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Hydrogen-Bond Acceptance of Bifunctional Ligands in an Alkyne−Metal π Complex

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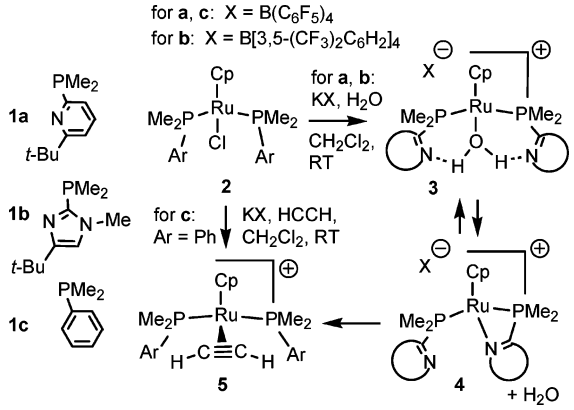
Typically, organometallic catalyst selectivity and reactivity have been controlled by variations in the metal and ancilliary ligands used, focusing on steric and electronic properties of the latter.[1,2] In contrast, nature's metalloenzymes use secondary interactions such as hydrogen bonding or proton transfer in the active site.[3] An increasing number of synthetic catalysts and related systems show the benefits of secondary interactions,[4] which are generally difficult to control. Using hydrogen bonding or proton transfer from or to imidazolyl[5] and pyridylphosphines,[4d,6,7] our group has reported rate enhancements in *anti*-Markovnikov alkyne hydration and alkene isomerization by factors of up to 10000. In studying the origin of remarkable rate enhancements in alkyne hydration, we have discovered hydrogen bonding between the terminal alkyne proton and a heterocyclic nitrogen. To probe this unusual structural feature, we report the first use of scalar coupling across a hydrocarbon C−H bond ($^{2h}J_{CN}$), a technique used to characterize hydrogen bonds in biological samples.[8]

Initial DFT calculations on the alkyne hydration pathway first suggested the importance of structures like **5** (Scheme 1).[9] However, in **5** the orientation of the alkyne alone does not allow us to conclude that there is C−H−N hydrogen bonding: in **5c**, a complex lacking the nitrogens, the same alkyne orientation is seen in both an X-ray crystal structure (with BF_4^- counterion)[10] and our calculations. It appeared from the literature[10] that to make an alkyne complex like **5** and study its structure before it isomerized to a vinylidene complex, we would need the smallest alkyne, phosphine, and ancilliary Cp ligand possible, making **5a**,**b** with ligands **1a** and **1b** our synthetic targets, with **1c** as a control.

Thus, ligands **1a**,[11] **1b**,[9] and **1c** were each converted to **2** using CpRu(COD)Cl. In the case of **2c**, ionization of the chloride (Scheme 1) was done in the presence of HCCH to give **5c**, which could be isolated and stored cold, but it converted smoothly to **6c** after 3 h at 50 °C (Scheme 2).

In contrast, early experiments made it very clear that extraordinary measures would be needed to isolate or even observe **5a** or **5b**. First (Scheme 1), the chlorides in **2a** and **2b** were ionized in the presence of water[12] to give aquo complexes **3a** or **3b**. Storage of **3a** or **3b** under vacuum led to loss of water and mixtures of **3** and **4**, with a greater amount of **4** in the case of **4b**. When cooled below −40 °C in CD_2Cl_2, chelate complex **4a** did not react at an appreciable rate with acetylene (Scheme 2), but near −40 °C was converted to symmetrical π complex **5a**, which isomerized smoothly to vinylidene **6a** at higher temperatures (0 °C, 3 h). In the imidazole case, **4b** was inert to acetylene until ca. 10 °C, where unsymmetrical addition product **7b** was the only product detected. Complex **7b** reasonably arises from unseen vinylidene **6b**. Interestingly, the NMR spectrum of **7b** (e.g., two sets of sharp resonances for the imidazoles at −40 °C) shows coalescence behavior at higher

Scheme 1. Precursor Synthesis



temperatures consistent with an equilibrium between **7b** and **6b** with $E_a = 15.9$ kcal mol^{-1}.

In summary, when imidazole derivative **4b** reacts with acetylene, alkyne complex **5b** is not seen, because of rapid conversion to **7b**, whereas, when starting with pyridyl analogue **4a**, alkyne complex **5a** can be observed at −40 °C, but at temperatures closer to 0 °C it evolves to **6a**. In contrast, control alkyne complex **5c** requires temperatures 50−90 °C higher for conversion to vinylidene **6c**, all showing the profound effects and assistance of the pendant bases on these transformations.

