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Perturbation of $^1J_{C,F}$ Coupling in Carbon-Fluorine Bonds on Coordination to Lewis Acids: A Structural, Spectroscopic, and Computational Study

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ABSTRACT: A lithiated $m$-terphenyl ligand bearing fluorine atoms at the ortho positions of the flanking aryl rings was synthesized and characterized using single crystal X-ray diffraction, variable-temperature multinuclear NMR spectroscopy, and computational methods. Changes in $^1J_{C,F}$ on coordination to lithium as a spectroscopic observable parametrizing the strength of the C–F···Li interaction are described, and a general, qualitative relationship between C–F bond lengths, $\Delta^1J_{C,F}$ values, and the extent of C–F bond activation as a result of Lewis acid coordination is proposed.
Introduction

The unique chemical properties of fluorinated substituents have made C–F bonds a common motif within agrochemical\(^1\) and pharmaceutical\(^2\) compounds, where they have been successfully used to alter bioactivities and other target properties. Among other effects, the incorporation of fluorine in bioactive organic compounds has the ability to modulate ligand binding affinities by way of introducing new electrostatic or hydrogen-bonding effects absent in the non-fluorinated analogues.\(^3\) In studying these compounds and their mechanisms of action, it is desirable, though frequently experimentally challenging, to quantify the strength of interactions between the relevant C–F bonds and the Lewis acid (L.A.) sites they may bind.\(^4\)

The past few years have witnessed a flurry of publications describing myriad related non-covalent interactions such as agostic,\(^5\) \(\pi-\pi\),\(^6\) cation-\(\pi\),\(^7\) and dispersion force interactions.\(^8\),\(^9\) More than minor contributors to molecular geometry and electronic structure, these relatively weak interactions often play important roles in determining the structures of transition metal complexes,\(^10\) biologically relevant macromolecules,\(^11\) and host-guest complexes.\(^12\)

In comparing these C–F…L.A. interactions to more broadly studied agostic interactions, in which C–H bonds coordinate to metal centers,\(^5\) we wondered if the two might necessarily share common spectroscopic signatures. Specifically, we hypothesized that the characteristic decreases in one-bond carbon-hydrogen NMR coupling constant \((^{1}J_{C,H})\) observed in agostic interactions as a result of three-center two-electron bonding should similarly manifest as changes in \(^{1}J_{C,F}\) values in systems featuring C–F…L.A. interactions. While it has been reported that cation binding by fluorinated cavitands tends to result in decreased \(^{1}J_{C,F}\) values,\(^13\)–\(^16\) the underlying mechanism causing these changes has not yet been addressed, so the generality of this phenomenon remains an important question.
To elucidate the cause of changes in $^1J_{C,F}$ values, we sought a diamagnetic, non-cavitand system in which a strong C–F···L.A. interaction could be prepared. To this end, we targeted the lithium complex of a substituted $m$-terphenyl ligand. Reported solid-state structures of unsolvated $m$-terphenyl lithium species frequently show close C$_{\text{arene}}$···Li or C–H···Li contacts,$^{17-19}$ suggesting that a fluorine-substituted analog might exhibit persistent C–F···Li interactions.

We envisioned the ligand Terph$^F$ ($\text{Terph}^{F} = 2,6$-bis(2,6-difluoro-4-trimethylsilylphenyl)-4-tert-butylphenyl) with the intent that the trimethylsilyl and tert-butyl groups would serve both to provide solubility in hydrocarbon solvents and as convenient and distinguishable NMR “handles”.$^{20}$ The synthesis of a related semifluorinated $m$-terphenyl has been reported,$^{21}$ and we developed a similar synthetic approach for our system.

