Homogeneous Catalysis

Gas-Phase Reactions of the $[(PHOX)IrL_2]^+$ Ion Olefin-Hydrogenation Catalyst Support an Ir^I/Ir^{III} Cycle**

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Since the introduction and elaboration of homogeneous catalytic hydrogenation, much work has been devoted to asymmetric hydrogenation by well-defined organometallic complexes. A particularly efficient example is the [(PHOX)-Ir(cod)]$^+$ X^- (PHOX = chiral phosphanyloxazoline ligand,[1] cod = 1,5-cyclooctadiene, X^- = weakly coordinating anion),

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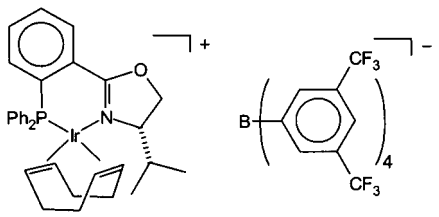
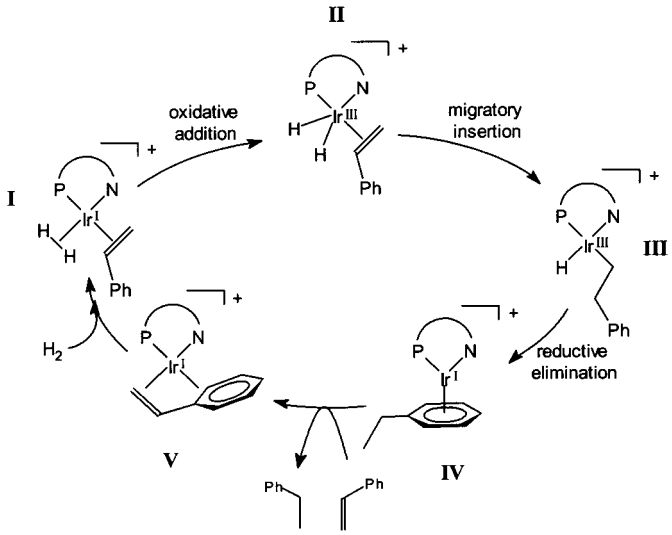


1–BArF

complex, for example, **1**-BArF (BArF = tetrakis-(3,5-di(trifluoromethyl)phenyl)borate), from Pfaltz and co-workers.[2]

This class of catalysts, developed from Crabtree's achiral [Ir(phosphane)(pyridine)] complexes,[3] shows exemplary properties in the asymmetric catalytic hydrogenation of unfunctionalized olefins under mild conditions. Turnover numbers (TON) and turnover frequencies (TOF) of >5000 and $5000\,h^{-1}$ with enantiomeric excesses (ee) $>95\%$ have been reported for olefinic substrates lacking the usual secondary-binding moieties. Given this background, the paucity of mechanistic information on the catalytic cycle and reactive intermediates is surprising. Recently, a computational study of a truncated model complex by Brandt, Hedberg, and Andersson[4] has suggested a catalytic cycle in which Ir^{III} and Ir^{V} intermediates play the decisive roles. We report herein an experimental investigation of the hydrogenation of styrene by the **1**-BArF by means of electrospray ionization tandem mass spectrometry which strongly suggests that, contrary to the computational study, the catalytic cycle proceeds by way of Ir^{I} and Ir^{III} intermediates, presumably by a "dihydride" catalytic cycle indicated in Scheme 1.[5]



Scheme 1. Presumed catalytic cycle via the dihydride intemediate.

The modified Finnigan-MAT TSQ-700 tandem mass spectrometer has been previously described.[6] Sample introduction from pressurized glass reactors to the electrospray source requires a short description because previous experience in hydrogenation and hydroformylation catalysts has shown that the expected dihydrogen complexes or dihydrides rapidly lose dihydrogen once they are removed from a dihydrogen-saturated solution. In this case, the active catalytic solution was introduced directly into the electrospray source by a fused silica capillary (150 μm × 100 cm) dipped into the solution in a pressurized reaction. The process pressure, 6 bar H_2, suffices to pump the solution ($<10^{-5}$ M **1** and 0.17–0.26 M styrene in 5 mL CH_2Cl_2, 28 °C) directly into the spray tip with a flow rate of 20 μL min^{-1}. A final section of narrow-bore capillary (80 μm × 17 cm) ensures that there is no pressure drop with consequent bubble formation prior to the spray tip. Unless otherwise specified, reactions of selected ions are performed with close to zero collision energy with neutral reagents in the octopole collision cell at a nominal pressure of 2.5 mtorr. Previous work has shown that these conditions mean on the order of 10^4 collisions of the ion with collision/reaction gas molecules within a transit time of a few milliseconds up to 100 ms.[6]

