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C–F bond activation of perfluorinated arenes by a bioxazoline-derived N-heterocyclic carbene†

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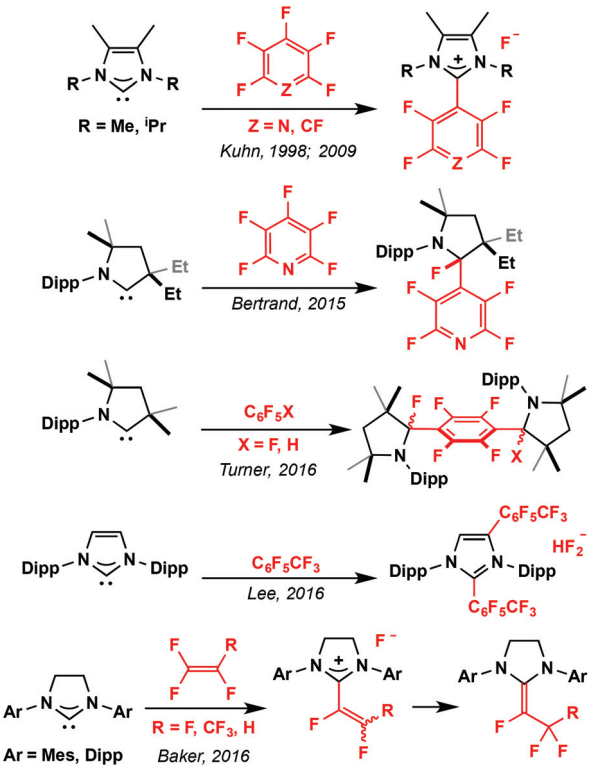
The N-heterocyclic carbene IBioxMe$_4$ enacts selective single and double C–F bond activation of octafluorotoluene and hexafluorobenzene, respectively. The formation of the fluoroarene substituted, zwitterionic imidazoliumolate products is consistent with a mechanism involving nucleophilic aromatic substitution and subsequent oxazoline ring opening by liberated fluoride.

In addition to finding diverse applications as ancillary ligands in organometallic chemistry and catalysis, N-heterocyclic carbenes (NHCs) have attracted considerable attention in their own right as organocatalysts and for their propensity for σ-bond activation.[1] Of the latter, notable landmarks include the cleavage of dihydrogen and insertion into the N–H bonds of ammonia.[2] In recent years examples demonstrating the activation of characteristically robust C–F bonds by NHCs have also begun to appear and highlight a new and potentially fertile avenue for exploration in synthetic organic chemistry.

Kuhn and co-workers were the first to describe C–F bond activation by an NHC in 1998; reactions involving the nucleophilic aromatic substitution of pentafluoropyridine by tetraalkylimidazol-2-ylidenes (Scheme 1).[3] This approach was later extended to the C–F bond activation of fluoroarenes including hexafluorobenzene, with products isolated by sequestration of fluoride as $[BF_4]^-$ by addition of $BF_3{\cdot}OEt_2$.[4] Conceptually related to transition-metal-based processes, Bertrand and co-workers went on to describe the formal oxidative addition of a C–F bond to a cyclic alkyl amino carbene in 2015 (Scheme 1).[5] To the best of our knowledge the only other examples of C–F bond activation reactions by NHCs are limited to very recent reports by Turner, Lee and Baker (Scheme 1).[6–8] The former is notable for its parallels to Bertrand's work and for the remarkable double C–H/C–F or C–F bond activation of pentafluorobenzene and hexafluorobenzene, respectively.



Scheme 1 Previous examples of C–F bond activation by NHCs. Mes = 2,4,6-$Me_3C_6H_2$; Dipp = 2,6-$^iPr_2C_6H_3$.