**Results and Discussion**

*Synthesis and Solid-State Structure of a Semifluorinated $m$-terphenyl Lithium*

The triazene-protected semifluorinated $m$-terphenyl 2 (Terph$^F$-N$_2$-NC$_4$H$_8$) was synthesized from the corresponding protected dibromide 1 by way of a palladium catalyzed double Negishi cross-coupling using two equivalents of 2,6-difluoro-4-(trimethylsilyl)phenylzinc chloride (Scheme 1). From this protected terphenyl, semifluorinated $m$-terphenyl iodide 3 (Terph$^F$-I) was prepared in 74% yield by refluxing with two equivalents of I$_2$ in degassed 1,2-dichloroethane for 16 hours. Lithiation of the resultant aryl iodide with $n$-BuLi in hexane furnished 4 ([Terph$^F$-Li]$_2$) in 82% yield (95% pure; by $^1$H NMR the only impurity is the protonated arene, Terph$^F$-H, 5).
Scheme 1: Convergent synthesis of semifluorinated \textit{m}-terphenyl lithium dimer 4. Synthesis of 1 from 2,6-dibromo-4-\textit{tert}-butylaniline (left). The protected, semifluorinated \textit{m}-terphenyl 2 is synthesized via a double Negishi cross-coupling utilizing 2,6-difluoro-4-trimethylsilylphenylzinc chloride and 1 (top). Deprotection of 2 with I_2 yields the corresponding terphenyl iodide, 3 (right), which is lithiated to yield 4 (bottom).

Colorless single crystals of 4 suitable for X-ray diffraction were obtained from a saturated \textit{n}-hexane solution at −40 °C. Like other base-free \textit{m}-terphenyl lithium species,\textsuperscript{17–19} 4 is dimeric in the solid-state, with two lithium atoms bridging the central carbons of the terphenyl units and C–Li distances ranging from 2.156(6) to 2.170(7) Å (Figure 1). The solid-state structure of the TerphF-Li dimer displays C–F…Li close contacts, with F–Li distances ranging from 1.925(4) to 1.945(5) Å. Each lithium center adopts a coordination geometry intermediate between square planar and tetrahedral, but best described as loosely tetrahedral (average τ_4 and τ_4′ for lithium:
0.67 and 0.66, respectively), and is coordinated by two fluorines, one from each terphenyl moiety of the dimer. Reflecting their coordination to a metal center, each of these C–F bonds are elongated by a small but significant distance (avg. 0.025 Å) relative to their corresponding unbound C–F bonds, a phenomenon that has been predicted computationally and observed in other systems with C–F⋯Li interactions evident in the solid-state.

Figure 1: Solid state structure of 4 with 50% probability ellipsoids. Hydrogen atoms, tert-butyl and trimethylsilyl groups, and lattice solvent molecules are omitted for clarity. Selected bond lengths (Å): C–Li range: 2.156(5)-2.170(7), F–Li range: 1.925(4)-1.945(5), average C–F\text{free}: 1.356(2), average C–F\text{Li bound}: 1.381(1). Average $\tau_4$ and $\tau_4'$ for lithium: 0.67 and 0.66, respectively.

Variable Temperature NMR Studies

The $^1$H NMR spectrum of 4 in C$_6$D$_6$ at room temperature exhibits four resonances, suggesting a time-averaged solution state structure in which both ligands, and both halves of each ligand, are equivalent (i.e. effective $D_{2h}$ symmetry). Unexpectedly, no signals were observed in the $^{19}$F NMR spectrum of 4 in C$_6$D$_6$ at room temperature. However, upon cooling a solution of 4 in
toluene-$d_8$ to $-10\, ^\circ C$, two signals in the 470 MHz $^{19}$F NMR spectrum appeared at $-113.58$ and $-135.63$ ppm corresponding to the free and lithium-coordinated fluorines, respectively. This implies that the absence of a $^{19}$F NMR signal at room temperature is due to peak coalescence over a 22 ppm range, leading to significant loss of signal intensity. Further cooling to $-60\, ^\circ C$ revealed a 32 Hz scalar coupling to $^7$Li ($I = 3/2$, 92.4% natural abundance, Figure S24) as observed in the peak at $-137.91$ ppm in the $^{19}$F NMR spectrum, directly indicating F–Li interactions in solution. The effects of these interactions are also apparent in the $^1$H NMR spectrum of 4 in toluene-$d_8$: below $-20\, ^\circ C$, the resonances corresponding to the two protons of each flanking aryl ring are resolved as distinct features (Figure 2), suggesting that motion of the flanking aryl rings becomes slow on the NMR timescale and that [Terph$_F$-Li$_2$]$_2$ adopts an effective $D_2$ geometry in solution at low temperature. Eyring analysis of the peak widths$^{23}$ of the $^{19}$F signals at different temperatures suggests this rotation barrier is enthalpically dominated ($\Delta H^\ddagger = 13.0(\pm0.8)$ kcal/mol), with a small, positive entropic contribution of 1.7(±0.1) cal/mol·K (Figure S1). This places an upper limit on the strength of the C–F⋯Li interaction of 13.0(±0.8) kcal/mol.
Figure 2: Variable-temperature 500 MHz $^1$H spectra of the aromatic region of 4 in toluene-$d_8$ between 22 and $-70$ °C.

