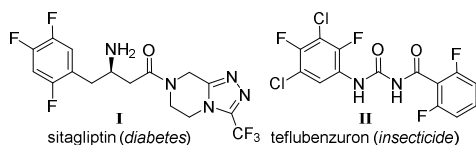


# Room Temperature Regioselective Catalytic Hydrodefluorination of Fluoroarenes with *trans*-[Ru(NHC)<sub>4</sub>H<sub>2</sub>] via a Concerted Nucleophilic Ru-H Attack Pathway

Mateusz K. Cybulski,<sup>[a]</sup> David McKay,<sup>[b]</sup> Stuart A. Macgregor,<sup>\*,[b]</sup> Mary F. Mahon<sup>[a]</sup> and Michael K. Whittlesey<sup>\*,[a]</sup>

**Abstract:** The efficient and highly selective room temperature hydrodefluorination (HDF) of fluoroarenes by the *trans*-[Ru(IME<sub>4</sub>)<sub>2</sub>H<sub>2</sub>] catalyst, **3**, is reported. Mechanistic studies show **3** acts directly in catalysis without any ligand dissociation and DFT calculations indicate a concerted nucleophilic attack mechanism. The calculations fully account for the observed selectivities which corroborate earlier predictions regarding the selectivity of HDF.

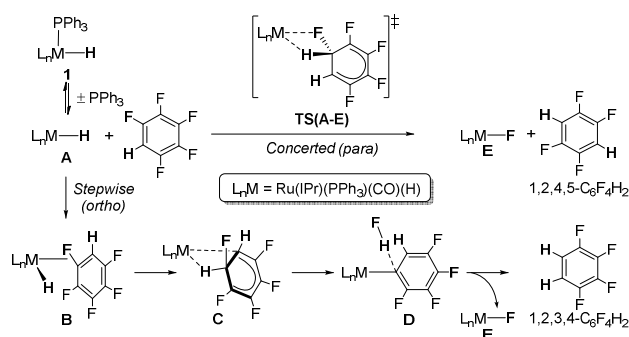
The presence of partially fluorinated aromatic rings in many high value pharmaceuticals and agrochemicals (e.g. **I** and **II**, Scheme 1)<sup>[1]</sup> has fuelled interest in the use of catalytic hydrodefluorination (HDF) as a route to such functionalities by F/H substitution of perfluorinated substrates.<sup>[2–4]</sup> However, to achieve this the development of more active and more selective HDF catalysts is still required, as highlighted by the very specific substitution patterns in **I** and **II**. This is challenging as HDF becomes increasingly difficult as the number of fluorine substituents decreases, and this difficult process must be achieved with a high degree of regiocontrol. Chemoselectivity is also an issue, as selective C–F activation must be targeted over potentially deactivating C–H activation pathways.



**Scheme 1.** Examples of commercially important fluorinated molecules.

In previous work on HDF catalysis using N-heterocyclic carbene (NHC) ruthenium hydride complexes we have combined experimental and computational data to develop a mechanistic framework for the logical design of new catalysts with improved activity and regiocontrol. While our first catalyst system, [Ru(IPr)(PPh<sub>3</sub>)<sub>2</sub>(CO)H<sub>2</sub>] (**1**)<sup>[5,6]</sup>, showed only modest activity, catalytic HDF of C<sub>6</sub>F<sub>6</sub> at 70 °C did proceed with a remarkably high and very unusual *ortho*-regioselectivity to give 1,2,3,4-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub>. DFT studies on the HDF of C<sub>6</sub>F<sub>5</sub>H characterised two mechanisms based on the nucleophilicity of a hydride ligand in the 5-coordinate intermediate **A** formed via PPh<sub>3</sub> loss from **1** (Scheme 2).<sup>[7,8]</sup> These were

a concerted pathway in which F/H exchange occurred in a single step, or, after fluoroarene coordination (**B**), a stepwise pathway featuring insertion into the Ru–H bond, HF elimination and protonolysis of Ru–aryl intermediate **D** to release C<sub>6</sub>F<sub>4</sub>H<sub>2</sub> and Ru–F species **E**. These two pathways exhibited different kinetic selectivities, the concerted mechanism leading to the *para*-HDF product 1,2,4,5-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub>, while the stepwise process favoured *ortho*-HDF and formation of 1,2,3,4-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub>. Overall, the stepwise pathway proved more accessible and so accounted for the observed regioselectivity.



**Scheme 2.** Nucleophilic hydride attack mechanism in [Ru(IPr)(PPh<sub>3</sub>)<sub>2</sub>(CO)H<sub>2</sub>] catalysed HDF.