As part of our work exploring the coordination chemistry of bioxazoline-derived imidazol-2-ylidenes developed by Glorius and co-workers,[9] in particular the synthesis of low-coordinate rhodium and iridium complexes of the tetramethyl substituted variant IBioxMe$_4$ in fluorinated solvents,[10] we discovered that these NHCs can enact interesting C–F bond activation chemistry. Whilst assessing the suitability of a range of fluoroarenes as solvents *in situ* using NMR spectroscopy, the chemical

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†Electronic supplementary information (ESI) available: Full experimental details, NMR spectra of isolated compounds, computational details and optimised geometries in xyz format. CCDC 1517965 for **1a**. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6ob02556k

non-innocence of $IBioxMe_4$ in neat perfluorinated benzene and toluene became readily apparent by complete consumption of the NHC ligand and concomitant formation of brightly coloured red solutions within 30 minutes of dissolution at RT. In contrast, no decomposition of $IBioxMe_4$ was apparent by ^1H NMR spectroscopy after 12 h at RT using a range of partially fluorinated benzene solvents: fluorobenzene, 1,2-difluorobenzene and 1,3,5-trifluorobenzene – solvents that instead resulted in homogeneous colourless solutions.

Seeking to understand these observations, $IBioxMe_4$ was reacted with 5 equiv. of octafluorotoluene at RT, using 1,2-difluorobenzene as an inert solvent. Analysis *in situ* by ^1H and ^{19}F NMR spectroscopy indicated the quantitative formation of zwitterionic imidazoliumolate **1a**,[11] which was subsequently isolated as an air and moisture sensitive crystalline solid on addition of cyclohexane and fully characterised (32% yield; Scheme 2, Fig. 1). Based on the literature precedents discussed above,[3,4,7,8] we account for the formation of **1a** by a mechanism involving initial nucleophilic aromatic substitution of octafluorotoluene by $IBioxMe_4$, followed by ring opening of one of the oxazolines by the liberated fluoride anion.

In the solid-state structure of **1a** (Fig. 1) the fluoroarene adopts an approximately orthogonal arrangement with respect to the imidazoliumolate ring (102.99(5)°), which shows broadly similar component bonding metrics to $IBioxMe_4$·HOTf;[9c] for instance the C3–C4 bond distance (1.3845(16) *vs.* 1.354(3) Å) and N2–C1–N5 angle (106.58(11) *vs.* 105.55(16)°). Moreover, the exocyclic C4–O11 bond distance (1.2492(14) Å) is in close agreement with related zwitterionic imidazoliumolates (*ca.* 1.25 Å).[11] The structure deduced by X-ray diffraction is fully corroborated in solution by NMR spectroscopy. Notably ^1H and ^{13}C NMR spectra demonstrate reduced symmetry compared to $IBioxMe_4$ (C_s *vs.* C_{2v}), the new H_2C–F linkage is characterised by resonances at δ_H 4.91 ($^2J_{FH}$ = 47.2 Hz), δ_C 86.1 ($^1J_{FC}$ = 176 Hz), and δ_F −224.59 ($^2J_{FH}$ = 47.2 Hz), and the $^{19}F\{^1H\}$ NMR spectrum features only two C(sp^2)–F resonances at δ_F −133.05 and −138.64.

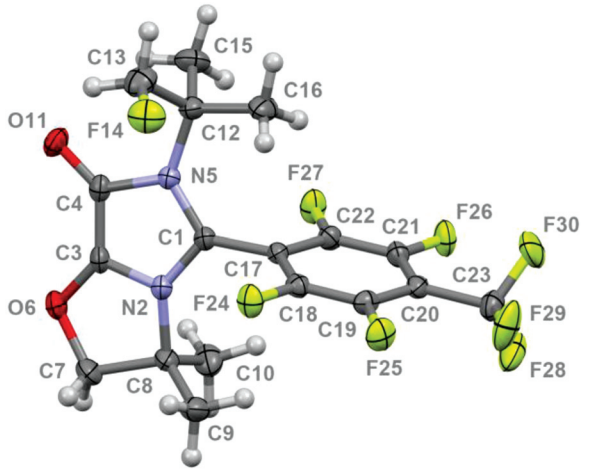
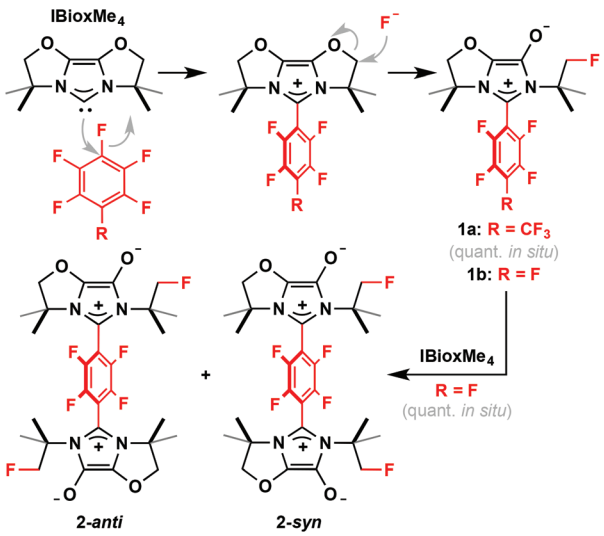


