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COMMUNICATION

Highly active iridium(I) complexes for the selective hydrogenation of carbon–carbon multiple bonds†

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New iridium(I) complexes, bearing a bulky NHC/phosphine ligand combination, have been established as extremely efficient hydrogenation catalysts that can be used at low catalyst loadings, and are compatible with functional groups which are often sensitive to more routinely employed hydrogenation methods.

Catalytic hydrogenation is a well-established method of elevated importance in organic synthesis.[1] Indeed, there are many known methods for the hydrogenation of double bonds under both heterogeneous[1b] and homogeneous[2] catalysis. Perhaps the most commonly used homogeneous hydrogenation complexes are the catalysts of Wilkinson[3] and Crabtree,[4] with the latter having been shown to display greater efficiency in a more general sense.[4b] Although Crabtree's iridium-based species is a very mild and effective catalyst, it is known to be thermally unstable and is prone to deactivation *via* the irreversible formation of inactive clusters.[5] In an effort to solve this problem, Nolan[6] and Buriak[7] have elegantly established that manipulation of the ligand sphere around the iridium centre can improve stability whilst maintaining the catalytic activity of the complex. Within our own laboratories, we have accessed a series of novel iridium(I) complexes containing bulky *N*-heterocyclic carbene (NHC) ligands alongside appreciably encumbered phosphine ligands (Fig. 1).[8] These complexes have shown themselves to be highly efficient hydrogen isotope exchange catalysts, with activity far in excess of the industry standard, Crabtree's catalyst.

Fig. 1 Iridium(I) complexes possessing bulky NHC and phosphine combinations.

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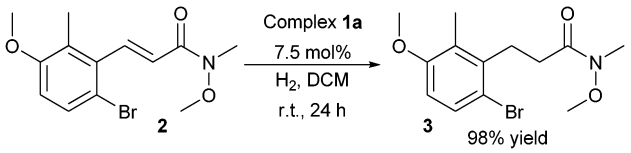
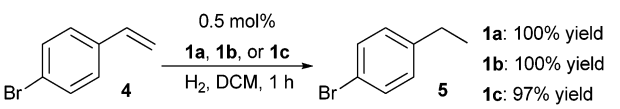
† Electronic supplementary information (ESI) available: Experimental protocols, catalyst preparation procedures, and full characterization data for novel compounds. See DOI: 10.1039/c1cc14367k

As part of a total synthesis project within our laboratories, a key step was the required reduction of an alkene in the presence of an aryl bromide, as in the Weinreb amide (**2**). Traditional catalysts such as Pd/C, PtO_2, Rh/alumina, and $Pd(OH)_2$/C failed to deliver the targeted product (**3**), and only debrominated material was observed.[9] However, when we employed our iridium complex **1a** in 7.5 mol%, we were pleased to obtain the desired product (**3**) in an excellent 98% yield (Scheme 1), with no concomitant dehalogenation.



Scheme 1 Selective hydrogenation of **2** with complex **1a**.

From this satisfying outcome, and based on the outstanding levels of activity shown in C–H activation,[8] we felt that these same iridium-based species (**1**) had the potential to act as selective hydrogenation catalysts in a more general sense. To investigate this hypothesis, we chose a number of substrates containing different functional groups which were potentially sensitive to hydrogenation conditions. We initiated this study with another aryl bromide, 4-bromostyrene (**4**), and, in turn, obtained high yields of the corresponding saturated product with only 0.5 mol% catalyst loading after 1 h (Scheme 2). As observed previously, the bromide unit also remained intact under the conditions employed. Notably, these results were entirely in line with those obtained when we applied Crabtree's catalyst (0.5 mol%, 1 h, quantitive yield), establishing that complexes **1a–c** were catalysts with, at least, competitive levels of activity for application in the field of hydrogenation.



Scheme 2 Hydrogenation of **4** with complexes **1a–c**.

The α,β-unsaturated ketone **6** was also successfully hydrogenated using complexes **1a** and **1c** (Scheme 3). Again, using only 0.5 mol% catalyst loading, high yields of the desired product were obtained after only 1 h. Moreover, using

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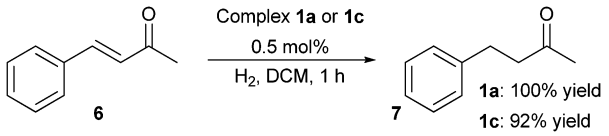
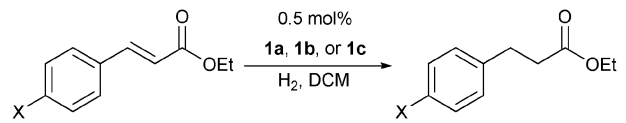


Scheme 3 Hydrogenation of **6** with complexes **1a** and **1c**.

