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Counter-ion effects switch ligand binding from C-2 to C-5 in kinetic carbenes formed from an imidazolium salt and $IrH_5(PPh_3)_2$

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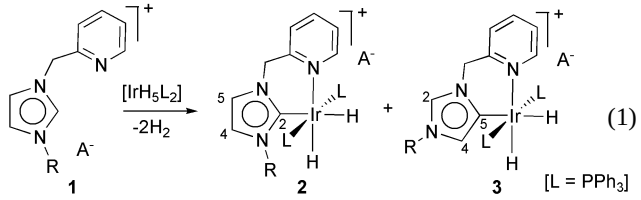
Changing the counter-anion in 2-pyridylmethyl imidazolium salts (Br, BF_4, PF_6, SbF_6) causes their kinetic reaction products with $IrH_5(PPh_3)_2$ to be switched from normal C-2 to abnormal C-5 binding.

N-Heterocyclic carbenes, increasingly used[1–4] as ligands in homogeneous catalysis, have a much more complicated organometallic chemistry than originally thought. For example, all other previous examples show normal metal binding[1–4] at C-2 (**2**) but abnormal C-5(4) binding (**3**) has been found in the products from eqn. (1), where R = Pr^i and A = BF_4.[5] In this communication, we report the remarkable role of the counter ion in switching the kinetic product between **2** and **3**.



(1)

As previously reported,[5b] the imidazolium metallation of eqn. (1) (R = Me; A = BF_4) gave a 45:55 ratio of C-2 and C-5 bound carbenes **2** and **3**. To help determine if this was a thermodynamic or kinetic ratio, we evaluated the energy difference between normal **2** and abnormal **3** isomers with combined QM/MM ONIOM (B3PW91/UFF) calculations† on the cationic anion-free models, normal **[4$^+$]** and abnormal **[5$^+$]** respectively. These species were described in full at the QM level except for the Pr^i and Ph substituents which were modeled at the MM level. The abnormal C-5 bound **[5$^+$]** was 10.1 kcal mol^{-1} higher in energy than **[4$^+$]**. In view of prior work in which ion pairing was significant,[6] we included the [BF_4^-] anion in the QM part of the ONIOM calculations. The difference in energy between **[4$^+$]**[BF_4^-] and **[5$^+$]**[BF_4^-], now only 1.6 kcal mol^{-1} in favor of the normal C-2 product, make the isomers essentially isoenergetic. The anion was hydrogen bonded to the C-2 C–H bond in **[5$^+$]**[BF_4^-] ion pair and to the C-5 C–H in **[4$^+$]**[BF_4^-]. This large influence of the anion on the relative energies of **4** and **5** led us to vary the anion experimentally in eqn. (1).

We now find that the choice of the anion in **1** (R = Me) can bias the experimental‡ kinetic product of the reaction to give either normal C-2 (**2**) or abnormal C-5 binding (**3**). The effects seen here go beyond the modest counter-ion effects[6b] usually seen on rates and selectivities of catalytic reactions in organometallic chemistry. In particular, normal **2** was by far the major product with A = Br but abnormal **3** was formed with A = SbF_6. Having the two materials in pure form allowed their identities to be unambiguously determined and led to secure identification of **2** and **3** in the mixture formed with A = BF_4. Examples of **3** (R = Pr^i and mesityl) have previously been unambiguously characterized *via* X-ray diffraction.[5]

The very different NMR characteristics of C-2 and C-5 bound isomers, fully discussed recently,[5b] allow secure spectroscopic identification of the isomers. In particular, the adjacent imidazole aromatic protons of normal **2** (R = Me, A = BF_4) C-4 and C-5, are relatively close in proton NMR chemical shift ($CDCl_3$), δ 7.44 and 6.31, as expected,[5b] while the nonadjacent aromatic protons of abnormal **3** (R = Me, A = BF_4), C-2 and C-4, are more separated, δ 8.66 and 4.88, again as expected,[5b] consistent with the acidic C-2 proton having a particularly low field shift. Also in line with previous data,[5b] the C-2 carbene has a lower field ^{13}C NMR shift, ($CHCl_3$) 169.9 ppm (BF_4 salt), than the C-5 carbene, 142.0 ppm (BF_4 salt).

We were also able to verify that **2** was not converted to **3** nor *vice versa* under neutral conditions, even after exchanging counter ions. HBF_4/CH_2Cl_2 completely (NMR) converts **2** to **3** (R = Bu^n, Pr^i), however. This suggests that although the energies of **2** and **3** may be quite close, the product ratio from eqn. (1) is kinetic in origin. The ion present during the synthesis decides the **2/3** ratio, not any subsequent change of anion.

Moving to a larger R group biases the **2/3** ratio in favor of the less hindered abnormal **3**. **1** (R = Pr^i, A = Br) gives the normal product **2** as major**,** but **1** (R = Pr^i, A = BF_4) gives only the abnormal product **3**. Table 1 lists the results from a variety of counter ions.