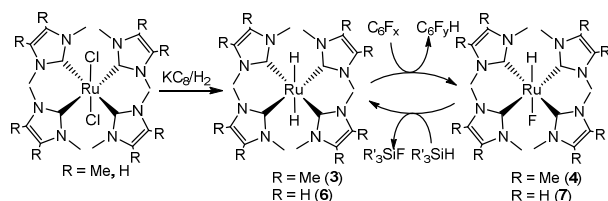
Having identified hydride nucleophilicity as a key element in these Ru-catalysed HDF reactions we turned to the more electron-rich, *trans*-dihydride complex [Ru(IEt<sub>2</sub>Me<sub>2</sub>)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>H<sub>2</sub>] (**2**).<sup>[9,10]</sup> This did indeed give higher activity, with C<sub>6</sub>F<sub>6</sub> being converted to difluorobenzene through four HDF cycles at 90 °C. However, this was counterbalanced by poorer regioselectivity, with both the 1,2- and 1,4-isomers of C<sub>6</sub>F<sub>2</sub>H<sub>4</sub> being formed. We reasoned that this may reflect the lability of the PPh<sub>3</sub> ligands in this system, resulting in a mixture of 5- and 6-coordinate Ru species in solution. The former could access both stepwise and concerted pathways, while for the latter, the concerted process would be the only option. We now report on catalytic HDF with a new catalyst, *trans*-[Ru(IME<sub>4</sub>)<sub>2</sub>H<sub>2</sub>] (**3**).<sup>[11]</sup> In this system the use of four strongly bound NHC ligands aims both to enforce coordinative saturation and enhance hydride nucleophilicity. We show that **3** is capable of taking C<sub>6</sub>F<sub>6</sub> to 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub> at room temperature; moreover the intermediate steps all occur in a highly selective fashion. DFT calculations rationalise the observed outcomes.

The *trans*-dihydride complex **3** (Scheme 3) was reported previously by Wolf upon reduction of [Ru(IME<sub>4</sub>)Cl<sub>2</sub>] with LiAlH<sub>4</sub>, although it could only be obtained as an impure solid in low yield.<sup>[12]</sup> If KC<sub>8</sub>/H<sub>2</sub> is instead used as the reductant, **3** can be isolated as an analytically pure yellow microcrystalline solid in high (80%) yield (Scheme 3). The high

[a] Mr M. K. Cybulski, Dr M. F. Mahon, Prof. M. K. Whittlesey  
Department of Chemistry, University of Bath, Claverton Down, Bath,  
BA2 7AY, UK. E-mail: m.k.whittlesey@bath.ac.uk

[b] Dr D. McKay, Prof. S. A. Macgregor  
Institute of Chemical Sciences, Heriot Watt University, Edinburgh,  
EH14 4AS, UK. E-mail: S.A.Macgregor@hw.ac.uk  
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symmetry of the molecule led to a very simple  $^1\text{H}$  NMR spectrum consisting of just three resonances at  $\delta = 3.37$ , 1.97 and -8.14 ppm in a 24:24:2 ratio.



**Scheme 3.** Synthesis and hydrodefluorination chemistry of *trans*-[Ru(NHC) $_4$ H $_2$ ].

Upon addition of a stoichiometric amount of  $\text{C}_6\text{F}_6$  to a benzene solution of **3** at room temperature, rapid HDF took place to afford [Ru(IME $_4$ ) $_4$ HF] (**4**) and  $\text{C}_6\text{F}_5\text{H}$ .<sup>[13]</sup> The X-ray structure of **4** (ESI) confirmed the same *trans*-H-Ru-F geometry as found in [Ru(IEt $_2$ Me $_2$ ) $_2$ (PPh $_3$ ) $_2$ HF] (**5**), albeit with a lengthening of the Ru-F distance (2.3070(18) Å vs 2.264(2) Å). **4** exhibits approximate  $C_4$  molecular symmetry around the H-Ru-F axis. The presence of the weakly coordinated fluoride ligand *trans* to hydride is reflected in the low frequency of the Ru-H chemical shift of **4** ( $\delta = -23.19$  ppm). Addition of 5 eq  $\text{Et}_3\text{SiH}$  to **4** brought about the rapid and clean reformation of **3** at room temperature (Scheme 3).<sup>[14]</sup>