At or below $-60$ °C in the $^1$H NMR spectrum, the four flanking aryl protons on the exterior of the Terph$_F$-Li dimer appear as a doublet at 6.93 ppm with a three-bond proton-fluorine coupling constant ($^3J_{H,F}$) of 8.8 Hz. The flanking aryl protons on the interior of the dimer appear as a “virtual triplet” at 6.66 ppm, with $^3J_{H,F}$ of 12.2 Hz. The virtual coupling observed in these protons results from coupling to magnetically-inequivalent fluorine atoms that engage in strong (ca. 35 Hz) through-space coupling across individual terphenyl units of the dimer, giving rise to an AA'XX' splitting pattern. Such through-space coupling indicates that 4 maintains its dimeric solid-state structure in hydrocarbon solution. These second order effects also manifest in the $-70$ °C $^{13}$C{$_1^1$H} NMR spectrum of 4 in toluene-$d_8$: the carbons of the C–F···Li unit appear as a
doublet of second-order multiplets shifted slightly ($\Delta \delta = -0.68$ ppm) from their free values in the exterior of the dimer (Figure 3).

![Experimental 13C{1H} NMR spectrum of [TerphF-Li]2 at −70 °C showing the carbons bound to fluorines (black trace) and corresponding numerical simulation as generated using Spinach24 (blue trace). Simulation parameters (see Figure S2 for atom labelling scheme): $^3J_{Ha,Fa}$: 8.8 Hz, $^1J_{Fa,Ca}$: 251.0 Hz, $^4J_{Fa,Cb}$: 7.0 Hz, $^3J_{Hb,Fb}$: 12.2 Hz, $^4J_{Fb,Ca}$: 7.0 Hz, $^1J_{Fb,Cb}$: 226.4 Hz, $J_{Fb,Fc}$: 35.0 Hz, $\delta_{Ca}$: 159.85 ppm, $\delta_{Cb}$: 159.17 ppm.]

As a result of strong C–F···Li interactions in solution, $^1J_{C,F}$ for the lithium-coordinated C–F bonds (226.4 Hz) on the interior of the dimer is 25 Hz smaller than that for the free C–F bonds of the dimer (251 Hz) at low temperature. At room temperature, this is observed as an average $^1J_{C,F}$ of 238.7 Hz, which is significantly lower than the $^1J_{C,F}$ values in 2, 3, and 5, which span the narrow range of 250.9 to 252.0 Hz.

**Figure 3**: Portion of the experimental $^{13}$C{1H} NMR spectrum of [TerphF-Li]$_2$ at −70 °C showing the carbons bound to fluorines (black trace) and corresponding numerical simulation as generated using Spinach$^{24}$ (blue trace). Simulation parameters (see Figure S2 for atom labelling scheme): $^3J_{Ha,Fa}$: 8.8 Hz, $^1J_{Fa,Ca}$: 251.0 Hz, $^4J_{Fa,Cb}$: 7.0 Hz, $^3J_{Hb,Fb}$: 12.2 Hz, $^4J_{Fb,Ca}$: 7.0 Hz, $^1J_{Fb,Cb}$: 226.4 Hz, $J_{Fb,Fc}$: 35.0 Hz, $\delta_{Ca}$: 159.85 ppm, $\delta_{Cb}$: 159.17 ppm.

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**Computational Studies of C–F Bond Coordination within a Semifluorinated m-terphenyl Lithium Dimer**
Having observed a perturbation in $^1J_{C,F}$, we next sought to investigate the system computationally so as to better understand the physical basis for the observed spectroscopic parameters. To this end, we studied a truncated variant of 4 (denoted as 4', see Figure 4) in which the trimethylsilyl and tert-butyl groups were replaced with hydrogens to minimize computational cost while maintaining a system that reproduced the essential physics of the C–F···Li interaction. Geometry optimization at the BP86 level with a def2-TZVP basis set for all atoms§§ reproduced the relevant geometric parameters of the C–F···Li unit well, with an average absolute error in bond length of 0.008 Å across the C–F, F–Li, Li–Li, and C–Li distances. Critically, the observed C–F bond elongation upon coordination to lithium was observed in the model (Table 1), and the average optimized F–Li distance of 1.946 Å closely matched that observed in the solid state structure of 4 (1.935 Å) (see Table S4 for a detailed comparison of structure metrics between 4 and 4').

