

Challenging the Limitations of the Streitwieser Lithium Indicator Acidity Scale with
Cyclopentadiene Derivatives

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ABSTRACT

This dissertation focuses on linking the Streitwieser Lithium Indicator (SLI) acidity scale to the aqueous Bronsted-Lowry scale to give true pK_a values to carbon acids measured on the SLI scale. To achieve this goal, we needed at least one carbon acid that is both water- and THF-soluble and that has an acidity appropriate to measurement on both scales. After considering various options, cyano-substituted cyclopentadiene derivatives were selected for our study. Because the published methods of synthesizing these compounds were not suited to a routinely equipped academic lab, we developed our own synthetic method based on electrophilic cyanation of cyclopentadiene derivatives using tosyl cyanide (TsCN) as the cyanizing reagent. Neutral cyanocyclopentadienes are thermally unstable (likely they polymerize), so we developed workup procedures that maintained these compounds in their anionic, conjugate-base forms (as potassium salts). Using this procedure, several potassium cyanocyclopentadienide derivatives were successfully synthesized in yields ranging from 44-64%. Of the salts synthesized, potassium 1,2-dicyanocyclopentadienide and its inseparable 1,3-isomer were subjected to acidity measurements using ^1H and ^{19}F NMR spectrometry in CD_3CN solution, bracketing their acidities between two “indicator” acids that were previously established on the SLI scale. This process revealed pK_{MeCN} , pK_{THF} (SLI acidity) and pK_a (“true” aqueous acidity) values for each compound. These compounds were then used to offset the SLI scale against the Bronsted-Lowry (aqueous) scale. Assuming this offset to be constant, all the acids heretofore measured on the SLI acidity scale were finally assigned “true” pK_a values.

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General Audience Abstract

Carbon acids are organic compounds that show a tendency toward the loss of hydrogen ion (H^+) from a carbon atom. Organic chemists use this tendency to help understand the mechanisms or “inner workings” of chemical reactions. Over time, lists or “scales” of numerous compounds have been collected so that the tendency toward loss of H^+ (acidity) can be correlated with molecular structure, and so that acidities of new compounds can be predicted by extrapolating these trends. The most common “scale” is the aqueous Bronsted-Lowry scale, which is taught even in high-school chemistry courses. This dissertation focuses on a particular “scale” known as the Streitwieser Lithium Indicator (SLI) acidity scale, which uses a different solvent (THF) because most organic compounds are not soluble in water, or because most organic compounds are not acidic enough to release hydrogen ion in water. Our main goal was to link these two scales by an “offset value” (some might say “fudge factor”) so that comparisons between the two scales, each of which has strengths and weaknesses, might be more readily made. To achieve this goal, synthesized a compound that could be measured using both methods. This synthesis required the development of a new synthetic method, whose scope we explored briefly. The acidity measurements required us to work around some technical problems, but we ultimately found that the “offset” between the aqueous Bronsted-Lowry and SLI methods is about 5 units on the standard logarithmic scale. Thus, in general, carbon acids of the

type that we explored (having large, delocalized structures) tend to be about 10^5 times as acidic in water, compared to their acidity in THF. These scales can now be considered “linked” so long as the offset is assumed to be constant.

Acknowledgements

I would like to thank Mr. Ken Knott-Sharpe and Dr. Murthy Shanaiah for optimizing our ^{19}F NMR and ^1H NMR spectroscopic methods. I thank Dr. Sherry Hildreth for running our HRMS measurements for our compounds. I thank Dr. Paul Deck, Dr. Sarah Swilley, and Ms. Danni Gonzalez for helpful discussions while experimenting and writing this dissertation. I would like to thank our undergraduate researchers, Tripp Aardema and Stephen Williams, for aiding me in the synthesis work. I would like to thank my family for supporting me, especially my grandma Opal. Last but not least, my girlfriend Elizabeth Wilkinson for supporting me and being there for me... Always and Forever.

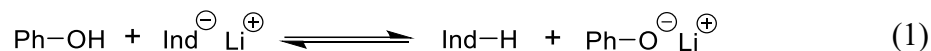
Table of Contents

Abstract	ii
General Audience Abstract	iii
Acknowledgements	v
Table of Contents	vi
Chapter 1: Dissertation Overview and Review of Background Literature	1
1.1: Research Objectives	
1.2: Introduction: Beyond Perfluoroaryl Substituents	
1.3: Cyanation & Carbon Acidity	
1.4: Exploring Alternative Cyanizing Reagents & Initial Work	
Chapter 2: Synthesis & Workup of HCNCps	17
Chapter 3: Acidity Measurements & Trends of HCNCps.....	52
Chapter 4: Supplemental Information	82
Chapter 5: References.....	113

Chapter 1: Dissertation Overview and Review of Background Literature

Research Objectives

Linking the SLI and Aqueous Acidity Scales. The primary objective of this project is to connect the Streitwieser Lithium Indicator (SLI) acidity scale to the aqueous Bronsted-Lowry acidity scale by synthesizing several compounds that can be measured precisely in both scales. Designing and experimental approach to this problem requires us to meet several simultaneous constraints. First, we need the test compounds to be soluble in both water and THF. For organic compounds, aqueous solubility is often a significant limitation. Second, the acidities of the compounds must be in the right range to measure using available indicators. In principle, one could imagine that a carbon-acidic indicator having an appropriate acidity on the SLI scale could be compared directly with an ordinary water-soluble Bronsted acid such as phenol ($pK_a = 10$), by measuring the equilibrium constant of the reaction shown in eq 1.



However, we have found that common organic acids based on OH and NH bonds are too labile – the equilibrium cannot be determined by our preferred NMR methods because it will be in fast NMR exchange. For example, if two proton peaks separated by 0.2 ppm in a 400 MHz NMR spectrometer have a rate of exchange faster than 178 Hz at room temperature, the peaks will coalesce together preventing accurate measurement of their acidities. However, cyclopentadiene derivatives exchange protons only very slowly – in the extreme slow-exchange regime of ordinary NMR spectroscopic methods. It is even slower than the rate of decoupling (~44 Hz) which is not observed at room temperature. Therefore, to link the SLI and aqueous acidity scales, we wanted to find, specifically,

cyclopentadiene derivatives that are soluble in water and that demonstrate appreciable aqueous acidity.

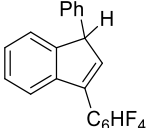
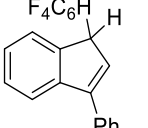
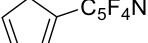
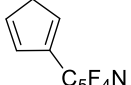
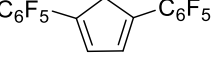
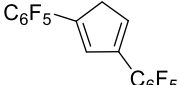
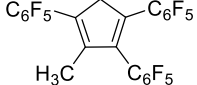
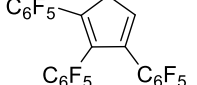
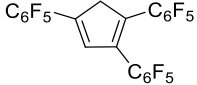
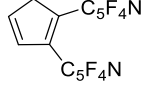
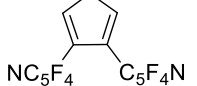
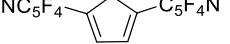
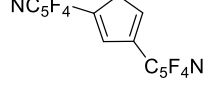
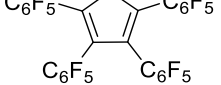
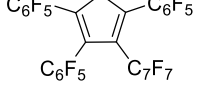
Fortunately, we were aware that Webster and co-workers had published the synthesis and the aqueous acidities of several cyclopentadiene derivatives that have cyano (CN) groups, which not only increase the acidity of the cyclopentadiene ring significantly, but they also afford aqueous solubility.¹ Therefore, we needed to retread some of Webster's work, with the goal of preparing one or two selected cyanocyclopentadiene derivatives (HCNCps) that have acidities in the right range to measure against our existing scale of SLI indicators. The SLI scale includes many carbon acids (Ex: Fluorene, 9-tert-butylfluorene, 2,3-benzofluorene, etc.) that are far too weak to be compared directly against common aqueous acids. Those of appropriate acidity are mostly perfluoroaryl-substituted cyclopentadienes prepared in our own laboratories. For reasons that will be discussed in more detail in Chapter 2, we needed to find alternatives to Webster's synthetic methods. Specifically, Chapter 2 describes new methods that we developed for attaching cyano groups (-CN) using tosyl cyanide (TsCN) as an electrophilic cyanizing reagent. To set this accomplishment in an appropriate context, this chapter will include a review of the literature of electrophilic cyanation in organic chemistry. This chapter also summarizes the background on carbon acidity measurements generally, with a focus on our NMR methods for characterizing cyclopentadiene derivatives. Chapter 3 delves into the details of our acidity measurements and our efforts to link the SLI and aqueous acidity scales using a constant offset.

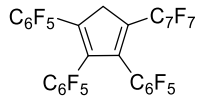
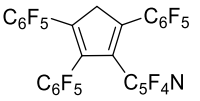
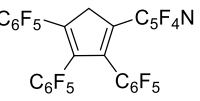
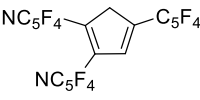
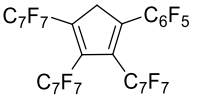
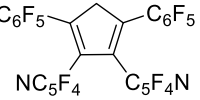
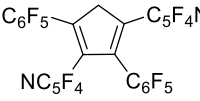
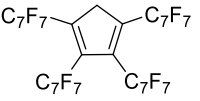
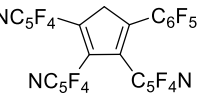
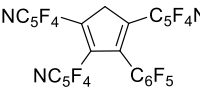
Introduction

Fluoroaryl Acidifying Substituents

In our previous research into enhancing the carbon acidity of cyclopentadiene, we had found great success in using fluoroaryl substituents including perfluorophenyl (-C₆F₅), perfluorotolyl (-C₇F₇), and perfluoropyridyl (-C₅F₄N).^{2,3} Beyond enhancing the acidity of cyclopentadiene, these fluoroaryl substituents allowed us to use ¹⁹F NMR spectroscopy as a method of measuring their pK_a values on the SLI scale. The use of ¹⁹F NMR spectroscopy came with several unique advantages including a large spectral range giving enhanced resolution between peaks, and the ability to determine the relative concentrations of all chemical species. With this method, we measured the acidities of 34 unique fluoroaryl cyclopentadiene derivatives. These measurements drove the SLI scale down to a new record low pK value of -5.99 (Table 1).

Table 1. A selection of 25 (from a total of 34) fluoroaryl-substituted cyclopentadienes and their SLI acidities of the aliphatic C-H bond, synthesized by the Deck Group.

Compounds	pK	Compounds	pK	Compounds	pK
	9.50		9.14		7.71
	6.73		6.31		5.88
	5.17		3.50		2.89
	1.97		1.42		0.62
	-0.03		-0.37		-1.54

	-1.65		-2.20		-2.47
	-3.81		-3.95		-4.01
	-4.17		-5.09		-5.88
	-6.01				

A rather obvious goal of our prior work was to see how far we could push the SLI scale! The practical “solvent limit” is set by the acidity of protonated THF ($C_4H_8OH^+$) in THF as the solvent ($pK_{THF} \approx -7-8$, $pK_a = -2.1$ in water).⁴ Any acid more acidic than this species will be considered “strong” in general chemistry language and will be “leveled” by the solvent. Thus, we knew that we would not be able to measure – in THF solvent – the acidities of any species more acidic than $C_4H_8OH^+$.

Despite our many previous successes in synthesizing cyclopentadiene derivatives and in measuring their acidities using ^{19}F NMR spectroscopic indicator methods, we had not reached the solvent limit of THF. Two key barriers prevented us from achieving this goal. First, our approach requires *incremental* changes in acidity that can be measured using NMR integration, which has a limited dynamic range. In practice, this means that simply adding another group (usually an easier synthetic problem) causes a change in acidity that is typically too large to measure. The first barrier is therefore a synthetic one: To get incremental acidity changes, we need to make *subtle* structural changes, so we need to prepare increasingly complex cyclopentadiene derivatives. Second, as the complexity of our derivatives increases, the resulting NMR spectra do, too, which causes more

interference between signals and limits the number of “clear” signals available for precise measurement. This complexity is further compounded by the issue of regioselectivity in synthesis, often resulting in an inseparable mixture of isomers that then needed to be characterized together. A “limiting” example of these problems is shown in Figure 1, which is based on the equilibrium shown in eq 2.

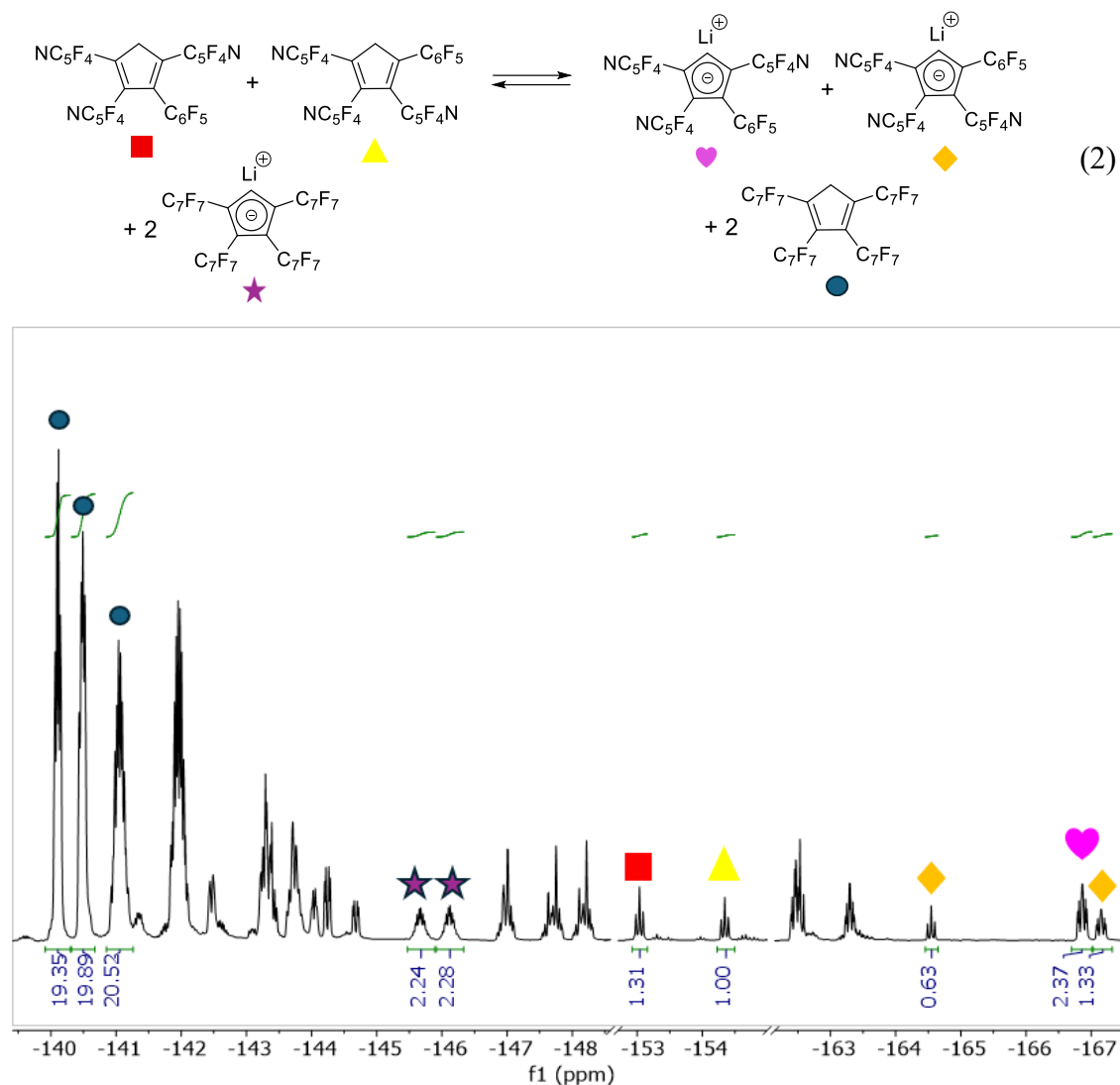


Figure 1. ^{19}F NMR spectrum (376 MHz, THF) of an equilibrium solution used to compare the acidities of the cyclopentadienes as represented in eq 2.

Although our NMR spectroscopic method only requires one peak for each constituent in the equilibrium, we find that including as many peaks as may be available increases our measurement precision which in turn keeps our overall propagated error low as we measure from one acid to another, in sequence.