Table 1 summarizes the results of catalytic HDF with **3** (5 mol%) in benzene with a silane as reductant.  $\text{C}_6\text{F}_6$  underwent two HDF cycles within ca. 5 min (TOF > 480 h $^{-1}$ ) at room temperature to give the para-HDF product, 1,2,4,5- $\text{C}_6\text{F}_4\text{H}_2$ . The reaction is therefore notable not only for taking place at room temperature,<sup>[15]</sup> but also in that **3** exhibits a different regioselectivity to **1**. 1,2,4,5- $\text{C}_6\text{F}_4\text{H}_2$  continued to react further, albeit far more slowly, undergoing another two HDF cycles over ca. 1 month to ultimately give 1,4- $\text{C}_6\text{F}_2\text{H}_4$  (entry 1). When the HDF of  $\text{C}_6\text{F}_6$  was performed at 90 °C, full conversion to 1,4- $\text{C}_6\text{F}_4\text{H}_2$  was complete in 10 h (entry 1). The formation of low fluorine-content products was investigated using a range of less fluorinated substrates (entries 2-5). HDF of 1,2,4,5- $\text{C}_6\text{F}_4\text{H}_2$  first formed 1,2,4- $\text{C}_6\text{F}_3\text{H}_3$ , which then reacted onwards to give 1,4- $\text{C}_6\text{F}_2\text{H}_4$  (entries 2 and 3). No further reduction of 1,4- $\text{C}_6\text{F}_2\text{H}_4$  to  $\text{C}_6\text{FH}_5$  was observed, although fluorobenzene could be formed from both the 1,2- and 1,3-isomers of  $\text{C}_6\text{F}_2\text{H}_4$  (entries 4 and 5). No reduction to benzene was observed.<sup>[16]</sup>

Variation of the silane reductant (entries 6-10) established that those with mixed aryl/alkyl substituents (PhMe $_2$ SiH, Ph $_2$ MeSiH), as well as secondary alkyl silanes (Et $_2$ SiH $_2$ ), performed similarly to Et $_3$ SiH, although lower reactivity was found with aryl silanes (Ph $_3$ SiH, Ph $_2$ SiH $_2$ ).<sup>[14]</sup> Replacement of the IME $_4$  ligand by the less donating 1,3-dimethylimidazol-2-ylidene (IME $_2$ ) ligand (Scheme 3) also had a noticeable effect, [Ru(IME $_2$ ) $_4$ H $_2$ ] (**6**; ESI) displaying lower activity than **3** (entries 11 and 12). This appeared to result from the relatively poor solubility of the corresponding hydride fluoride complex, [Ru(IME $_2$ ) $_4$ HF] (**7**; ESI) in solution; even at 90 °C, a fine yellow precipitate of **7** could be observed in catalytic HDF reactions.

Given the coordinative saturation of both **3** and **5**, the potential for dissociation of an NHC from either ruthenium complex was probed. The strength of metal-NHC bonds<sup>[17]</sup> has led to carbenes being considered as innocent spectator ligands which do not dissociate readily from metal centres.<sup>[18]</sup> Indeed, no exchange between **3** and free IEt $_2$ Me $_2$  (3 eq) was observed at room temperature, and so any involvement of unsaturated species such as [Ru(IME $_4$ ) $_3$ H $_2$ ] can be ruled out in the HDF reactions in Table 1 conducted at room temperature. However, upon heating at 90 °C,

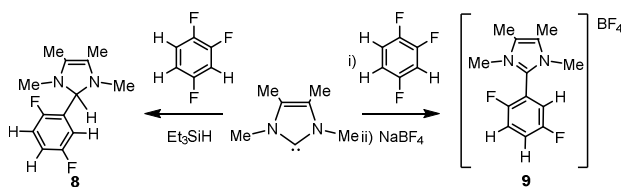
**Table 1.** [Ru(NHC) $_4$ H $_2$ ] catalysed hydrodefluorination.<sup>a</sup>

