PERSPECTIVE

Dalton
www.rsc.org/dalton

C–H Activation approaches for the application of molecular recognition to organometallic chemistry and homogeneous catalysis †

Robert H. Crabtree
Yale Chemistry Department, P.O. Box 208107, New Haven, CT. 06520-8107, USA.
E-mail: robert.crabtree@yale.edu.

Received 14th April 2003, Accepted 9th May 2003
First published as an Advance Article on the web 22nd September 2003

A series of metal complexes of 2-aminobenzoquinoline prepared by C–H activation show molecular recognition effects. For example, ketones bound both by N–H···O hydrogen bonding and by coordination to a metal show selectivity of binding and dynamic properties not found when the hydrogen bonding function is omitted. N-heterocyclic carbenes (NHCs) are prepared by C–H activation reactions of imidazolium salts with the goal of understanding and using molecular recognition effects in homogeneous catalysis. Abnormal binding *via* C[5] is seen in some cases.

C–H activation [1–6] is now sufficiently advanced for applications to other problems to be envisaged. This paper covers recent examples from our group in which C–H activation has been applied to a number of molecular recognition problems in organometallic chemistry and catalysis. The work has relied heavily on collaborations with Odile Eisenstein and Eric Clot (Montpellier) in computational chemistry, Jack Faller (Yale) in structural studies and Eduardo Peris (Castellón) in organometallic synthesis. In the ion pairing aspect of the problem, a collaboration with Alceo Macchioni (Perugia) has also been invaluable.

Enzymes [7] use a molecular recognition function together with a catalytic function to bring about catalysis with very high selectivity and rate. Organometallic catalysts have tended to limit their recognition ability to simple steric effects, as in asymmetric catalysis [8,9] with ligands like diop, duPhos or binap. Proteins use a much wider range of recognition functions [10] notably aromatic stacking (AS), hydrogen bonding (HB) and ion pairing (IP). The aim of our work is therefore first to apply AS, HB and IP functions to organometallic catalysts to learn how to use them to get more enzyme-like selectivity without sacrificing catalytic rates. We hope to analyze the more successful systems in detail to understand why they work; improvements may then be possible based on such understanding.

It should be possible to tune the recognition for the optimal degree of interaction, since AS, HB and IP forces have a wide range of energies from 2 kcal mol^{-1} for AS to *ca.* 15 kcal mol^{-1} for IP, with HB occupying the middle range; these forces are also solvent-sensitive.[10] Our work to date has mainly concentrated on the two strongest forces, HB and IP. We need to do much more than just tune the overall strength of force involved, however. The hardest part of the project is ensuring that the recognition forces are stronger in the transition state (TS) for the turnover limiting step of a catalytic reaction than in the substrate or product-bound states of the catalyst. If we use recognition forces to lower the TS energy and at the same time stabilize substrate binding to an equal extent, for example, no net catalytic acceleration is expected. We believe that to lower the TS energy relative to the other states will prove to be the biggest challenge. In view of the recognized flexibility [11] of enzymes, we propose that this aim may best be achieved by endowing the recognition function of the synthetic catalyst with an appropriate degree of constrained flexibility. Since passage of a transition state is a dynamic process, the recognition element may need to track this motion for efficient TS stabilization. The flexibility has to be constrained because we do not want the recognition function also to stabilize related TSs for undesired pathways.

Remarkably few broad ligand classes have been found to support useful levels of organometallic catalytic activity. We found that phosphines, PR_3, the main such ligands used today, pose significant difficulties in attempted modification to incorporate recognition groups. The R groups point away from the metal so are not ideally placed to interact with substrates. Changing the R groups also involves significant changes in the electronic and steric effects of the PR_3 ligand, so the resulting catalytic changes may well be hard to interpret in terms of recognition. Phosphine synthesis is often somewhat elaborate and we anticipated that it might be hard to modify PR_3 to incorporate all the recognition groups we want. Finally, flexible linkers may be hard to incorporate.

We next moved to a 2-aminobenzoquinolinate system where an NH bond of the amino group points to the adjacent coordination site, making bifunctional binding possible. In this

† Based on the presentation given at Dalton Discussion No. 6, 9–11th September 2003, University of York, UK.

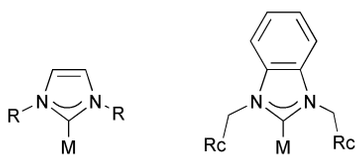
Bob Crabtree, educated at New College Oxford with Malcolm Green, did a Ph.D. with J. Chatt at Sussex University and spent four years in Paris with Hugh Felkin at the CNRS. At Yale since 1977, he is now Professor. He has been A.P. Sloan Fellow, Dreyfus Teacher–Scholar, ACS and RSC organometallic chemistry awardee, H.C. Brown Lecturer, Mack Awardee, Baylor Medallist, and has chaired the ACS Inorganic Division. He is the author of an organometallic textbook now in its 3rd edition. Early work on catalytic alkane C–H activation and functionalization was followed by C–F bond activation, H_2 complexes, dihydrogen bonding, and halocarbon and HF complexation. His homogeneous hydrogenation catalyst is widely used. Some of his present interests are reviewed here.

Bob Crabtree

DOI: 10.1039/b304125p

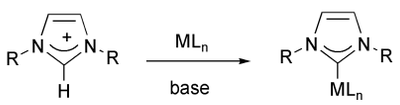
case, catalysis was considered unlikely and so we only expected to get data on selective ligand binding. Encouraging results were obtained, as reviewed here.