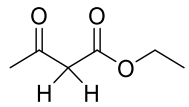
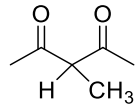
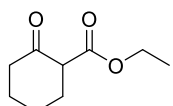
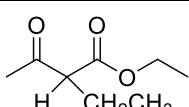
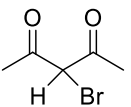
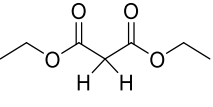
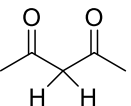
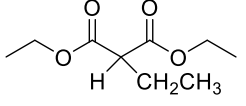
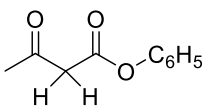
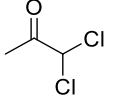
We also considered cyano substituents in our quest to approach the THF solvent limit for carbon acidity, because we knew from Webster's work that they are strong electron-withdrawing groups, but also because they are *not fluorinated* and could help simplify our spectra. So, we set out to prepare a selection of cyclopentadienes bearing both fluoroaryl and cyano groups. However, we quickly learned that the acidification factor afforded by one CN group was so strong that we would have faced a lot of synthetic trial-and-error before finding the two or three compounds that we still needed to approach the THF solvent limit in stepwise fashion. Ultimately, we decided that "strongest carbon acid" or "reaching the end of the scale" were not as important as some of our other scientific aims.

Cyanation & Carbon Acidity

To understand the acidifying power of the -CN group has, it is instructive to look at the work undertaken by Pearson and Dillon.⁵ As part of their studies into the rates of ionization of pseudo acids (i.e., slowly ionizing acids), Pearson and Dillon were able to create a table (Table 2) of simple carbon acids with their pK_a values as well as the forward and backward rate constants of hydroxide-catalyzed proton transfer (k_1 and k_{-1} respectively).⁵ They achieved this by amalgamating their own data from kinetic halogenation studies with previously reported values.⁵⁻¹⁸ Pearson and Dillon then plotted $\log k_1$ as a function of pK_a to demonstrate the rough relationship between K_a and k_1 (Figure 2).⁵ Note that the plot in Figure 2 has several outlying points removed, which we believe the authors also excluded

in their work, as we could not reproduce their slope otherwise. From there, the acidities of even weaker acids in their series (including acetonitrile **22**) were extrapolated, because the practical limits of their kinetic isotope-exchange measurements were exceeded.^{5, 12, 17} From Table 2, it can be seen that the acidifying power of individual substituents on carbon acids goes in the following order:⁵ $-\text{NO}_2 > -(\text{C}=\text{O})- > -\text{SO}_2 > -\text{CO}_2\text{H} > -\text{CO}_2\text{R} > -\text{CN} \approx -\text{CONH} > -\text{X} > -\text{H} > -\text{R}$. One amusing fact is that the foregoing analysis, checked by assumptions and approximations, is the ultimate source of the widely-quoted “textbook” value for the pK_a value of acetonitrile.

Table 2. Condensed table of carbon acids with their aqueous Bronsted-Lowry pK_a values and their ionization rate constant (k_1) values in H_2O at STP. Recreated from Pearson & Dillon.⁵

No.	Compounds	pK_a	k_1, min^{-1}	No.	Compounds	pK_a	k_1, min^{-1}
1	$\text{CH}(\text{NO}_2)_3$	≤ 0	N/A	12		10.7	7.2×10^{-2}
2	$\text{CH}(\text{SO}_2\text{CH}_3)_3$	≤ 0	N/A	13		11	5×10^{-3}
3	$\text{CH}(\text{CN})_3$	≤ 0	N/A	14	$\text{CH}_2(\text{CN})_2$	11.2	9.0×10^{-1}
4	$\text{CH}_2(\text{NO}_2)_2$	3.6	50	15		11.5	5.8×10^{-4}
5	$\text{CH}(\text{COCH}_3)_3$	5.8	N/A	16		12.7	4.5×10^{-4}
6		7	1.4	17		13.3	1.5×10^{-3}
7		9	1.0	18		15	2×10^{-5}
8		9.4	6.6×10^{-1}	19		15	4.4×10^{-5}

9		10	2	20		16.5	3.3×10^{-6}
10	CH_3NO_2	10.2	2.6×10^{-6}	21		20	2.8×10^{-8}
11		10.5	1.4×10^{-1}	22	CH_3CN	25	4×10^{-12}

While the $-\text{CN}$ group is not the most acidifying substituent, it is a step up from halogens just like fluoroaryl substituents are. In a subsequent section, we will have a better opportunity to compare CN more directly to C_6F_5 and its congeners.

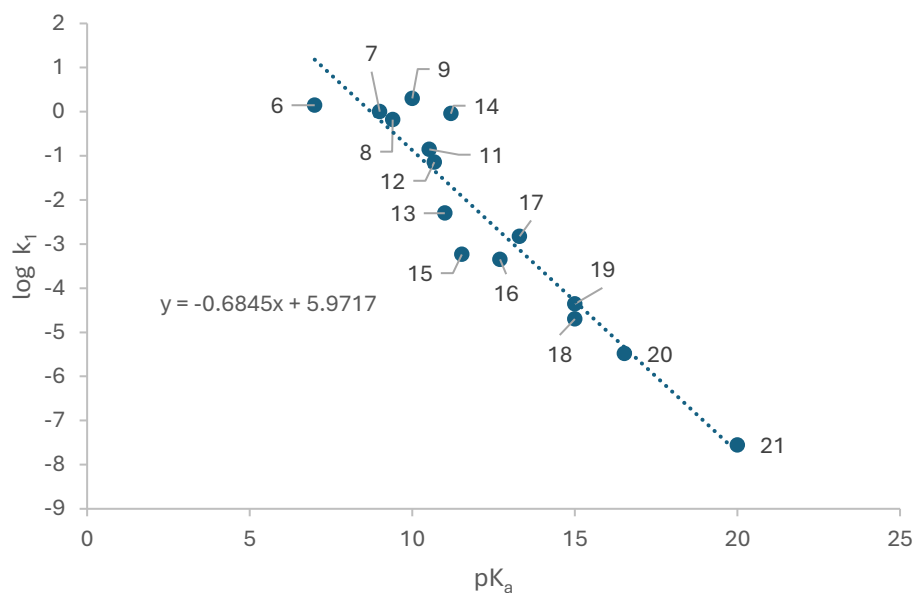


Figure 2. Modified plot of $\log k_1$ as function of pK_a of the acids shown in Table 2 Recreated from Pearson & Dillon.⁵


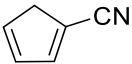
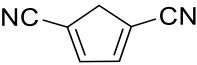
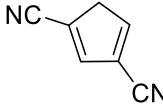
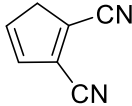
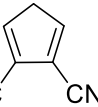
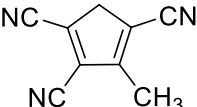
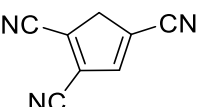
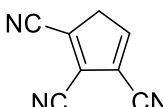
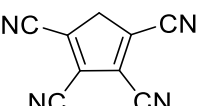
Table 2 also illustrates the power of polysubstitution of acidifying groups, as cyanoform ($\text{CH}(\text{CN})_3$) among others reached pK_a values below zero despite being based structurally on a very weak acid (methane, $\text{pK}_a \approx 50$). Cyanoform is not only acidic because of polysubstitution, but also of the proximity and availability of direct resonance

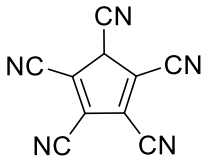
stabilization of the anion. Indeed, all the cyano-substituted species in Table 2 have the $-\text{CN}$ group directly on the acidic carbon. However, there is a noticeable saturation effect that results in a nonadditive increase in the acidity of the carbon-hydrogen bond with diminishing returns with each new substituent.⁵ Cram blamed the nonadditive increase in acidity on the compounding steric effects of substituents, which he theorized caused the conjugate base to form a nonplanar motif that would limit the resonance stabilizing effects of the substituents.¹⁹ The nitro group is a good example: There are “diminishing returns” when comparing CH_4 ($\text{pK} \sim 50$) to CH_3NO_2 (10) to $\text{CH}_2(\text{NO}_2)_2$ (3.6), and Cram was essentially arguing that both nitro groups of the $\text{CH}(\text{NO}_2)_2$ anion cannot be simultaneously coplanar on steric grounds. But we performed a quick quantum-mechanical geometry optimization on the $\text{CH}(\text{NO}_2)_2$ anion and theory (B3LYP, 6-31G*) predicts an entirely planar structure in the gas phase. Nevertheless, clearly the additivity effect is much stronger with the nitriles, when comparing CH_4 ($\text{pK} \sim 50$) to CH_3CN (25) to $\text{CH}_2(\text{CN})_2$ (11). Regardless, these results prompt us to consider what acidities could be reached if polycyanation of more acidic carbon acids could be achieved.

As part of his research into cyanocarbons and their potential commercial applications, Webster (presumably with coworkers) at DuPont synthesized a series of HCNCps via electrophilic addition of $-\text{CN}$ groups and measured their pK_a values (Table 3).^{1,20} Webster had the long-term goal to promote “cyanocarbons” as being a class of compounds that could be just as useful as halocarbons, owing to the “pseudohalogen” nature of the cyano group. To measure the acidity values of the HCNCps, Webster employed the spectroscopic titration method first described by Chantooni and coworkers.^{1, 20, 21} In this method, the HCNCps were titrated with a strong acid (such as HClO_4) in water or acetonitrile until the

half neutralization point was determined (i.e. $[\text{CNCp}^-] = [\text{HCNCp}]$) via UV-Vis spectroscopy.²¹ Once the half neutralization point was met, a pH reading would be taken to determine the pK_a as described by the Henderson-Hasselbalch equation (Eq. 3-4).²¹

Table 3. Recreated and modified chart of Webster's HCNCps and their pK_a values¹

Compound	$\text{pK}_a^{\text{H}_2\text{O}}$	$\text{pK}_a^{\text{MeCN}}$	Calculated $\text{pK}_a^{\text{H}_2\text{O}}$
	15 ^a	–	–
	9.78	–	–
	2.40	–	–
	1.40	–	–
	0.81	9.81	0.81
	0.81	9.81	0.81
	–	3.40	–5.7
	–	3.00	–6.1
	–	1.44	–7.8
	–	≈ 0	≈ -9.1

	–	< –2	< –11
HClO ₄	–6.7	1.83	–7.3

To determine the pK_a values of individual isomers that could not be separated from each other, a modification of the Henderson-Hasselbalch equation was derived (eq 5–7).¹ To measure the isomeric ratios under equilibrium conditions, an instrument with adequate resolution and sensitivity must be employed. We do not have access to the raw data for this experiment, but we speculate that resolving the two dienes (1-cyano- and 2-cyanocyclo-pentadiene) in the UV-vis spectrum would be very difficult.

$$\text{pK}_a = \text{pH} - \log \frac{[\text{CNCp}^-]}{[\text{HCNCp}]} \quad (3)$$

$$\text{pK}_a = \text{pH} \text{ (at half-neutralization)} \quad (4)$$

$$[\text{CNCp}^-] = [\text{HCNCp}^1] + [\text{HCNCp}^2] \text{ at the half-neutralization point} \quad (5)$$

$$\text{pK}_a^1 = \text{pH} - \log \frac{[\text{CNCp}^-]}{[\text{HCNCp}^1]} = \text{pK}_a^{\text{observed}} - \log \frac{[\text{HCNCp}^1] + [\text{HCNCp}^2]}{[\text{HCNCp}^1]} \quad (6)$$

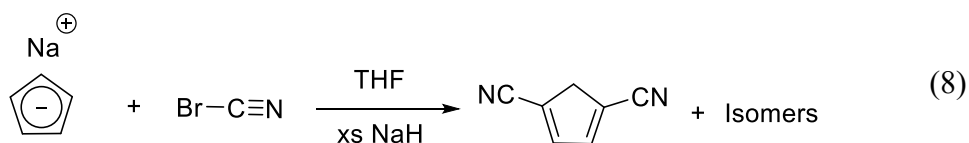
$$\text{pK}_a^1 = \text{pK}_a^{\text{observed}} - \log \left(1 + \frac{[\text{HCNCp}^2]}{[\text{HCNCp}^1]} \right) \quad (7)$$

Webster's results provide an excellent jumping off point for our line of research for two main reasons. First, he confirms what we expected from the findings of Pearson and Dillon – that the CN group has a strongly acidifying effect when attached to cyclopentadiene. Second, he provides a synthetic method that seems, at least initially, to be quite simple – electrophilic cyanation of cyclopentadienyl anion using cyanogen chloride (ClCN).¹ This approach is virtually the same as the synthetic method we

employed for the development of our fluoroaryl cyclopentadienes (electrophilic arylation using perfluoroarenes such as hexafluorobenzene (C₆F₆). Unfortunately, cyanogen chloride is a highly volatile and toxic asphyxiant that is classified as a chemical warfare agent subject to various international treaties! While still used in limited synthesis applications today, using ClCN would have required significant changes to our lab infrastructure to safely handle this compound. In addition, the only samples available to us commercially were dilute and expensive gas mixtures (thousands of dollars for a small cylinder). Therefore, we need to find an alternative cyanizing reagent if we were to have any hope of referencing the SLI scale to 1,2-dicyanocyclopentadiene. The selection of the latter compound for scale referencing is described in more detail in Chapter 3.

Exploring Alternative Cyanizing Reagents & Initial Work

In our initial work, we decided to explore cyanogen bromide (BrCN) as our alternative cyanizing reagent, eq 8.



While still very toxic (LD₅₀ = 25-50 mg/kg), BrCN is a liquid at standard temperature and pressure and thus is much safer to handle in our laboratory. We were also able to acquire BrCN inexpensively (\$119.70 for 100 g). Our initial hypothesis was that since BrCN is in the same family of compounds as ClCN, it should act very similarly to ClCN – as an electrophilic cyanizing reagent. Our assertion was backed up by BrCN’s extensive literature precedent as a cyanizing reagent for Grignard reagents and amines in drug

synthesis.²²⁻³³ There was even one publication that managed to cyanize a nucleophilic carbon, in this case 1-cyanopentane was converted to 1,1-dicyanopentane.³⁴ In most of these publications, BrCN acted purely as a cyanizing reagent and the only cases we found where bromination occurred was when there was significant steric hindrance around the reactive sites of certain Grignard reagents. We concluded that BrCN was worth trying as a cyanizing agent for cyclopentadienyl anions.

However, our initial work with BrCN gave peculiar results. We first tried to derivatize 1,2,4-tris(perfluorophenyl)cyclopentadiene (Figure 3). The substrate is simple because its conjugate base is symmetrical (two equivalent sites for cyanation). We anticipated that by using LC-MS, we could identify the addition of the $-CN$ group via an exact mass measurement. Dr. Sherry Hildreth (VT-MSI) used LC-ESI-MS to characterize our product mixtures. Initial experiments produced mostly unreacted starting material as well as both cyanized and brominated products. Refinement of the experimental conditions eliminated the starting material, but the main products were now apparently brominated (Figure 3)!

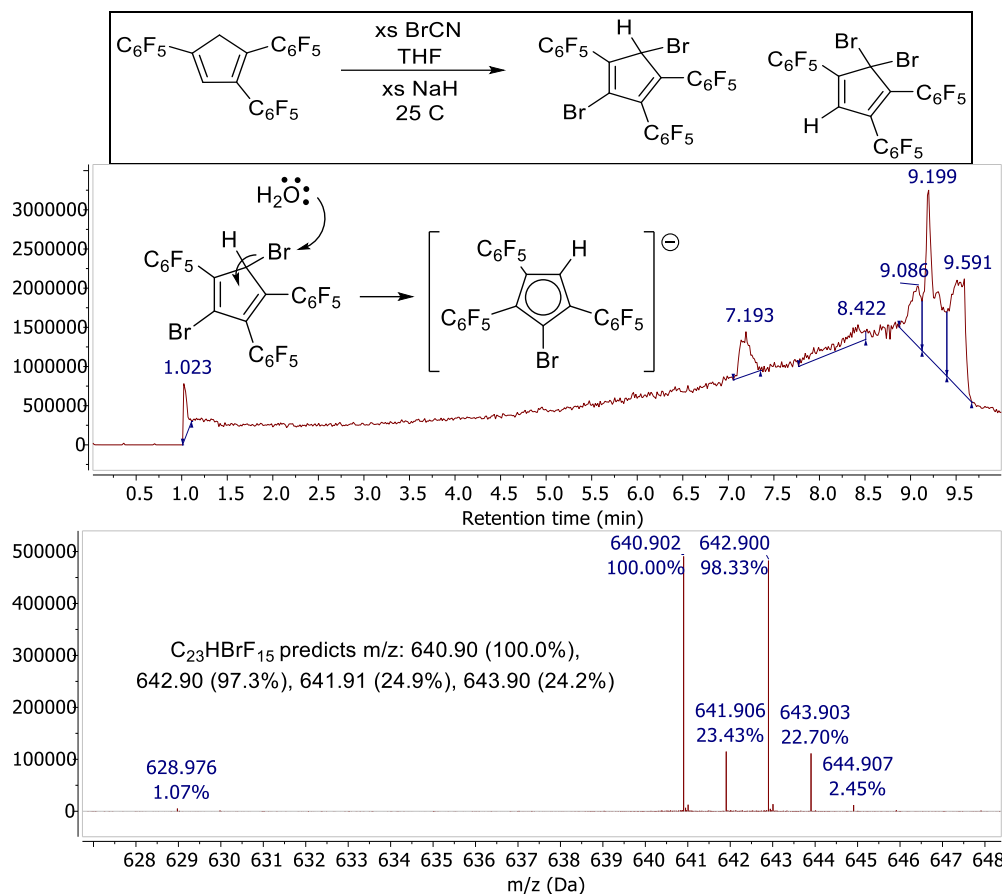


Figure 3. Negative-ion LC-MS of the product mixture for the reaction shown. Top: Total-ion chromatogram (TIC). Bottom: Mass spectrum corresponding to a retention time of 9.2 min (largest peak in the TIC).