Entry	Cat	Substrate	Reductant	Product	T [°C]	t [h]	TON
					25	740	80
1	<b>3</b>	$\text{C}_6\text{F}_6$	Et $_3$ SiH	1,4- $\text{C}_6\text{F}_2\text{H}_4$	25/90 <sup>b</sup>	10	80
2	<b>3</b>	1,2,4,5- $\text{C}_6\text{F}_4\text{H}_2$	Et $_3$ SiH	1,4- $\text{C}_6\text{F}_2\text{H}_4$	90	10	40
3	<b>3</b>	1,2,4- $\text{C}_6\text{F}_3\text{H}_3$	Et $_3$ SiH	1,4- $\text{C}_6\text{F}_2\text{H}_4$	90	9	20
4 <sup>c</sup>	<b>3</b>	1,2- $\text{C}_6\text{F}_2\text{H}_4$	Et $_3$ SiH	$\text{C}_6\text{FH}_5$	120	157	20
5 <sup>c</sup>	<b>3</b>	1,3- $\text{C}_6\text{F}_2\text{H}_4$	Et $_3$ SiH	$\text{C}_6\text{FH}_5$	120	539	20
6	<b>3</b>	$\text{C}_6\text{F}_6$	PhMe $_2$ SiH	1,4- $\text{C}_6\text{F}_2\text{H}_4$	25	740	80
7	<b>3</b>	$\text{C}_6\text{F}_6$	Ph $_2$ MeSiH	1,4- $\text{C}_6\text{F}_2\text{H}_4$	90	17	80
8 <sup>d</sup>	<b>3</b>	$\text{C}_6\text{F}_6$	Ph $_3$ SiH	$\text{C}_6\text{F}_5\text{H}$ (79%) + 1,2,4,5- $\text{C}_6\text{F}_4\text{H}_2$ (21%)	25	740	18.5
9	<b>3</b>	$\text{C}_6\text{F}_6$	Et $_2$ SiH $_2$	1,4- $\text{C}_6\text{F}_2\text{H}_4$	25/90 <sup>b</sup>	9	80
10	<b>3</b>	$\text{C}_6\text{F}_6$	Ph $_2$ SiH $_2$	1,2,4,5- $\text{C}_6\text{F}_4\text{H}_2$	25	264	40
11	<b>6</b>	$\text{C}_6\text{F}_6$	Et $_3$ SiH	1,2,4,5- $\text{C}_6\text{F}_4\text{H}_2$	25	6	40
12	<b>6</b>	$\text{C}_6\text{F}_6$	Et $_3$ SiH	1,4- $\text{C}_6\text{F}_2\text{H}_4$	90	103	80

[a] Reaction conditions: 0.1 M fluoroarene, 0.5 M silane, 5 mol% **3** or **5**, 0.5 mL  $\text{C}_6\text{H}_6$ , conversions determined by  $^{19}\text{F}$  NMR spectroscopy. [b] Temperature raised to 90 °C after ca. 5 min at 25 °C. [c] Solvent = toluene. [d] Product distribution is % of main products/total % of all HDF products.

new hydride resonances were observed in the same  $\delta = -8$  ppm hydride region of the proton NMR spectrum as **3**, suggesting that carbene dissociation and exchange is possible at higher temperature.<sup>[19]</sup>

To address whether any dissociated IME $_4$  could therefore play a similar role to that recently found for alkylphosphines in catalysing HDF,<sup>[20]</sup> free IME $_4$  was heated between 70-90 °C with 1,2,4- $\text{C}_6\text{F}_3\text{H}_3$  in the presence of Et $_3$ SiH. The addition product **8** (ESI) and Et $_3$ SiF were formed in a 1:1 ratio (Scheme 4). Activation at the 2-position (i.e. *para* to H rather than *para* to F) was confirmed by structural characterisation of the imidazolium salt **9**, which was formed when IME $_4$  and 1,2,4- $\text{C}_6\text{F}_3\text{H}_3$  were heated together in the absence of any silane (ESI).<sup>[21]</sup> Crucially, heating **7** at 90 °C in both the presence and absence of Et $_3$ SiH resulted in <15% conversion to 1,4- $\text{C}_6\text{F}_4\text{H}_2$  upon fluoroarene elimination. This shows there is only a low level of the NHC-mediated stoichiometric HDF and confirms the need for Ru in the reactions of **3**. Moreover, the absence of **8** at the end of catalytic runs with **3** shows that 16e [Ru(IME $_4$ ) $_3$ H $_2$ ] is not catalytically relevant even in the high temperature HDF runs.

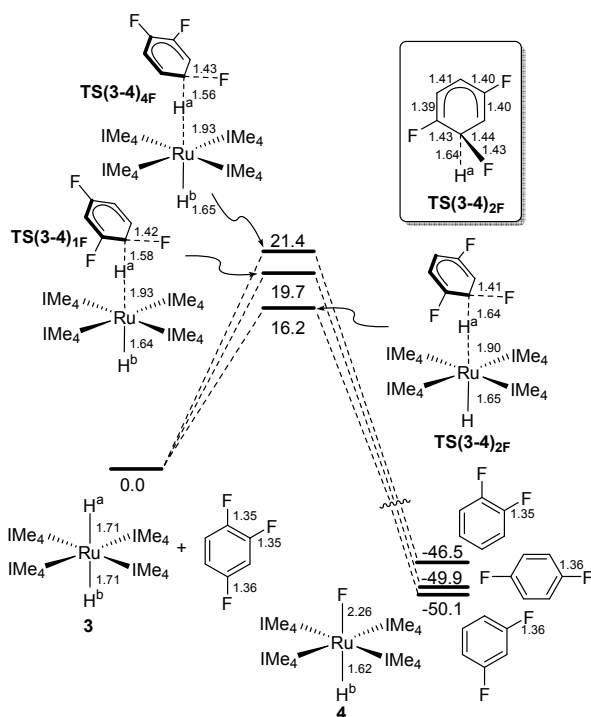


**Scheme 4.** Stoichiometric C-F activation reactions of 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> with IMe<sub>4</sub>.