**Figure 4:** Depiction of structure 4' as optimized at the BP86/def2-TZVP level. Carbon is shown as gray, fluorine as green, hydrogen as white, and lithium as purple.
The calculated $^{13}\text{C}$ and $^{19}\text{F}$ chemical shifts of $4'$ (BP86/pcSseg-2) are in good agreement with those observed in $4$ (Table 1). In particular, the relative $^{19}\text{F}$ and $^{13}\text{C}$ chemical shift differences between atoms in lithium-bound and free C–F bonds ($\Delta \delta^{19}\text{F}$ and $\Delta \delta^{13}\text{C}$) for $4'$ of 26.88 ppm and 0.73 ppm, respectively, closely match those observed in $4$ at low temperature (24.33 ppm and 0.68 ppm). The through space $^{19}\text{F}–^{19}\text{F}$ coupling and scalar $^{19}\text{F}–^{7}\text{Li}$ coupling observed in $4$ is also replicated well in $4'$, providing further assurance that the computed NMR parameters of $4'$ accurately approximate the real spin system present in $4$. Accordingly, we can confidently discuss the $^1J_{C,F}$ values of $4'$ as proxies for those observed in $4$.

**Table 1:** Comparison of various experimentally observed parameters in $4$ with the average values calculated for $4'$. Values in parentheses are standard errors for bond lengths (ESDs for crystallographically determined metrics, and population standard deviations where enough parameters were available from computed structures) or uncertainties for NMR $J$-couplings (the reciprocal of acquisition time for experimentally determined values, and population standard deviations where enough parameters were available from computed NMR parameters).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Experimental ($4$)</th>
<th>Calculated ($4'$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Bound</strong></td>
<td><strong>Free</strong></td>
</tr>
<tr>
<td>$C–F_{\text{avg}}$ Dist. (Å)</td>
<td>1.381(2)</td>
<td>1.356(4)</td>
</tr>
<tr>
<td>$^1J_{C,F}$ (Hz)</td>
<td>226(1)</td>
<td>251(1)</td>
</tr>
<tr>
<td>$\delta^{13}\text{C}$ (ppm)</td>
<td>159.17</td>
<td>159.85</td>
</tr>
<tr>
<td>$\delta^{19}\text{F}$ (ppm)</td>
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<td>-113.58</td>
</tr>
<tr>
<td>$J_{F,F}$ (Hz)</td>
<td>c.a. 35</td>
<td>n/a</td>
</tr>
<tr>
<td>$^1J_{F,Li}$</td>
<td>32(1)</td>
<td>n/a</td>
</tr>
</tbody>
</table>

The average $^1J_{C,F}$ value for the free C–F bonds ($-243.5$ Hz) in $4'$ is calculated to be larger in magnitude than that of the bound C–F bonds ($-234.7$ Hz; see Figure 5 for a graphical depiction). The most important contributors to $^1J_{C,F}$ in $4'$ are the paramagnetic spin-orbit (PSO) and Fermi terms, all other terms either being vanishingly small or relatively constant ($<5$ Hz difference) between the free and bound C–F bonds. Detailed descriptions of the PSO and Fermi coupling
mechanisms are available elsewhere, and it is sufficient here to state that the PSO coupling mechanism involves interactions between occupied and energetically accessible unoccupied orbitals, and is frequently a reporter of π-bonding character, whereas the Fermi mechanism couples spins through σ-bonds with nonzero s-orbital character.

**Figure 5:** Graphical depiction of the Fermi contact (FC) and paramagnetic spin-orbit (PSO) components of $^1J_{C,F}$ for the free (light blue) and lithium coordinated (dark blue) C–F bonds in 4′ as calculated at the BP86/pcsSeg-2 level of theory.