The recent rise of imidazole-based carbenes (**1**) as useful stabilizing ligands for a broad range of homogeneous catalysis[12] has changed the picture. In these ligands, the wingtip R groups point towards the metal and so should readily interact with catalytic substrates. A move to benzimidazole or related azoles with steric bulk remote from the metal was expected to encourage the R groups to adopt the desired conformation (**2**).



1 **2**

Synthesis of the imidazolium precursors from imidazole and an alkylating agent is extremely easy, although it has to be admitted that subsequent transfer to the metal – a reaction involving C–H activation at the imidazole 2-position – can be challenging (eqn. (1)). The electronic and steric effects of the recognition groups should have a small influence on the electronic effect of the carbene ligand, specially if there is a $–CH_2–$ linker group between the recognition group (Rc) and the ring. This $–CH_2–$ group may also introduce the right degree of flexibility, the proposed need for which was discussed above; alternatively, a wide range of linkers is possible.

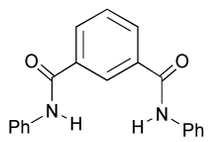


(1)

There are two levels of effect that we can expect on incorporating AS, HB and IP functionality into organometallic compounds. The first and simplest involves traditional molecular recognition effects[10] such as selective binding of external ligands, where we already have useful data. With some understanding attained at this first level, we have moved to look into selectivity effects in homogeneous catalysis. We are currently at the stage of exploring ways of metallating the functionalized imidazolium salts under mild conditions. This study is needed because traditionally the 2-H of the salt has been removed by strong base (*e.g.*, Bu^{n}Li) prior to introduction of the metal. This is clearly of limited use when the imidazolium salt bears reactive HB or IP functionality that could interact either with Bu^{n}Li or with the free carbene center prior to metal binding. In what follows we show examples of selective metallation reactions (that are also necessarily CH activation reactions) of imidazolium salts and the unexpected problems that have arisen.

Early attempts with modified phosphines

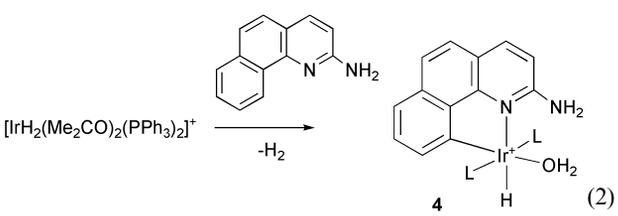
Before we adopted carbene ligands, we made attempts[13] to modify phosphines by appending hydrogen bonding groups. $Ph_2P(m\text{-}C_6H_4CONHPh)$ (= L^{HB}) was synthesized and successfully incorporated into the corresponding cationic iridium complexes such as $[IrH_2(Me_2CO)_2(L^{HB})_2]X$. We did not see any useful recognition-based cooperative effects in which a substrate bound both to the metal and to the NH group. This was perhaps because the conformation of the complex tends to direct the NH to the exterior of the molecule and away from the metal binding site. Indeed, we noticed strong binding to the external anion X^- in this iridium complex that led us to devise and look at the properties of a series of purely organic anion receptors of type ($m\text{-}C_6H_4\{CONHPh\}_2$) (**3**) and their sulfonyl analogs.[14] These proved to be powerful anion receptors and were extensively studied and applied to a number of molecular recognition problems, such as Lewis acid catalysis and electrochemical anion sensing by ferrocene derivatives, that are not relevant to the present discussion.[15]



3

Benzoquinoline chemistry

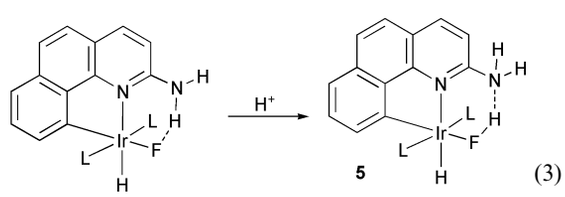
In an attempt to produce a system with a convergent binding site where both the N–H and the metal could cooperate in binding an external ligand, we turned to benzoquinoline (Hbq). This can readily be functionalized at the 2 position by $NaNH_2$ to give 2-aminobenzoquinoline ($Hbq–NH_2$), which readily cyclometallates – a CH activation reaction – to give the desired $Ir(bq–NH_2)$ aqua species, **4** (eqn. (2)). The high *trans* effect of the aryl group of the cyclometallated bq ensures that the solvated binding site remains *cis* to the NH_2 group, allowing cooperative binding.



4 (2)

Fluoride and HF complexes

Fluoride ion readily binds to **4** to give a species in which F is bound *via* a conventional Ir–F bond and *via* an N–H ··· F hydrogen bond (eqn. (3)).[16a] The latter is revealed by the crystal structure, showing a short N ··· F distance, combined with the appearance of a ^1J(H,F) coupling of 52 Hz in the ^{1}H NMR spectrum. More interestingly, when the fluoro complex is protonated at −80 °C, an HF complex (**5**) is formed, the first of its kind. They are related to the known[16b] bifluoride complexes M(FHF) in the sense that the terminal F is replaced by the pendant NH_2 group. Complex **5** decomposes with loss of HF above −20 °C, so no crystal structure could be obtained, but the ^{1}H NMR spectrum at low temperature shows a ^1J(H,F) coupling of 440 Hz, only consistent with the presence of an HF hydrogen bonded to the amino group. If the NH_2 is absent or replaced by an isosteric, non-HB functionality such as CH_3, no HF complex is formed; instead the HF dissociates on protonation.