Bonding in vinylidenes **6a** and **6c** was compared using isotopomers derived from $H^{13}C^{13}CH$. Significantly, nearly identical values for $^1J_{CC}$ (Scheme 2) are consistent with the same C−C bond length and degree of backbonding in each case.[13]

To clarify the structure of **5a**, various unsuccessful attempts were made to grow crystals at −40 °C. Instead, spectroscopic characterization[14] of alkyne bonding in **5a** and **5c** was made using $H^{13}C^{13}CH$, resulting in **5a**- and **5c**-$(^{13}C)_2$. At −40 °C the ten-line AA′XX′ pattern could be analyzed[13] to show that there were significant differences in couplings involving the hydrogens (Scheme 2). Data above for $^1J_{CC}$ in **6a** and **6c** show that the electronic effects of the two ligands are identical, consistent with almost identical $^1J_{CC}$ values in the π complexes. We could find no experimental data on effects of hydrogen bonding on alkyne NMR coupling constants and only a single theoretical paper (on HCCH−OH_2).[15] Comparing alkyne and hydrogen-bonded alkyne, the changes in $^1J_{CH}$ and $^2J_{CH}$ seen by us experimentally (+1.5 and +1.9 Hz) resemble those predicted[15] for HCCH−OH_2 (+2.55 and +1.65 Hz).[16] In short, the differences in NMR couplings are for those couplings to *hydrogen*, and we attribute this to effects of hydrogen bonding in **5a**. Attempts were made to engage the CH bonds of π complex **5c** in hydrogen bonding. Instead, addition of imidazole **8** led to *addition to the alkyne* (**9**).

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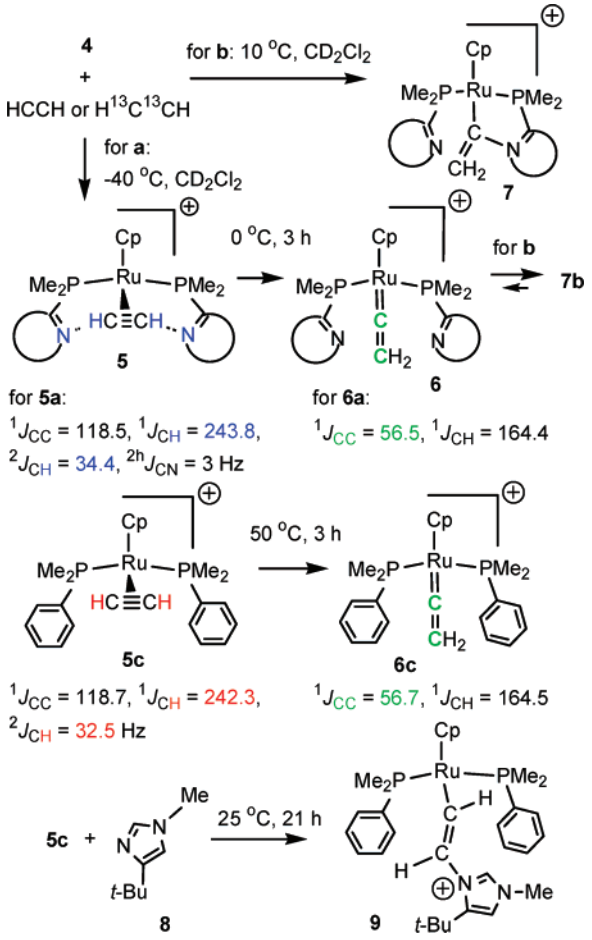
Scheme 2. Alkyne Hydrogen Bonding and Enhanced Reactivity of Bifunctional Complexes



Because NMR coupling constants are a novel tool for studying alkyne hydrogen bonding, we wanted to provide additional evidence for structure **5a**. The remarkable discovery of scalar couplings across hydrogen bonds has stimulated a great deal of experimental work on proteins, DNA, and supramolecular interactions[8] and theoretical investigations of simple systems, but there appears to have been no use in coordination or organometallic chemistry. Ligand **1a**-^{15}N was made[9] and converted to **3a**-(^{15}N)$_2$ and **4a**-(^{15}N)$_2$. Addition of acetylene at low temperature led to **5a**-(^{15}N)$_2$, whose ^{13}C NMR spectrum acquired at −50 °C with decoupling of both ^{1}H and ^{31}P allowed observation of a somewhat broadened[17] doublet ($^{2h}J_{CN}$ = 3 ± 0.5 Hz) as expected for coupling of one natural abundance acetylene ^{13}C to the nearest ^{15}N nucleus, whereas a similar spectrum of **5a** showed a singlet.

Previous theoretical work by Del Bene et al. on a simple system[18] showed that when the C−H−N angle is near 135°, $^{2h}J_{CN}$ would be approximately one-third the magnitude when the hydrogen bond is linear. Indeed, DFT calculations on **5a** itself show a slightly unsymmetrical structure with two C−H−N angles (124.5 and 135.7°).[19] Determining the strength of the hydrogen bonds in **5a** remains a subject for future study, but as an estimate, we note that calculations on conversion of **5c** to **6c** indicate that $\Delta G = -17.9$ kcal mol^{-1} whereas for similar conversion of **5a** to **6a**, $\Delta G = -12.7$ kcal mol^{-1}. The difference may be attributed to thermodynamic stabilization of **5a** by two hydrogen bonds. Despite this effect, experiments show a pronounced kinetic acceleration by the heterocycles on isomerization of alkyne to vinylidene (**5** to **6**), and importantly, **3a** is a very competent catalyst (>99% yield of hexanal from 1-hexyne after 5 h at 70 °C using 2 mol % **3a**).