The coordinated C–F bonds in 4′ have average Fermi components of $^1J_{C,F}$ higher in magnitude (more negative, opposite to the overall change in $^1J_{C,F}$) by an average of 12.5 Hz relative to their free counterparts, suggesting that upon coordination to a Lewis acid, the atomic s-character of the C–F bond increases slightly. This is a result of two competing effects. While coordination to a Lewis acid partially depletes the bonding electron density of the C–F bond and thus acts to reduce the magnitude of the $J$-coupling value (bonding electron density being a critical mediator of coupling), the slight elongation of the C–F bond on coordination raises the magnitude of the Fermi term, and is the dominant effect in this case. One chemically plausible explanation for the latter phenomenon, which is reflected in the computational data, is that upon C–F bond
elongation, the system takes on more \([\text{Caryl}^+][\text{F}^-]\) character. In this limiting resonance contributor, electron density is drawn from a carbon centered orbital of predominantly \(p\) character (on basis of its lower ionization energy) and shifted to fluorine to give a fully occupied set of \(s\) and \(p\) orbitals. This depletion of electron density at carbon is in turn compensated for by donation of additional electron density from neighboring carbon atoms, which acts to preserve the valence of the carbon bound to fluorine and distribute the positive charge over multiple nuclei. The net result of this is an increase in overall electron density on carbon and fluorine and a concomitant increase in \(s\) electron density at both carbon and fluorine, resulting in an increase in the Fermi term for the bond. We acknowledge that this analysis is convoluted slightly in that L.A. binding also draws electron density away from the fluorine, but evidently this has less effect on the Fermi term than the previously mentioned factors.

The increase in magnitude of the Fermi term is similarly reported by \(^3J_{H,F}\), where the coupling strength between the flanking aryl protons nearest the lithium and their associated bound fluorines in 4, 12.2 Hz, is higher than that observed for the opposite pairs, 8.8 Hz, due to increased atomic \(s\)-character in the bonds mediating the coupling on the interior of the dimer (\(^3J_{H,F}\) range for 2, 3, and 5: 6.6–6.9 Hz). \(^3J_{H,F}\) is overwhelmingly dominated by the Fermi coupling relayed through a C–H, C–C, and C–F bond, so the increase in \(s\)-character of the C–F bond raises the Fermi term for the whole system.

The observed reduction in magnitude of \(^1J_{C,F}\) in the bound C–F bonds of 4' relative to their free counterparts is a result of changes to the PSO part of the coupling value that are larger in magnitude and opposite in sign to the change in the Fermi component. Specifically, while the average PSO contribution to \(^1J_{C,F}\) in the free C–F bond is negative (PSO\(_{\text{iso}}\): −9.8 Hz) the same value is positive for coordinated C–F bonds (PSO\(_{\text{iso}}\): 6.3 Hz). Reported isotropic PSO
components of $^{1}J_{C,F}$ in typical $sp^{3}$ hybridized systems (where $\pi$-effects are small) are also positive, suggesting that an increasingly positive PSO term may be indicative of reduced carbon-fluorine $\pi$-bonding character. While this trend has not yet been established for carbon-fluorine bonds, similar relationships between the value of the PSO term and multiple-bonding character have been demonstrated for carbon-carbon bonds.

The sum of these considerations begins to suggest that the absolute value of $^{1}J_{C,F}$ should necessarily decrease in systems where Lewis acid binding perturbs a carbon-fluorine $\pi$-interaction (as in aryl fluorides). This proposal, that coordination of an aryl C–F bond to a Lewis acid should generally result in a decrease in $|^{1}J_{C,F}|$, is explored in the following section.

The General Relation Between $\Delta^{1}J_{C,F}$ and C–F Bond Activation

Having established that the reduced $^{1}J_{C,F}$ value of the lithium coordinated C–F bonds of 4 was the sum of two opposing effects, it was still unclear whether or not this decrease in coupling constant on C–F bond coordination to Lewis acidic sites was a phenomenon to be generally anticipated. To further assess this possibility, we conducted a survey of reported $^{1}J_{C,F}$ values for systems with clear aryl C–F···L.A. interactions. At the time of writing, the Cambridge Structural Database contains 383 reported structures containing aryl C–F···L.A. interactions. The following analysis pertains to 17 structures that satisfy the following criteria, as well as compound 4 reported in this work:

- In solution, the C–F···L.A. interaction is maintained, and multi-site exchange does not occur. This precludes most structures with polyfluorinated aryl rings for which ring rotation is not slow on the NMR timescale.

- High resolution, interpretable $^{13}C\{^{1}H\}$ or $^{13}C$ NMR data for both the Lewis-acid bound complex and the “free” complex exists. For macrocycles that engage in Lewis-acid
binding, the “free” complex refers to the neutral macrocycle. For complexes where the
Lewis acid is bound by an anionic ligand, the “free” complex refers to the protonated
ligand, or where unavailable, the ligand halide. This excludes paramagnetic complexes
for which $^{13}$C NMR linewidths may exceed $^{1}J_{C,F}$, as well as diamagnetic complexes for
which incomplete NMR data are reported.

