Application of the $\pi$-accepting ability parameter of N-heterocyclic carbene ligands in iridium complexes for signal amplification by reversible exchange (SABRE)$^\dagger$

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The new $\pi$-accepting ability parameter (PAAP) appears to be the best tool to analyse the electronic properties of NHC ligands in [Ir(H)$_2$(NHC)(Py)$_3$]$^+$ complexes for SABRE. Together with the buried volume, the efficiency of hyperpolarisation transfer in SABRE, depending on the exchange rate of pyridine, can be described.

NMR is a powerful analytical tool that is widely used in the fields of chemistry, material science, and medicine. Because of the small population differences between the nuclear spin states in a magnetic field, however, NMR is intrinsically a relatively insensitive technique. This relative insensitivity can be overcome by using hyperpolarisation techniques to produce non-Boltzmann spin-state distributions. A promising approach is Signal Amplification By Reversible Exchange (SABRE), which was first described by Duckett et al.$^1$ In this method hyperpolarisation is achieved by the temporary association of a substrate and $p$-H$_2$ in the coordination sphere of a transition metal, whereupon polarisation can be transferred from the $p$-H$_2$-derived hydride ligands to the bound substrate via scalar coupling (Fig. 1).$^2$ The hyperpolarised substrate then dissociates into the solution resulting in strongly enhanced NMR signals of its unbound form.

Since the discovery of SABRE, several small molecules,$^{3,4}$ mainly aromatic nitrogen heterocycles,$^{5-8}$ have been successfully hyperpolarised. However, for the development of the SABRE technique to a level where NMR can also be used for biomedical (imaging) applications some further problems must be addressed. Recently, much progress has been made, including the development of 2D-NMR methods,$^6$ analytical applications,$^9,10$ quantification methods,$^{11}$ and compatibility with high magnetic fields$^{12-14}$ and aqueous media.$^{15-17}$ In this perspective, development and optimisation of heterogeneous$^{18,19}$ and homogeneous catalysts$^{20-25}$ are also important; detailed insight in the catalytic process can lead to a more rational design of the next generation of catalysts.

We reported earlier$^{20}$ on the influence of the steric and electronic properties of NHC ligands in iridium complexes for SABRE as quantified by the buried volume (\%$V_{\text{bur}}$)$^{26,27}$ and an analogue of the Tolman Electronic Parameter (TEP), respectively (Fig. 2).$^{28}$ We measured the performance of the catalyst in terms of pyridine signal enhancement and exchange rate. The TEP had little distinguishing power in this series of NHC ligands, and there appeared to be no correlation with the chemical shift, exchange rate, or hyperpolarisation of pyridine. Inversely, the exchange rate increases generally with \%$V_{\text{bur}}$, which is consistent with a dissociative mechanism for the exchange of pyridine. The Ir-complex with IMes$^5$ had the optimum value for exchange rate and \%$V_{\text{bur}}$, resulting in the highest enhancement factor.$^{20,21}$ We also postulated that the property that has the strongest influence on the enhancement factor is the aromatic character of the substituent.
The contribution of the π-accepting ability of the NHC ligand to the metal-NHC bond has been recognised for some time, and a new electronic parameter to describe this ability was developed only recently by Nolan, Cavallo and co-workers. They defined the π-accepting ability parameter (PAAP) as the $^{77}$Se chemical shift of the corresponding selenium in the corresponding £complex. We have previously synthesised a series of $[$Ir(Cl)(COD)-(NHC)$]$ complexes and have evaluated their performance in the hyperpolarisation transfer in SABRE. We have shown earlier that in general a higher steric bulk leads to a higher exchange rate. While unsaturated ligands (e.g. ImNPr 4, IMes 7) have slightly less steric bulk than their saturated analogues (e.g. SImNPr 3, SIMes 6), these subtle differences did not properly explain the large differences in the observed exchange rate; imidazolium derived ligands had exchange rates that are approximately 3–5 times larger than those of their saturated counterparts. These exchange rates are, however, nicely correlated with the PAAP of the ligands as shown in Fig. 4. Moreover, as noted by Cavallo et al., there is an intriguing difference in $^{77}$Se values (90 and 101 respectively) for IPent 10 and IMes 7 and IPr 9 and we show here that this is reflected in the exchange rate of pyridine.

These examples demonstrate that the PAAP represents the best tool to analyse the electronic properties of NHC ligands and contributes in this case to a better understanding of the observed reactivity. It should be kept in mind, however, that this electronic effect is certainly not the only factor that influences the exchange rate of pyridine, and an exception to the general trend can be noted in Fig. 4. Ligand SImNPr 3 has an exchange rate three times faster than its unsaturated counterpart ImNPr 4, which is in line with the large difference in PAAP. The low absolute exchange rate of SImNPr 3 can probably be attributed to the aliphatic nature of the R group and its relatively small buried volume. To illustrate the effect of buried volume further, IPr 9 was compared to the new IPent 10 catalyst. These imidazoliums with 2,6-substituted aryl groups exhibit similar $^{77}$Se values (90 and 101 respectively), but IPent 10 has a significantly higher buried volume than IPr 9 (approx. 5% based on the Se crystal structure). Based on the general trend (exchange rate $Py = 0.12115(\delta_{Se}) + 0.00246(\delta_{Se})^2 + 4.28856$, $R^2 = 0.99863$) an exchange rate of 41.6 s$^{-1}$ is expected for IPent 10, but in fact a much higher exchange rate, higher than that of any of the previously reported catalysts was observed, which must be explained by the much larger steric

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bulk (see ESI† for details). These two examples illustrate that it is important to consider all properties of a ligand at all times.

Conclusions

It is important to have a good understanding of the precise nature of the NHC-metal bond as control of the electronic and steric properties of NHC ligands can help in the design of significantly more active and selective catalyst systems. When the PAAP was introduced by Nolan, Cavallo and co-workers, it was predicted that this parameter would be suitable for more general use. Here we have shown that it indeed offers a tool to better understand the observed reactivity in a series of SABRE catalysts. The PAAP helps to explain, better than before, the observed difference in exchange rate of pyridine, which is crucial in the catalytic hyperpolarisation transfer process, between saturated and unsaturated NHC ligands. The parameter also gives insight in the remarkable difference in activity between the structurally similar ligands IMes 6 and IPr 9. Although PAAP gives a more adequate description of electronic effects than TEP, it should be kept in mind that steric effects are also important as we have demonstrated in the case of 2,6-substituted aryl ligands. Ligands IPr 9 and IPent 10 have similar PAAP values, but steric properties control the observed reactivity. To conclude, the PAAP is a valuable new addition to the current set of parameters to characterise the electronic and steric properties of NHC ligands and offers more insight in the reactivity of NHC-metal catalysts in general.

Acknowledgements

We thank the European Union (EFRD, European Fund for Regional Development) and the provinces of Gelderland and Overijssel for financially supporting the Ultrasense NMR project. The authors kindly thank Ad Swolfs and Ruud Aspers for their assistance with the 77Se NMR experiments, and Paul Tinnemans for performing the X-ray crystallographic analysis.

Notes and references