This mass spectrum (Figure 3) suggests the formation of monobrominated product, but the NMR measurements (Figure 4) were more consistent with the formation of two dibrominated isomers. We do not know which structure corresponds to each signal. The ^{19}F spectrum likewise shows two products, each containing three chemically inequivalent C_6F_5 groups, in approximately the same mole ratio as shown in Figure 4. This finding rules out the assignment of either structure to a compound having an unsubstituted methylene (CH_2). The remaining question is why the MS data shows a single monosubstituted product. We surmise that in the electrospray ionization process, bromine is lost formally

as Br^+ which results in the formation of the single carbanion proposed in Figure 3. The doubly-allylic Br atoms of the species proposed in Figure 4 might well be quite labile.

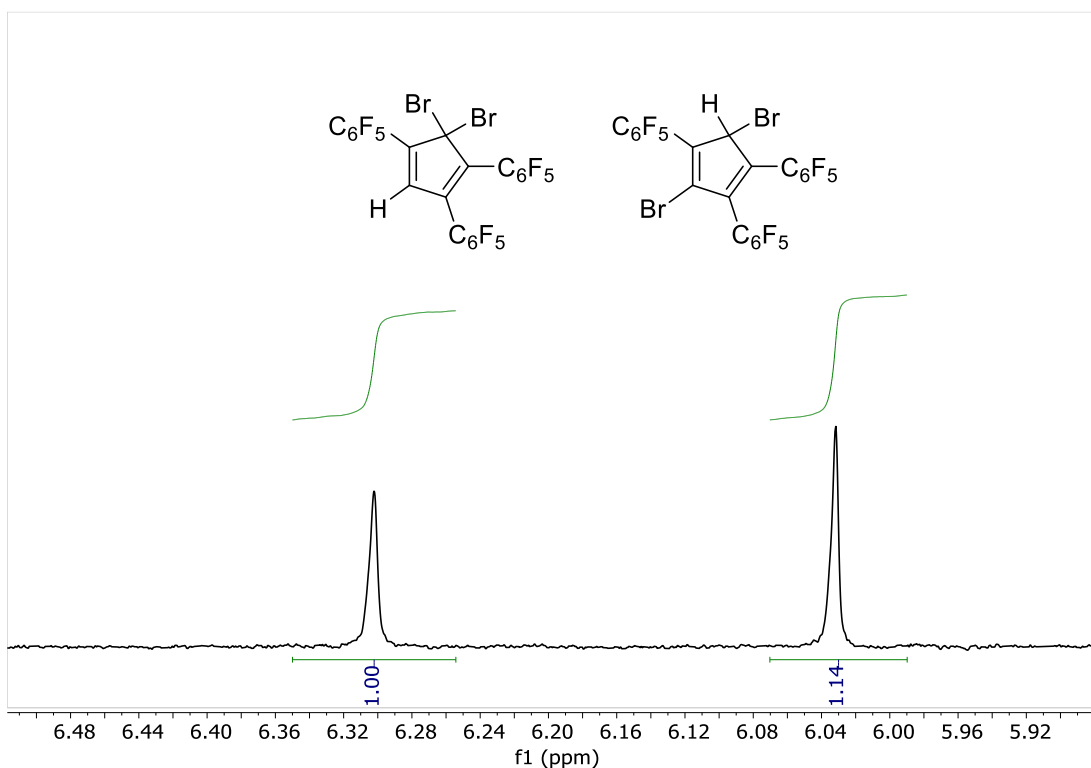
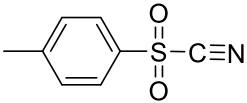
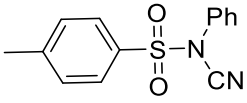
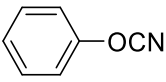
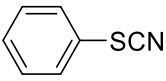
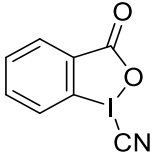


Figure 4. Proton NMR spectrum (CDCl_3 , 400 MHz) of the products thought to result from treatment of 1,2,4-tris(perfluorophenyl)cyclopentadiene with BrCN and NaH .

Having confirmed our results, we searched through the literature again to determine if our synthesis was unprecedented and thus worthy of publication. Alas, we found one obscure publication that showed that β -aminoenones, which at their core are delocalized carbon nucleophiles like cyclopentadienide, are brominated rather than cyanized.³⁵ In recent years, another publication has shown that 1,3-diketones can undergo the same bromination reaction.³⁶ While this outcome was still interesting in its own right, we decided that we would not be able to control the reaction for monobromination, and the likely reactivity of the bromine atoms in the 5-position, during acidity measurements, put us off. We moved on to find another alternative cyanizing reagent.

In the field of electrophilic cyanizing reagents there are 5 broad classes: thiocyanates, cyanates, cyanamides, hypervalent iodine compounds, and TsCN.³⁷⁻³⁹ To determine which compounds would best suit our synthesis, we defined our desired criteria as shown in Table 4.

Table 4. Best cyanizing reagent candidates based on our criteria

Compounds	No catalyst required	No side reaction or follow up reaction	Literature precedent of reacting with delocalized carbon nucleophiles	Price (USD/25g)
 (TsCN)	✓	✓	✓	\$130
 (NCTS)	✓	✓	✓	\$163
 (PhOCN)	✓	✓	✓	\$6400
 (PhSCN)	✗	✓	✓	\$242
	✓	?	✓	\$760

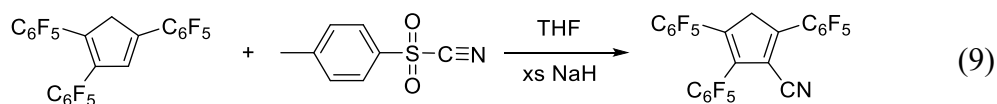
First, our alternative cyanizing reagent had to be commercially available at a reasonable price for our lab. After a cost analysis of the best candidates for each compound, TsCN was found to be the cheapest cyanizing reagent (Table 4). On the other hand, the most prohibitively expensive compound is phenyl cyanate at \$254/g (ca. \$6400 for 25 g). While

phenyl cyanate could be synthesized, it would require the use of cyanogen bromide, which as previously stated is highly toxic,⁴⁰ but mostly we wanted a reagent that we could buy off-the-shelf. Second, our ideal cyanizing reagent should also react with our nucleophile in ethereal solvents under alkaline conditions without the aid of a catalyst. At this hurdle, many thiocyanates fall short as most known uses of thiocyanates as a cyanizing reagent require a catalyst of some sort.^{41, 42} In addition, our cyanizing reagent should only behave as a cyanizing reagent under our conditions. It should also not be susceptible to causing side product formation either through a side reaction or an additional synthesis following the formation of our product. Some thiocyanates such as benzyl thiocyanate fail in this regard as there is literature precedent where under alkaline conditions cyanization or thiocyanization of a nucleophile can occur.⁴³

Ideally, our alternative cyanizing reagent would also have some literature precedent of cyanizing delocalized carbon nucleophiles such as enolates. While there is literature precedent in all categories, the two compounds that stand out the most are TsCN and NCTS.^{37, 38, 44} After some deliberation, we decided to try TsCN as our alternative cyanizing reagent for our proposed HCNCp syntheses. The next chapter summarizes our foray into this interesting project in synthetic methodology.

Chapter 2: Synthesis & Characterization of Cyanocyclopentadienes.

Having narrowed down our choices to TsCN, NCTS, and hypervalent iodine compounds, we opted to try TsCN first as it was the cheapest of the three options. For our initial synthesis (eq 9), we opted to react excess TsCN (0.4 mmol) and NaH (1 mmol) with 1,2,4-tris(perfluorophenyl)cyclopentadiene (0.2 mmol) in dry THF. All our synthetic work used anaerobic conditions (Schlenk technique, glovebox, purified solvents) as needed to preserve reactive species like hydrides and carbanions.



Our initial crude product showed two main signals in the ^1H NMR spectrum (Figure 5).

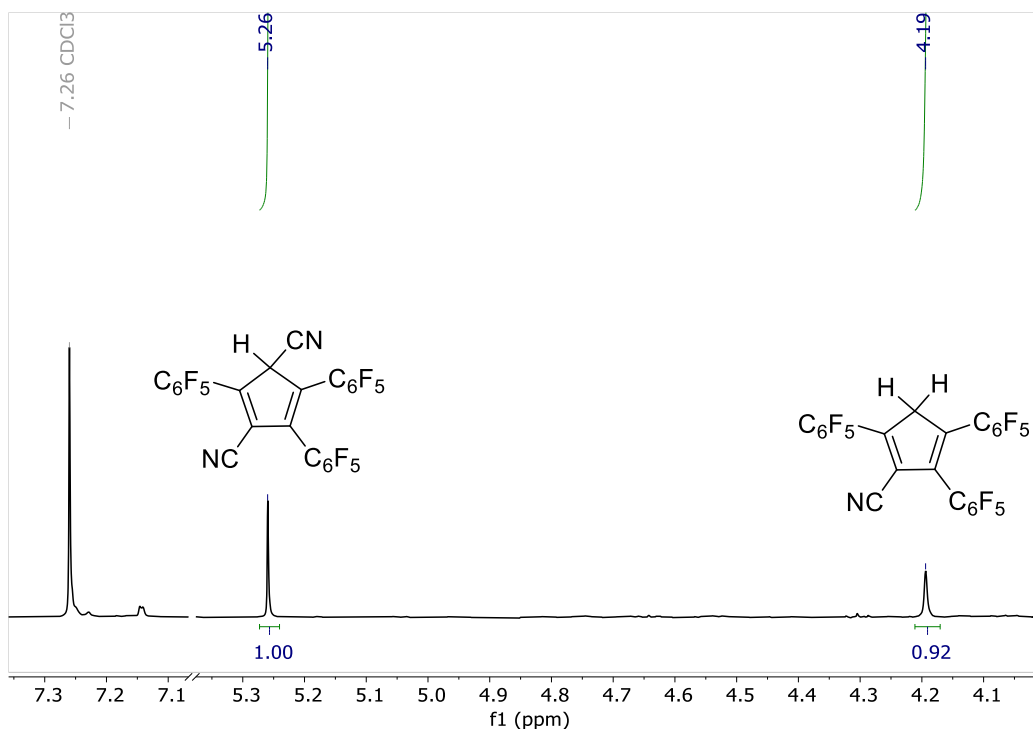


Figure 5. ^1H NMR (376 MHz, CDCl_3) spectrum of the product mixture formed from the reaction shown in eq 9. Assignment of the second product (to the signal at 5.26 ppm) is probably not correct, as explained in the text, but we do not have a better alternative.

We assigned the upfield singlet at 4.19 ppm to the CH₂ group of 2-cyano-1,3,4-tris(perfluorophenyl)cyclopentadiene, while the singlet at 5.26 ppm was assigned to the CH(CN) of 2,5-dicyano-1,3,4-tris(perfluorophenyl)cyclopentadiene, shifted downfield by the proximity of the CN group attached to the same carbon atom. The corresponding ¹⁹F NMR spectrum (Figure 6) confirms the assignment of the spectrum in Figure 5 but only after working through an additional puzzle. Across the spectral range, we see that the peaks corresponding to 2,5-dicyano-1,3,4-tris(perfluorophenyl)cyclopentadiene are more upfield than those corresponding to 2-cyano-1,3,4-tris(perfluorophenyl)cyclopentadiene. This result is odd because attachment of the second cyano group should have deshielded the local nuclei and shifted their signals more downfield – a golden rule in our chemistry so far. The second piece in the puzzle is the apparent twofold symmetry present in the spectrum we are assigning to 2,5-dicyano-1,3,4-tris(perfluorophenyl)cyclopentadiene. The two triplets at -157.1 ppm and -157.4 ppm are present in a ratio of 2:1, respectively. This pattern is echoed near -139 ppm and near -163 ppm. Both of these “puzzles” can be addressed by proposing that 2,5-dicyano-1,3,4-tris(perfluorophenyl)cyclopentadiene was autoionizing in the NMR solution. Formation of the carbanion would cause the fluorine nuclei to shift upfield (shielding effect). We understand that CDCl₃ is not a solvent that generally supports the spontaneous formation of ions. We can possibly justify autoionization by noting that the upfield portion of the ¹H NMR spectrum (not shown in Figure 5) indicates that there is a significant amount of residual THF in the sample, left over from the synthesis. However, this result leaves the compound without any hydrogen nuclei, so the corresponding ¹H NMR spectrum would be silent. Thus, one possibility is that the signal at 5.26 that we are assigning to 2,5-dicyano-1,3,4-tris(perfluorophenyl)-

cyclopentadiene is actually something else – an additional compound that we cannot assign. The only alternative at our disposal to explain the apparent twofold molecular symmetry in 2,5-dicyano-1,3,4-tris(perfluorophenyl)cyclopentadiene is fast exchange, a [1,3] type hydrogen shift that might be catalyzed by adventitious THF. This alternative, unfortunately, does not account for the upfield signal shifts in the ^{19}F NMR spectrum. In the end, we decided that whatever this second compound is, it's not what we wanted to synthesize, so we focused on isolating the monocyno derivative and improving its yield.

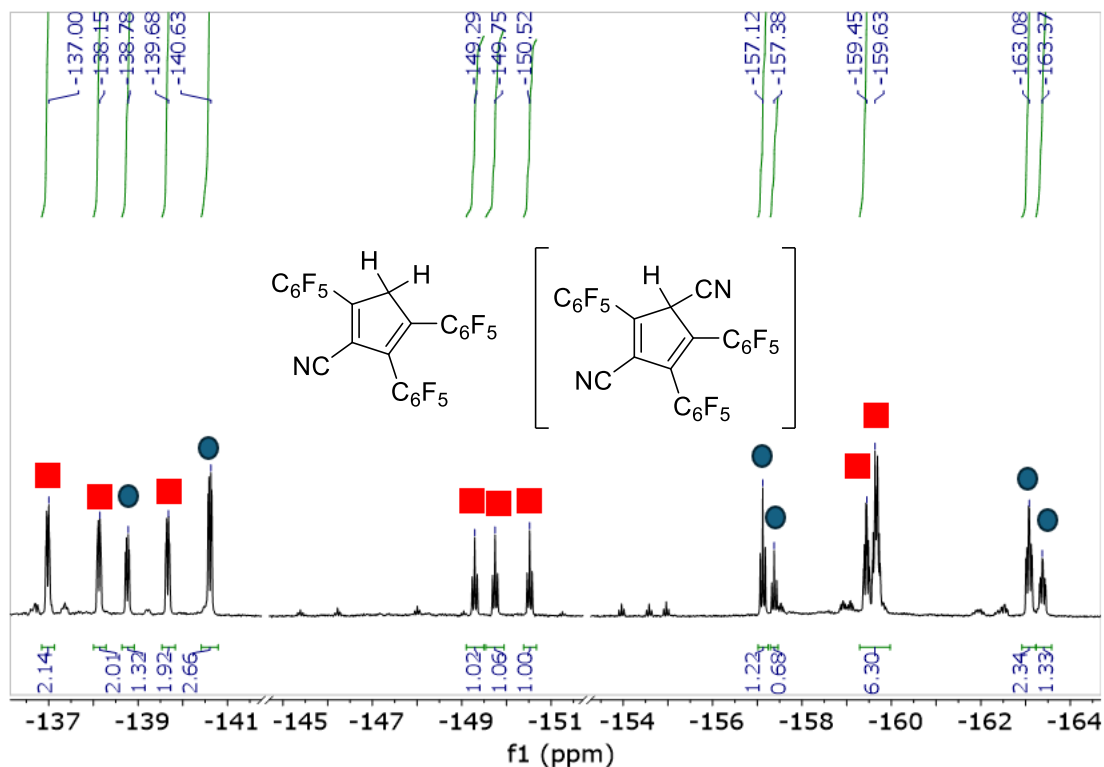


Figure 6. ^{19}F NMR spectrum (376 MHz, CDCl_3) of the product mixture arising from the reaction shown in eq 9. The left compound is confidently assigned to the signals marked by red squares. The right compound is tentatively assigned to the signals marked with blue circles.

Regardless, from these results it was clear that excess TsCN was unnecessary for our reaction, unlike our SnAr syntheses with perfluoroaryl compounds, and that a mole-to-mole ratio would suffice for the addition of one $-\text{CN}$ group. After adjusting our amount of

TsCN to a 1:1 ratio of TsCN:Cp, we managed to synthesize just 2-cyano-1,3,4-tris(perfluorophenyl)cyclopentadiene (Figure 7). The ^1H NMR spectrum showed an aliphatic proton peak at 4.21 ppm this time instead of the previously seen 4.19 ppm, which might be the result of small differences in the amounts of certain polar impurities such as THF. The pure compound was analyzed via flow injection-mass spectroscopy (FI-MS) to give an exact mass of 587.988 (Figure 9, Calculated Exact Mass: 588.990). Recrystallization using hexanes and toluene as our solvents provided a crystal of good enough quality to get an X-ray crystallographic structure from, further validating our results (Figure 8).