5 (3)

Thanks to a collaboration with Eisenstein and Clot, computational work[17] was carried out on the system that suggests that the binding site is ideally suited for HF binding. The calculated (DFT, B3PW91. Quantum model: $[IrH(bqNH_2)(FH)(PH_3)_2]^+$) geometry is indicated in Fig. 1 and the calculated HF binding energy is 32.5 kcal mol^{-1}. The calculations also suggest that the aqua complex (**4**), for which we lack experimental structural data, also has a similar hydrogen bonding network.

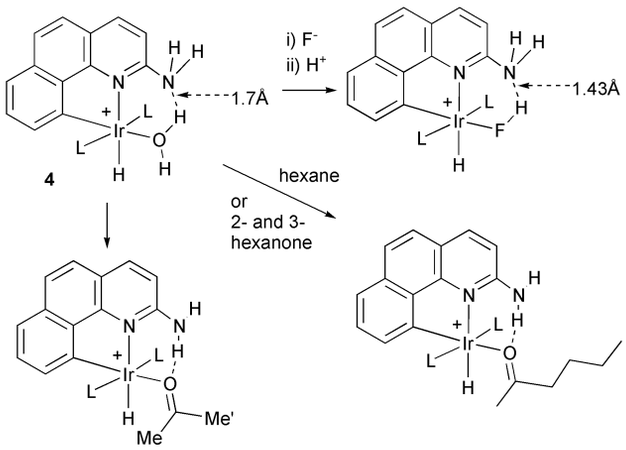


Fig. 1 Some transformations of the bq–NH_2 molecular recognition system, **4**. The structural data for the HF complex comes from calculations (DFT, B3PW91. Quantum model: $[IrH(bqNH_2)(FH)(PH_3)_2]^+$) by Clot and Eisenstein.[17]

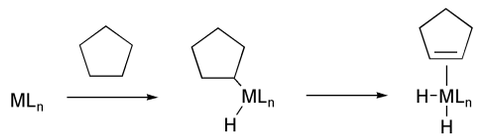
Selectivity and dynamics of the ketone complexes

We were amazed to find that when **4** was recrystallized from diethyl ether–hexane, crystals of the 2-hexanone complex were formed (Fig. 1).[18] This was traced, not to an exotic CH activation process, but to the presence in the hexane of a small percentage of 2- and 3-hexanone. The latter, normally present in aged hexane thanks to radical autoxidation by air, do not usually make their presence felt. In this case, we have a site that so avidly binds ketones of type MeCOR, in part thanks to the bifunctional binding, that the trace ketone impurity is now scavenged from the hexane solvent. One ketone O lone pair is bound by Ir and the other engages with the NH group of the HB functionality. The result of this double binding is that the ketone is necessarily held in the bq plane. The result of this conformational restriction is that only 2-hexanone can bind well because its terminal Me group does not come into repulsive contact with the adjacent Ir–H ligand, while 3-hexanone fails to bind at all under any conditions we tried, presumably because its larger terminal Et group now interferes sterically with the adjacent Ir–H ligand. When the NH_2 is absent on the bq ligand, NMR data suggests that both 2- and 3-hexanones can now bind, there being no rigid conformational restriction, but they do so more weakly because the additional binding of the HB group is now absent. This indicates that the presence of the HB functionality very greatly alters the selectivity of ligand binding, a result that augurs well for our larger catalytic program.

The acetone complex of **4** is interesting in showing two acetone methyl ^1H NMR resonances at low temperature as a result of the binding with the NH group of the HB functionality. This binding must be broken for the *endo* and *exo* methyl groups to exchange. In contrast, in the system lacking the NH_2 group acetone undergoes free rotation at all accessible temperatures. This indicates that the HB functionality also constrains the dynamics of the bound ligand to a significant extent, again a relevant point in relation to our broader goals.

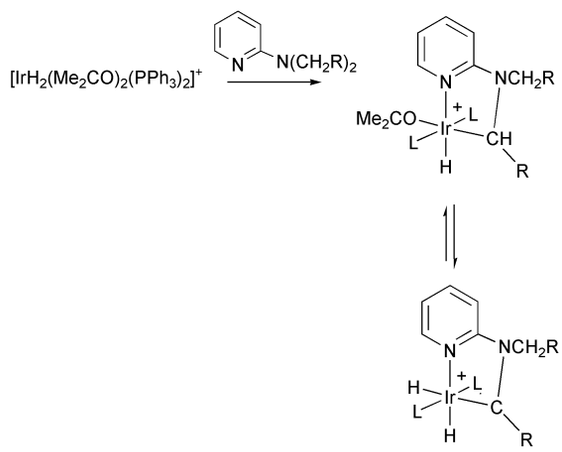
Carbene ligands *via* double geminal CH activation

As mentioned earlier, the next step of the program exploits the properties of carbene ligands for obtaining useful molecular recognition effects in catalysis. CH activation reactions played a vital part in the development of this area, too, because our first direct contact with carbenes came from a C–H activation project in a substituted aminopyridine.[19] Alkane C–H activation followed by β-elimination (eqn. (4)) is a well-established route to alkenes that can be either stoichiometric or catalytic.[1–6] C–H activation followed by α-elimination has recently proved possible where a π-donor heteroatom such as N or O is located



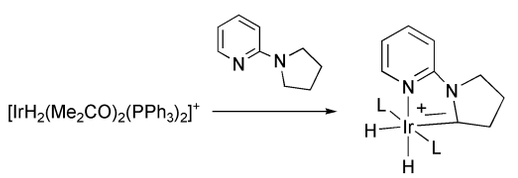
(4)

adjacent to the site of C–H activation. The result is a double geminal C–H activation with formation of a heteroatom stabilized carbene as product (eqn. (5)).