DFT calculations were used to account for the selectivity of the various HDF reactions in Table 1.<sup>[22]</sup> As a stepwise HDF process based on initial NHC/fluoroarene substitution can be ruled out experimentally, the calculations focused on the concerted mechanism and applied this to the full range of fluoroarenes C<sub>6</sub>F<sub>6-n</sub>H<sub>n</sub> (n = 0-5). The results obtained with 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> are typical and details are provided in Figure 1. The lowest energy pathway involves attack of the hydride ligand at the C2 position of the arene and proceeds with a free energy barrier (relative to **3** + free 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub>) of 16.2 kcal/mol. The transition state involved, **TS(3-4)<sub>2F</sub>**, features a near-linear {Ru...H<sup>a</sup>...C2} moiety (171.9°) and elongated Ru...H and C2-F2 distances of 1.90 Å and 1.41 Å respectively. As this occurs, the new C2-H<sup>a</sup> bond begins to form (1.64 Å) and a shortening of the *trans* Ru-H<sup>b</sup> distance is seen (1.65 Å) in response to the weakening of the Ru-H<sup>a</sup> interaction. The orientation of the approaching fluoroarene (as defined by the C<sub>6</sub> plane) is offset by approximately 40° relative to the best-fit plane containing Ru and the four C2 carbons of the IMe<sub>4</sub> ligands. **TS(3-4)<sub>2F</sub>** exhibits a Meisenheimer-type geometry with elongation of the *Cipso-Cortho* bonds (see inset, Figure 1), although H-transfer onto C is more progressed than the C-F bond cleavage, the C2-F2 bond being only 0.06 Å longer than in free 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub>. The Ru...F2 distance is also rather long (3.70 Å), but characterisation via IRC calculations confirms that F2 does move onto the metal centre to generate **4** and release the 1,4-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub> product all in one step.<sup>[23]</sup> This HDF process is extremely exergonic (ΔG = -49.9 kcal/mol).

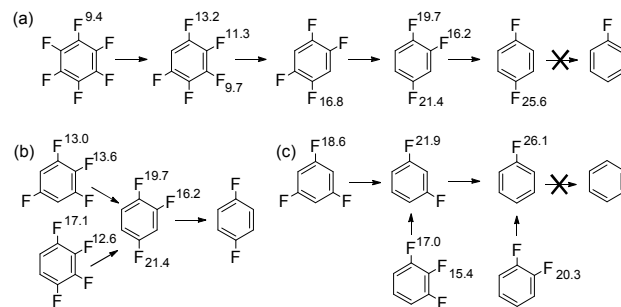
The alternative HDF at the C1 and C4 positions of 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> proceed via transition states **TS(3-4)<sub>1F</sub>** and **TS(3-4)<sub>4F</sub>** at +19.7 kcal/mol and +21.4 kcal/mol respectively. These display similar geometries to **TS(3-4)<sub>2F</sub>**, although with somewhat longer Ru...H<sup>a</sup> and shorter C1/C4...H<sup>a</sup> distances. These later geometries (in terms of H-transfer) are consistent with the higher computed barriers which indicate a clear kinetic preference for HDF at the 2-position, in line with experiment where only that process is observed (Table 1, entry 3).

The DFT study was extended to the HDF of other fluoroarenes by **3** starting with C<sub>6</sub>F<sub>6</sub>. Results are shown in Figure 2(a) as calculated barriers (relative to **3** and the appropriate fluoroarene in each case) for each HDF step. As seen previously,<sup>[7b]</sup> there is a general increase in the barrier as the number of F-substituents is reduced and this is reflected in the more forcing conditions that are required experimentally to achieve HDF with lower fluorinated substrates. The pattern of the F-substituents also directs the selectivity. We have previously shown that the concerted mechanism is favoured most by the presence of *ortho*-F substituents which cause a weakening of the target C-F bond; *meta*-F substituents also reduce barriers (although to a lesser extent), while *para*-F substituents can actually cause a slight increase in the barrier.<sup>[7b]</sup> These patterns are borne out here, with C<sub>6</sub>F<sub>5</sub>H reacting at the 4-position (this having two *ortho*-F and two *meta*-F substituents) and, as seen in Figure 1, 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> reacts at the 2-position (its *ortho*-F and *meta*-F substituents trumping the 1-position which has one *ortho*-F and one *para*-F substituent). HDF of 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub> has a high predicted barrier of 25.6 kcal/mol and so,



