Deprotonation of Organic Compounds Bearing Acid Protons Promoted by Metal Amido Complexes with Chiral Diamine Ligands Leading to New Organometallic Compounds

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*Summary: Well-defined 16-electron metal amido complexes bearing chiral Ts-diamine ligands readily react with nitromethane, acetone, or phenylacetylene to give new organometallic compounds in almost quantitative yields. For example, an Ir amido complex, Cp*Ir[(R,R)-Tscydn], reacts with nitromethane at room temperature to give quantitatively a nitromethyl Ir complex, Cp*Ir-(CH_2NO_2)[(R,R)-Tscydn], as a single diastereomer. The isolable organometallic compounds with chiral amine ligands are relevant to active catalysts for asymmetric C−C bond formation.*

Chiral transition-metal complexes with a metal/NH bifunctional synergetic effect have been recently developed as practical asymmetric transfer hydrogenation catalysts for the synthesis of optically active alcohols, in which both chiral metal amido and chiral metal amine hydrido complexes are involved as catalysts and intermediates.[1,2] In particular, the coordinatively unsaturated 16-electron metal amido complexes Ru(Ts-diamine)(η^6-arene)[1] and Cp*M(Ts-diamine)[1e,3] (Cp* = pentamethylcyclopentadienyl, Ts-diamine = *N*-(*p*-toluenesulfonyl)-1,2-diamine, M = Rh, Ir) have suitable Brønsted basicity on the amido group to react with hydrogen donors such as alcohols and formic acid to produce metal amine hydrido complexes. This hydrido complex reacts readily with carbonyl compounds, possibly through a pericyclic six-membered transition state as shown in Figure 1[1d,2] to regenerate the amido complex and release the reduction product. If the amido complex could react with certain organic compounds which have suitable acidic protons to give an amino complex bearing a metal-bonded *C*-nucleophile and could then be followed by further reactions with carbonyl compounds, catalytic enantioselective C−C bond formation could be achieved. To accomplish this asymmetric catalysis process, we first examined the reaction of these chiral metal amido complexes with a series of acidic organic compounds and found that a C−H bond of these compounds readily adds across the M−N bond of the amido complex, leading to new organometallic compounds.[4]

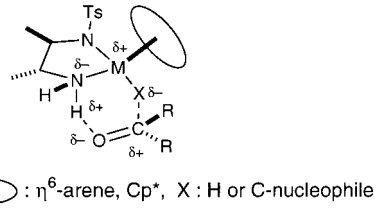

Figure 1. Possible transition state for hydrogen transfer between alcohols and ketones.

A 16-electron metal amido complex, Cp*Ir(Ts-diamine) or Ru(Ts-diamine)(η^6-arene), has now been proven to react smoothly with nitromethane (pK_a = 10.2) at room temperature to give a nitromethyl complex (Scheme 1). Since there is a structural similarity between these amido complexes, they exhibit similar reactivity toward nitromethane, but the outcome of the reaction is delicately affected by the electronic properties of the ligands and the central metal. For example, the reaction of Cp*Ir[(*R*,*R*)-Tscydn] (**1a**; (*R*,*R*)-TsCYDN = (1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-cyclohexanediamine)[1f,3] with 1 equiv of nitromethane in CH_2Cl_2 gave quantitatively a pale yellow complex, Cp*Ir(CH_2NO_2)[(*R*,*R*)-Tscydn] (**1b**) as a single dia-

(1) (a) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562−7563. (b) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 285−288. (c) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738−8739. (d) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97−102. (e) Murata, K.; Ikariya, T.; Noyori, R. *J. Org. Chem.* **1999**, *64*, 2186−2187. (f) Murata, K.; Okano, K.; Miyagi, M.; Iwane, H.; Noyori, R.; Ikariya, T. *Org. Lett.* **1999**, *1*, 1119−1121. (g) Okano, K.; Murata, K.; Ikariya, T. *Tetrahedron Lett.* **2000**, *41*, 9277−9280. (h) Koike, T.; Murata, K., Ikariya, T. *Org. Lett.* **2000**, *2*, 3833−3836.

(2) (a) Alonso, D. A.; Brandt, P.; Nordin, S. J. M.; Andersson, P. G. *J. Am. Chem. Soc.* **1999**, *121*, 9580−9588. (b) Yamakawa, M.; Ito, H.; Noyori, R. *J. Am. Chem. Soc.* **2000**, *122*, 1466−1478. (c) Casey, C. P.; Singer, S. W.; Powell, D. R.; Hayashi, R. K.; Kavana, M. *J. Am. Chem. Soc.* **2001**, *123*, 1090−1100.