(5)

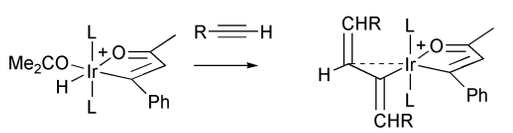
This reaction was known even for THF[20] but our case involved activation by N not O. It is rare to find an α-elimination where a β-elimination is possible (eqn. (5), R = CH_3), but here the adjacent N activates this C–H bond strongly enough for this to be possible. A second unusual feature is the reversibility of the second, α-elimination step (eqn. (3), R = H). The related pyrrolidine also reacts readily, but irreversibly, to give the N-heterocyclic carbene (eqn. (6)).



(6)

Attempted C–C coupling with double C–H activation

We have tried to use a related enone cyclometalation reaction[21] to bring about C–C coupling with alkynes. Instead of the expected enone/alkyne coupling, two alkyne molecules rearrange to vinylidine and successively insert into the MH bond to give a rare η^2-butadienyl (eqn. (7)). The most interesting feature of this reaction is that crossover studies with RCCH and R^1CCD indicate that the CH proton of each alkyne migrates from the 1 to the 2 position within each alkyne to give a vinylidene without crossover or exchange with any other protons; the Ir–H proton ends up in the position expected for a double vinylidene insertion into Ir–H.

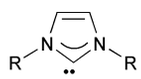


(7)

N-Heterocyclic carbenes (NHCs) as ligands

Shortly after the discovery of the Fischer (heteroatom stabilized) carbene ligand, early work by Öfele,[22] Wanzlick and Schonher[23] and Lappert and coworkers[24] showed that N-heterocyclic carbenes formally derived from imidazole-2-ylidene (**1**) with two adjacent heteroatoms are excellent ligands. Not only do they bind very strongly to transition metals but, as

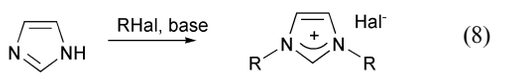
was already shown[25] even during the 1970s, they can also act as stabilizing spectator ligands in homogeneous catalysis. Interest in the area was greatly enhanced by Arduengo's isolation of stable examples[26] of type **6** with bulky R groups (e.g., 1-adamantyl) to protect the reactive carbon center.



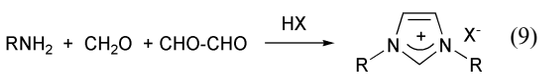
6

Until Herrmann[12] described a series of such catalysts from the mid 1990s, NHCs remained a rarity in the role of stabilizing ligand in catalysis, however. Perhaps the most striking use of NCHs in catalysis came from the great improvement of the Grubbs olefin metathesis catalyst[27] caused by replacement of one PCy_3 group with an NHC.

The precursor imidazolium salt is very readily synthesized with any of a wide variety of wingtip groups.[28] The two most common pathways are illustrated in eqns. (8) and (9). In the simplest, imidazole is alkylated; for example, a benzylic R group is easily installed in this way. In the second, the heterocyclic ring is constructed from amine, CH_2O and $(CHO)_2$ by the Radizewski synthesis to give the imidazolium salt directly. This is most appropriate for aryl wingtip groups.

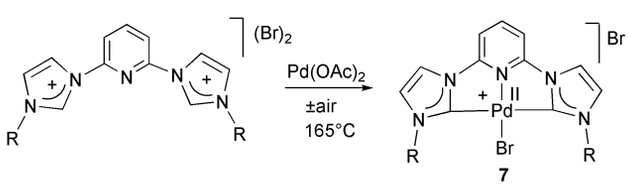


(8)



(9)

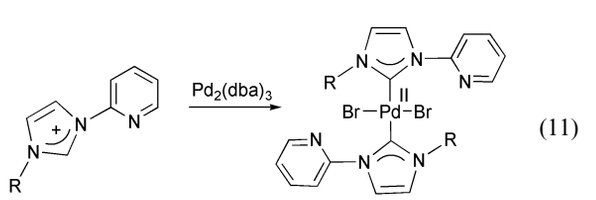
We now need to effect CH activation by metallation under mild conditions. A conceptually very simple way of installing the carbene is to start from the precursor salt and a metal acetate in the hope of metallating *via* σ-bond metathesis. We tested this route using a carbene pincer precursor with $Pd(OAc)_2$ to give pincer complex **7** (eqn. (10)).[29] This required 165 °C but the process occurred even in air, a testament to the great thermal stability of metal NHC complexes. The resulting complex and several similar ones[30] proved to be active for typical Pd catalyzed coupling reactions, without Pd(0) being formed. However, we judged that the high temperature metallation route required was too harsh for our purposes.