**Figure 1.** Computed profiles (ωB97xD//BP86, free energies in benzene, kcal/mol) for the HDF of 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> by [Ru(IMe<sub>4</sub>)<sub>4</sub>H<sub>2</sub>], **3**. Selected distances are shown in Å and the inset provides additional information for **TS(3-4)<sub>2F</sub>**.

experimentally, the catalytic HDF of C<sub>6</sub>F<sub>6</sub> proceeds to, but stops at, 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub>. Figures 2(b) and (c) consider a range of other fluoroarene substrates. Both 1,2,3,4- and 1,2,3,5-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub> are predicted to form 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> and hence 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub> (Figure 2(b)). Figure 2(c) shows that HDF of both 1,2,3- and 1,3,5-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> is predicted to be accessible (barriers of 15.4 kcal/mol and 18.6 kcal/mol respectively), and that both species will form 1,3-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub>. The *meta*-disposition of the F-substituents in this isomer (compared to the unfavourable *para*-arrangement in 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub>) makes HDF to C<sub>6</sub>FH<sub>5</sub> possible via a barrier of 21.9 kcal/mol. As expected, the *ortho* F atom arrangement in 1,2-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub> makes HDF even more accessible (ΔG<sup>‡</sup> = 20.3 kcal/mol) and so fluorobenzene can also be accessed via this route, as is indeed observed experimentally. HDF of fluorobenzene has a significantly higher barrier of 26.1 kcal/mol and is not observed.



**Figure 2.** Selectivity of HDF for a range of fluoroarene substrates: (a) C<sub>6</sub>F<sub>6</sub> gives 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub>; (b) 1,2,3,4-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub> and 1,2,3,5-C<sub>6</sub>F<sub>4</sub>H<sub>2</sub> give 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub>; and (c) 1,3,5-

C<sub>6</sub>F<sub>3</sub>H<sub>3</sub>, 1,2,3-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> and 1,2-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub> give C<sub>6</sub>FH<sub>5</sub>. In each case the calculated barrier is indicated in kcal/mol (ωB97XD/BP86, free energies in benzene).

In summary, room temperature, selective catalytic HDF of C<sub>6</sub>F<sub>6</sub> to 1,4-C<sub>6</sub>F<sub>2</sub>H<sub>4</sub> has been demonstrated with the *trans*-[Ru(IME<sub>4</sub>)<sub>2</sub>H<sub>2</sub>] catalyst, **3**. Fluorobenzene can also be accessed from 1,3,5-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub> and 1,2,3-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub>. The highly electron rich character of **3** promotes the HDF reaction, which DFT calculations show proceeds via a concerted nucleophilic attack mechanism. Experimental studies indicate that **3** acts directly in catalysis and that alternative pathways based on initial ligand loss are not relevant. This also accounts for the high selectivity observed experimentally, in contrast to earlier mixed NHC/PR<sub>3</sub> catalysts.<sup>[9]</sup> Our findings corroborate earlier work that predicted the effects of the presence of other F-substituents on selectivity.<sup>[7b]</sup> Thus controlling the mechanism also controls the synthetic outcome and this insight will hopefully allow for the development of new HDF catalysts that have greater utility in synthesis.

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**Keywords:** hydrodefluorination • ruthenium • NHC • catalysis • DFT calculations

[1] a) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320-330; b) D. O'Hagan, *J. Fluorine Chem.* **2010**, *131*, 1071-1081; c) J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok and H. Liu, *Chem. Rev.* **2014**, *114*, 2432-2506.

[2] For recent reviews of HDF, see: a) M. F. Kuehnel, D. Lentz and T. Braun, *Angew. Chem. Int. Ed.* **2013**, *52*, 3328-3348; *Angew. Chem.* **2013**, *125*, 3412-3433; b) M. K. Whittlesey and E. Peris, *ACS Catal.* **2014**, *4*, 3152-3159; c) J. D. Weaver, *Synlett* **2014**, *25*, 1946-1952; d) J.-Y. Hu and J.-L. Zhang, *Top. Organomet. Chem.* **2015**, *52*, 143-196.