We note in passing that although we have excluded systems exhibiting multi-site exchange
from our analysis, the $^{1}J_{C,F}$ values for a coordinated C–F bond undergoing exchange with free
C–F bonds can be well-approximated by understanding the observed $^{1}J_{C,F}$ value as an average.
By comparing the observed coupling constant with the “free” coupling constant, one can
calculate the approximate $^{1}J_{C,F}$ value for a coordinated C–F bond involved in exchange without
requiring exchange process be slow on the NMR timescale, and could in principle extend this
analysis to these more complex systems.

Candidate data sets include a diverse array of Lewis acidic sites, including multiple group 1
and 2 elements (lithium$^{13,28,29}$ sodium$^{13,30,31}$ potassium$^{13,32}$ rubidium$^{33}$ cesium$^{16,34}$ and
calcium$^{35}$), as well as several transition elements (zirconium$^{29,36}$ hafnium$^{29}$ and palladium$^{37}$).
The aggregate data qualitatively agree with the statement that stronger C–F···L.A. interactions
lead to lower $^{1}J_{C,F}$ values: a simple plot of observed $^{1}J_{C,F}$ versus coordinated C–F bond length
shows a downward trend which, when fit to an empirical linear model ($R^2 = 0.64$) suggests that
$^{1}J_{C,F}$ values decrease at a rate of about 6 Hz per 0.01 Å elongation (Figure S4).

$^{1}J_{C,F}$ values depend on both the specific ligand as well as its coordination state, however, so we
next studied the relationship between coordinated C–F bond length and the change in $^{1}J_{C,F}$ value
from the “free” ligand value upon coordination ($\Delta^{1}J_{C,F}$) as a means of providing some level of
referencing. Plotting $\Delta^{1}J_{C,F}$ versus C–F bond length (d$_{C–F}$) yields little initial insight, as there is
no clear correlation between $d_{C-F}$ and change in $^1J_{C,F}$ (Figure 6). This observation suggested that a more complex relationship between $\Delta^1J_{C,F}$, $d_{C-F}$, and the strength of a C–F···L.A. interaction existed. To elucidate this relationship, we undertook a systematic computational study, utilizing as a model system embodying a representative Caryl–F···L.A. interaction: the fluorobenzene–tris(dimethylether)lithium cation ([C₆H₅F···Li(OMe)₃]⁺) (Figure 7). This system was chosen for its chemical simplicity, and there is little reason to expect that the use of another Lewis acidic center would significantly change the outcome of this study; it need only be true that the model system incorporate an aryl C–F bond acting as a Lewis base and a site with a vacant orbital acting as a Lewis acid.

**Figure 6:** Plot showing decreases in $^1J_{C,F}$ values in reported structurally characterized systems featuring static, non-exchanging C–F···L.A. interactions in solution from their “free” values
versus C–F bond length as determined by X-ray crystallography (blue points). The solid state structures, NMR parameters, and CCDC accession codes for each data point are tabulated in Table S1, and are labelled from 1-17 in the same manner they are on this plot. Dashed contour lines show, for a given C–F bond length and decrease in $^1J_{C,F}$, what portion of the C–F bond order is lost due specifically to coordination (rounded to the nearest 0.01), as calculated using the [C$_6$H$_5$F...Li(OMe$_2$)$_3$]$^+$ model system.