7

(10)

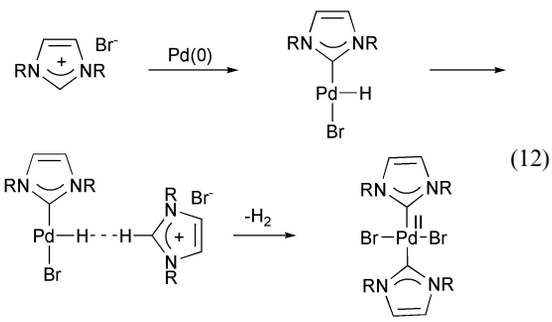
A direct C–H activation of the critical 2-CH bond to a low valent metal seemed a good alternative. As shown by eqn. (11), this occurs at very modest temperatures with $Pd_2(dba)_3$, a standard Pd(0) source, but surprisingly, the bis-carbene complexes were always formed, never the expected mono-carbene



[R = mesityl]

(11)

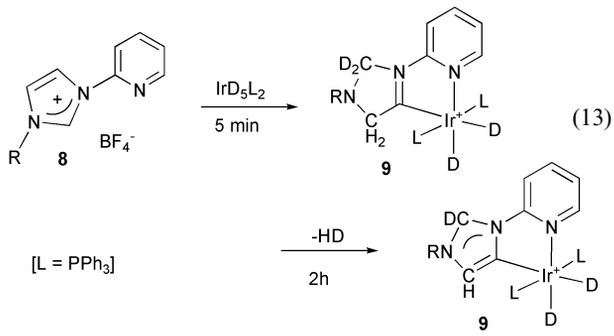
hydrides that are presumably transient intermediates.[31] This result suggests that the proposed intermediate hydride might react very rapidly with the 2-C–H hydrogen of a second molecule of imidazolium salt. This could happen because the hydride plausibly being particularly hydridic, could form a dihydrogen bond[32] with the 2-C–H of the imidazolium salt, facilitating reaction (eqn. (12)).



(12)

As a test of the hypothesis that a hydridic hydride should react rapidly with an imidazolium salt we looked at the reaction of $IrH_5(PPh_3)_2$ with pyridine **8**.[33] This reaction proved possible (eqn. (13)) but to our very great surprise, the imidazolium ring metalated in the wrong way, *i.e.*, at the normally less reactive C^5, not at the usual C^2 position. This kind of 'wrong way' binding, never observed before, must now be considered as a possibility in any work with NHCs. At present, however, some NHC catalysts are made *in situ* from metal salts and imidazolium salts with the assumption that only binding at C^2 will occur, but without checking the nature of the binding; this approach could lead to problems. Our resulting carbene at C^5 is now stabilized by just one and not two adjacent N atoms, with the result that it is apparently thermodynamically less stable than the C^2 isomer. C^5 to C^2 isomerization can be carried out with strong acid at least when the wingtip R is M or Pr^i, but not with the bulky mesityl.[34]

A clue for the mechanism of formation of the C^5 isomer came from the observation that a wrong-way hydrogenated carbene **9** was formed at short reaction times (eqn. (13)). For small R groups, this intermediate quickly converts to the right-way aromatic carbene, but for the bulky R, mesityl, the hydrogenated form could be isolated in a pure form and its X-ray structure obtained. This, together with the ^1H NMR spectrum, definitely proves the structure. Using $IrD_5(PPh_3)_2$ gave the result shown in eqn. (13), where the deuterium is found only on the remote methylene group while the methylene closest to the metal is fully protonated. As a working hypothesis, we proposed the mechanism shown in Fig. 2 to explain this transformation and the labeling pattern seen. Because three Ds are proposed to be distributed over four sites in the product, the deuteration level drops by a quarter, as observed; the sites having this diluted label are denoted d in the diagram. If this mechanism is correct, the 'right carbene' is formed from a C–H activation but the 'wrong carbene' is formed by an insertion of a ring C=N bond into an Ir–H bond, a very unexpected reaction. If so, the final C^5 product is only an apparent C–H activation.



[L = PPh_3]

(13)

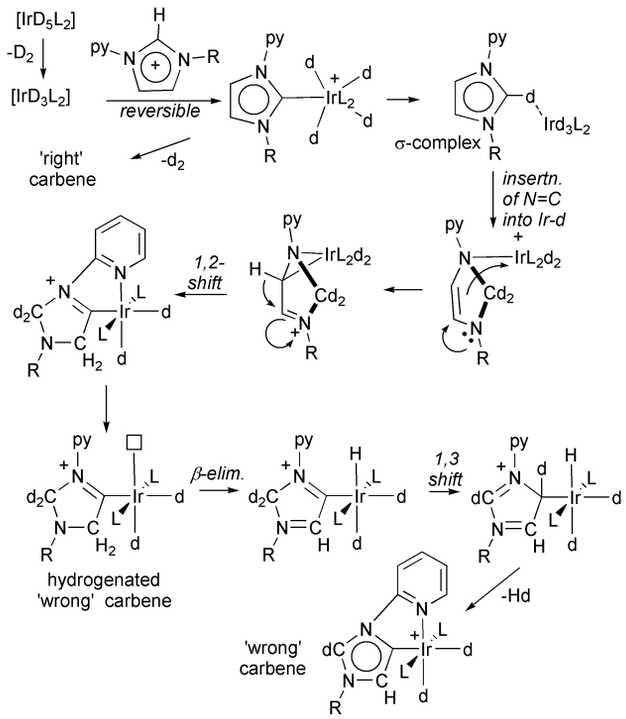


Fig. 2 The mechanism proposed to explain the CH activation reaction.[33] D represents a fully labelled position and d a position with 75% labelling as a result of exchange between three D and one H.

