{AB}} = 12.0$ Hz, ${}^{3}J_{BX} = 2.0$ Hz, NHCHH), 4.27 (ABX, ${}^{2}J_{AB} = 12.0$ Hz, ${}^{3}J_{AX} =$ 10.0 Hz, NHCHH), 6.80–7.48 (m, 25 H, aromatic), 7.72 (d, ${}^{3}J = 7.5$ Hz, 2 H, aromatic). ${}^{13}C{}^{1}H$ NMR (CD₂Cl₂, 125 MHz, -30 °C): δ 20.88, 20.94 (tolyl CH3); 63.26 (NCH2Ph); 82.63, 84.25 (C 3, 4 of Cp); 102.86, 102.91 (C 2, 5 of Cp); 116.09, 119.39, 126.18, 126.24, 127.56, 127.68, 127.78, 128.25, 128.34, 128.38, 129.17, 129.90, 130.38, 131.68, 132.26, 132.50, 136.79, 137.56, 137.66, 141.45, 143.35, 144.76 (aromatic);²⁵ 162.74 (C1 of Cp); 198.53, 200.92 (CO).

[2,5-Ph₂-3,4-Tol₂(η^4 -C₄CO)](CO)₂RuNH₂C₆H₄-*p*-NHCH₂Ph (9). **Procedure A.** A solution of 4-amino-*N*-(benzylidene)aniline (4.0 mg, 0.02 mmol) was added to a solution of 2 (11.4 mg, 0.02 mmol) in toluene-*d*₈ (0.5 mL) at -78 °C. The solution was slowly warmed to -30 °C to give a 1:1 mixture of 8:9. Upon warming to room temperature, 8 isomerized to 9 within 20 min. The final ratio of 8:9 was 4:96. Solvent was evaporated under vacuum to give a green solid which was recrystallized from hexane at -10 °C to give pure 9 as a yellowish green precipitate (10 mg, 67% yield).

Procedure B. 4-(*N*-Benzylamino)aniline (20.0 mg, 0.1 mmol) was added to a CD₂Cl₂ suspension of ruthenium cyclopentadienone dimer (**3**) (57 mg, 0.05 mmol), and the mixture was stirred for 30 min, until all the material dissolved. Solvent was evaporated under vacuum to give a green solid which was recrystallized from hexane at -10 °C to give pure **9** as a yellowish green precipitate (6.5 mg, 84%), mp 176–178 °C (dec). IR (CH₂Cl₂): 2015 (s), 1956 (s) cm⁻¹. ¹H NMR (C₆D₆, 500 MHz): δ 1.78 (s, 6 H, tolyl CH₃), 3.06 (t, ³*J* = 5.8 Hz, NH), 3.69 (d, ³*J* = 5.5 Hz, CH₂), 3.75 (br s, NH₂), 5.91 (d, ³*J* = 8.5 Hz, 2 H, aromatic), 6.18 (d, ³*J* = 8.5 Hz, 2 H, aromatic), 6.67–7.12 (m, 11 H, aromatic), 7.21 (d, ³*J* = 8.5 Hz, 4 H, aromatic), 8.14 (d, ³*J* = 8.5 Hz, 4 H, aromatic). ¹³C{¹H} NMR (CD₂Cl₂, 125 MHz): δ 21.17 (tolyl CH₃); 48.69 (NCH₂Ph), 84.39 (C

⁽²³⁾ Bushweller, C. H.; O'Neil, J. W.; Bilofsky, H. S. Tetrahedron 1972, 28, 2697.

⁽²⁴⁾ If none of the aryl resonances were accidentally equivalent, then 24 peaks would be expected; 21 were seen.

⁽²⁵⁾ If none of the aryl resonances were accidentally equivalent, then 24 peaks would be expected; 22 were seen.

3, 4 of Cp); 103.46 (C 2, 5 of Cp); 113.19, 120.03, 126.70, 127.50, 127.79, 128.02, 128.60, 128.88, 129.03, 131.03, 132.25, 133.25, 137.70, 137.90, 139.84, 145.61 (aromatic); 163.55 (C1 of Cp); 200.25 (CO). HRMS (ESI) (M + H)⁺ calcd for $C_{46}H_{38}N_2O_3^{102}Ru$, 769.2005; found, 769.2015.

Procedure for Trapping Experiments will be illustrated with a specific example. A 50 μ L aliquot of a standard toluene- d_8 solution of *N*-benzylidenemethylamine (0.40 M, 20 μ mol) and isopropylamine (0.40 M, 20 mmol) was added via a gastight syringe to a solution of **2** (11.4 mg, 20 mmol, 0.044 M) in toluene- d_8 (0.45 mL) and cooled to -78 °C. The sample was inserted into an NMR spectrometer precooled to -60 °C, and spectra were acquired.

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Supporting Information Available: General experimental information, preparation of solutions of **2**, preparation of **7** and **10**, kinetics of amine exchange reactions, T_1 measurement of **2**, DFT calculations, and X-ray structure of **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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