Fig. 1 Solid-state structure of **1a**; minor disordered components (CH_2F and CF_3 groups) and solvent omitted for clarify. Thermal ellipsoids drawn at the 50% probability level. Selected bond lengths (Å) and angles (°): C1–N2, 1.3359(17); C1–N5, 1.3670(14); C1–C17, 1.4704(18); C3–C4, 1.3845(16); C3–O6, 1.3635(17); C4–O11, 1.2492(14); C3–C4–O11, 133.64(14); N2–C1–N5, 106.58(11); LSplane(C1–N5) < LSplane (C17–C22), 102.99(5)°.



Scheme 2 Reactions and proposed mechanism associated with the C–F bond activation of octafluorotoluene and hexafluorobenzene by $IBioxMe_4$.

On turning to the equivalent reaction between $IBioxMe_4$ and hexafluorobenzene (5 equiv., RT in 1,2-difluorobenzene), analysis of the reaction mixture *in situ* by ^1H and ^{19}F NMR spectroscopy indicated the selective and quantitative formation of **2**, as a mixture of two rotamers (*ca.* 1 : 1 ratio), resulting from double C–F bond activation. The new bis-imidazoliumolate crystallises from the reaction mixture on standing, enabling its isolation as an extremely air and moisture sensitive red microcrystalline solid (19% yield). The structure of **2** was established spectroscopically in solution, with the double C–F bond activation of the fluoroarene confirmed by the presence of one 4F integral C(sp^2)–F resonance at δ_F −133.71/−133.63 and one 2F integral C(sp^3)–F resonance at δ_F −223.44 ($^2J_{FH}$ = 47.3 Hz)/−223.89 ($^2J_{FH}$ = 47.3 Hz) for each rotamer (*i.e.* C_i/C_{2v} symmetry). Moreover, the NMR data for the imidazoliumolate groups show good agreement with those of **1a**. Despite repeated attempts we have been so far unsuccessful in determining a suitably high quality solid-state structure of **2** (see ESI† for optimised structures).

The formation of **2** is suggested to proceed *via* a mechanism analogous to that of **1a**, *i.e. via* intermediate formation of **1b** (Scheme 2). Similar double C–F bond activation of hexafluorobenzene was observed by Kuhn.[4] The presence of an excess of hexafluorobenzene during the formation of **2** implies that the imidazoliumolate group is significantly more activating than a fluorine substituent alone. Although a more detailed computation analysis is required, corroborating this suggestion the calculated natural charge of the *para*-disposed fluoroarene carbon in **1b** is more positive that the carbon atoms of hexafluorobenzene (+0.302 *cf.* +0.290; see ESI†).

In summary, we have demonstrated that while bioxazoline-derived imidazol-2-ylidene $IBioxMe_4$ is stable in a range of partially fluorinated arene solvents (fluorobenzene, 1,2-difluorobenzene and 1,3,5-trifluorobenzene), in the presence of octafluorotoluene and hexafluorobenzene C–F bond activation ensues. These reactions result in the formation of zwitterionic imidazoliumolates presumably *via* a mechanism involving nucleophilic aromatic substitution by the NHC ligand and subsequent oxazoline ring opening by liberated fluoride. In the case of hexafluorobenzene, the substituted arene appears to be more activated towards nucleophilic attack, ultimately leading to double C–F bond activation. These reactions help further substantiate the potential of NHCs to mediate challenging bond disconnections of contemporary interest.

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