Ion pairing [35]

Since ion pairing is a force we hope to use in recognition, we have looked at the possibility that it might occur in our organometallic salts. We first saw contact ion pairing in the closely related molecule $[IrH_2(bipy)L_2]BF_4$ where the BF_4 anion proved by solution NMR studies in collaboration with Alceo Macchioni,[35b] to be located near the dipyridyl C^3 and $C^{3'}$ positions (Fig. 3), surprisingly remote from the metal. The origin of this structure was traced in computational studies by Clot and coworkers [35b] to the strongly positive character of the C^2 and $C^{2'}$ carbons in the complex, the aromatic C=N bonds being strongly polarized by metal binding. These positions are not directly accessible to the counterion which can only approach the adjacent C^3 and $C^{3'}$ positions.

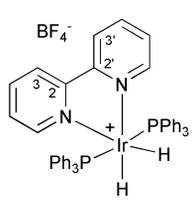
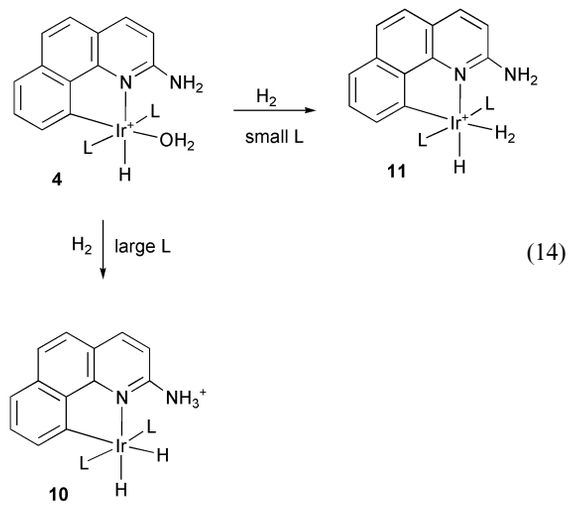


Fig. 3 The average solution structure of the ion pair, $[IrH_2(bipy)L_2]BF_4$, from NMR studies by Alceo Macchioni.[35]

Alerted to the importance of ion pairing, we have looked for it in other systems. Computational work by Clot and Eisenstein suggested that there should also be contact ion pairing between the 2-CH bond of the wrong-way carbene and the counterion.[36] This indeed proved to be true, as shown by the large ^1H NMR spectral shifts found for this 2-CH proton resonance as the nature of the anion was varied. Titration studies showed that on addition of Br^- to the SbF_6^- salt, the lower field resonance of the CH ··· $FSbF_5$ adduct smoothly moves to the higher field position assigned to the CH ··· Br adduct. The total shift of $\Delta\delta$ of 2 during the process seems rather large but is entirely consistent with the behavior seen for the free imidazolium salt, so the metal does not seem to play any special role in the ion pairing.

This result encouraged us to look for counterion effects on the course of the reaction. Surprisingly changing counterion completely reversed the outcome, bromide giving the 'right' carbene and the SbF_6 salt mainly giving the 'wrong' isomer. Accounting for this result will require much more study but ion pairing presumably has opposite, or at least very different effects on the transition states (TSs) for the two pathways.[35,36]

In one other related case, we have proposed that contact ion pairing determines the product isomer adopted.[37] The bq–NH_2 aqua complex **4** reacts with H_2 to give one of two isomers, the hydride **10** or the dihydrogen complex, **11** (eqn. (14)). These are related by proton transfer from H_2 to the –NH_2 group. Surprisingly, the phosphine basicity did not determine the outcome, because P(cyclohexyl)$_3$ gives the hydride **10** even though, as the most basic ligand tried, it should have increased the basicity of the Ir–H group. Large phosphines turned out to favor the H_2 form **11** and small phosphines the hydride form **10**.



(14)

Thanks to computational work with Clot and Eisenstein, the origin of the effect was traced to vicinal ion pairing (i.e., near the H_2), possible only for small phosphines (Fig. 4) stabilizing the dihydrogen form and distal ion pairing (i.e., near the –NH_3^+), enforced by large phosphines, stabilizing the hydride form.

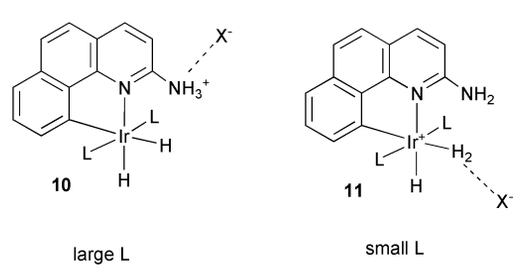
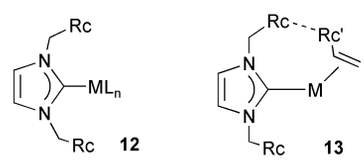


Fig. 4 The proposed ion pair structures of the two isomers of type **10** and **11** from DFT studies by Clot and Eisenstein.[37] The bulk of the phosphine is proposed to determine the position of ion pairing which in turn decides the structure.