Catalytically active solutions (confirmed by product monitoring) were prepared from **1**-BArF according to the literature procedure.[2] Sampling of the reactor when it is pressurized with inert gas produces in the electrospray mass spectrometer a clean signal for **1**, which upon addition of the approximately 20000-fold molar excess of styrene[7] and H_2 pressure shows three new peaks (after 15 min), whose masses correspond to the compositions $[(PHOX)Ir(styrene)(H_2)_2]^+$, $[(PHOX)Ir(styrene)(H_2)]^+$ (the latter being species **I**–**IV** in Scheme 1) and $[(PHOX)Ir(styrene)]^+$ (species **V** in Scheme 1). The mass alone, especially for the first two species, does not provide an unambiguous structural assignment, but mechanistic information can nevertheless be extracted from the experiment. The same two peaks are also very sensitive to even small increases in the tube lens potential, that is, more rigorous "desolvation" conditions,[8] which lead to loss of dihydrogen. At shorter times, that is, < 5 min, other species are visible in the mass spectrum in which the cyclooctadiene moiety is not yet completely reduced. Control experiments in which the cyclooctadiene in **1**-BArF, is replaced with 3-methyl-1,5-cyclooctadiene[9] (to shift the mass of the diene complexes) confirm that all of the initial diene complex is reduced within the first 5 min and therefore does not contribute to the mass spectrum 15 min after initiation of the reaction. If the H_2 pressure in a reactor containing the catalyst, **1**-BArF, styrene, and H_2 is released, a sample taken immediately afterwards shows principally $[(PHOX)Ir(styrene)_2]^+$, underlining the importance of the in situ sampling technique described above.

We found two gas-phase reactions that are instructive with regard to the catalytic cycle. Bearing in mind that the present apparatus (with only two stages of MS/MS) does not allow more than two consecutive reactions, that is, we cannot do controlled turnover in the gas phase, we examined the reactions of selectively prepared intermediates. $[(PHOX)Ir(H_2)]^+$, produced by "hard" desolvation conditions applied to electrosprayed ions from a solution of **1**-BArF and H_2, was then subjected to multiple collisions with ethylbenzene, producing, among other species, an ion with the composition $[(PHOX)Ir(ethylbenzene)]^+$. The ion, assumed to be species **IV**, was isolated in the gas phase by selection according to its

m/*z* ratio. Collision-induced dissociation (CID) of **IV** with argon leads to exceedingly facile loss of dihydrogen, producing the styrene complex **V**. If 1,3-diethylbenzene or 1,3,5-triethylbenzene are used instead of ethylbenzene, multiple dehydrogenations are observed. Because the selectively prepared gas-phase species **IV** has no opportunity to go "forward" in Scheme 1—-the substrate-for-product ligand exchange is shut off, it traverses the catalytic cycle backwards until it undergoes the irreversible (in the gas-phase) step in which dihydrogen dissociates and leaves. Note that the facile production of **V** does not mean that complex **V** is the most stable species in the catalytic cycle, but merely that **V** is the product of a step that is irreversible under the experimental conditions. In the second instructive MS/MS experiment, a single isotopomer of **V** is prepared and isolated by its *m*/*z* ratio, and then treated under soft conditions (initial collision energy of 6.9 kcal mol^{-1} or less in the center-of-mass frame) with D_2 gas. The sole observable products are **V**, [D_1]**V**, and [D_2]**V** (Figure 1).

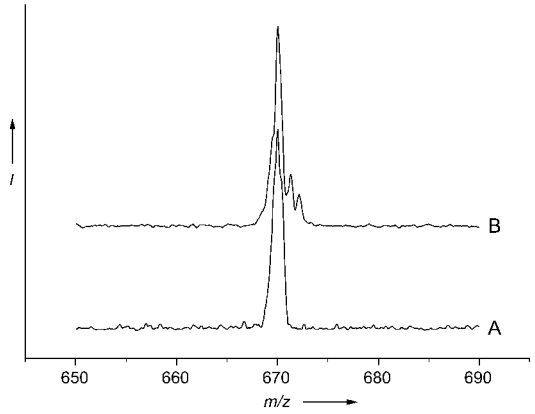


Figure 1. Daughter-ion mass spectrum generated by mass selection of one isotopomer of **V** at *m*/*z* 670 (Trace A), and treatment of the mass-selected ion with D_2 (Trace B) at a collision energy set to 6.9 kcal mol^{-1} in the center-of-mass frame. Under comparable conditions, the reaction of **V** with H_2 does not form an adduct mass, but rather returns only **V** back. Mono- and dideuteration is clearly visible in the experiment with D_2.

