Crabtree's catalyst revisited; Ligand effects on stability and durability

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The extent of time-dependent deactivation of monophosphine monoamine iridium hydrogenation catalysts by trimer formation is strongly dependent on ligand structure; attempts to counter this process lead to the observation of an oligomerisation resistant catalyst.

The discovery of active cationic iridium catalysts was one of the milestones of homogeneous hydrogenation.[1] Crabtree's work with complex **1a** demonstrated a high level of reactivity, particularly for highly substituted alkenes, which contrasted with the then known rhodium and ruthenium catalysts. Further work demonstrated their effectiveness in directed hydrogenation of cyclic alkenes carrying coordinating substituents such as OH, CO_2R or $CONR_2$.[2] A general drawback of these catalysts has been their sensitivity to extraneous proton-bearing impurities. In addition there is a tendency to form an inactive trimeric heptahydride **2** under turnover conditions at low alkene concentration by an irreversible process, shown in Fig. 1. The trimer formally requires the addition of the neutral 16-electron species. $[IrH_3(PCx_3)L]$ to two molecules of $[IrH_2(PCx_3)L]^+$ and the formation of the former requires the presence of free base, implying N-ligand dissociation.

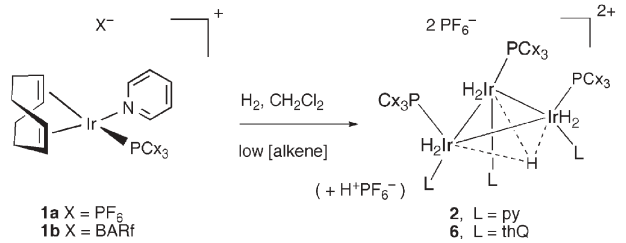

Fig. 1 The deactivating trimerisation process in classical Ir homogeneous hydrogenation; (thQ = 5,6,7,8-tetrahydroquinoline).

Pfaltz's development of enantiomerically pure PN-chelating ligands, typified by **3**, adds a new dimension, since it extends asymmetric hydrogenation to new classes of reactant.[3] The importance of this advance has been recognised in subsequent contributions from several groups, notably Andersson and Burgess.[4] In most applications save the reduction of 1,1′-disubstituted alkenes, high pressures of H_2 are required.[5] Like their simple achiral analogues, the catalysts are prone to deactivation by trimerisation,[6] and there is a high degree of sensitivity to traces of water. The use of large non-coordinating counteranions and especially BARf (*tetrakis*-(3,5-*bis*-trifluoromethylphenyl)borate) provides a practical solution to these difficulties provided that rigorously anhydrous conditions are applied.[7]

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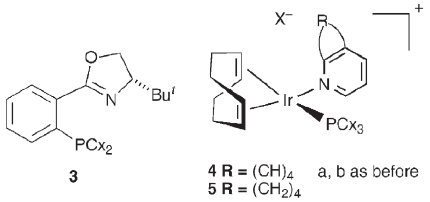


Our interest in the topic centred on efforts to prepare non-chelate asymmetric catalysts. This needed further information on the lability of both the phosphorus and nitrogen ligands under catalytic turnover conditions, and also the stability of the monomeric catalyst. On analysis of the X-ray structure of the all *syn*-trimer **2**, it was clear that increase in the steric bulk of one of the two ligands might inhibit its formation. Indeed the X-ray structure indicates close HH contacts for both P and N ligands. Correspondingly, we prepared the analogues from quinoline, **4a**, and from 5,6,7,8-tetrahydroquinoline **5a**, the latter being characterised by X-ray (Fig. 2a). PM3 calculations were carried out on the putative trimer from the cation of **5a**, using these X-ray structural parameters together with those of the original Ir trimer **2**.[8] These revealed that the minimum energy structure possessed considerable repulsive H–H interactions, several below 2.1 Å.

Hydrogenation of complexes **4a** and **5a** in CD_2Cl_2 solution was followed by ^1H NMR, and by ES-MS. For the quinoline complex **4a** (PF_6^-), the characteristic hydridic peaks at δ −3.7 (q, J_{PH} 50 Hz) (bridging) and −19.2, −26.0 ppm (terminal) appeared as the COD ligand was reduced.† The analogue **5a** has a significantly bulkier imine ligand, but complex oligomeric hydrides were still observed in the ^1H NMR right from the onset of its hydrogenation under similar conditions. The "conventional" trimer **6** analogous