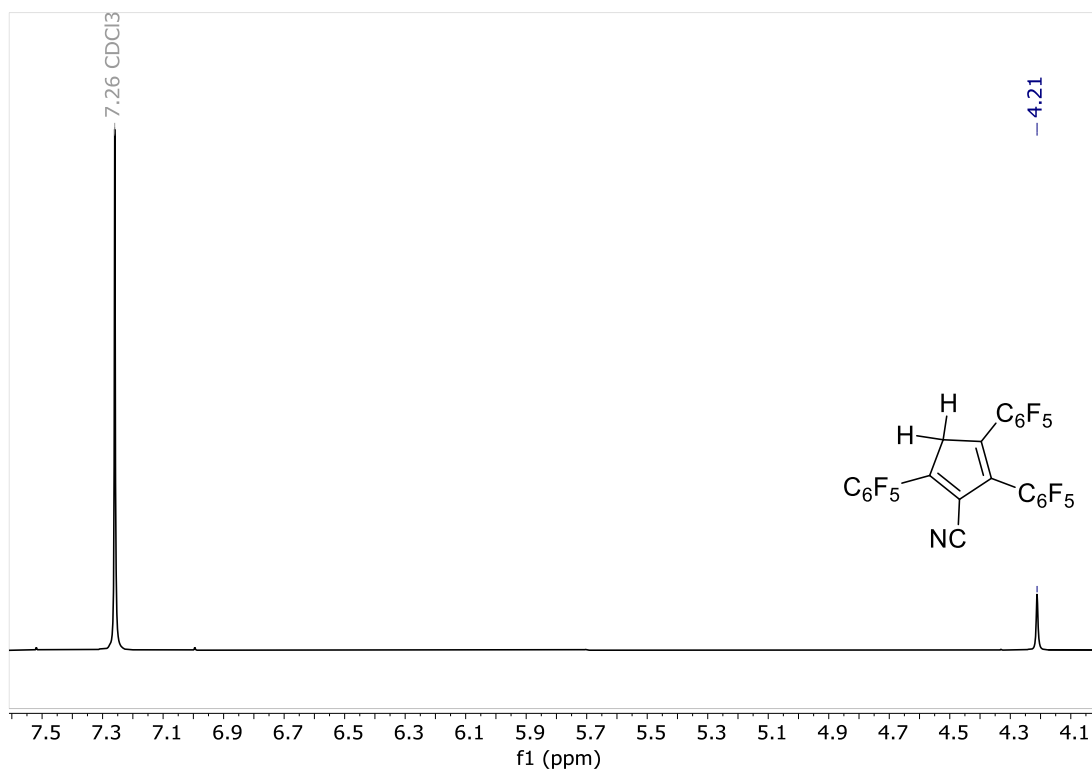


Figure 7. ^1H NMR (376 MHz, CDCl_3) spectrum of the monocyanoated product obtained from the reaction shown in eq 9 with 1:1 reactant stoichiometry.

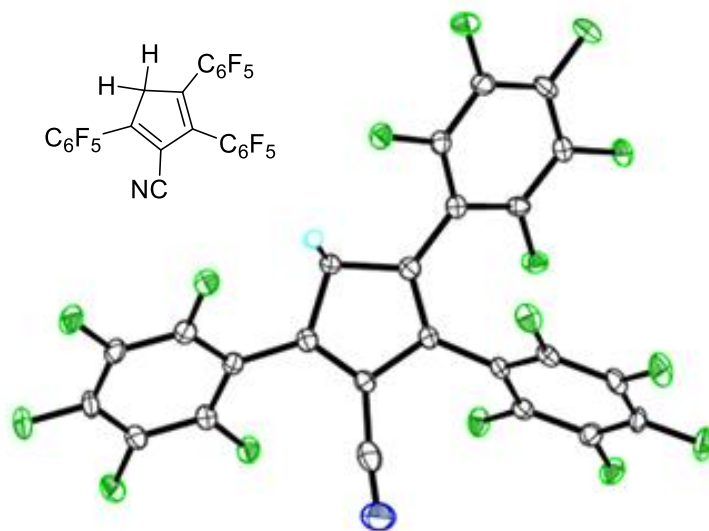


Figure 8. Thermal ellipsoid plot (50% probability) of the molecular structure of the compound shown in the diagram (1,2,4-trisperfluorophenyl-3-cyanocyclopentadiene), in the crystalline state. (Crystals were grown from a hexane / toluene mixture). Dark blue = nitrogen; light blue = hydrogen; green = fluorine, gray = carbon.

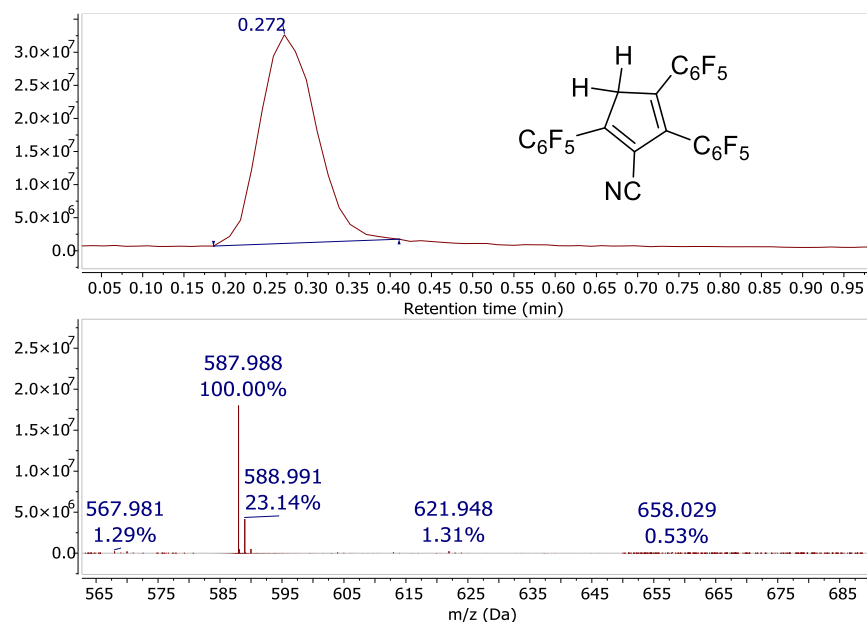


Figure 9. ESI-MS (negative ion) of the compound shown in the diagram. **Top:** Total ion chromatogram showing the single peak expected for the derivatized cyclopentadienide anion (loss of H). **Bottom:** Mass spectrum. The M+1 signal intensity (23%) is roughly consistent with a C₂₄ formula.

While successful, the reaction did not provide enough product to run multiple acidity measurements. Thus we increased the scale to 1 mmol and tried again. However, scaling the reaction up resulted in a new unknown aliphatic peak forming at 4.19 ppm (Figure 10).

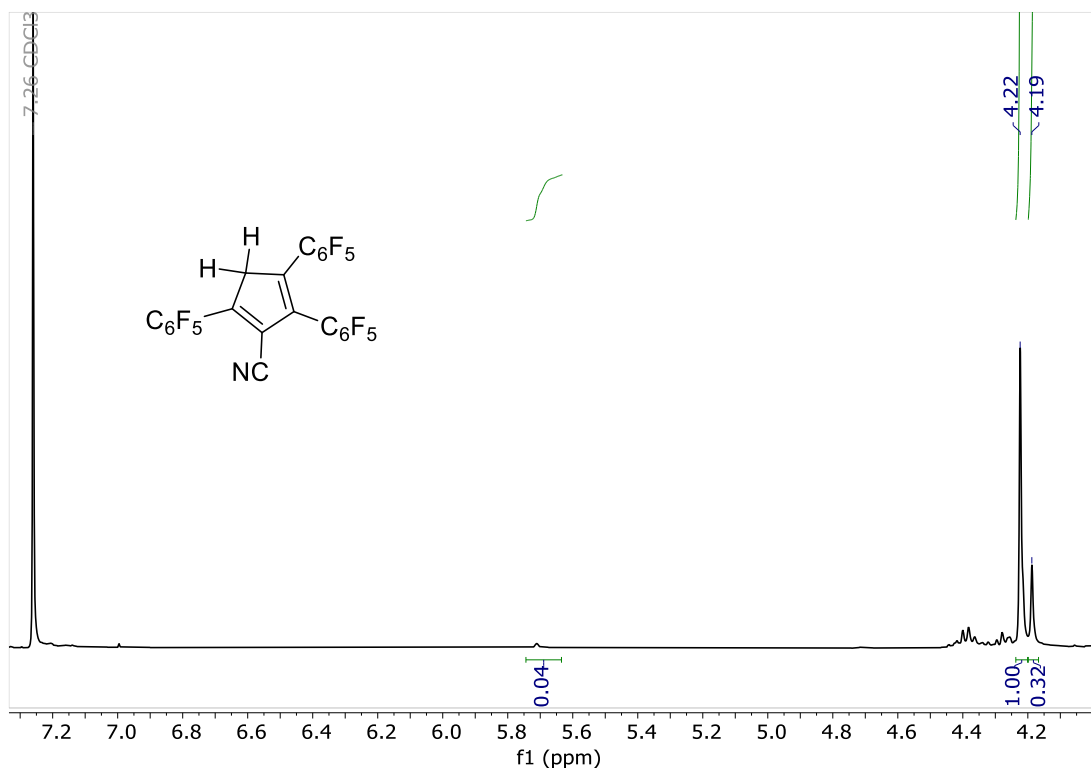


Figure 10. ¹H NMR (376 MHz, CDCl₃) spectrum of the compound shown, obtained from an upscaled synthesis of the compound shown in the diagram.

Additional peaks in the ¹⁹F-NMR spectrum (Figure 11) confirmed that an additional fluorinated product was forming. Neither the proton or fluorine peaks corresponded to starting material, and structural isomerization of the product should have been theoretically impossible given that we used a single isomer of the starting material. Adding insult to injury, recrystallization of the product from the larger-scale synthesis did not result in a useful outcome. We therefore were left with sufficient compound to run one preliminary acidity measurement, which will be described later.

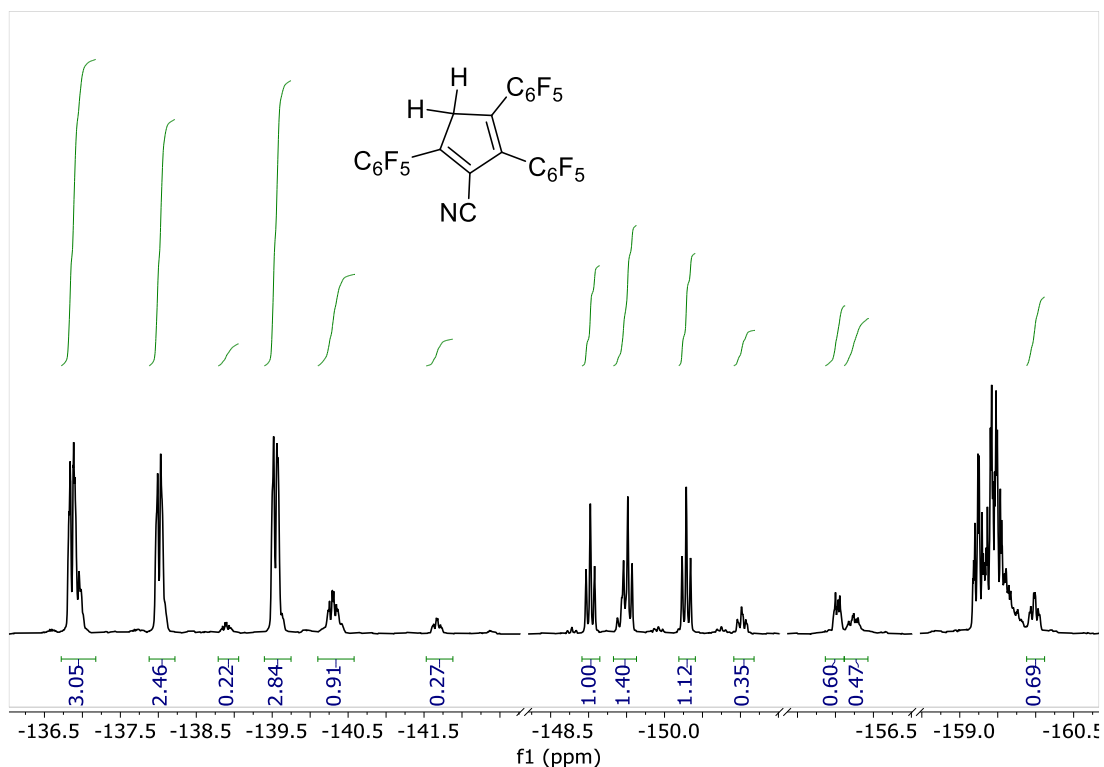
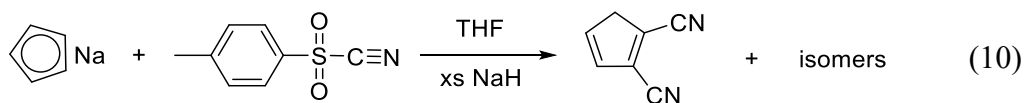


Figure 11. ^{19}F NMR (376 MHz, CDCl_3) spectrum of the spectrum of 2-cyano-1,3,4-tris(perfluorophenyl)cyclopentadiene and unknown by-product(s).

After declaring a partial victory in the addition of $-\text{CN}$ groups to 1,2,4-tris(perfluorophenyl)cyclopentadiene, we attempted to replicate Webster's work in synthesizing dicyanocyclopentadienes (eq 10) using our preferred reagent system. As we will explain in Chapter 3, these compounds were expected to play a central role in aligning the aqueous and SLI acidity scales.



In our first attempt, 5 mmol of NaCp was reacted with 10 mmol (2 equiv) of TsCN and excess NaH in THF. To better control the exothermic additions of TsCN, a solution of TsCN in THF was cannulated into a graduated, pressure-equalizing addition funnel for

dropwise addition to the reaction, instead of adding the TsCN as a solid in a single portion. The reaction flask was also placed in an ice bath for the first hour of the reaction to help improve reaction selectivity. As the TsCN was added, a white precipitate formed because the leaving group, tosyl anion (Ts^-), forms a sodium salt that is insoluble in THF. We could not find anywhere specifically stated in literature if TsNa is insoluble in THF.⁴⁵ The insolubility of TsNa in THF was confirmed by mixing 225 mg of pure TsNa in 20 mL of THF (Figure 12). Here we emphasize the distinction between tosyl (Ts) and tosylate (TsO).

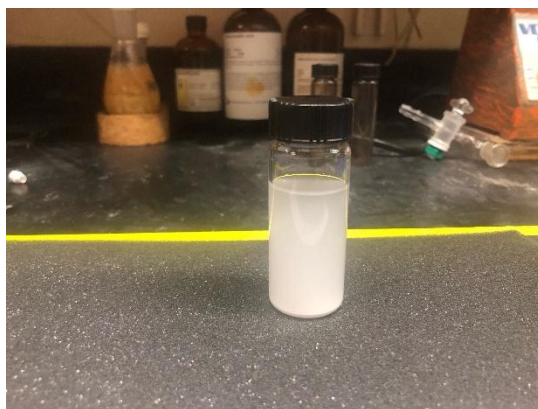


Figure 12. Photograph of a slurry of 225 mg of TsNa and 20 mL of THF demonstrating the insolubility of the salt.

After adding the TsCN, the reaction mixture took on a noticeable darker color. After 24 h, the reaction was filtered anaerobically to separate the dissolved product species (which should be sodium cyclopentadienide derivatives) from the TsNa precipitant and from unreacted NaH, which is also entirely insoluble in THF. The filtrate was then evaporated, leaving a solid product mixture that was transferred to the glove box for sampling and spectroscopic analysis. At this point it is important to recognize that there has been no “work up” or “hydrolysis” of the product mixture, so the cyclopentadiene derivatives should all be present as their conjugate bases.

The NMR spectrum (Figure 13) reports a peculiar result: Three singlets at 6.62, 6.22, and 5.68 ppm, respectively. After comparing our NMR data to Webster's, we confirmed that the singlet peak at 5.68 corresponded to NaCp starting material. Though slightly offset from Webster's reported chemical shift data, the peaks at 6.62 and 6.22 ppm most likely represent the 1,2,3 and 1,2,4 isomers of tricyanocyclopentadiene, respectively. Thus, our synthesis had "jumped" the mono- and disubstituted intermediates and left us with a crude product consisting of undesired $(\text{CN})_3\text{Cp}^-$ and starting material.