(3) Previously, we reported that the Ir amido complex was obtained from the reaction of Cp*IrH[(*R*,*R*)-Tscydn] with acetone as a yellow crystal.[1e] However, the structure of this isolable yellow complex was later confirmed by X-ray crystal structural analysis to be Cp*Ir(CH_2COCH_3)[(*R*,*R*)-Tscydn] (**1c**). A careful stoichiometric reaction of the Ir hydrido species and acetone in CH_2Cl_2 gave a purple complex. The structure of the complex was determined to be Cp*Ir[(*R*,*R*)-Tscydn] (**1a**) on the basis of NMR analysis and elemental analysis. The complex **1a** can be conveniently obtained by the reaction of Cp*IrCl[(*R*,*R*)-Tscydn][1e] with 1 equiv of NaOH in CH_2Cl_2−H_2O quantitatively. **1a**: ^{1}H NMR (CD_2Cl_2) δ 0.8−2.2 (cyclohexane ring protons, 9H), 1.77 (s, 15H, $C_5(CH)_3$), 2.38 (s, 3H, CH_3 of Ts), 2.71 (m, 1H, C*H*-NTs), 5.64 (br s, 1H, N*H*), 7.22, 7.73 (4H, aromatic ring protons). Anal. Calcd for $C_{23}H_{33}N_2O_2SIr\cdot H_2O$: C, 45.15; H, 5.77; N, 4.58. Found: C, 45.06; H, 5.49; N, 4.60.

(4) During the preparation of this paper, an effective stepwise C−H bond activation with a coordinatively saturated Ru amido complex with diphosphane ligands, followed by subsequent Ru−C bond formation, was reported by Bergman's group: Fulton, J. R.; Bouwkamp, M. W.; Bergman, R. G. *J. Am. Chem. Soc.* **2000**, *122*, 8799−8800.

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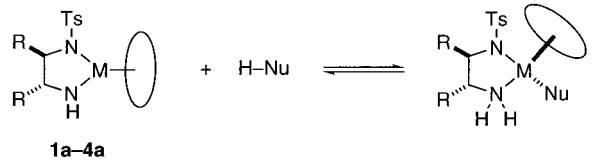
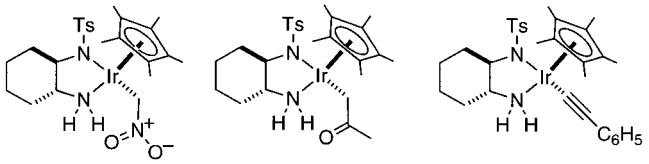
Scheme 1



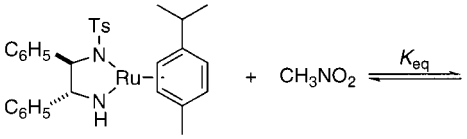
1a–4a

1a: Cp*Ir[(*S*,*S*)-Tscydn] 3a: Cp*Ir[(*S*,*S*)-Tsdpen]
2a: Ru[(*S*,*S*)-Tscydn](*p*-cymene) 4a: Ru[(*S*,*S*)-Tsdpen](*p*-cymene)
H–Nu: CH_3NO_2, CH_3COCH_3, $HC{\equiv}CC_6H_5$

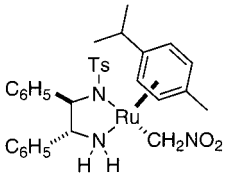


1b **1c** **1d**

Scheme 2



4a



4b

stereomer after 0.5 h.[5,6] The analogous nitromethyl Ru complex **2b** was obtained in 90% yield from the reaction of nitromethane and the Ru complex **2a**, which was in situ generated from the reaction of RuCl[(*R*,*R*)-Tscydn](*p*-cycmene) with NaOH. In contrast, the reaction of Ir or Ru amido complex with a less electron donating TsDPEN ligand (TsDPEN = *N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine), **3a** or **4a**, with nitromethane under otherwise identical conditions gave an equilibrium mixture of the amido complex **3a** or **4a**, nitromethane, and the nitromethyl complex **3b** or **4b** in the ^{1}H NMR spectra. An equilibrium constant of $K_{eq} = 2.4 \times 10^2$ for the reaction of **4a** and nitromethane in CD_2Cl_2 at 22 °C could be estimated from a linear van't Hoff plot obtained at several different temperatures (Scheme 2). The use of 10 equiv of nitromethane with **4a** caused an equilibrium shift to the right, leading to the nitromethyl Ru complex in almost quantitative yield in the solution. These results indicate that the TsCYDN complex exhibits stronger basicity than the TsDPEN complex and that the deprotonation with the amido complexes proceeds reversibly as shown in Scheme 2. In fact, the treatment of isolable complexes **1b** with CD_3NO_2 resulted in deuterium incorporation in the nitromethyl group of **1b** without loss of the chirality of the metal center. Noticeably, nitroethane reacted stereoselectively

(5) More conveniently, the reaction of the Ir chloride complex Cp*IrCl[(*R*,*R*)-Tscydn] with nitromethane in CH_2Cl_2 containing 1 equiv of NaOH gave **1b**, quantitatively.