The absence of even an adduct mass in the gas-phase reaction of **V** with H_2 would mean either that there is no reaction at all, only coordination followed by a fast dissociation, or that none of the species **I**–**IV** lies in such a deep well that it would be long-lived enough to be observed before the irreversible loss of H_2 regenerated **V**. The D_2 experiment indicates unambiguously that the latter case is operative. In other words, isotopic exchange in **V** confirms the intermediacy of at least species **I**–**III** even if they are not directly observed in the mass spectrum.

Mere observation of a species formed in situ during a catalyzed reaction does not prove its participation in the catalytic cycle. It could be reservoir species, an unreactive spectator, or even a catalyst deactivation product. Moreover, the inability to observe a particular species does not show that it is absent in the catalytic cycle because those species in the catalytic cycle with the highest rate constants for subsequent reaction will occur with the lowest concentration at steady-state. An observed species can, however, be assigned as an intermediate in the cycle with reasonable certainty if it can be shown that the species is competent in the subsequent elementary reaction steps needed for turnover. The mass spectrum of a catalytically active solution of **1**-BArF suggests that **II**, or a species of the mass of **II**, could be the resting-state species. The competence of the putative **II** to enter into the elementary reactions in Scheme 1 is supported by the two gas-phase reactions. In the absence of either H_2 or excess olefin, **IV** dehydrogenates to **V**, connecting the hydrogenation product mechanistically to the substrate olefin complex. In the other direction, production of [D_1]**V**, and [D_2]**V** from the reaction of **V** and D_2, shows that both dihydrogen cleavage and the insertion of the substrate olefin into the Ir–H bond are facile and reversible when turnover is blocked. The gas-phase experiments by themselves do not identify unambiguously which of the isobaric ions **I**–**IV** is the actual resting state in the catalytic cycle, but they do show that the overall cycle with the species **I**–**V** is mechanistically plausible. Auxiliary evidence, for example, ^{1}H NMR spectroscopy results by Drago, Pregosin, and Pfaltz,[10] can be interpreted to suggest that a dihydride such as **II** is more stable than a dihydrogen complex such as **I**, which leads one to presume that the resting state is in fact **II**. Lastly, the experiments strongly suggest that trihydrides, for example, Ir^V species, play no significant role in the hydrogenation reaction. Given the computations by Brandt, Hedberg, and Andersson,[4] the demonstrated catalytic activity by well-characterized iridium polyhydrides,[11] as well as experimental evidence for a minor route through polyhydrides from Crabtree's catalyst by Brown and coworkers,[12] we have looked for the Ir^{III} hydrido dihydrogen/Ir^V trihydrido complexes. ESI-MS analysis of the activated catalyst solution under H_2 pressure does show ions with the compositions [(PHOX)Ir(styrene)(H_2)]$^+$ and [(PHOX)Ir(styrene)(H_2)$_2$]$^+$. The former corresponds to species **I**–**IV** in Scheme 1. The latter possesses the mass and the composition of the Ir^{III} hydrido dihydrogen complex or the Ir^V trihydrido species predicted in the calculation.[13] Although a species of that composition appears to be present in solution under active catalytic conditions, the gas-phase experiment suggests that it plays no major role in the catalytic cycle. Given that the ion isolated as **V** was treated with D_2 under conditions where it underwent approximately 10^4 collisions with D_2 in the timeframe of a few to 100 ms, we estimate a gas-phase collision frequency on the order of 10^6 s^{-1}. If one were to characterize the diffusion-controlled encounter rate of a catalyst molecule in solution with dissolved H_2 using $k_{2nd\ order} \approx 10^9$–$10^{10}$ L mol^{-1} s^{-1} and [H_2] in the millimolar range,[14] then one concludes that the gas-phase and solution-phase encounter rates are similar and that a species of the composition [(PHOX)Ir(styrene)(D_2)$_2$]$^+$ had the opportunity to form in the gas-phase (and subsequently dissociate again) if it were an important species in solution. If there were a favorable mechanism for hydrogenation for species of this composition, then one would expect to see trideuterated [(PHOX)Ir(styrene)]$^+$ products in the **V** + D_2 reaction[15] because, given the reversibility of elementary steps in the