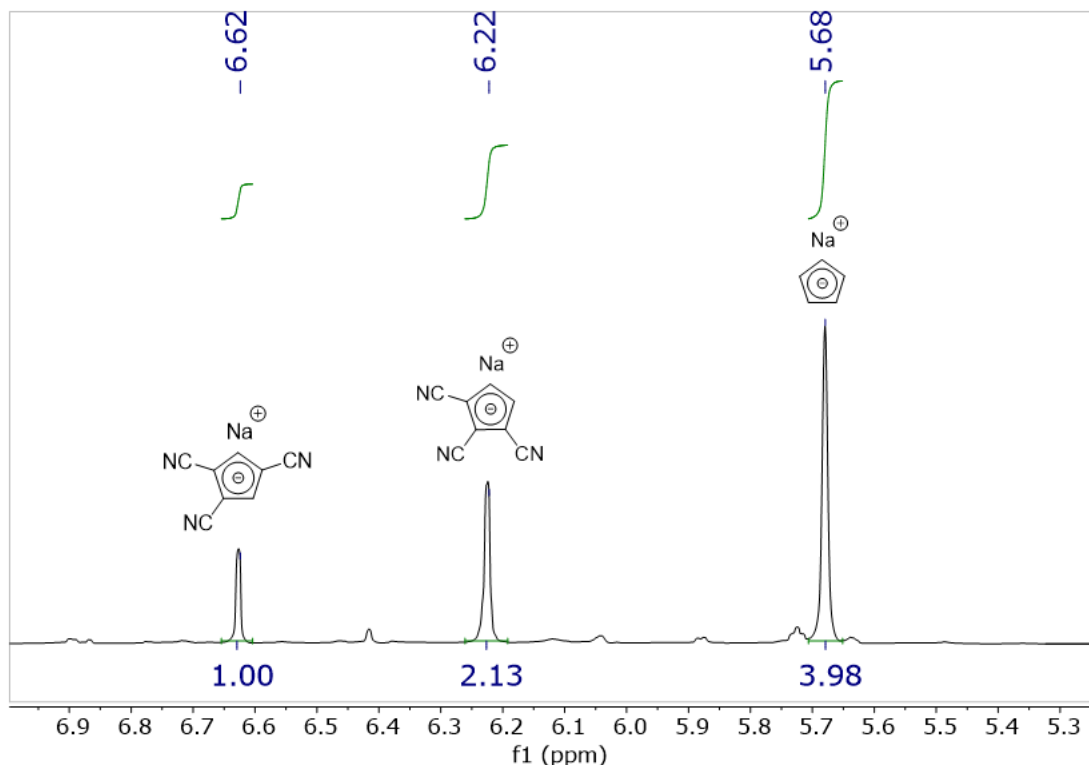
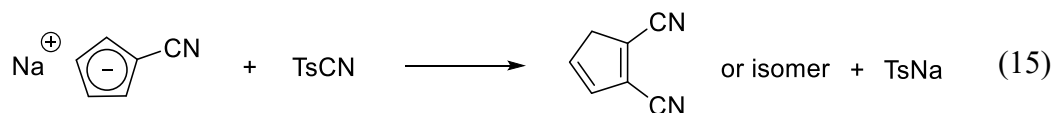
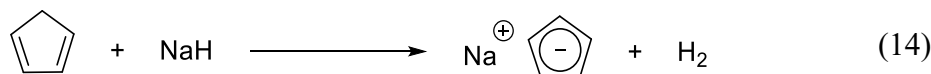
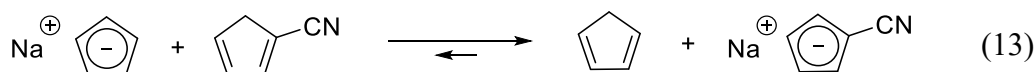
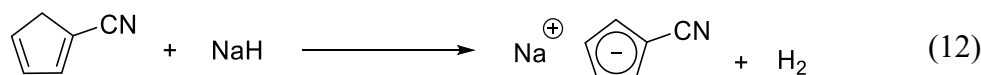
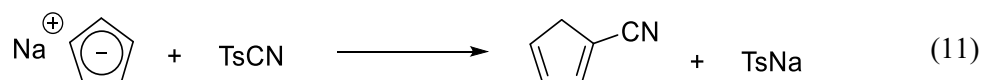


Figure 13. ^1H NMR spectrum (400 MHz, CD_3CN) of the product mixture resulting from the reaction shown in eq 10.

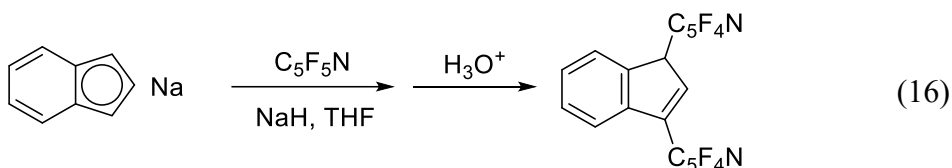
This result can be rationalized by considering the relative rates of the different processes involved. The initial substitution (eq 11), and subsequent substitutions (starting with eq 15) are apparently fast. In addition, proton exchanges among cyclopentadienes (eq 13) are fast, too. We assumed, based on prior work using C_6F_6 and similar compounds as the

electrophilic reagents, that the return of unsubstituted cyclopentadiene to its anion form (eq 14) would be fast enough to keep up with the other reactions. However, this apparently is not true. Likewise, the equilibrium shown in eq 13 lies strongly to the right. This thermodynamic bias, along with the apparent relative slow rate of the return of cyclopentadiene to a reactive state (eq 14), results in the buildup of neutral cyclopentadiene in the reaction. After all of the TsCN has been consumed, the reaction shown in eq 14 would continue at its relatively slow rate, apparently concluding before workup or analysis, resulting in a significant quantity of observed NaCp in the reaction mixture. To summarize, neutral cyclopentadiene, generated by a fast, thermodynamically biased proton exchange (eq 13), represents a “dead end” because cyclopentadiene is insufficiently reactive toward sodium hydride to return it to its anionic form.



This outcome suggests that TsCN is *much more reactive* than our “historical” electrophilic reagents like hexafluorobenzene or octafluorotoluene. This outcome is also consistent with an isolated outcome among our unpublished results. Our group found that sodium indenide

reacted with 1.0 equiv of pentafluoropyridine and excess sodium hydride to give a 40% yield of 1,3-bis(tetrafluoro-4-pyridyl)indene and unreacted indene (eq 16). We now believe that the same kind of kinetic effect was operating, as indene is even less reactive toward NaH than cyclopentadiene.



To alleviate this issue, we swapped NaH for the more reactive KH to keep neutral cyclopentadiene from building up in the reaction. We knew from synthetic experiments that KH is considerably more reactive. And in fact, the use of KH did increase the rate at which neutral cyclopentadiene is returned to its anionic form, allowing us to exert better control over our reaction outcome by adjusting the amount of TsCN in the synthesis. After the reaction was complete, the mixture was evaporated to dryness and subjected to a normal acidic-aqueous workup. This process differs from the preceding example in that the products are present as neutral dienes, not as carbanions. An NMR sample was taken immediately after completion of the workup (Figure 14).

Using the multiplicities, integrals, placement, and coupling constants of the peaks we were able to assign the spectrum shown in Figure 14. For 1,2-dicyanocyclopentadiene, the aliphatic protons correspond to the peak at 3.67 ppm (there is a minor interference) while the vinyl peaks correspond to the two doublets-of-triplets at 6.9 ppm and 6.7 ppm. The multiplet shoulder signal at 3.66 ppm corresponded to the aliphatic protons of 1,3-dicyanocyclopentadiene. This assignment was confirmed by the vinyl peaks at 7.58 ppm sharing the same integration as the shoulder multiplet. This finding also helped us assign

the other vinyl peak at 7.39 ppm that was hidden beneath the vinyl peak of 1,4-dicyanopentadiene at 7.38 ppm. The vinyl peak of 1,4-dicyanopentadiene was coupled with the aliphatic peak at 3.73 ppm because of their equal integration and sharing the same coupling constant of 1.6 Hz. By process of elimination, the vinyl peak at 7.46 ppm and the aliphatic peak at 3.57 ppm correspond to the 2,3-dicyanocyclopentadiene which was confirmed by their shared coupling constant of 1.38 Hz.

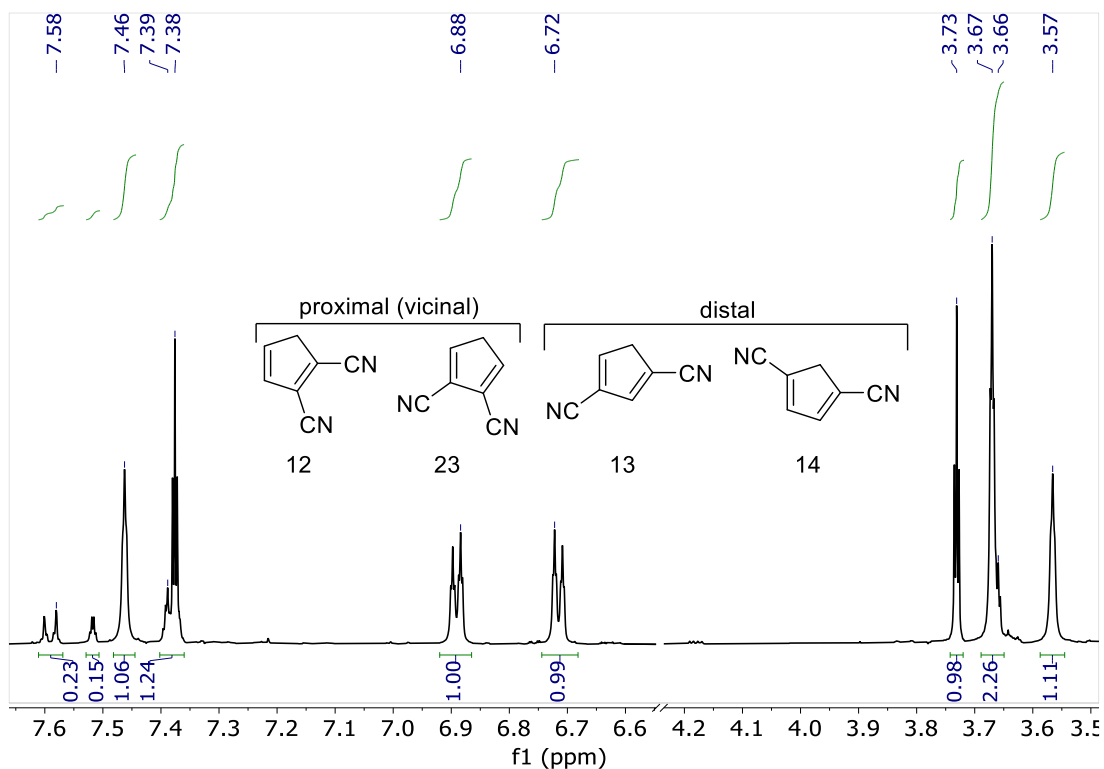


Figure 14. ^1H NMR (400 MHz, CD_3CN) spectrum of the mixture of dicyanocyclopentadiene isomers obtained from the reaction shown in eq 10.

However, after 24 h under ambient conditions, the crude dicyanocyclopentadiene product converted itself from a dark lumpy powder to a shiny dark glass. This transition was reflected in the proton NMR spectrum (Figure 15) which showed our recognized product peaks to be gone and replaced by a forest of new aliphatic peaks and some vinyl peaks.

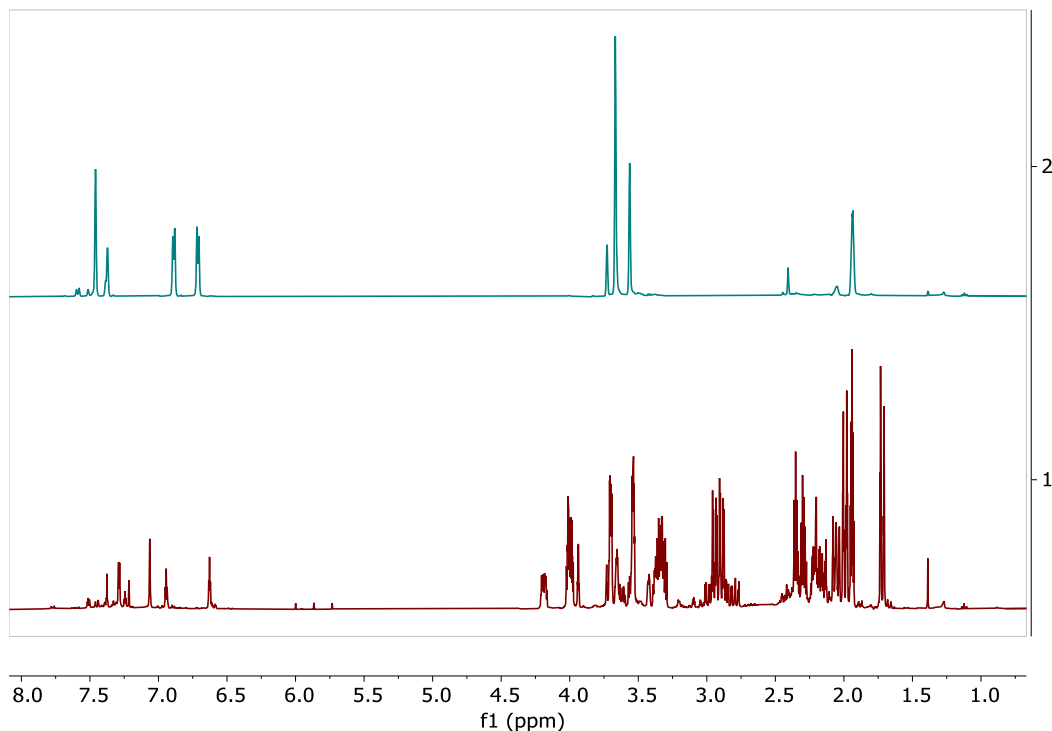


Figure 15. ^1H NMR spectra (400 MHz, CDCl_3) spectrum of the crude dicyanocyclopentadiene product immediately after workup (**Top**) and after 24 h at 25 $^\circ\text{C}$ (**Bottom**).

These results were further validated by mass spectroscopy which showed masses that were higher than we anticipated for our products (Figure 16). These results led us to conclude that the dicyanocyclopentadienes are unstable at room temperature, likely through some kind of polymerization process. Whether this process is a radical-type reaction or cationic in nature cannot be estimated from the observations at hand. For some of the isomers, dimerization by Diels-Alder reaction could be possible, too.

To address this decomposition issue, we retained all of the polycyanocyclopentadiene products of all future syntheses as Na/K salts. Experience within our group teaches us that certain cyclopentadiene derivatives (such as phenylcyclopentadiene) are unstable in the same way. While keeping the products as salts is easy “on paper,” in practice it made the

synthetic workup more difficult, and of course we lost the ability to separate isomers using silica gel chromatograph – a significant concession to the challenges of our chemistry.

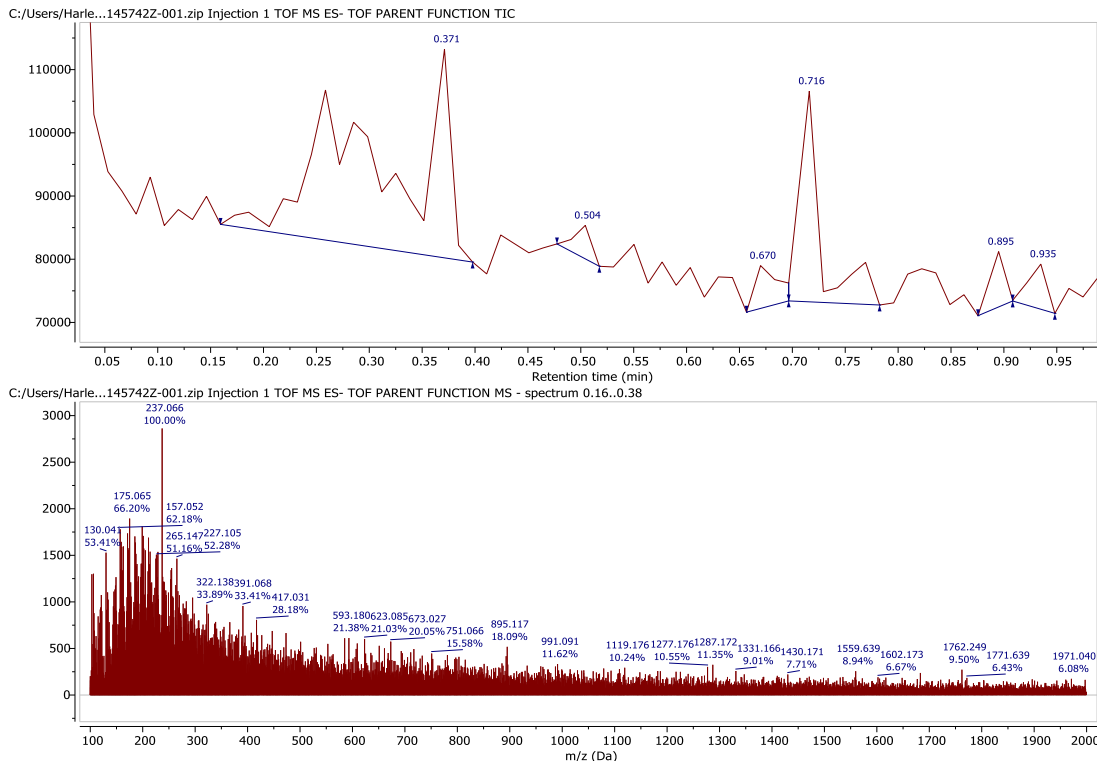


Figure 16. FIA-MS of crude dicyanocyclopentadiene product after 24 h.