To evaluate the effect of Br^- on the relative product energies, we calculated **[4$^+$]**[Br^-] and **[5$^+$]**[Br^-] with ONIOM (Br^- in the QM part). The energy difference of 3 kcal mol^{-1} is more in favor of normal **2** than for [BF_4^-]. Some of this difference may be present in the product-determining transition state since Br^- favors **2** experimentally. Ligands such as **1** are therefore bifunctional—the most intrinsically thermodynamically stable normal carbene has weaker H bonding ability (**2**) and *vice versa* (**3**)—both factors seem to be involved in the reaction.

Ion pairing occurs preferentially between the acidic CH of the starting salt **1** and counter ions, as shown by the sensitivity of the proton NMR shift of the 2-C–H to the nature of the anion. For example, for the model imidazolium salt **6**, the resonance shifts ($CDCl_3$) are as follows: Br^-, δ 10.45; BF_4^-, δ 9.85; PF_6^-, δ 8.79; SbF_6^-, δ 8.50. The same interaction is detected in the abnormal carbene **3**, where the acidic CH is directed away from the metal. The shifts seen are : Br^-, δ 9.71; BF_4^-, δ 8.66; PF_6^-, δ 8.44; SbF_6^-, δ 8.38. Br can readily replace SbF_6^- (or BF_4^-) as ion pairing partner in **6**, as shown by the change in chemical shift of the 2-C–H from that of the SbF_6 salt to that of the Br^-

Table 1 Ratio of **2** to **3** in eqn. (1) for various alkyl groups, R, and anions, A

R	A	**2**	**3**
Me	Br	91	9
Me	BF_4	45	55
Me	PF_6	50	50
Me	SbF_6	11	89
Pr^i	Br	84	16
Pr^i	BF_4	0	100

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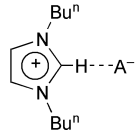
salt on addition of NBu_4Br in $CDCl_3$. The titration curve suggests K_{eq} is 1.6 in favor of Br. Similar ion pairing effects in imidazolium salts have been reported.[7]



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The origin of this counter-ion effect on the product ratio is not yet understood but work is currently in hand. The relative energies of the transition state *vs.* the ground state ion pair must be affected by the change of anion. Presumably, charge redistribution is substantially different in the C-2 *vs.* C-5 transition states, leading to a different response to the nature of the anion.

The results signal that it may not be safe to assume that the choice of counter ion is insignificant for selectivity in organometallic reactions and suggest a potential opportunity in that it may be fruitful to use anion effects more widely to influence such reactions in desired ways.

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Notes and references

† The ONIOM calculations[8] (B3PW91[9]/UFF[10]) have been carried out with Ph of PPh_3 and imidazole Pr^i in the MM part. The Stuttgart–Bonn Effective Core Potentials and associated basis sets[11] augmented by polarization function[12] were chosen for Ir and P. C, N and H were treated with a 6-31G** basis set.[13] Geometry optimizations, starting from solid state geometries, were carried out without any symmetry restriction with Gaussian 98.[14]

‡ *Typical synthesis*: a mixture of **1** (R = Me, A = SbF_6, 33 mg, 0.08 mmol) and insoluble $IrH_5(PPh_3)_2$ (55 mg, 0.08 mmol) in THF (5 ml) was vigorously refluxed in air for 2 h. After cooling to room temperature, 50 ml of pentane was added. A yellowish precipitate was filtered off and dried *in vacuo*. Yield: 71 mg (80%). Pure **3** can be obtained by recrystallization from $CHCl_3$/pentane.

^{1}H NMR ($CDCl_3$, 298 K): δ 8.38 (s, 1H, NCHN), 8.22 (d, 1H, $^3J_{HH}$ 5.5 Hz, py-*H*), 7.38–7.18 (m, 32H, py-*H*, Ph-*H*), 6.10 (t, 1H, $^3J_{HH}$ 6.6 Hz, py-*H*), 4.89 (s, 1H, im-*H*), 4.58 (s, 2H, CH_2), 3.38 (s, 3H, CH_3), −10.86 (dt, $^3J_{HH}$ 5.0, $^2J_{PH}$ 19.8 Hz, IrH), −21.53 (dt, $^3J_{HH}$ 5.0, $^2J_{PH}$ 18.6 Hz, IrH); ^{13}C{^{1}H} NMR ($CDCl_3$, 298 K): δ 161.97 (C_{py}), 152.7 (C_{py}), 142.43 (t, J_{PC} 6.5 Hz, $C_{carbene}$), 137.23 (C_{py}), 134.87 (t, J_{PC} 26.5, C_{Ph}), 133.61 (t, J_{PC} 6.3, C_{Ph}), 133.39 (NCN), 129.65 (C_{Ph}), 128.0 (C_{im}), 127.87 (t, J_{PC} 4.8, C_{Ph}), 125.5 (C_{py}), 124.21 (C_{py}), 55.36 (CH_2), 34.57 (CH_3); ^{31}P{^{1}H} NMR ($CDCl_3$, 298 K): δ 21.0.

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