Crabtree's catalyst, only 54% of **6** was converted to **7** under the same reaction conditions. Disappointingly, in this case, complex **1b** proved to be rather unreliable, delivering irreproducible results. Nevertheless, levels of enhanced efficiency over Crabtree's catalyst were beginning to emerge.

In order to probe the scope of tolerated functional groups, we next investigated three *para*-substituted arenes: an aryl bromide, a benzyl protected phenol, and a nitro arene (Table 1). At only 0.5 mol% catalyst loading, high yields of the desired saturated compounds were obtained. These reactions proceeded in short reaction times of 1–1.25 h for substrates **8** and **10**, and over a slightly longer period of 4 h for compound **12**. Importantly, the potentially sensitive bromo, benzyl, and nitro units remained intact following reactions with all three catalysts (**1a–c**), further illustrating the mild and selective nature of the emerging systems. Although Crabtree's catalyst performed well with substrate **12** (4 h; full conversion; 87% yield), it was less active in the hydrogenation of **8** and **10**, resulting in incomplete reactions after 1 h (92% and 28% conversions, respectively) under the conditions shown in Table 1.

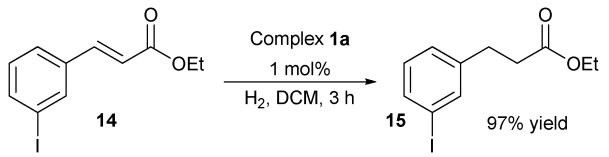
Table 1 Hydrogenation studies with substrates **8**, **9**, and **12**[a]



Entry	Complex	X	Substrate	Product	Time	Yield[b]
1	**1a**	Br	**8**	**9**	1 h	99
2	**1b**	Br	**8**	**9**	1 h	94
3	**1c**	Br	**8**	**9**	1 h	100
4	**1a**	OCH_2Ph	**10**	**11**	1 h	100
5	**1b**	OCH_2Ph	**10**	**11**	1.25 h	100
6	**1c**	OCH_2Ph	**10**	**11**	1 h	98
7	**1a**	NO_2	**12**	**13**	4 h	100
8	**1b**	NO_2	**12**	**13**	4 h	90
9	**1c**	NO_2	**12**	**13**	4 h	94

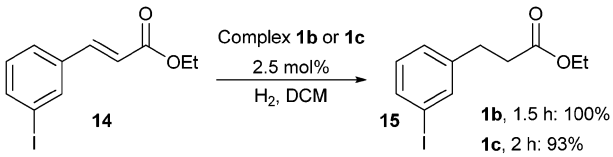
[a] Reaction conditions: substrate (0.2 mmol), complex **1a**, **1b**, or, **1c** (0.001 mmol), DCM (4 mL), r.t., H_2 (1 atm). [b] Isolated yields.

In the hydrogenation of substrate **14**, containing the halogen in the *meta*-position, we were pleased to obtain the desired saturated product **15** in an excellent 97% yield using complex **1a**, despite a slightly higher catalyst loading (1 mol%) being required (Scheme 4). Additionally, no cleavage of the aryl iodide was observed. When Crabtree's catalyst was employed under the same reaction conditions, only 1% conversion to product **15** was observed.



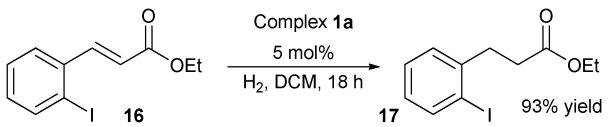
Scheme 4 Hydrogenation of **14** with complex **1a**.

With regards to complexes **1b** and **1c** and the same substrate (**14**), use of 2.5 mol% catalyst was required to produce high yields of product **15** (Scheme 5). However, even at this slightly elevated loading, these complexes remained more active than Crabtree's catalyst (1.5 h; 39% conversion).



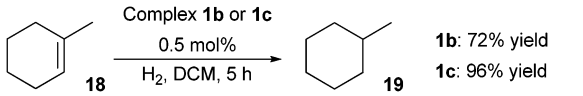
Scheme 5 Hydrogenation of **14** with complexes **1b** and **1c**.

Based on the results accumulated to this stage, the tribenzylphosphine complex **1a** was emerging as the catalyst of choice. In relation to this and in terms of a more sterically encumbered substrate, the potentially more challenging *ortho*-iodo α,β-unsaturated ester **16** was investigated. In this instance, 5 mol% of complex **1a** was required over an 18 h reaction time to deliver the desired product in 93% yield (Scheme 6). Under the same conditions using Crabtree's catalyst, only 60% of the substrate was converted to product, again illustrating the elevated catalytic activity of complex **1a**. Unfortunately, complexes **1b** and **1c** were not efficient in the reduction of **16**.