Another significant concession, which we will address in more detail in Chapter 3, was the presence of Na^+ and K^+ as the counterions of these carbanions, whereas the SLI measurement requires Li^+ as the counterion! Nevertheless, we were able to develop a two-part workup that was good enough to allow us to attempt some preliminary acidity measurements of some HCNCps. The first part of the workup removed the NaTs (and KTs) from the crude product via anaerobic filtration followed by evaporation of the reaction solvent (THF) and slurring the resulting residue in either diethyl ether or hexane. The second part of the workup took advantage of the difference in acidity between NaCp (KCp) and its cyano-substituted analogues (difference of 5-6 pK_a units) to selectively re-protonate

the NaCp (KCp) to HCp. To complete the second step, the HCp, now dissolved in the ether solvent, would be separated from the solid ionic CNCp salts by a second anaerobic filtration (Figure 17). These worked-up salts would then be washed with ether before being evacuated on the Schlenk line overnight and taken into a nitrogen-rich glovebox for storage.

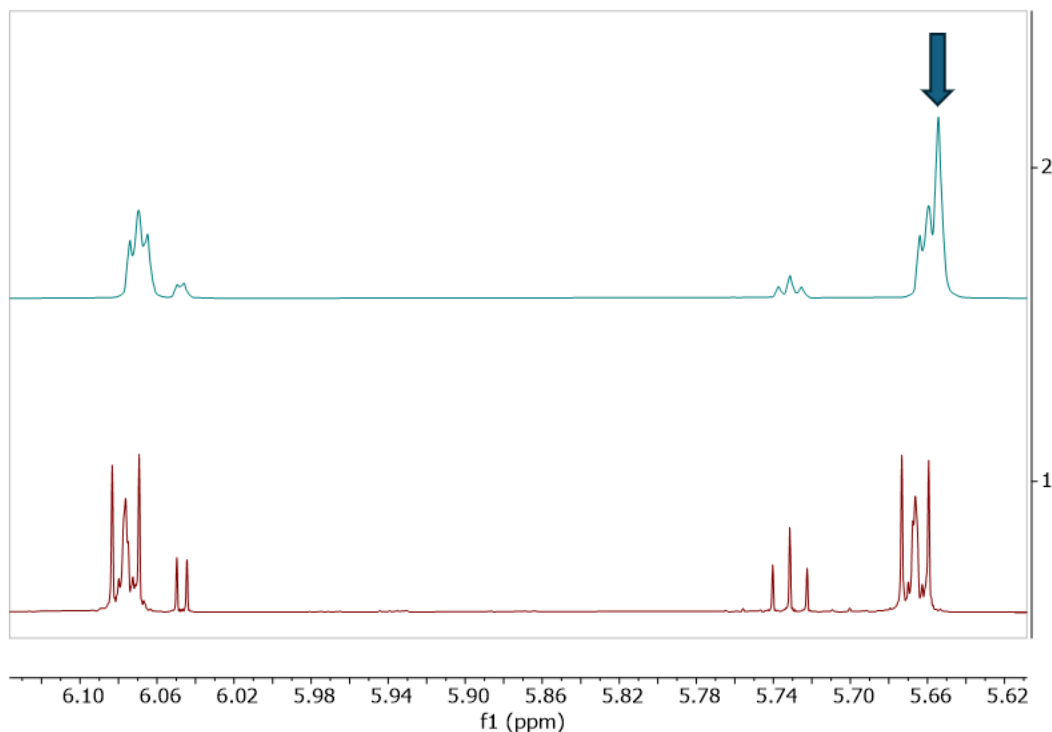


Figure 17. ^1H NMR spectra (CD_3CN , 400 MHz) of the monocyanocyclopentadiene product mixture from the reaction shown in eq 10. **Top:** Same spectrum as Crude product containing CpCN anion (major, 5.67 and 6.08 ppm), Cp anion (5.65 ppm, indicated by the arrow) and $\text{Cp}(\text{CN})_2$ (minor). The triplet at 5.73 ppm corresponds to 1,2- $\text{Cp}(\text{CN})_2$ and the doublet at 6.04 ppm corresponds to 1,3- $\text{Cp}(\text{CN})_2$. **Bottom:** Crude product after selective re-protonation and filtration.

Our initial success with this selective acidification process, coupled with preliminary acidity tests suggesting that the ΔpK between 1,2-dicyanocyclopentadiene and 1,3-dicyanocyclopentadiene may be significant, led us to attempt to remove the 1,4- and 1,3-dicyanocyclopentadiene isomers (distal regioisomers, neutral dienes) from the 1,2-

dicyanocyclopentadienide (vicinal regioisomer, carbanion). Unfortunately, our attempts were in vain as the ΔpK was still too close for us to accomplish this separation selectively (Figure 18).

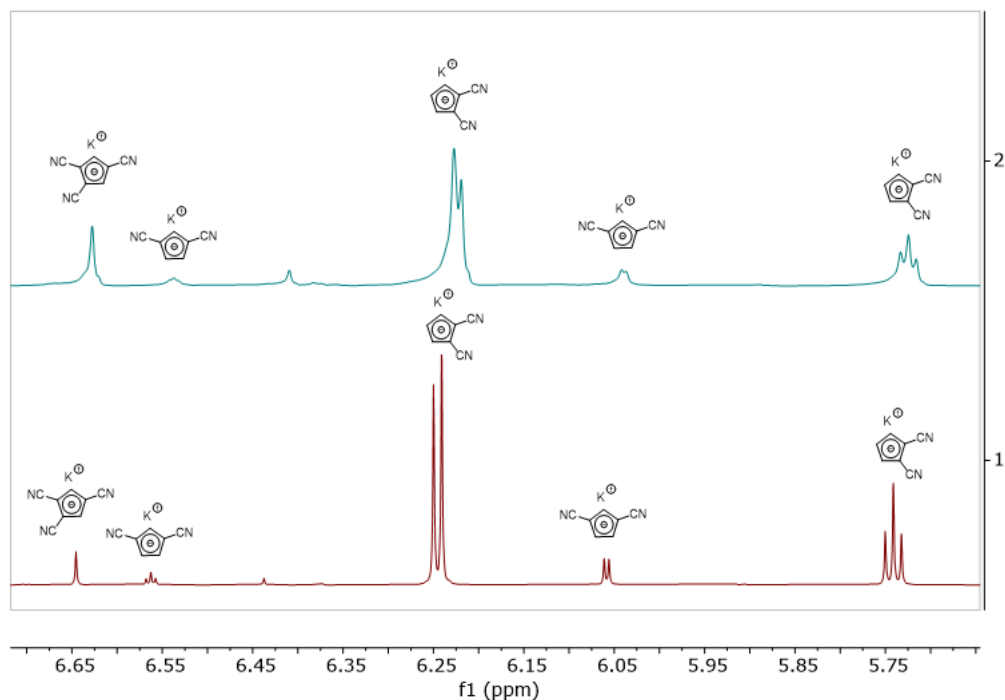













Figure 18. Stacked ¹H NMR (400 MHz, CD₃CN) spectrum of the 1,3- and 1,2-dicyanocyclopentadienide isomeric mixture before (**Bottom**) and after (**Top**) attempting to separate the 1,3-dicyanocyclopentadienide from the rest of the mixture via selective re-protonation.

Having optimized the synthesis and workup of cyanocyclopentadiene compounds, we successfully applied this total procedure as a template to synthesize several cyanocyclopentadiene derivatives both known and novel (Table 5). All of this was achieved thanks to the help of our undergraduate researcher, Tripp Aardema. Any remaining starting material in the crude mixture, as determined by NMR spectroscopic analysis, was removed via selective acidification. Higher order derivatives were left in the product and accounted for in future acidity tests (see Chapter 3). Syntheses that used sodium 1,2-dimethylcyclopentadienide and sodium t-butylcyclopentadienide as started

material were observed to have a higher proportion of higher-order derivatives than sodium cyclopentadienide.

Table 5. Product yields resulting from addition of cyano groups to cyclopentadienes and alkylcyclopentadienes. Asterisk indicates a possible product whose yield cannot be determined by ^1H NMR for lack of a resolved signal. Mass ratios (individual product percentages) are normalized to a total of 100%.

Starting Material	Molar Eq. of TsCN	Yield	Mass Ratios							
										
	1	61%	6.7%	51%	27%	5.4%	0.0%	0.0%		
	2	64%	0.0%	0.0%	69%	14%	2.5%	0.0%		
	1	44%	4.8%	30%	48%	14%	0.0%*			
	2	54%	0.0%	0.0%	0.0%	0.0%	100%			
	1	35%	9.0%	9.3%	16%	36%	17%	11%	0.0%	0.0%
	2	68%	0.0%	0.0%	1.3%	49%	12%	7.8%	10%	15%

The presence of the alkyl substituents results in a less acidic cyclopentadiene ring, causing the deprotonation of any neutral cyclopentadiene derivative (eq 14) to be less reactive toward KH, and we know from synthetic experiments that the reactions of cyclopentadienes with KH are *much slower* when the ring is alkylated. We believe that with alkylated cyclopentadienes, the reaction with KH (analogous to eq 14) has become so slow that even at the time of workup, there is present a significant quantity of the neutral cyclopentadiene derivative (starting material), but it is not observed in the product mixture because neutral dienes would be lost during filtration. This explains both the formation of more highly cyanated derivatives and the low overall yield. In principle, we could use a could be increased again by replacing KH with a stronger base. However, alternative options for a faster *non-nucleophilic* base are quite limited. Any nucleophilic base would be in competition with the alkylated cyclopentadienides for the nitrile carbon of TsCN. For

example, it is known in our lab that BrCN will react with lithium diisopropylamide (LDA) to form an aminonitrile. So we would need to be selective even among the well-known “hindered” bases. The additional steric bulk associated with lithium bis(trimethylsilyl)amide (LHMDS) may prove adequate in preventing nucleophilic competition, but that is work for a future student. Another possible reason why these alkylated cyclopentadienylsodium compounds gave multiple cyanations is that their assays were probably low, as I used older samples that were prepared some time ago (possibly years). For example, if sodium dimethylcyclopentadienide was partially decomposed sitting in the glove box resulting in only a 50% assay of reactant, then the ratio of TsCN to carbanion is 2:1, not 1:1. This difference in ratio would obviously promote multiple cyanations.

Our first novel cyano-substituted cyclopentadiene derivative was a mixture of mono- and dicyanodimethylcyclopentadienide derivatives. Following the General Synthesis Procedure, we combined sodium 1,2-dimethylcyclopentadienide with 1.0 equiv each of TsCN and KH in dry THF. We optimized at 1.0 equiv of KH to avoid dealing with a large excess of KH in the TsNa by-product, which would require potentially hazardous quenching. After 1 h at 0 °C and 3 h at 25 °C, the reaction mixture was filtered anaerobically to give a red-orange powder. A sample of the powder (a mixture of carbanions) was dissolved in CD₃CN and analyzed by ¹H NMR spectrometry (Figure 19).

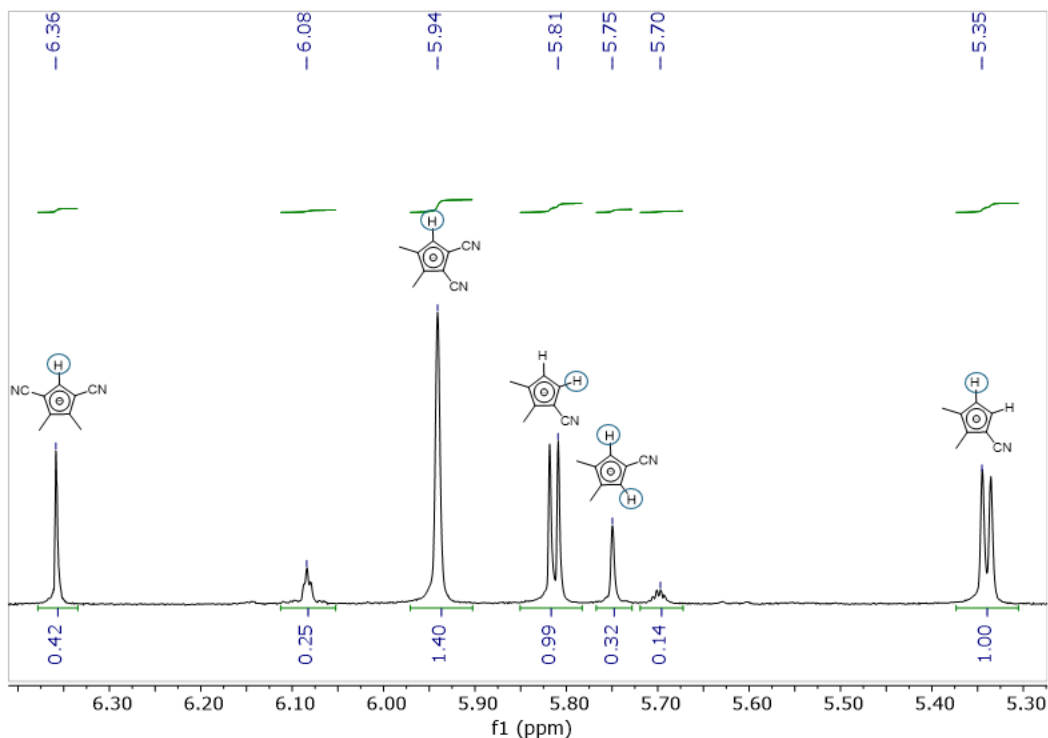


Figure 19. ¹H NMR spectrum (400 MHz, CD₃CN) of the products from the reaction of 1,2-dimethylcyclopentadienylsodium with tosyl cyanide. Each peak is labeled with both the structure they belong to and the proton they represent with a blue circle.

The methyl groups of the different products were not resolved in the NMR spectra. Only the aromatic signals could be used to give tentative assignments of compounds in the mixture. The equally integrating pair of doublets at 5.81 ppm and 5.35 ppm ($J = 3.7$), in the most upfield portion of the “aromatic region” was assigned to 1-cyano-2,3-dimethylcyclopentadienide. The most upfield singlet at 5.75 ppm was assigned to the symmetrical isomer, potassium 1-cyano-3,4-dimethylcyclopentadienide. The next downfield singlet at 5.94 ppm was assigned to potassium 1,2-dicyano-3,4-dimethylcyclopentadienide (ring proton adjacent to one cyano group and one methyl group), and the singlet furthest downfield, at 6.36 ppm was assigned to potassium 1,4-dicyano-2,3-dimethylcyclopentadienide (ring proton adjacent to two cyano groups). The

signals at 5.70 ppm and 6.08 ppm were not assigned – except to some sort of impurity or decomposition by-product that we could not identify.

These assignments are consistent with our observations for the spectrum of the potassium dicyanocyclopentadienide mixture (Figure 20), in which the downfield-most triplet is assigned to the ring proton between the two cyano groups of potassium 1,3-dicyanocyclopentadienide, and the upfield-most triplet is assigned to the ring proton between two hydrogen atoms in potassium 1,2-dicyanocyclopentadienide.

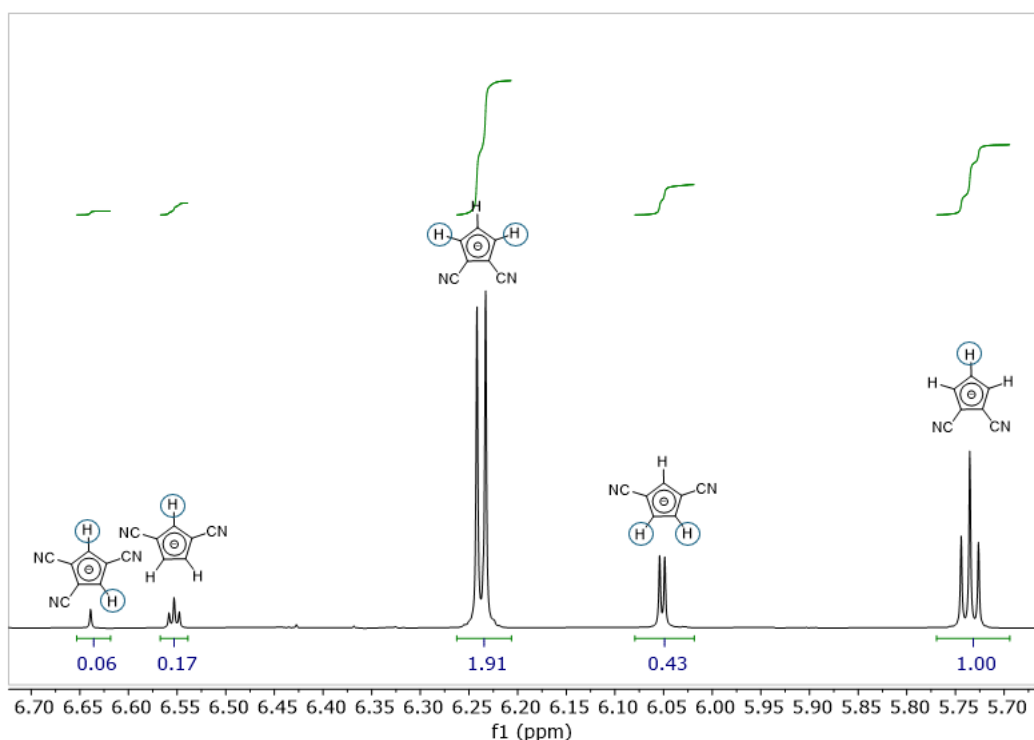


Figure 20. ¹H-NMR spectrum (400 MHz, CD₃CN) of the product mixture resulting from the reaction of cyclopentadienylsodium and TsCN. Each peak is labeled with both the structure they belong to and the proton they represent with a blue circle.