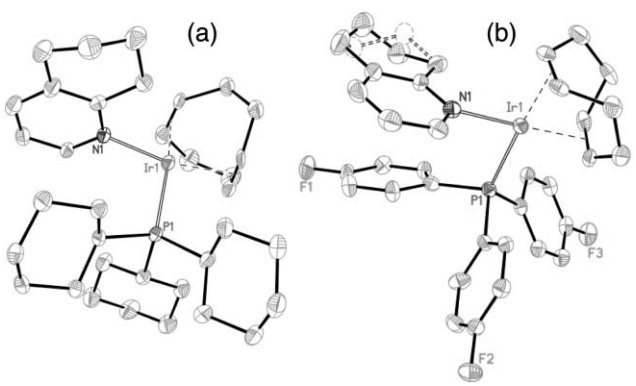
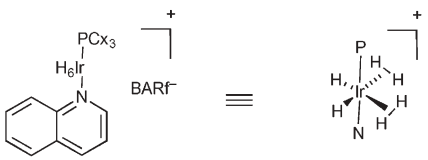


Fig. 2 ORTEP diagrams of the X-ray structures of the cationic part of complexes (a) **5a**, NPIr = 93.6°, and (b) **8a**, NPIr = 90.3°, with H-atoms omitted for clarity. The second complex exhibits conformational disorder in the tetrahydroquinoline entity.[9]

to **2** was the minor species in this case, accompanied by a novel tetrameric iridium species currently under investigation, and which will shortly be the subject of an independent publication.[10]

Much recent iridium catalysis has been carried out with BARf as counteranion, and in the simple case of the recently prepared complex **1b** the hydrogenation of 1-octene is somwhat faster than with **1a**.[11,12] Consequently we monitored the stiochiometric hydrogenation of **4b** by ^{1}H NMR, and noted that trimer formation as described earlier was accompanied by the formation of an intermediate, with a characteristic resonance at −16.0 ppm. In the ES-MS of this same sample a strong monoiridium peak at *m*/*z* 608.2993 is observed (calc. 608.2997), corresponding uniquely to the cationic hexahydride **7**. Diphosphine analogues of this structure are known and have also been computationally characterised.[13] DFT calculations support a similar $2\eta^2$, $2\eta^1$ configuration for hydridic entities of the PN-complex.[14] The analogous species is not seen, however, in the parallel experiment when PF_6^- is employed as the anion in CD_2Cl_2. Once observed, the hexahydridic species was seen in other cases. When hydrogenation of the PF_6^- complex **4a** was carried out in Bu^{t}OMe, the same intermediate monohydridic species was seen by ES-MS.



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The relative reluctance of complex **5** to form an inert trimer under hydrogenation conditions encouraged us to test it in catalysis. β-Pinene was selected as a moderately hindered alkene. Under the hydrogenation reaction conditions in dichloroethane,[15] interconversion with the more stable trisubstituted alkene α-pinene is rapid.[16] The uptake of H_2 was monitored in a constant volume rig operating at *ca.* 1.3 bar initial pressure. When complex **1a** was employed, there was a significant tail-off in hydrogenation rate close to the point of completion, as would be expected as deactivation sets in through trimerisation (Fig. 3). Over the same region of the hydrogenation reaction, the loss of activity was less pronounced when **5a** was employed as catalyst under otherwise identical conditions. Although promising, this represented an incremental improvement rather than an advance. In view of earlier results,[11] we compared the reactivity of PF_6 and BARf complexes. In our hands, hydrogenation of β-pinene with **4b** (0.5 mol%) was if anything slightly slower than with **4a** under comparable conditions.

Variation of the electronic properties of the phosphorus ligand was considered next. In the iridium asymmetric hydrogenation of 2-substitiuted pyridines to piperidines with arylphosphino analogues of ligand **3**, the 4-fluorophenyl complex was the most effective.[17] Although arylphosphine-derived relatives of complex **1** have only rarely been applied in catalysis,[18] we decided to synthesise complex **8** for comparison. The desired iridium complex **8a** was readily prepared and characterised by X-ray (Fig. 2b). It proved to be an effective hydrogenation catalyst that is clearly superior in the rate of H_2 uptake close to completion. The lack of tail-off indicates a lower tendency towards deactivation (Fig. 3).

In order to test the mechanism of trimerisation further, a crossover experiment was devised. In this a mixture of complexes **1b** and **8b** was hydrogenated in CD_2Cl_2 and the ^{1}H NMR monitored over the course of reaction (Fig. 4).

The previously characterised trimer **2** was observed with only minor amounts of other hydridic species apparent. The ES-MS spectrum showed a predominant dication peak at 660.3304 (calc. 660.3306) with two other dications at about 10% of its intensity. The first of these was (**2**–pyridine)$^{2+}$; as a general observation in these MS studies, loss of a nitrogen ligand from the trimeric

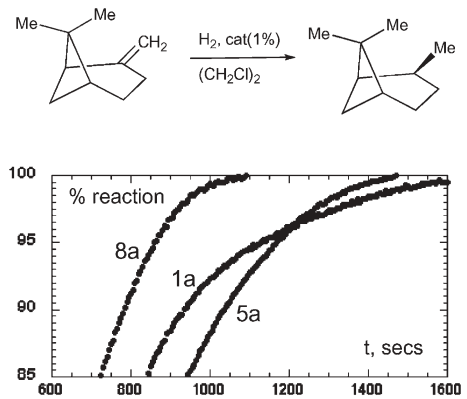

Fig. 3 Hydrogenation of β-pinene with three different Ir complexes in dichloroethane showing the last 15% of hydrogen take-up.