gas-phase reaction, even a transient Ir^V intermediate with three chemically equivalent deuterides (and an alkyl group with one deuterium atom) would produce at least partial incorporation of more than two deuterium atoms into the styrene substrate.[16] Examination of Figure 1 shows that the trideuterated styrene complexes are absent. We believe that the observed mechanism differs from the computationally predicted one because the computation employed a markedly truncated substrate and complex with less steric constraints and different electronic properties in the search for the minimum-energy reaction path.

In conclusion we report gas-phase reactions of selected organometallic ions that reveal a plausible mechanism for the catalytic hydrogenation of olefins by the $[(PHOX)Ir(cod)]^+X^-$ family of catalysts. In contrast to the results of a computational study, the most likely mechanism is found to involve the more expected cycle with Ir^I and Ir^{III} species. There is no evidence for the participation of Ir^V complexes. In contrast to in situ spectroscopic studies which rely primarily on identification of species in solution whose role in the reaction must be subsequently ascertained by independent means, the preference for the Ir^I/Ir^{III} cycle over the alternative Ir^{III}/Ir^V mechanism is supported by gas-phase reactivity data which are diagnostic even if the purported intermediates are present in such low steady-state concentration so as not to be directly observable.

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[1] G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336.
[2] A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem.* **1998**, *110*, 3047; *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2897; D. G. Blackmond, A. Lightfoot, A. Pfaltz, T. Rosner, P. Schnider, N. Zimmermann, *Chirality* **2000**, *12*, 442; A. Pfaltz, J. Blankenstein, R. Hilgraf, E. Hörmann, S. McIntyre, F. Menges, M. Schönleber, S. P. Smidt, B. Wüstenberg, N. Zimmermann, *Adv. Synth. Catal.* **2003**, *345*, 33.
[3] R. Crabtree, *Acc. Chem. Res.* **1979**, *12*, 331.
[4] P. Brandt, C. Hedberg, P. G. Andersson, *Chem. Eur. J.* **2003**, *9*, 339.
[5] L. D. Vázquez-Serrano, B. T. Owens, J. M. Buriak, *Chem. Commun.* **2002**, 2518; report *para*-hydrogen-induced polarization (PHIP) NMR spectroscopic evidence that the "dihydride" mechanism through Ir^I/Ir^{III} is in fact operative for catalysts related to **1**-BArF but the experiment does not prove that an alternative mechanism is not also running in parallel.
[6] C. Hinderling, D. A. Plattner, P. Chen, *Angew. Chem.* **1997**, *109*, 272; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 243; C. Hinderling, D. Feichtinger, D. A. Plattner, P. Chen, *J. Am. Chem. Soc.* **1997**, *119*, 10793; D. Feichtinger, D. A. Plattner, *Angew. Chem.* **1997**, *109*, 1796; *Angew. Chem. Int. Ed. Engl. Angew. Chem. Int. Ed.* **1997**, *36*, 1718; D. Feichtinger, D. A. Plattner, P. Chen, *J. Am. Chem. Soc.* **1998**, *120*, 7125; C. Hinderling, C. Adlhart, P. Chen, *Angew. Chem.* **1998**, *110*, 2831; *Angew. Chem. Int. Ed.* **1998**, *37*, 2685; C. Hinderling, P. Chen, *Angew. Chem.* **1999**, *111*, 2393; *Angew. Chem. Int. Ed.* **1999**, *38*, 2253; Y. M. Kim, P. Chen, *Int. J. Mass Spectrom.* **1999**, *185–187*, 871; C. Adlhart, C. Hinderling, H. Baumann, P. Chen, *J. Am. Chem. Soc.