Biological applications of para-hydrogen

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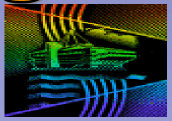
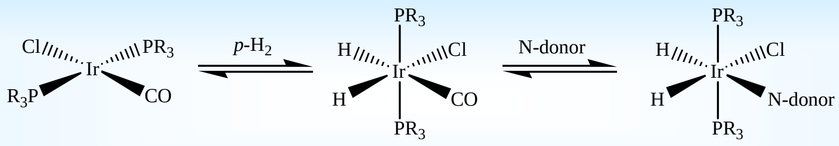


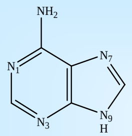
- The addition of hydrogen to $IrCl(CO)(PR_3)_2$ has been extensively studied
- Conducting this reaction with para-hydrogen in the presence of a suitable nitrogen-donor molecule yields a new set of complexes
- These complexes can be identified by their enhanced hydride resonances

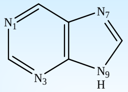


PR_3 = a triarylphosphine

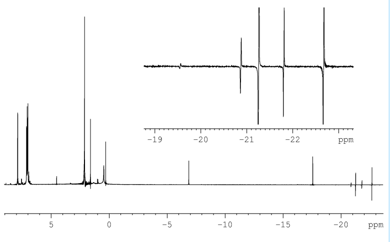
- The resultant enhanced hydride resonances appear in the high-field region of the ^1H NMR spectrum, at approximately δ -20
- Using pyridine as the nitrogen-donor, the resultant complex has been characterised using ^1H, ^{13}C, ^{15}N, ^{31}P and ^1H NOESY methods

Reactions with adenine and purine



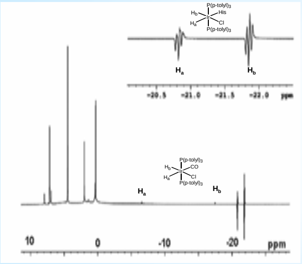


- For purine, four pairs of enhanced hydride signals are observed, corresponding to purine coordinating via each of the four N-sites.
- The N_9 site is accessed via tautomerisation
- For the major N1 product, the enhancement magnitude allows the acquisition of the coordinated purine ^{15}N chemical shift in less than 15 minutes *at natural abundance*
- Analogous results are observed for adenine



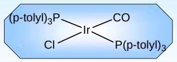
This spectrum shows the products arising from the addition of p-H_2 to a sample containing 0.1 mmol of $IrCl(CO)(PPh_3)_2$ and 0.1 mmol of purine, in d_8-toluene at 305 K. Over a range of temperatures, four separate products are observed.

Reactions with amino acids



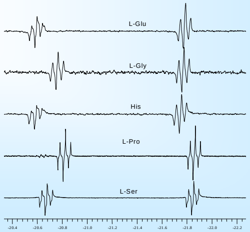
^1H NMR spectrum of a sample of $Ir(Cl)(CO)[P\text{-}(p\text{-}tolyl)_3]_2$ reacting with p-H_2 in the presence of histidine (**a**) Limited hydride signals for $Ir(H)_2(Cl)(CO)[P\text{-}(p\text{-}tolyl)_3]_2$, (**b**) strongly enhanced signals for $Ir(Cl)(histidine)[P\text{-}(p\text{-}tolyl)_3]_2$

The bio sensor



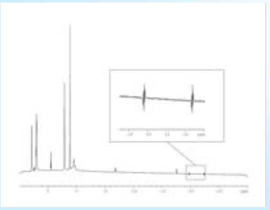
Vaska's analogue

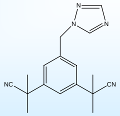
NMR spectra showing the polarised hydride resonances seen for the indicated amino acid complexes. The position of the signals for the hydride ligand which is *trans* to chlorine (right) do not change significantly while those for hydrides ligands which are ***trans* to an amino acid (left) move substantially and are indicative of the amino acid**



Reactions with drugs and their metabolites

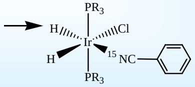
- •The drug anastrazole, used in the treatment of breast cancer has been detected by virtue of its binding to $IrH_2Cl(CO)(PR_3)_2$.
- •A 0.01mM solution of anastrazole in toluene gives rise to the 1H NMR spectrum observed below.

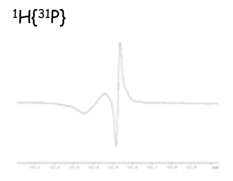




Anastrazole

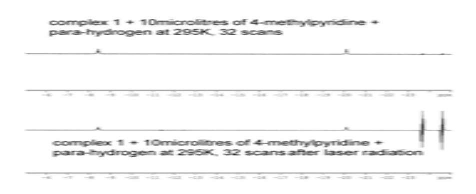
- •Using 15N-labelled substrates, unambiguous characterisation of the corresponding substrate bound metal complexes can be achieved.
- •The 15N gives rise to an extra splitting in the hydride *trans* to the substrate.





Other protocols

Additional increases in sensitivity are possible when using *in-situ* laser irradiation. Approximately 20 times the signal enhancement is observed when using this methodology



Acknowledgements

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