Another interesting observation is the variation in coupling constants. Potassium 1,3-dicyanocyclopentadienide shows narrower four-bond coupling (⁴J = 2.1 Hz) while potassium 1,2-dicyanocyclopentadienide shows wider three-bond coupling (⁴J = 3.5 Hz).

Knowing that often ${}^4J \sim {}^3J$ in metallocene compounds such as ferrocene derivatives, these coupling constants, on their own, would not be definitive for assignment. However, we can conclude that they correspond to 4J and 3J , respectively, based on the sound chemical shift arguments. Therefore, the trend in coupling constants is, by itself, a useful finding that may help us characterize other product mixtures in the future.

This proximity to the $-CN$ groups result in significant deshielding of the vicinal proton and thus it is more downfield than its corresponding isomeric proton. These observations suggest that proximity to EWGs as well as the number of EWGs present on the compound result in more downfield proton peaks. Note that this trend tends to be generally true for cyclopentadienyl *anions* but not *cyclopentadienes*, which have a butadiene system that has its general rule for what is upfield vs. downfield (the “inside” hydrogen atoms of a 1,3-butadiene system are usually downfield).

Having successfully synthesized a mixture of monocyano- and dicyano derivatives of 1,2-dimethylcyclopentadienide derivatives, we hoped to optimize the synthesis to produce only dicyanized derivatives. To this end, we increased the amount of TsCN and KH to 2 equiv each. NMR spectrometric analysis of the resulting red-brown powder product, however revealed no aromatic (ring) signals at all! Instead, only a single aliphatic multiplet at 2.03 ppm could be associated with our product along with an assortment of impurities (Figure 21). This aliphatic peak was given the tentative assignment of potassium 1,2,3-tricyano-4,5-dimethylcyclopentadienide. Again we believe the “ k_4 problem” (see eq 14) is at work. Neutral 1,2-dimethylcyclopentadiene is deprotonating only very slowly with KH, which tends to increase the number of cyano groups that are attached. We considered ordering MS analyses of these products mixtures to at least confirm the number of cyano groups

present in each product, but we also knew that the ESI method typically includes acid hydrolysis which would result in even more complex isomeric mixtures and probably a lot of decomposition, too. Considering the cost of the analysis we did not try.

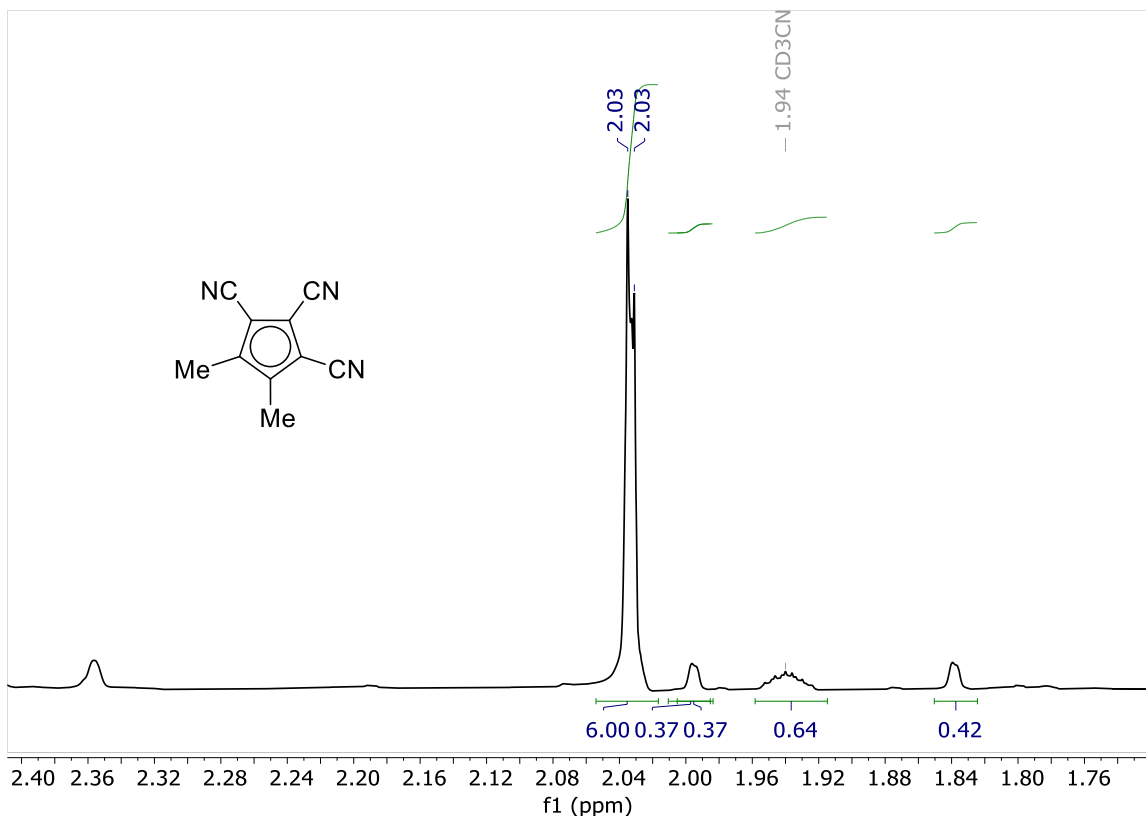


Figure 21. ¹H NMR spectrum (400 MHz, CD₃CN) of potassium 1,2,3-tricyano-4,5-dimethylcyclopentadienide (tentative assignment).

Having explored what was possible with sodium 1,2-dimethylcyclopentadienide, we turned our attention to sodium tert-butylcyclopentadienide in an effort to expand the scope of our methods and to understand its potential limitations. Following the General Synthesis Procedure, we conducted two syntheses, one with 1 equiv of TsCN and the other with 2 equiv TsCN. We first conducted NMR analysis on the latter reaction because we suspected it would be easier to assign the spectrum since the multiplicities suggested that all the

products contained two $-\text{CN}$ groups or more. In Figure 22, we observed that the doublet peaks at 5.63 ppm and 6.04 ppm had the same coupling constant (3.7 Hz).

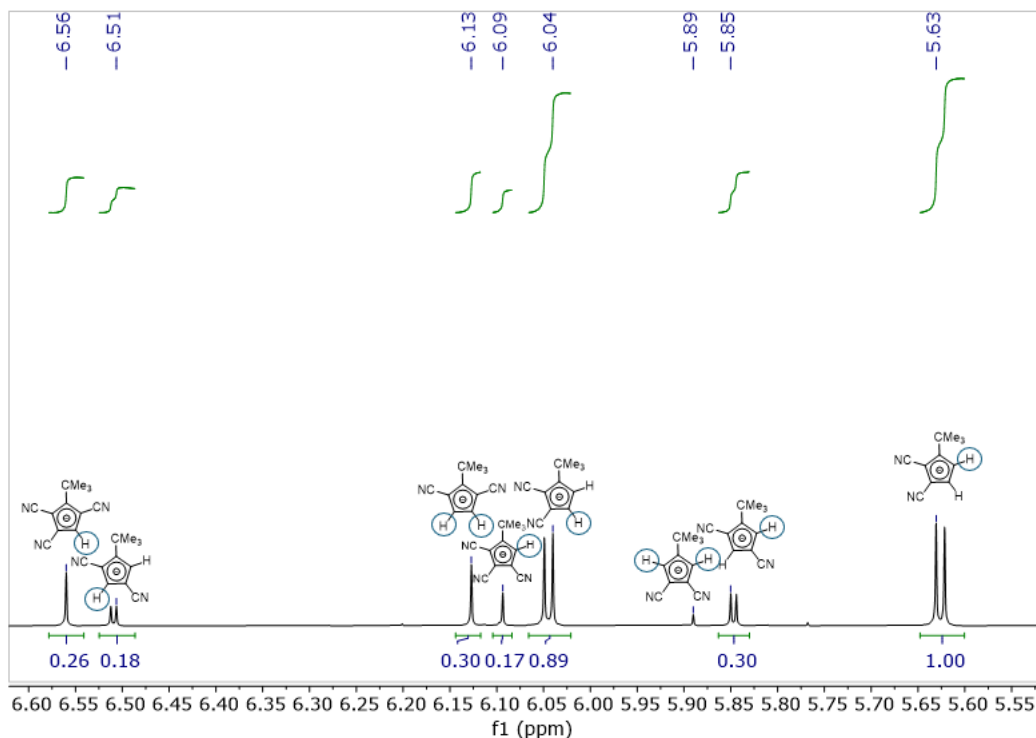


Figure 22. ^1H NMR (400 MHz, CD_3CN) spectrum of the product mixture resulting from sodium *tert*-butylcyclopentadienylsodium and 2 equiv each of TsCN and KH. Each peak is labeled with both the structure they belong to and the proton they represent with a blue circle.

We also observed the doublet peaks at 5.85 ppm and 6.51 ppm shared the same coupling constant (2.40 Hz). From their multiplicities, we could determine that each set of peaks either corresponded to potassium 1,2-dicyano-3-*tert*-butylcyclopentadienide or potassium 1,3-dicyano-4-*tert*-butylcyclopentadienide. Referring back to our analysis of the NMR spectrum in Figure 20, we also see that $^4J < ^3J$ in these compounds, which further supports the assignment. Using this information, we assigned the signals at 5.85 and 6.51 ppm to potassium 1,3-dicyano-4-*tert*-butylcyclopentadienide and the signals at 5.63 and 6.04 ppm to potassium 1,2-dicyano-3-*tert*-butylcyclopentadienide. To assign the remaining singlets,

we first recognized that potassium 1,2,4-tricyano-3-tert-butylcyclopentadienide would have the most downfield ^1H peak because of its three $-\text{CN}$ groups and the fact that its proton is proximal (vicinal) to two of them. Therefore, we assigned the peak at 6.56 ppm to potassium 1,2,4-tricyano-3-tert-butylcyclopentadienide. We also recognized that potassium 1,2-dicyano-4-tert-butylcyclopentadienide should have the most upfield singlet as it has only two $-\text{CN}$ groups and its proton is proximal to both a nitrile group and the t-butyl group. Therefore, the small peak at 5.89 ppm was tentatively assigned to potassium 1,2-dicyano-4-tert-butylcyclopentadienide (tentatively just because it's a minor product).

To assign the singlets at 6.09 and 6.13 ppm, we compared the spectra obtained after reactions of tert-butylcyclopentadienylsodium with 2 equiv each of TsCN and KH (same spectrum as in Figure 22) and with 1 equiv each of the same reagents (Figure 23).

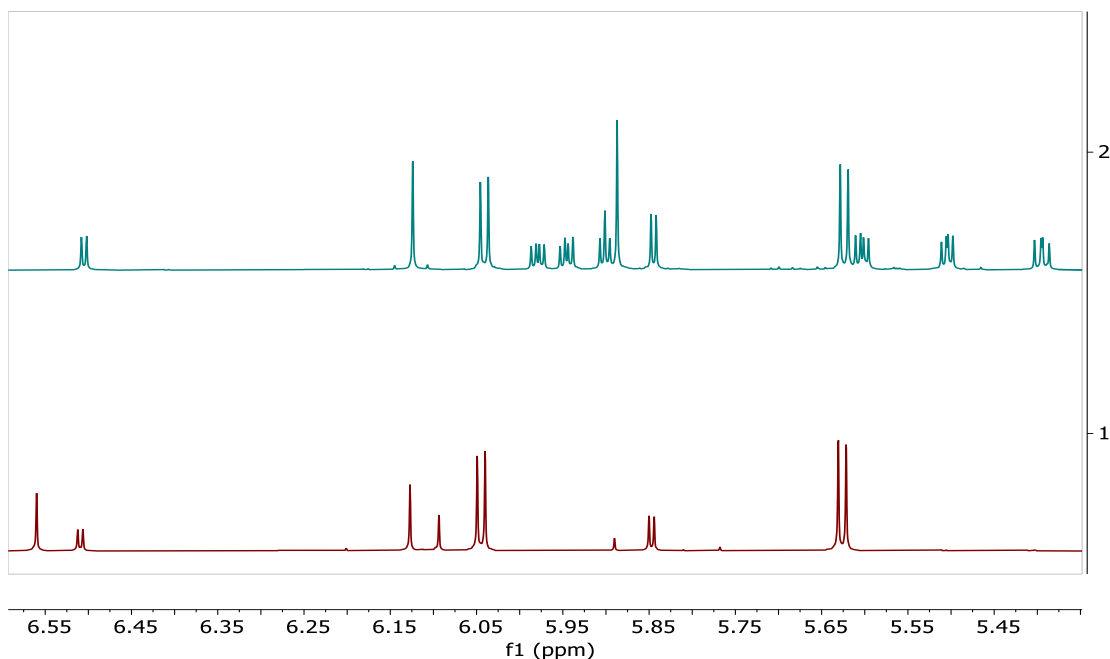


Figure 23. ^1H NMR spectra (400 MHz, CD_3CN) obtained after reactions of 1,2-dimethylcyclopentadienylsodium with (**Top**) 1 equiv each of TsCN and KH and with (**Bottom**, same as Fig. 22) 2 equiv each of the same reagents.

By stacking the spectra together, we observed that the signal at 6.13 ppm appears in both product mixtures, while the signal at 6.09 ppm only appears in the mixture obtained by using two equiv of reagents. Thus, the ^1H peak at 6.09 ppm is associated with a higher order cyanized product than the ^1H peak at 6.13 ppm. Therefore, we assigned the signal at 6.09 ppm to potassium 1,2,3-tricyano-4-tert-butylcyclopentadienide and the signal at 6.13 ppm to potassium 1,3-dicyano-2-tert-butylcyclopentadienide.

Having assigned the spectra of tricyano- and dicyano-tert-butylcyclopentadienide derivatives, we turned our attention back to the monocyno congeners (Figure 24).

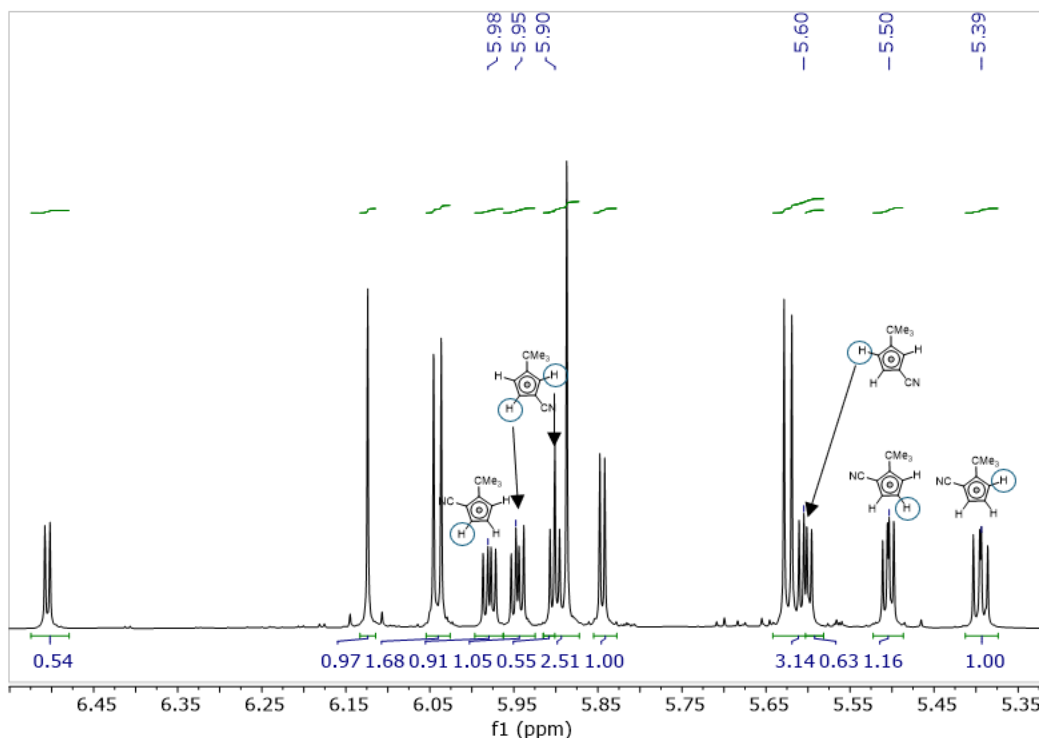


Figure 24. ^1H NMR spectrum (400 MHz, CD_3CN) of the product mixture obtained by reaction of 1,2-dimethylcyclopentadienylsodium with 1 equiv each of KH and TsCN (same spectrum as the Top chart in Figure 23). Unassigned signals were assigned in Figure 22.