(6) The analogous nitromethyl Cp*Rh complex was obtainable from the reaction of Cp*RhCl[(*R*,*R*)-Tscydn] with nitromethane in CH_2Cl_2 containing 1 equiv of NaOH.

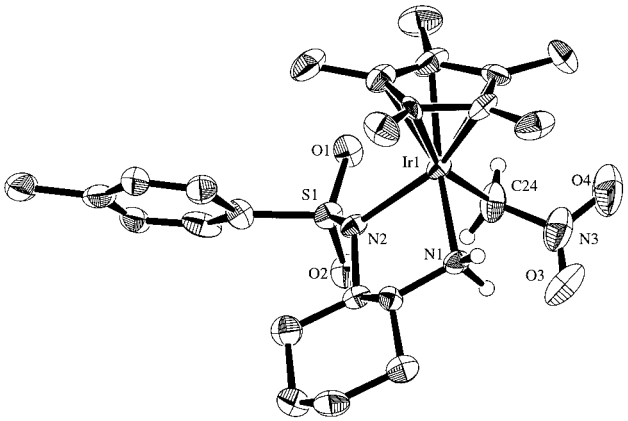


Figure 2. ORTEP view of (η^5-pentamethylcyclopentadienyl)(nitromethyl)[(1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-cyclohexanediamine)iridium (**1b**) (all hydrogen atoms except for NH_2, CH of the cyclohexyl group, and CH_2 of the nitromethyl group have been omitted for clarity). Selected bond lengths (Å): Ir(1)−C(24), 2.16(2); Ir(1)−N(1), 2.12(1); Ir(1)−N(2), 2.18(1); C(24)−N(3), 1.43. Selected bond angles (deg): C(24)−Ir(1)−N(1), 89.2(6); C(24)−Ir(1)−N(2), 87.1(6); N(1)−Ir(1)−N(2), 78.6(5); Ir(1)−C(24)−N(3), 113(1). Priority for the assignment of absolute configuration at Ir: Cp* > NTs > NH_2 > CH_2.

with **4a** under otherwise identical conditions to give the corresponding nitroethyl complex as a single diastereomer in the NMR spectrum, in which **4a** could discriminate the enantiotopic hydrogen atoms of nitroethane.

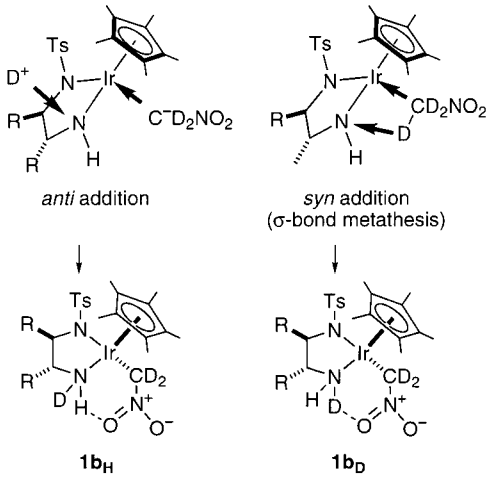
The single-crystal X-ray crystallographic analysis of the nitromethyl complex (*R*,*R*)-**1b**, as illustrated in Figure 2, confirmed that it has a three-legged pianostool coordination environment with Cp*, amino, sulfonamino, and nitromethyl ligands.[7] The chirality of the (*R*,*R*)-diamine ligand determines the *S* configuration around the central metal, as observed in the metal hydrido and chlorido complexes.[1f] It should be noted that **1b** has a nitromethyl group with an Ir−C bond length of 2.16 Å, and there is a short O···NH distance of 2.06 Å, which is ascribed to an intramolecular hydrogen bond. The ^{1}H NMR spectrum of **1b** at room temperature displays one AB quartet due to the diastereotopic methylene protons at δ 5.58 and 5.66 ppm. Two inequivalent acidic NH protons of the amino group were observed at δ 3.57 and 4.62 ppm. The signal at the lower field can be assigned to the proton that interacts with the oxygen atom of the nitro group through hydrogen bonding.[1b]