[3] For specific examples from the last five years, see: a) J. J. Wu and S. Cao, *Chemcatchem* **2011**, *3*, 1582-1586; b) S. H. Yow, S. J. Gates, A. J. P. White and M. R. Crimmin, *Angew. Chem. Int. Ed.* **2012**, *51*, 12559-12563; *Angew. Chem.* **2012**, *124*, 12727-12731; c) W. W. Zhao, J. J. Wu and S. Cao, *Adv. Synth. Catal.* **2012**, *354*, 574-578; d) J. H. Zhan, H. B. Lv, Y. Yu and J. L. Zhang, *Adv. Synth. Catal.* **2012**, *354*, 1529-1541; e) H. Lv, J.-H. Zhan, Y.-B. Cai, Y. Yu, B. Wang and J.-L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 16216-16227; f) P. Fischer, K. Gotz, A. Eichhorn and U. Radius, *Organometallics* **2012**, *31*, 1374-1383; g) Z. Chen, C. Y. He, Z. S. Yin, L. Y. Chen, Y. He and X. G. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 5813-5817; *Angew. Chem.* **2013**, *125*, 5925-5929; h) G. Podolan, D. Lentz and H.-U. Reissig, *Angew. Chem. Int. Ed.* **2013**, *52*, 9491-9494; *Angew. Chem.* **2013**, *125*, 9669-9672; i) Y. He, Z. Chen, C. Y. He and X. G. Zhang, *Chin. J. Chem.* **2013**, *31*, 873-877; j) S. Sabater, J. A. Mata and E. Peris, *Nat. Commun.* **2013**, *4*, 2553-2559; k) J. Xiao, J. J. Wu, W. W. Zhao and S. Cao, *J. Fluorine Chem.* **2013**, *146*, 76-79; l) H. Lv, Y.-B. Cai and J.-L. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 3203-3207; *Angew. Chem.* **2013**, *125*, 3285-3289; m) L. Zámostná, M. Ahrens and T. Braun, *J. Fluorine Chem.* **2013**, *155*, 132-142; n) O. Ekkert, S. D. A. Strudley, A. Rozenfeld, A. J. P. White and M. R. Crimmin, *Organometallics* **2014**, *33*, 7027-7030; o) H. Nakai, K. Jeong, T. Matsumoto and S. Ogo, *Organometallics* **2014**, *33*, 4349-4352; p) S. M. Senaweera, A. Singh and J. D. Weaver, *J. Am. Chem. Soc.* **2014**, *136*, 3002-3005; q) T. L. Gianetti, R. G. Bergman and J.

Arnold, *Chem. Sci.* **2014**, *5*, 2517-2524; r) S. M. Senaweera and J. D. Weaver, *J. Am. Chem. Soc.* **2016**, *138*, 2520-2523; s) A. Matsunami, S. Kuwata and Y. Kayaki, *ACS Catal.* **2016**, *6*, 5181-5185; t) V. H. Mai and G. I. Nikonov, *ACS Catal.* **2016**, *6*, 7956-7961; u) J. Krüger, C. Ehm and D. Lentz, *Dalton Trans.* **2016**, *45*, 16789-16798.

[4] For a review of non-transition metal catalysed HDF, see: T. Stahl, H. F. T. Klare and M. Oestreich, *ACS Catal.* **2013**, *3*, 1578-1587.

[5] S. P. Reade, M. F. Mahon and M. K. Whittlesey, *J. Am. Chem. Soc.* **2009**, *131*, 1847-1861.

[6] IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene.

[7] a) J. A. Panetier, S. A. Macgregor and M. K. Whittlesey, *Angew. Chem. Int. Ed.* **2011**, *50*, 2783-2786; *Angew. Chem.* **2011**, *123*, 2835-2838; b) S. A. Macgregor, D. McKay, J. A. Panetier and M. K. Whittlesey, *Dalton Trans.* **2013**, *42*, 7386-7395; c) D. McKay, I. M. Riddlestone, S. A. Macgregor, M. F. Mahon and M. K. Whittlesey, *ACS Catal.* **2015**, *5*, 776-787.

[8] A. Nova, R. Mas-Ballesté and A. Lledós, *Organometallics* **2012**, *31*, 1245-1256.

[9] M. K. Cybulski, I. M. Riddlestone, M. F. Mahon, T. J. Woodman and M. K. Whittlesey, *Dalton Trans.* **2015**, *44*, 19597-19605.

[10] IET<sub>2</sub>Me<sub>2</sub> = 1,3-diethyl-4,5-dimethylimidazol-2-ylidene.

[11] IME<sub>4</sub> = 1,3,4,5-tetramethylimidazol-2-ylidene.

[12] R. Wolf, M. Plois and A. Hepp, *Eur. J. Inorg. Chem.* **2010**, 918-925.

[13] **4** was also formed cleanly upon reaction of **3** with the less fluorinated substrate 1,2,4-C<sub>6</sub>F<sub>3</sub>H<sub>3</sub>, although more slowly (see ESI).

[14] See ESI for a study of the stoichiometric reaction of **3** with Ph<sub>3</sub>SiH.

[15] Multiple HDF steps typically require forcing conditions. See refs [3f] and [3n].