To map the electronic landscape of various C–F…L.A. interaction strengths, we performed a series of constrained geometry optimizations, holding the C–F–Li angle fixed at 135° and the F–Li distance at either 2.0, 2.2, 2.4, 2.6, 3.0, 3.5, or 5.0 Å,† the shorter and longer distances serving as representative cases of strong and weak C–F…L.A. interactions, respectively. For each F–Li distance, the C–F distance was varied between 1.34 and 1.40 Å in increments of 0.01 Å, and the $^1J_{C,F}$ value for each optimized structure was calculated. Taking as a metric for interaction strength the calculated C–F bond Mayer bond order, we compared the C–F bond orders of each computed structure with the corresponding values obtained for the neutral fluorobenzene molecule with C–F distances similarly varied between 1.34 and 1.40 Å. This allowed us to determine, for a given C–F bond length, how activated a bond was as a direct result of interactions with a Lewis acid, and what change in $^1J_{C,F}$ this corresponded to. These results are plotted as contours showing Mayer bond order decrease (rounded to the nearest 0.01) resulting directly from Lewis acid binding in Figure 6 alongside the data obtained from the literature survey for comparison.
Figure 7: Depiction of the $[\text{C}_6\text{H}_5\text{F} \cdot \cdot \cdot \text{Li(OMe}_2)_3]^+$ system utilized to study changes in $^{1}J_{C,F}$ as a function of $d_{C-F}$ and $d_{F-Li}$. Geometry optimizations followed by NMR calculations at the BP86/pcsSeg-2 level were performed for C–F bond distances between 1.34 and 1.40 Å in increments of 0.01 Å, and for F…Li distances of 2.0, 2.2, 2.4, 2.6, 3.0, 3.5, and 5.0 Å with a fixed C–F–Li angle of 135° to yield $^{1}J_{C,F}$ values and C–F bond Mayer bond orders. Carbon is shown as gray, fluorine as green, hydrogen as white, lithium as purple, and oxygen as red.

The results of this calculation show a clear trend: longer Lewis acid coordinated C–F bonds with large reductions in $^{1}J_{C,F}$ show the greatest extent of activation or, equivalently, the strongest C–F–L.A. interactions. Previous work has frequently discussed the strength of C–F–L.A. interactions in context of C–F bond elongations, but this work further asserts a relation between $^{1}J_{C,F}$ and the extent of C–F bond activation. An additional critical finding of this analysis is that “long” C–F bonds do not necessarily imply greater activation relative to shorter analogues, and that for a given C–F bond length, varying degrees of activation are possible. A simple demonstration of this statement is found in comparing 4 with analogous semifluorinated $m$-terphenyl silylium ion complex $[2,6-bis(2,6-difluorophenyl)phenyl]dimethylsilylium tetrakis(pentafluorophenyl)borate (herein referred to as [Terph$^{F-}$$\cdot$$\cdot$$\cdot$$\cdot$$\cdot$SiMe$_2$][B(C$_6$F$_5$)$_4$]), where a
formally cationic silicon center acts as the Lewis acidic site. The Lewis acid bound C–F bonds in [TerphF–SiMe2]⁺ are on average significantly longer than those in 4 (1.416 Å vs. 1.381 Å), which, when considered alone, suggests that the C–F bonds of [TerphF–SiMe2]⁺ are more activated. The C–F···L.A. interaction energies (as gauged by activation energies for ring rotation) in these two species, however, suggest the opposite: for 4 this value is approximately 13 kcal/mol, whereas for [TerphF–SiMe2]⁺ it was calculated (the process being fast on the NMR timescale down to 233 K) to be 4.5 kcal/mol. Discussion of Δ¹JC,F values for each system provides a more complete picture: for [TerphF–SiMe2]⁺ Δ¹JC,F is 16 Hz,†† whereas for 4 it is 25 Hz. Qualitatively weighing these values alongside the C–F bond lengths in context of the broad trends presented in Figure 6 suggests instead that the coordinated C–F bonds in 4 and [TerphF–SiMe2]⁺ are both quite activated—probably to similar extents—in spite of their differing metrical parameters. This suggests that utilizing C–F bond lengths as the sole descriptor of C–F···L.A. interactions is ill-advised, and that a more complete description of these interactions should also include a discussion of NMR or computational data, or a combination of all three.

This point is made more obvious by considering the metric of C–F bond lengths in a general sense: analysis of the nearly 29,000 structures in the CSD containing uncoordinated aryl C–F bonds shows that while each of the 18 structures analyzed in Figure 6 has a C–F bond length longer than the average aryl C–F bond (1.347 Å), two fall within one standard deviation of the average (1.365 Å), and 12 fall within two standard deviations (1.383 Å), including 4. In general, there is a significant overlap between reported Lewis acid coordinated aryl C–F bond lengths and free aryl C–F bond lengths, the numeric spread for both data sets being comparable in magnitude to the differences between each set’s average, further complicating the use of C–F bond length as
a reliable parameter (Figure 8). This could presumably be ameliorated by referencing coordinated C–F bond lengths to the same bond lengths in the absence of a Lewis acid, though crystallographic characterization for these metal-free compounds is less frequently reported, and in some cases (where the relevant compound is not a solid, for instance) may not be feasible.