* **2000**, *122*, 8204; C. Hinderling, P. Chen, *Int. J. Mass Spectrom. Ion Processes* **2000**, *195/196*, 377; Y. M. Kim, P. Chen, *Int. J. Mass Spectrom. Ion Processes* **2000**, *202*, 1; C. Hinderling, C. Adlhart, P. Chen, *Chimia* **2000**, *54*, 232; C. Adlhart, P. Chen, *Helv. Chim. Acta* **2000**, *83*, 2192; C. Adlhart, M. A. O. Volland, P. Hofmann, P. Chen, *Helv. Chim. Acta* **2000**, *83*, 3306; M. A. O. Volland, C. Adlhart, C. A. Kiener, P. Chen, P. Hofmann, *Chem. Eur. J.* **2001**, *7*, 4621; P. Chen, *Angew. Chem.* **2003**, *115*, 2938; *Angew. Chem. Int. Ed.* **2003**, *42*, 2832; C. Adlhart, P. Chen, *Helv. Chim. Acta* **2003**, *86*, 941; X. Zhang, P. Chen, *Chem. Eur. J.* **2003**, *9*, 1852; X. Chen, X. Zhang, P. Chen, *Angew. Chem.* **2003**, *115*, 3798; *Angew. Chem. Int. Ed.* **2003**, *42*, 3798; G. Gerdes, P. Chen, *Organometallics* **2003**, *22*, 2217; G. Gerdes, P. Chen, *Organometallics* **2004**, *23*, 3031; X. Zhang, X. Chen, P. Chen, *Organometallics* **2004**, *23*, 3437.
[7] R. Crabtree, M. F. Mellea, J. M. Quirk, *J. Chem. Soc. Chem. Commun.* **1981**, 1217; report that styrene is a poor substrate for Crabtree's catalyst. Styrene behaves unremarkably with **1**-BArF.
[8] The rigor of desolvation is controlled by the tube lens potential in the TSQ-700 mass spectrometer. There is a qualitative range from soft to hard, corresponding to tube lens potentials of 10–150 V.
[9] 1,5-Cyclooctadiene in **1**-BArF can be readily replaced by equilibrating **1**-BArF in a large excess of by 3-methyl-1,5-cyclooctadiene and then pumping off all volatile components. The control experiment was necessary because the cyclooctadiene complex has a mass very similar to that of styrene or ethylbenzene.
[10] D. Drago, P. S. Pregosin, A. Pfaltz, *Chem. Commun.* **2002**, 286.
[11] R. H. Crabtree, M. Lavin, L. Bonneviot, *J. Am. Chem. Soc.* **1986**, *108*, 4032; A. S. Goldman, J. L. Halpern, *J. Am. Chem. Soc.* **1987**, *109*, 7537.
[12] J. M. Brown, A. E. Derome, G. D. Hughes, P. K. Monaghan, *Aust. J. Chem.* **1992**, *45*, 143.
[13] Although we have no definitive experimental evidence, we believe that this ion is actually $[(PHOX)Ir(ethylbenzene)(H_2)]^+$.
[14] For example, see: E. Brunner, *Ber. Bunsen-Ges.* **1979**, *83*, 715.
[15] Ref. [12] and D. Hou, J. Reibenspies, T. J. Colacot, K. Burgess, *Chem. Eur. J.* **2001**, *7*, 5391; M. C. Perry, Cui, M. T. Powell, X. D. Hou, J. H. Reibenspies, K. Burgess, *J. Am. Chem. Soc.* **2003**, *125*, 113; report an alternate mechanism for the incorporation of more than two deuterium atoms by the reversible formation of π-allyl intermediates. This mechanism cannot operate in the present case with styrene as the substrate because there are no allylic positions for the exchange.
[16] A solution-phase control experiment in which styrene (0.1 mL) and **1**-BArF (0.1 mg; S/C ≈ 15000; S/C = substrate-to-catalyst ratio) are degassed (5× freeze-pump-thaw) in CH_2Cl_2 (5 mL) and then treated at 28 °C with 6 bar D_2 was checked at 2, 5, 10, 20, 40, and 85 min by GC/MS, showed up to 50% conversion to ethylbenzene (at 85 minutes) with no deuterium incorporation in the residual styrene at any time. The ethylbenzene product was cleanly dideuterated. This is consistent with the gas-phase results if one considers that 1) the high D_2 pressure selectively lowers the energy of those intermediates and transition states in which the elements of D_2 are included, and 2) turnover is not blocked because ligand exchange of styrene for ethylbenzene is now possible. While the solution-phase experiment alone is not completely definitive, it is consistent with the conclusion from the gas-phase studies that Ir^V polyhydrides play no significant role in the catalytic cycle.