Catalytic studies

At the moment, we are extending these studies by building molecules of type **12** to look for recognition effects between Rc groups and the substrate.[38] For example, diagram **13** shows how this might alter the stabilities of TS's for 1,2 *vs.* 2,1 insertion



and therefore alter the ratio of Markovnikov products in hydrosilylation, for example. In addition to testing aromatic stacking with the series Rc = C_6H_{11}, C_6H_5, C_6F_5, using aromatic substrates such as PhC≡CH, we are also testing hydrogen bonding with Rc = *m*-$C_6H_5NHCOMe$ and ion pairing with Rc = *m*-$C_6H_5NMe_3^+$ groups. This should provide a useful general strategy for obtaining homogeneous catalysts with desired properties. Clues from the prior literature suggest that this is an achievable aim.

In the bioorganic realm, a theoretical analysis of a catalytic antibody points to the key roles of hydrogen bonds and stacking interactions in determining selectivity.[39] In work on ester hydrolysis, a rate acceleration of 10^7 was attributed to the stacking effects of aromatic substituents.[40] Chemical, kinetic and theoretical approaches led to the proposal that stacking effects caused an unexpected double benzylation of acetophenone under phase transfer catalysis conditions.[41] Several synthetic organic receptors have proved to be catalysts, typically for hydrolysis and acyl transfer.[10] In a Pd-catalyzed Heck reaction, Pregosin, Albinati and coworkers[42] proposed a strong stacking influence on an asymmetric reaction and estimated that a 4 kcal mol^{-1} stabilization came from π–π stacking. Perhaps the strongest evidence that stacking has a key role in catalytic selectivity comes from product studies, solvent effect, Hammett studies and X-ray data discussed by Sharpless and coworkers[43] for asymmetric osmylation with a phthalazine ligand. Anion effects on product distributions in catalysis have been reported in several papers.[44,45] Cation–π interactions have been invoked to explain high ee's in certain asymmetric reactions.[46]

Conclusion

We have used C–H activation to synthesize species relevant to the problem of applying molecular recognition effects to organometallic chemistry and catalysis. After attempts to work with phosphines failed, we moved to 2-substituted benzoquinolinates where selectivity and dynamic effects were seen on guest molecule binding. For future catalytic work, we have now moved to NHC ligands. The need to develop mild synthetic routes for metallating the precursor imidazolium salts led us to look at σ bond metathesis and CH oxidative addition. We also found a new abnormal metallation product formed by a mechanism that is believed to involve C=N insertion into the M–H bond. Ion pairing and hydrogen bonding are shown to have a number of significant effects on the products formed in the systems studied.

Acknowledgements

We thank our collaborators Odile Eisenstein, Eric Clot, Jack Faller, Eduardo Peris and Alceo Macchioni, as well as the US DOE and Johnson Matthey for funding.