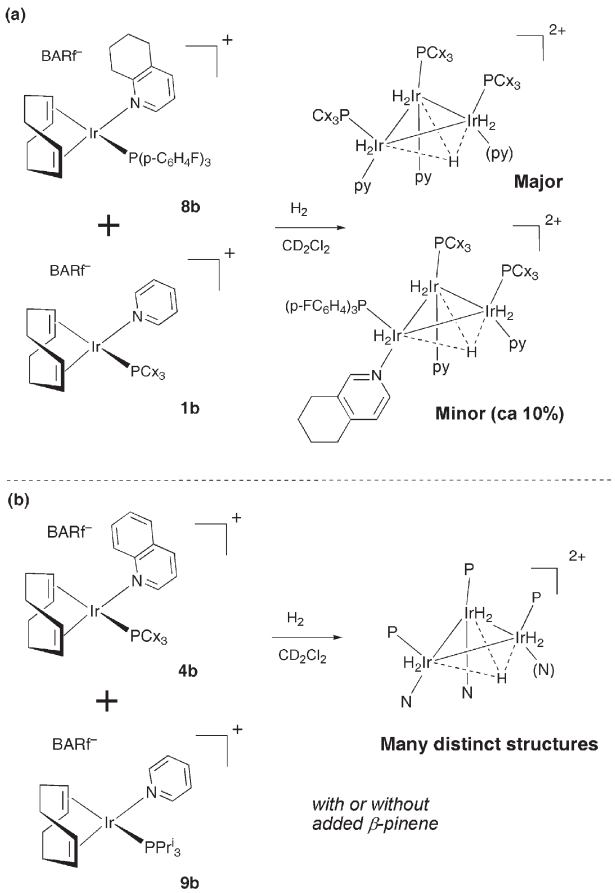

Fig. 4 The two crossover experiments described in the text. Equimolar amounts of the two complexes were employed in each case.

complexes is commonplace whereas phosphine loss is not observed. The second was a mixed cluster containing two (Cx_3P Ir py) units and one (ArFP Ir thq) unit; no other products of crossed trimerisation could be detected.

The inference is clear; ligand dissociation from the cation of **8** is an unfavourable process during hydrogenation. By contrast, a similar experiment in which a mixture of **4b** and the electronically similar complex **9b** was hydrogenated showed extensive scrambling. In the ^{1}H NMR spectrum, a proliferation of peaks in the −15 to −20 ppm region corresponding to different trimers was observed. In the ES-MS spectrum taken immediately following the completion of hydrogenation, the dicationic trimer from **4b**, but not that from **9b**, was observed as its [M-Quinoline] ion. In addition at least nine crossover products were observed, each lacking a single imine ligand. This experiment demonstrates that trimerisation is a consequence of ligand lability, more likely Ir–N bond dissociation.

These experiments provide a rational framework for the synthesis of novel asymmetric iridium catalysts. Recognising the likely involvement of ligand dissociation in formation of unreactive trimers is a key to development of oligomerisation resistant catalysts.

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Notes and references

† For the parent dication **2**, the corresponding values are δ −3.4 (q, J_{PH} 50 Hz) (bridging) and −20.1, −25.9 ppm (terminal).

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9 Crystal data for **5a**: $C_{35}H_{56}IrNP^+$, M = 714.38; triclinic, $P\bar{1}$; a = 10.0545(2), b = 11.8176(2), c = 15.5293(3) Å, α = 97.6584(8)°, β = 103.4087(9)°, γ = 99.2889(11)°, V = 1743.13(6) Å^3; T = 150 K; Z = 2; μ = 3.980 mm^{-1}; orange-red plate. Reflections collected = 25277; independent reflections =7896 (R_{int} = 0.062); R values [$I > 3\sigma(I)$, 6887 reflections]: $R1$ = 0.0415, w$R2$ = 0.0489 (all data). Crystal data for **9a**: $C_{35}H_{35}F_3IrNP^+$, M = 750.21; monoclinic, $P\ 2_1/n$; a = 15.2914(2), b = 12.2710(2), c = 17.6370(3) Å, α = 90°, β = 91.7169(6)°, γ = 90°, V = 3307.93(9) Å^3; T = 150 K; Z = 4; μ = 4.211 mm^{-1}; orange block. Reflections collected = 44293; independent reflections = 7880 (R_{int} = 0.059); final R values [$I > 3\sigma(I)$, 5480 reflections]: $R1$= 0.0278, w$R2$ = 0.0293 (all data). For crystallographic data in CIF or other electronic format, see: CCDC 654176, 654177. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b711979h.

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