Scheme 6 Hydrogenation of **16** with complex **1a**.

To further explore the capabilities of these catalysts, the investigation was extended to tri- and tetrasubstituted olefins, **18** and **20**. It has been shown previously that Crabtree's catalyst is effective in the hydrogenation of these more sterically encumbered olefins,[4,7b] Pleasingly, by employing complex **1b** or **1c**, substrate **18** was successfully hydrogenated (Scheme 7), producing methylcyclohexane (**19**) in high yields (72% and 96%, respectively). It should also be noted that increasing the catalyst loading of complex **1c** to 1 mol% delivered a 93% yield of **19** after only 30 min reaction time. Complex **1a** was unsuccessful in the hydrogenation of this same substrate. This result with trisubstituted olefin **18** was perhaps not surprising, with complex **1a** possessing the most sterically demanding ligand set from the catalysts investigated in this series.



Scheme 7 Hydrogenation of **18** with complexes **1b** and **1c**.

Similar observations were made in the hydrogenation of tetrasubstituted olefin **20**. In this case, 5 mol% of complex **1c** produced a 72% yield of **21**, whereas increasing the the

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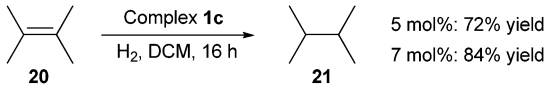
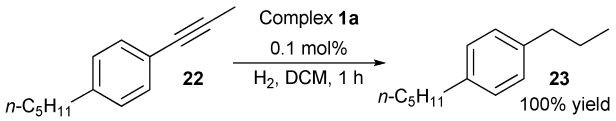
catalyst loading to 7 mol% delivered an improved 84% yield of the desired saturated product (Scheme 8).



Scheme 8 Hydrogenation of **20** with complex **1c**.

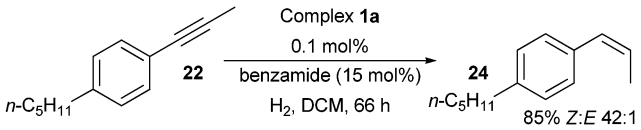
Finally, since the reduction of carbon–carbon double bonds was so successful, we decided to probe the applicability of our complexes in alkyne hydrogenation and, indeed, the semi-hydrogenation of the same class of substrate. Using the internal alkyne (**22**) we initially employed complex **1a** at 0.1 mol% loading, and, after a reaction time of only 1 h, the alkyne was reduced completely, yielding the alkane (**23**) quantitatively (Scheme 9).



Scheme 9 Complete hydrogenation of alkyne **22**.

From this result, it was clear that complex **1a** was extremely active in the hydrogenation of alkynes and so, in order to be able to achieve the selective reduction of the alkyne to the alkene, the catalytic efficiency of the complex would have to be lessened. In this regard, an effective way to tune the reactivity of transition metal complexes is to use a suitable poison, with this method often being employed within palladium catalysis.[10] With a view to finding a suitable poison for our catalysts, we considered an additive compound which has previously been found to be a challenging substrate within associated hydrogen–deuterium exchange reactions, namely benzamide.[11] Although complexes **1a–c** are capable of labelling this substrate at low catalyst loadings,[8] the levels of deuteration are less elevated than those typically observed for other substrates. This is thought to be due to strong coordination of this substrate to the iridium centre hindering the progress of the required catalytic cycle. Thus, we thought that benzamide could be an effective poison to allow the selective hydrogenation of alkynes with the emerging class of catalysts (**1**). Indeed, when 15 mol% of benzamide was employed with 0.1 mol% of complex **1a**, we were pleased to obtain an 85% conversion of alkyne **22** to alkene **24**, with an excellent selectivity for the *Z*-alkene (Scheme 10).[12]

In summary, new iridium(I) complexes (**1**) bearing a bulky NHC/phosphine ligand combination have been established as extremely efficient hydrogenation catalysts.† These species can be used at low catalyst loadings over short reaction times and



Scheme 10 Selective hydrogenation of alkyne **22**.

are compatible with functional groups which are sensitive to alternative and more widely employed hydrogenation methods. Complex **1a** has emerged as the most generally effective of the three complexes and leads to hydrogenation efficiencies that are elevated over those displayed by Crabtree's catalyst. Additionally, with more demanding, tri- and tetrasubstituted, olefin substrates the less encumbered complex (**1c**) shows activity levels which are, again, at least competitive with those shown with Crabtree's catalyst. Furthermore, employing benzamide as a poison, catalyst **1a** has been shown to selectively hydrogenate an alkyne to an alkene with high *Z*-selectivity.

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12 Following this process, the organic mass balance was made up of alkyne starting material **22** (5%) and the fully saturated alkane **23** (10%).

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