In the addition of the C−H bond to the M−N bond of the amido complex[8] to form a nitromethyl complex, two pathways are possible, as illustrated in Scheme 3: a concerted σ-bond metathesis[9] and a proton transfer[4]

(7) An X-ray crystallographic analysis of **1b** was performed. The structures were resolved with SHELX86 and DIRDIF94. **1b**·CH_3NO_2: $C_{24}H_{36}N_3O_4SIr{\cdot}CH_3NO_2$, M_r = 715.89, orthorhombic, space group $P2_12_12_1$ (No. 19), a = 13.198(10) Å, b = 22.501(10) Å, c = 9.39 (1) Å, V = 2787(3) Å^3, Z = 4, D_c = 1.706 g/cm^3, μ(Mo Kα) = 49.2 cm^{-1}, T = 253 K, R (R_w) = 0.050 (0.059) for 2938 observed reflections ($I > 2.00\sigma(I)$). All hydrogen atoms were calculated from ideal geometries, fixed, and included in the calculation of the structural factor.

(8) Reactions of metal amido complexes with alkanes and alkynes: (a) Bashall, A.; Collier, P. E.; Gade, L. H.; McPartlin, M.; Mountford, P.; Trösch, D. J. M. *J. Chem. Soc., Chem. Commun.* **1998**, 2555−2556. (b) Cummins, C. C.; Baxter, S. M.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8731−8733.

Scheme 3



through an ion pair intermediate, leading to the complex **1b$_D$** and a mixture of isotopomers, **1b$_H$** and **1b$_D$**, respectively. Monitoring the reaction of **1a** with 1 equiv of CD_3NO_2 revealed that the addition of the C−H bond to the Ir−N bond of the amido complex possibly proceeds via proton transfer from the carbon to the nitrogen which is bonded to the Ir metal. The ^{1}H NMR spectrum of the reaction mixture of **1a** at −80 °C in CD_2Cl_2 shows two signals due to NH_2 protons at 3.57 and 4.62 ppm (vide infra) with a 1:3 ratio of the relative intensity, indicating that the complex **1b$_H$** bearing a hydrogen-bonded NH proton is initially formed in an *anti* fashion, possibly through a proton transfer followed by Ir−C bond formation. An increase in the temperature of this reaction mixture to −50 °C resulted in formation of a 1:1 mixture of isotopomers, **1b$_H$** and **1b$_D$**, without loss of the chirality of the metal center. Rapid H/D exchange in the NH_2 group with a trace amount of water impurity in the solvent might be taking place even at low temperatures.[1b] It should be noted that no detectable formation of the *O*-bound isomer of **1b** was observed in these NMR studies, even with heating.[10]

In a manner similar to the reaction of nitromethane, **1a** reacted with acetone ($pK_a = 20$) and phenylacetylene ($pK_a = 18.5$) to give quantitatively the corresponding organometallic compounds **1c** and **1d**, respectively (Scheme 1).[11,12] Complex **3a** did not deprotonate acetone at all under the same conditions, while the reaction of **4a** with acetone gave an equilibrium mixture of **4a** and **4c** in an almost 1:1 molar ratio. Isotope labeling experiments on the reaction of acetophenone ($pK_a = 19$) with **4a** revealed that an addition of the C−H bond across the M−N bond occurred reversibly, although no detectable amount of benzoylmethyl Ru complex was observed in the solution.

In summary, the 16-electron metal amido complex bearing the chiral Ts-diamine ligand readily reacts with acidic organic compounds to give new organometallic compounds of these acidic compounds. The Brønsted basicity on the amido group in the amido complexes is responsible for an effective C−H bond activation. Thanks to the bifunctionality of the amido complex, the asymmetric catalytic nitroaldol reaction with these amido complexes was examined.[13,14] Preliminary experimental results showed that although **1a**, **2a**, or **3a** exhibited low catalytic activity for the reaction, (*S*,*S*)-**4a** (2 mol %) effected the nitroaldol reaction of cyclohexanecarboxaldehyde with 2 equiv of nitromethane in 2-methyl-2-butanol (0.2 M) at 30 °C for 24 h to give (*S*)-1-nitro-2-cyclohexyl-2-ethanol with good enantioselectivity, 75% ee, albeit in low yield (18% yield). Further studies on the mechanism and the scope of this new type of enantioselective catalytic C−C bond formation are now under way.[15]

Acknowledgment. We thank Professor Masakatsu Shibasaki of Tokyo University for discussions and information about nitroaldol products. This work was financially supported by a grant-in-aid from the Ministry of Education, Science, Sports and Culture of Japan (No. 12305057).