References

1 R. H. Crabtree, *J. Chem. Soc., Dalton Trans.*, 2001, 2951; R. H. Crabtree, *Chem. Rev.*, 1985, **85**, 245; R. H. Crabtree, *Chem. Rev.*, 1995, **95**, 987.
2 C. Hall and R. N. Perutz, *Chem. Rev.*, 1996, **96**, 3125.
3 S. S. Stahl, J. A. Labinger and J. E. Bercaw, *J. Am. Chem. Soc.*, 1996, **118**, 5961.
4 W. D. Jones, *Acc. Chem. Res.*, 2003, **36**, 140.
5 W. W. Xu, G. P. Rosini, M. Gupta, C. M. Jensen, W. C. Kaska, K. Krogh-Jespersen and A. S. Goldman, *Chem. Commun.*, 1997, 2273.
6 B. A. Arndtsen, R. G. Bergman, T. A. Mobley and T. H. Peterson, *Acc. Chem. Res.*, 1995, **28**, 154.
7 C. Walsh, *Enzymatic Reaction Mechanisms*, Freeman, San Francisco, 1979.
8 R. Noyori, *Adv. Synth. Catal.*, 2003, **345**, 15.
9 H. B. Kagan, *Adv. Synth. Catal.*, 2001, **343**, 227.
10 H. J. Schneider and A. Yatsimirsky, *Principles and Methods of Supramolecular Chemistry*, Wiley, New York, 2000.
11 M. Akke, *Curr. Opin. Struct. Biol.*, 2002, **12**, 642; S. Piana, P. Carloni and M. Parrinello, *J. Mol. Biol.*, 2002, **319**, 567; G. H. Peters and R. P. Bywater, *J. Mol. Recognit.*, 2002, **15**, 393; Y. E. Shapiro, E. Kahana and V. Tugarinov, *Biochemistry*, 2002, **41**, 6271; J. Broos, *Biocatal Biotransform.*, 2002, **20**, 291.
12 W. A. Herrmann, *Angew. Chem., Int. Ed.*, 2002, **41**, 1291.
13 K. Kavallieratos and R. H. Crabtree, unpublished data, 1997.
14 K. Kavallieratos, S. R. deGala, D. J. Austin and R. H. Crabtree, *J. Am. Chem. Soc.*, 1997, **119**, 2325.
15 K. Kavallieratos, S. Hwang and R. H. Crabtree, *Inorg. Chem.*, 1999, **38**, 5184; K. Kavallieratos and R. H. Crabtree, *Chem. Commun.*, 1999, 2109.
16 (*a*) B. P. Patel and R. H. Crabtree, *J. Am. Chem. Soc.*, 1996, **118**, 13105; (*b*) D. C. Roe, W. J. Marshall, F. Davidson, P. D. Soper and V. V. Grushin, *Organometallics*, 2000, **19**, 4575; M. K. Whittlesey, R. N. Perutz, B. Greener and M. H. Moore, *Chem. Commun.*, 1997, 187; V. J. Murphy, T. Hascall, J. Y. Chen and G. Parkin, *J. Am. Chem. Soc.*, 1996, **118**, 7428.
17 E. Clot, O. Eisenstein and R. H. Crabtree, *New J. Chem.*, 2001, **25**, 66.
18 K. Gruet, R. H. Crabtree, D.-H. Lee, L. Liable-Sands and A. L. Rheingold, *Organometallics*, 2000, **19**, 2228.
19 D.-H. Lee, J. Chen, J. W. Faller and R. H. Crabtree, *Chem. Commun.*, 2001, 213.
20 G. Ferrando-Miguel, J. N. Coalter, H. Gerard, J. C. Huffman, O. Eisenstein and K. G. Caulton, *New J. Chem.*, 2002, **26**, 687; E. Gutierrez-Puebla, A. Monge, M. C. Nicasio, P. J. Perez, M. L. Poveda and E. Carmona, *Chem. Eur. J.*, 1998, **4**, 2225.
21 X. Li, C. D. Incarvito and R. H. Crabtree, *J. Am. Chem. Soc.*, 2003, **125**, 3698.
22 K. Ofele, *Angew. Chem., Int. Ed.*, 1969, **8**, 916.
23 H. W. Wanzlick and H. J. Schonher, *Angew. Chem., Int. Ed.*, 1968, **7**, 141.
24 B. Cetinkaya, P. Dixneuf and M. F. Lappert, *Chem. Commun.*, 1973, 206.
25 J. E. Hill and T. A. Nile, *Transition Met. Chem.*, 1978, **3**, 315.
26 A. J. Arduengo, R. L. Harlow and M. Kline, *J. Am. Chem. Soc.*, 1991, **113**, 361.
27 T. M. Trnka, J. P. Morgan, M. S. Sanford, T. E. Wilhelm, M. Scholl, T. L. Choi, S. Ding, M. W. Day and R. H. Grubbs, *J. Am. Chem. Soc.*, 2003, **125**, 2546.
28 M. R. Grimmett, *Imidazole and Benzimidazole Synthesis*, Academic Press, New York, 1997.
29 E. Peris, J. A. Loch, J. Mata and R. H. Crabtree, *Chem. Commun.*, 2001, 201.
30 J. A. Loch, M. Albrecht, E. Peris, J. Mata, J. W. Faller and R. H. Crabtree, *Organometallics*, 2002, **21**, 700; M. Albrecht, J. Miecznikowski, A. Samuel, J. W. Faller and R. H. Crabtree, *Organometallics*, 2002, **21**, 3596.
31 S. Gründemann, M. Albrecht, A. Kovacevic, J. W. Faller and R. H. Crabtree, *J. Chem. Soc., Dalton Trans.*, 2002, 2163.
32 R. H. Crabtree, P. E. M. Siegbahn, O. Eisenstein, A. L. Rheingold and T. F. Koetzle, *Acc. Chem. Res.*, 1996, **29**, 348–54.
33 S. Gründemann, A. Kovacevic, M. Albrecht, J. W. Faller and R. H. Crabtree, *J. Am. Chem. Soc.*, 2002, **124**, 10473.
34 A. Kovacevic and R. H. Crabtree, unpublished data, 2002.
35 (*a*) D. Drago, P. S. Pregosin and A. Pfaltz, *Chem. Commun.*, 2000, 286; (*b*) A. Macchioni, C. Zuccaccia, E. Clot, K. Gruet and R. H. Crabtree, *Organometallics*, 2001, **20**, 2367.
36 A. Kovacevic, S. Gründemann, J. R. Miecznikowski, E. Clot, O. Eisenstein and R. H. Crabtree, *Chem. Commun.*, 2002, 2580.
37 K. Gruet, E. Clot, O. Eisenstein, D.-H. Lee, B. Patel, A. Macchioni and R. H. Crabtree, *New J. Chem.*, 2003, **27**, 80.
38 J. R. Miecznikowski, A. Chianese, R. H. Crabtree, unpublished data, 2003.
39 X. Y. Zhang, Q. L. Deng, S. H. Yoo and K. N. Houk, *J. Org. Chem.*, 2002, **67**, 9043.
40 S. Negi and H. M. Schneider, *Tetrahedron Lett.*, 2002, **43**, 411.
41 E. DiezBarra, A. delaHoz, A. Loupy, A. MartinezGonzalez, V. MartinezMerino, S. Merino, R. Paugam, P. SanchezVerdu, J. Sansoulet and J. Torres, *Tetrahedron*, 1997, **53**, 3659.
42 P. Dotta, A. Magistrato, U. Rothlisberger, P. S. Pregosin and A. Albinati, *Organometallics*, 2002, **21**, 3033.
43 H. C. Kolb, P. G. Andersson and K. B. Sharpless, *J. Am. Chem. Soc.*, 1994, **116**, 1278.
44 D. J. R. O'Mahony, D. B Belanger and T. Livinghouse, *Synlett*, 1998, 443.
45 D. Drago, P. S Pregosin and A. Pfaltz, *Chem. Commun.*, 2002, 286.
46 L. S. Kaanumalle, J. Sivaguru, N. Arunkumar and V. Ramamurthy, *Chem. Commun.*, 2003, 116.