![Figure 8: Histogram showing the frequencies of all C–F bond lengths for coordinated and free aryl C–F bonds reported in the CSD.](image)

Fewer issues arise when considering changes in $^1J_{C,F}$ on coordination as a metric for describing the strength of an aryl C–F···L.A. interaction. While it remains true that, for a given decrease in $^1J_{C,F}$, the precise strength of the interaction may vary, a decrease in $^1J_{C,F}$ on coordination is strongly indicative of the presence of a C–F···L.A. interaction in solution. This is due to the fact that, over the chemically relevant range of C–F bond lengths (between about 1.30 and 1.41 Å), longer, uncoordinated bonds are expected to yield higher $^1J_{C,F}$ values (Figure S5, *vide supra*).

It is important to note that the converse of this statement is not universally true, and that Lewis acid binding of aryl C–F bonds cannot be expected to always cause reductions in $^1J_{C,F}$. This is shown in Figure 6 where it is evident that, for long, relatively weakly activated C–F bonds, the
$^1J_{C,F}$ value is expected to *increase* on coordination to a Lewis acidic site. To the best of our knowledge, this phenomenon has not yet been conclusively observed experimentally.

We conclude this section by stating that, much like $d_{C-F}$, $\Delta^1J_{C,F}$ values are not a metric to be used in isolation, but rather an additional parameter that may aid the practicing chemist in describing C–F···L.A. interactions they may encounter in their work. In conjunction with $d_{C-F}$ values, $\Delta^1J_{C,F}$ values can offer more insight into the bonding within Lewis acid coordinated C–F bonding motifs than either value can alone.

**Conclusion**

To summarize, we have synthesized a new, semifluorinated $m$-terphenyl lithium featuring close C–F···Li contacts in the solid-state, and shown by multinuclear NMR spectroscopy that these interactions persist in solution. Eyring analysis allowed us to establish an upper limit on the enthalpy of the C–F···Li interaction of 13(±0.8) kcal/mol. Computational analysis of the NMR $J$-couplings within the C–F···Li unit suggest that the characteristic decrease in $^1J_{C,F}$ is due predominantly to changes in the extent of $\pi$-delocalization of the fluorine lone pairs into the arene $\pi$-system. In-depth computational analysis of the [C$_6$H$_5$F···Li(OMe)$_2$)$_3$]$^+$ model system suggests that, in general, decreases in $|^1J_{C,F}|$ on aryl C–F bond coordination to a Lewis acid are indicative of interactions of at least moderate strength, and that, taken together, C–F bond lengths and $\Delta^1J_{C,F}$ values can qualitatively describe the strength of C–F···Lewis Acid interactions more completely than either metric could in isolation.

**ASSOCIATED CONTENT**

The following files are available free of charge at http://pubs.acs.org.

Crystallographic data for 4 (CIF)

Crystallographic data for 5 (CIF)
Experimental procedures, NMR data, crystallographic data, and computational data (PDF)

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Notes

The authors declare no competing financial interests.

§ The through-space $^{19}\text{F}^{19}\text{F}$ coupling constant was obtained by globally fitting the low temperature $^1\text{H}$ and $^{13}\text{C}^{1\text{H}}$ NMR spectra. See Figure S3 and Figure 3.

§§ This functional and basis set were selected for their demonstrated utility in satisfactorily describing relevant interactions.\textsuperscript{38}

† While experimental $^{1}J_{\text{C,F}}$ values are frequently reported as absolute values, it is understood that the sign of these values is generally negative, as is found for computed $^{1}J_{\text{C,F}}$ values. NMR experiments capable of determining the relative sign of coupling constants exist, but are in general not routine.

† These F–Li distances were chosen to afford Mayer bond order decreases between 0.18 and 0.06, in increments of approximately 0.02.

†† $^{1}J_{\text{C,F}}$ for Terph$^{\text{F}}$–SiMe$_2$H is 247 Hz, while $^{1}J_{\text{C,F}}$ for [Terph$^{\text{F}}$–SiMe$_2$]$^{+}$, where only one signal is observed for all fluorinated carbons, is 239 Hz. Assuming Lewis acid coordination has little
effect on $^{1}J_{C,F}$ for non-coordinated C–F bonds (as observed in 4), we calculate the $^{1}J_{C,F}$ value for the silylium-coordinated C–F bonds to be 231 Hz.

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