Supporting Information Available: Tables giving single-crystal X-ray information on the complexes **1b**, **1c**, and **1d** and text giving physical and NMR data of the complexes **1b**, **1c**, **1d**, **2b**, **3b**, and **4b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) (a) Lee, J. C., Jr.; Peris, E.; Rheingold, A. L.; Crabtree, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 11014−11019. (b) Niu, S.; Hall, M. B. *J. Am. Chem. Soc.* **1998**, *120*, 6169−6170. (c) Musashi, Y.; Sakaki, S. *J. Am. Chem. Soc.* **2000**, *122*, 3867−3877.

(10) Naota, T.; Tannna, A.; Murahashi, S.-I. *J. Am. Chem. Soc.* **2000**, *122*, 2960−2961.

(11) The precise structures of **1c** and **1d** were determined by the single-crystal X-ray analysis, indicating that they have structures similar to that of the nitromethyl Ir complex with an *S* configuration around the central metal. **1c**: $C_{26}H_{39}N_2O_3SIr{\cdot}C_6H_5CH_3$, monoclinic, space group *C*2 (No. 5), $a = 24.426(8)$ Å, $b = 13.461(9)$ Å, $c = 9.418(6)$ Å, $\beta = 102.71(5)°$, $V = 3020(2)$ Å^3, $Z = 4$, $D_c = 1.636$ g/cm^3, μ(Mo Kα) = 45.3 cm^{-1}, $T = 253$ K, R (R_w) = 0.052 (0.056) for 2141 observed reflections ($I > 2.00\sigma(I)$). All hydrogen atoms were calculated from ideal geometries, fixed, and included in the calculation of the structural factor. **1d**: $C_{31}H_{39}N_2O_2SIr{\cdot}C_6H_5CH_3$, monoclinic space group $P2_1$ (No. 4), $a = 10.705(3)$ Å, $b = 13.313(5)$ Å, $c = 13.190(3)$ Å, $\beta = 107.98(2)°$, $V = 1787.9(2)$ Å^3, $Z = 2$, $D_c = 1.464$ g/cm^3, μ(Mo Kα) 38.36 cm^{-1}, $T = 253$ K, R (R_w) = 0.041 (0.035) for 2389 observed reflections ($I > 3.00\sigma(I)$). All hydrogen atoms were calculated from ideal geometries, fixed, and included in the calculation of the structural factor. **1c** and **1d**: **1c** and **1d** were also obtained quantitatively by the reaction of Cp*IrCl[(*R*,*R*)-Tscydn] with acetone or phenylacetylene in the presence of 1.0 equiv of NaOH(aq) in CH_2Cl_2.

(12) (a) Matsumoto, K.; Uemura, H.; Kawano, M. *Inorg. Chem.* **1995**, *34*, 658−662. (b) Venturelli, A.; Rauchfuss, T. B.; Verma, A. K. *Inorg. Chem.* **1997**, *36*, 1360−1365. (c) Lin, Y.-S.; Misawa, H.; Yamada, J.; Matsumoto, K. *J. Am. Chem. Soc.* **2001**, *123*, 569−575.

(13) For catalytic asymmetric C−C bond formation after C−H bond activation: (a) Rodewald, S.; Jordan, R. F. *J. Am. Chem. Soc.* **1994**, *116*, 4491−4492. (b) Sawamura, M.; Hashimoto, H.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 8295−8296. (c) Kuwano, R.; Miyazawa, H.; Ito, Y. *J. Chem. Soc., Chem. Commun.* **1998**, 71−72. (d) Davies, H. W.; Hansen, T.; Churchill, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 3063−3070. For reviews of C−C bond activation and transformation, see: (e) Murai, S. *Activation of Unreactive Bonds and Organic Synthesis*; Springer-Verlag: Berlin, Heidelberg, New York, 1999. (f) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *39*, 1698−1712. (g) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879−2932.

(14) Leading review paper for catalytic asymmetric nitro aldol reaction: Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1236−1256 and references therein.

(15) $RuH_2[P(C_6H_5)_3]_4$-promoted C−C bond formation was reported to proceed via oxidative addition followed by metal enolate formation: Murahashi, S.-I.; Naota, T.; Taki, H.; Mizuno, M.; Takaya, H.; Komiya, S.; Mizuno, Y.; Oyasato, N.; Hiraoka, M.; Hirano, A.; Fukuoka, A. *J. Am. Chem. Soc.* **1995**, *117*, 12436−12451.