In summary, the presence of C−H−N hydrogen bonding in an alkyne π complex was revealed using NMR coupling information, from both data within the alkyne ligand as well as between alkyne and pyridine ($^{2h}J_{CN}$). Ongoing experimental and theoretical studies are designed to elucidate further the favorable effects of bifunctional ligands in alkyne hydration and related reactions, and these will be reported in due course.

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Supporting Information Available: Details of compound preparation and characterization and calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313−348.
(2) Cooney, K. D.; Cundari, T. R.; Hoffman, N. W.; Pittard, K. A.; Temple, M. D.; Zhao, Y. *J. Am. Chem. Soc.* **2003**, *125*, 4318−4324.
(3) Lippard, S. J.; Berg, J. M. *Principles of Bioinorganic Chemistry*; University Science Books: Mill Valley, CA, 1994.
(4) For reviews, see: (a) Rowlands, G. J. *Tetrahedron* **2001**, *57*, 1865−1882. (b) Noyori, R.; Yamakawa, M.; Hashiguchi, S. *J. Org. Chem.* **2001**, *66*, 7931−7944. (c) Helmchen, G.; Steinhagen, H. *Angew. Chem., Int. Ed.* **1996**, *35*, 2339−2342. (d) Grotjahn, D. B. *Chem. Eur. J.* **2005**, *11*, 7146−7153. (e) Borovik, A. S. *Acc. Chem. Res.* **2005**, *38*, 54−61.
(5) Grotjahn, D. B.; Incarvito, C. D.; Rheingold, A. L. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 3884−3887.
(6) Grotjahn, D. B.; Lev, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 12232−12233.
(7) See also Labonne, A.; Kribber, T.; Hintermann, L. *Org. Lett.* **2006**, *8*, 5853−5856.
(8) Grzesiek, S.; Cordier, F.; Jaravine, V.; Barfield, M. *Prog. Nucl. Magn. Reson. Spectrosc.* **2004**, *45*, 275−300.
(9) See Supporting Information for details.
(10) Lomprey, J. R.; Selegue, J. P. *J. Am. Chem. Soc.* **1992**, *114*, 5518−5523.
(11) Baur, J.; Jacobsen, H.; Burger, P.; Artus, G.; Berke, H.; Dahlenburg, L. *Eur. J. Inorg. Chem.* **2000**, 1411−1422.
(12) Remarkably, direct ionization in the *absence* of water did not give **4** cleanly, even after prolonged reaction times or heating.
(13) Grotjahn, D. B.; Zeng, X.; Cooksy, A. L.; Kassel, W. S.; DiPasquale, A. G.; Zakharov, L. N.; Rheingold, A. L. *Organometallics* **2007**, *26*, 3385−3402.
(14) IR spectroscopy has been a major tool for studying hydrogen bonding of organic alkyne derivatives (e.g., refs 14a−e), but the high reactivity of **5a** thus far has precluded observing its IR spectrum. (a) Steiner, T. *Adv. Mol. Struct. Res.* **1998**, *4*, 43−77. (b) Kreevoy, M. M.; Charman, H. B.; Vinard, D. R. *J. Am. Chem. Soc.* **1961**, *83*, 1978−1983. (c) Jeng, M. L. H.; DeLaat, A. M.; Ault, B. S. *J. Phys. Chem.* **1989**, *93*, 3997−4000. (d) Jeng, M. L. H.; Ault, B. S. *J. Phys. Chem.* **1989**, *93*, 5426−5431. (e) Sundararajan, K.; Sankaran, K.; Viswanathan, K. S. *J. Mol. Struct.* **2004**, *733*, 187−192.
(15) Pecul, M.; Leszczynski, J.; Sadlej, J. *J. Chem. Phys.* **2000**, *112*, 7930−7938.
(16) Our calculations predict that $^{1}J_{CH}$ and $^{2}J_{CH}$ increase from **5c** to **5a**, and ascribe the shift to the Fermi contact contribution. This contribution increases with the s-character of the CH bonding MO, as the CCH bond angle becomes more linear (**5c**, 154°; **5a**, 162°) with hydrogen bonding. These effects are a subject of future study.
(17) At −20 °C, coupling was obscured by broadening, presumably due to alkyne rotation. See for example: Carbó, J. J.; Crochet, P.; Esteruelas, M. A.; Jean, Y.; Lledos, A.; Lopez, A. M.; Onate, E. *Organometallics* **2002**, *21*, 305−314. $^{1h}J_{NH}$ was not observed, but this could be expected to be less than 1 Hz.
(18) Del Bene, J. E.; Perera, S. A.; Bartlett, R. J.; Yanez, M.; Mo, O.; Elguero, J.; Alkorta, I. *J. Phys. Chem. A* **2003**, *107*, 3222−3227.
(19) In addition, preliminary calculation of $^{2h}J_{CN}$ gave values of −3.4 and −6.7 Hz, averaging to −5 Hz. Comparison of the other experimentally determined NMR coupling constants shown in Scheme 2 with calculated values shows that the latter are consistently about 20% too high.

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