[16] HDF of monofluoarenes has been reported only rarely. a) R. J. Young and V. V. Grushin, *Organometallics* **1999**, *18*, 294-296; b) S. Kuhl, R. Schneider and Y. Fort, *Adv. Synth. Catal.* **2003**, *345*, 341-344 c) ref [3j]; d) ref [3k]; e) ref [3q].

[17] a) J. Huang, L. Jafarpour, A. C. Hillier, E. D. Stevens and S. P. Nolan, *Organometallics* **2001**, *20*, 2878-2882; b) R. Dorta, E. D. Stevens, N. M. Scott, C. Costabile, L. Cavallo, C. D. Hoff and S. P. Nolan, *J. Am. Chem. Soc.* **2005**, *127*, 2485-2495.

[18] a) T. Weskamp, F. J. Kohl, W. Hieringer, D. Gleich and W. A. Herrmann, *Angew. Chem. Int. Ed.* **1999**, *38*, 2416-2419; *Angew. Chem.* **1999**, *111*, 2573-2576; b) J. Schwarz, V. P. W. Böhm, M. G. Gardiner, M. Grosche, W. A. Herrmann, W. Hieringer and G. Raudaschl-Sieber, *Chem. Eur. J.* **2000**, *6*, 1773-1780.

[19] For examples of NHC substitution: a) P. B. Hitchcock, M. F. Lappert and P. L. Pye, *J.C.S. Dalton* **1978**, 826-836; b) L. Titcomb, S. Caddick, F. G. N. Cloke, D. J. Wilson and D. McKercher, *Chem. Commun.* **2001**, 1388-1389; c) D. P. Allen, C. M. Crudden, L. A. Calhoun and R. Wang, *J. Organomet. Chem.* **2004**, *689*, 3203-3209; d) V. Lavallo and R. H. Grubbs, *Science* **2009**, *326*, 559-562; e) D. Canseco-Gonzalez, A. Petronilho, H. Müller-Bunz, K. Ohmatsu and M. Albrecht, *J. Am. Chem. Soc.* **2013**, *135*, 13193-13203.

[20] A. Arévalo, T.-A. A., M. Flores-Alamo and J. J. García, *J. Am. Chem. Soc.* **2014**, *136*, 4634-4639.

[21] Similar reactivity has been found for more fluorinated substrates: a) N. Kuhn, J. Fahl, R. Boese and G. Henkel, *Z. Naturforsch B* **1998**, *53*, 881-886; b) E. Mallah, N. Kuhn, C. Miaichle-Mössner, M. Steimann, M. Ströbele and K.-P. Zeller, *Z. Naturforsch B* **2009**, *64*, 1176-1182; c) S. Styra, M. Melaimi, C. E. Moore, A. L. Rheingold, T. Augenstein, F. Breher and G. Bertrand, *Chem. Eur. J.* **2015**, *21*, 8441-8446; d) Z. R. Turner, *Chem. Eur. J.* **2016**, *22*, 11461-11468; e) Y. Kim and E. Lee, *Chem. Commun.* **2016**, *52*, 10922-10925.

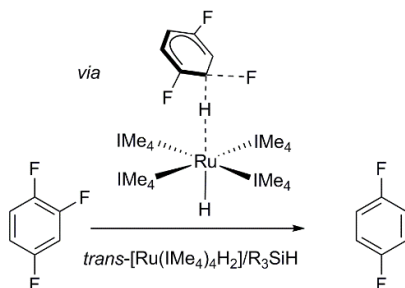
[22] DFT calculations were run with Gaussian 03/09 and were based on geometries optimised with the BP86 functional. Energies were re-computed with the ωB97XD functional and quoted free energies include a correction for C<sub>6</sub>H<sub>6</sub> solvent (PCM approach). See ESI for full details.

[23] Test calculations including the effect of benzene solvent in the optimisation procedure gave similar results. See ESI for details.

## Hydrodefluorination

Mateusz K. Cybulski, David McKay,  
Stuart A. Macgregor,\* Mary F. Mahon  
and Michael K. Whittlesey\* \_\_\_\_\_  
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Room Temperature Regioselective  
Catalytic Hydrodefluorination of  
Fluoroarenes with  $\text{trans-[Ru(NHC)}_4\text{H}_2]$   
via a Concerted Nucleophilic Ru-H  
Attack Pathway.



*Efficient and selective hydrodefluorination of fluoroarenes by a  $\text{trans-[Ru(NHC)}_4\text{H}_2]$  catalyst is reported. DFT calculations indicate that the observed selectivities are fully consistent with a concerted nucleophilic attack mechanism without any prior ligand dissociation.*