We found immediately that the use of integrations to match corresponding ^1H peaks was largely hopeless, first because of underlying impurities or poor resolution between peaks, and, second, because the two monocyano derivatives were present in similar amounts! Using coupling constants was also difficult as they all shared similar coupling constants. These issues prompted us to collect a TOCSY spectrum in hopes of distinguishing between our two sets of ^1H peaks from each other (Figure 25).

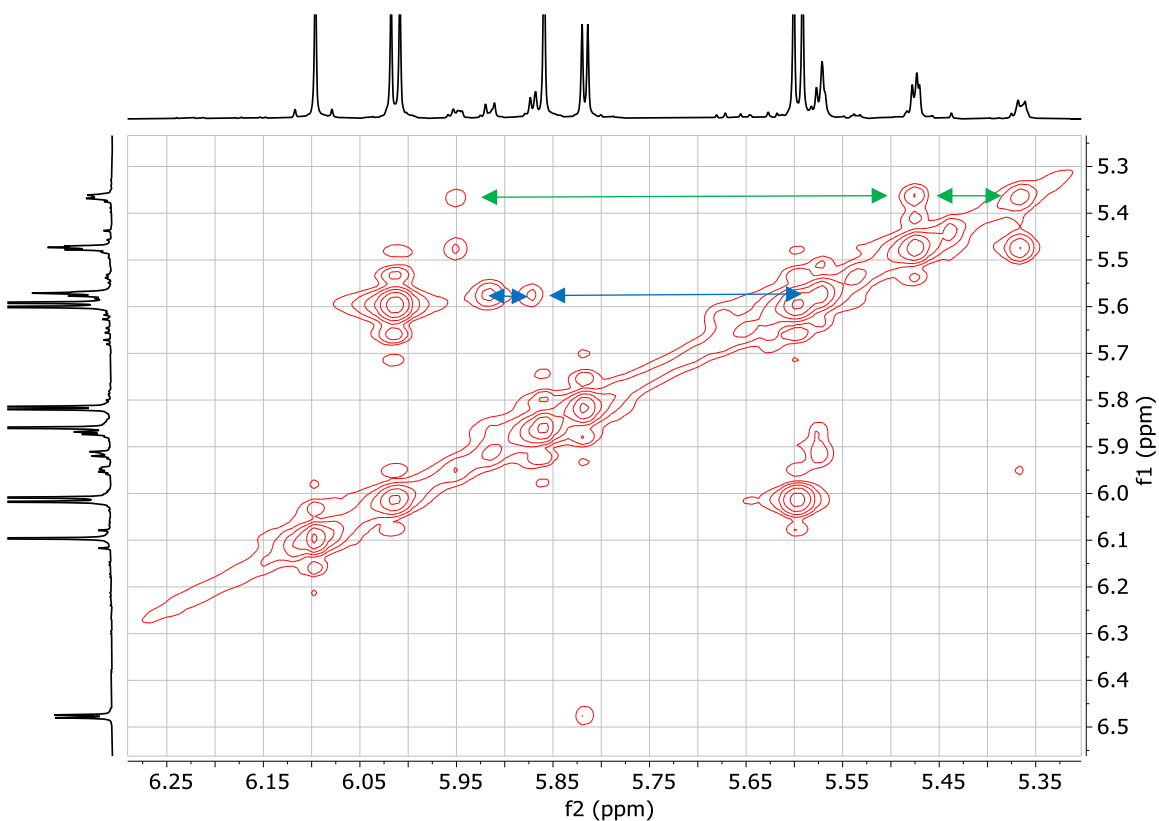


Figure 25. TOCSY NMR spectrum (400 MHz, CD_3CN) of the product mixture obtained by reaction of 1,2-dimethylcyclopentadienylsodium with 1 equiv each of KH and TsCN. Blue arrows show correlations for 1-cyano-3-tert-butylcyclopentadienide ion, and green arrows show correlations for 1-cyano-2-tert-butylcyclopentadienide ion.

From Figure 25, we observed that the signals at 5.39, 5.50, and 5.98 ppm were associated with one another through cross peaks. Likewise, we observed association among the

signals at 5.60, 5.90, and 5.95 ppm. Because TOCSY gives “total” correlation, we knew that each set of three signals must correspond to separate chemical species. The presence of two downfield signals for one set suggested that the compound associated with those peaks had to have two protons that were proximal to the –CN group. Therefore, the ^1H peaks at 5.60, 5.90, and 5.95 were tentatively assigned to potassium 1-cyano-3-tert-butylcyclopentadienide. Thus, the remaining ^1H peaks at 5.39, 5.50, and 5.98 ppm were tentatively assigned to potassium 1-cyano-2-tert-butylcyclopentadienide.

Clearly, all of these reactions yield complex mixtures of products. Like all synthetic methods, more effort could be applied toward optimizing for selectivity, for example by variations in temperature. On the other hand, the kinetic picture includes a significant conceptual barrier: The “ k_4 problem.” This issue will only be made worse by lowering the temperature in the hopes of realizing better selectivity. Then, there is the issue of reactant assay. Future work on this project would need to involve manufacture of fresh samples of these nucleophilic carbanion reactants to test our hypotheses under better-controlled conditions – as well as syntheses of other CpNa derivatives to expand the scope of the method even further. Finally, these mixtures are not amenable to chromatographic separation because of they would need to be hydrolyzed the corresponding dienes, which we know are unstable. For now, we can only conclude that these reactions give complex mixtures of products, which can be weighted in favor of less substitution vs. more substitution by varying the reaction stoichiometry. Here it is worth noting that in his original papers, Webster also did not isolate neutral CN-substituted cyclopentadienes, but he typically isolated tetraalkylammonium salts of the corresponding carbanions. Unfortunately he did not *explain* why this step was necessary. We assumed that he found

it convenient to purify his samples by recrystallization, although it appears that this process still resulted in isomeric mixtures. Only upon retreading some of his original work using our new methods did we learn how unstable the CN-substituted neutral dienes are.

Procedures

General Synthesis Procedure

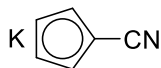
The following entire procedure is carried out anaerobically using only flame-dried, nitrogen-flushed glassware. Inside a nitrogen glove box, a 100-mL Schlenk flask is charged with the NaCp derivative and KH and fitted with a magnetic stir bar and a rubber septum. This flask is connected to a nitrogen Schlenk line and fitted under an N₂ counterstream with a graduated pressure-equalizing addition funnel that is capped with a rubber septum. The funnel is charged with 25 mL of THF using a syringe, and this solvent is drained into the reaction flask to form a slurry. The reaction flask is then chilled using an ice-water bath and stirred magnetically. A second Schlenk flask is charged with TsCN and THF to form a solution, which is transferred to the addition funnel using a cannula. The TsCN solution is then added dropwise to the NaCp/KH slurry, with stirring at 0 °C, over a period of about 1 h. Precipitation of off-white TsK is observed. Evolution of H₂ may also be observed depending on the rate and overall scale of the reaction. After the 1-h addition period, the funnel is replaced by a rubber septum, and the reaction is stirred under nitrogen at 0 °C for another hour and then for additional time at room temperature. After the desired total reaction time, the mixture is passed through a medium-porosity fritted-glass filter into a third Schlenk flask to remove the TsK by-product and any unreacted KH. The filtrate is then evaporated to dryness using a vacuum pump and an LN₂-cooled trap to condense THF vapor. Thorough removal of the THF solvent is

important; a sticky intermediate at this stage is undesirable. The residue is then triturated for 12-15 h (overnight) with 50 mL of hexane or anhydrous diethyl ether. The trituration mixture is then passed through a medium-porosity fritted-glass filter to separate the cyanated cyclopentadienide salt products from the solvent. The filter is pumped dry for several hours and then transferred to a nitrogen glove box to collect and store the solid for characterization and further use.

Selective Acidification Procedure

In a nitrogen glove box, an NMR tube is charged with a known mass of product mixture. The NMR tube is capped and transferred to a Schlenk adapter (a device that allows the tube, when uncapped, to be protected by a stream of nitrogen). Using a syringe, 0.55 mL of CD₃CN is added to the NMR tube, which is then capped, mixed, and submitted for NMR analysis. The resulting spectrum is then analyzed to determine the relative quantities of products that need to be removed by titration. Then, the remainder of the product mixture is transferred to a second Schlenk flask in the glove box. Ether or hexanes is added to form a slurry. Then, sufficient trifluoroacetic acid (TFA) is added to neutralize the basic component according to the determination of its assay in the product mixture. The resulting slurry is stirred for 1 h and filtered anaerobically. The filtrate is washed with ether or hexane to remove residual TFA and then dried using a vacuum pump for at least 15 h before transferring the solid to a glove box for further use and characterization.

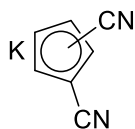
Synthesis of potassium monocyanocyclopentadienide



The general synthesis procedure was followed. NaCp (5.00 mmol, 0.440 g), KH (5.00 mmol, 0.200 g), and TsCN (5.00 mmol, 0.906 g, dissolved in

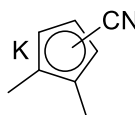
25 mL of THF) were used. The reaction time at room temperature was 3 h. The trituration solvent was ether. The yield was 0.396 g, 3.11 mmol, 61% of a brown solid. A breakdown of the composition of this mixture is shown in Table 5.

Synthesis of Potassium Dicyanocyclopentadienide (Isomeric Mixture)



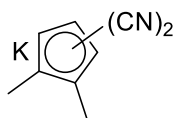
The general synthesis procedure was followed. NaCp (5.00 mmol, 0.440 g), 10.0 mmol (0.400 g) of KH, and 10.0 mmol (1.81 g) of TsCN dissolved in 25 mL of THF were used. The reaction time at room temperature was 3 h. The trituration solvent was ether. The yield was 0.495 g, 3.21 mmol, 64% of an orange solid. A breakdown of the composition of this mixture is shown in Table 5.

Synthesis of Potassium Monocyanodimethylcyclopentadienide Isomeric Mixture



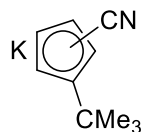
The general synthesis procedure was followed. Na[1,2-C₅H₃(CH₃)₂] (5.00 mmol, 0.581 g), 5.00 mmol (0.200 g) of KH, and 5.00 mmol (0.906 g) of TsCN dissolved in 25 mL of THF were used. The reaction time at room temperature was 3 h. The trituration solvent was ether. The yield was 0.349 g, 2.22 mmol, 44% of a red-orange solid. A breakdown of the composition of this mixture is shown in Table 5.

Synthesis of Potassium Dicyanodimethylcyclopentadienide Isomeric Mixture



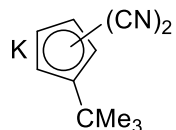
The general synthesis procedure was followed. Na[1,2-C₅H₃(CH₃)₂] (5.00 mmol, 0.440 g), 10.0 mmol (0.400 g) of KH, and 10.0 mmol (1.81 g) of TsCN dissolved in 25 mL of THF were used. The reaction time at room temperature was 3 h. The trituration solvent was ether. The yield was 0.495 g, 2.71 mmol, 54% of a red-brown solid. A breakdown of the composition of this mixture is shown in Table 5.

Synthesis of Potassium Monocyano-*tert*-butylcyclopentadienide Isomeric Mixture



The general synthesis procedure was followed. Sodium *tert*-butylcyclopentadienide (5.00 mmol, 0.721 g), 5.00 mmol (0.200 g) of KH, and 5.00 mmol (0.906 g) of TsCN dissolved in 25 mL of THF were used. The reaction time at room temperature was 3 h. The trituration solvent was ether. The yield was 0.329 g, 1.78 mmol, 35% of a light brown solid. A breakdown of the composition of this mixture is shown in Table 5.

Synthesis of Potassium Dicyano-*tert*-butylcyclopentadienide Isomeric Mixture



The general synthesis procedure was followed. Sodium *tert*-butylcyclopentadienide (5.00 mmol, 0.440 g), 10.0 mmol (0.400 g) of KH, and 10.0 mmol (1.81 g) of TsCN dissolved in 25 mL of THF were used. The reaction time at room temperature was 3 h. The trituration solvent was ether. The yield was 0.495 g, 2.71 mmol, 54% of a light brown solid. A breakdown of the composition of this mixture is shown in Table 5.

Chapter 3: Acidity Measurements & Trends of HCNCps

After our initial success with synthesizing and purifying 1,2-dicyanocyclopentadienide and 2,3-dicyanocyclopentadienide, we tried measuring the acidities of their respective carbon acids. After all, this compound is one that could help us unify the SLI and aqueous Bronsted-Lowry acidity scales. However, before delving into that data, a brief review of our method is in order. For over 20 years, our group has been measuring carbon acidities of cyclopentadiene derivatives using an **indicator method**, whereby an acid of unknown acidity is measured against another acid with a known acidity, the indicator (eq 17).



By knowing the concentrations of all four principal components, the ΔpK between the two acids could be calculated (eq 18). With this ΔpK and the previously known pK value of the indicator, the unknown pK value of the measured acid could be calculated.

$$\Delta\text{pK} = \text{pK}_{\text{HInd}} - \text{pK}_{\text{HA}} = -\log \frac{[\text{HInd}]}{[\text{Ind}^{\ominus}]} + \log \frac{[\text{A}^{\ominus}]}{[\text{HA}]} = -\log \left(\frac{[\text{HInd}][\text{A}^{\ominus}]}{[\text{Ind}^{\ominus}][\text{HA}]} \right) \quad (18)$$

In previous studies, championed by Streitwieser, UV-vis spectroscopy was the predominant method used to find concentrations of the conjugate bases in the system. The clear advantage of UV-Vis is sensitivity, using very dilute solutions where the formation of ion-pairs and triple-ions should be minimized. The disadvantage of UV-vis is that only the conjugate base concentrations $[\text{Ind}^{\ominus}]$ and $[\text{A}^{\ominus}]$ are measured directly; the acid concentrations $[\text{HInd}]$ and $[\text{HA}]$ must be obtained by mass balance, which introduces several large sources of experimental error from encroachment by adventitious moisture, oxygen, impurities in the compounds themselves, etc. Our lab's work swapped UV-vis

spectroscopy for ^{19}F NMR spectroscopy. The use of ^{19}F NMR spectroscopy came with several built-in advantages. First and by far the most important was that the relative concentrations of all four of the mixture components could be measured in the NMR spectrum simultaneously, so long as each component had at least one well resolved peak. This eliminated the need for mass balance determinations. The NMR method was also more robust regarding the presence of impurities or side reactions. Essentially, anything besides the four principal components can be present, as long as it does not interfere with the signals to be integrated. This advantage is complemented by ^{19}F NMR's superior resolution, which increased the likelihood of finding at least one well-resolving peak of each component. The disadvantage of the NMR technique stems from the intrinsic insensitivity of NMR as an analytical measurement. Moreover, unless the spectrum is rigorously free of impurities, integration of small signals can be quite uncertain. To avoid small signals, as mentioned in the first chapter, the acid (HA) and indicator (HInd) must have comparable acidities. For example, if $|\Delta\text{pK}| = 2$, from eq 18, one canonical set of concentration ratios that will satisfy this condition is $[\text{Hind}]/[\text{Ind}^-] = [\text{A}^-]/[\text{HA}] = 10$. In practice even these ratios challenge the limits of reproducible integration.

With our shift to nitriles, however, we are forced to shift from ^{19}F NMR to ^1H NMR spectroscopy. While sharing the same ability to measure the relative concentrations of all equilibrium components, ^1H NMR spectroscopy has three key constraints. First, it has a much narrower spectral range than ^{19}F NMR, increasing the likelihood of component peaks overlapping with each other. Second, impurities in general (for instance, small bits of solvent left in a compound after synthesis) tend to have more proton peaks than fluorine peaks and thus the likelihood of impurities affecting the measurement are higher. Finally,

there are fewer proton peaks available for measurement for our cyanocyclopentadienes compared to the number of fluorine peaks available for our perfluoroaryl cyclopentadiene derivatives. These three constraints leave us with a much tighter margin of error to work with. Nevertheless, we were able to get preliminary measurements for 1-cyano-2,3,4-tris(perfluorophenyl)cyclopentadiene and 1-monocyanocyclopentadiene, and we succeeded in obtaining complete and careful measurements for 1,2- and 2,3-dicyanocyclopentadiene. These are detailed below.

Our initial work began by determining the pK_{THF} of 1-cyano-2,3,4-tris(perfluorophenyl)cyclopentadiene in THF. At this stage, we were still chasing the “solvent limit” of the SLI scale and eager to find ways to synthesize exciting new carbon superacids. In the end, the “cyano effect” on the acidity value was “too much of a good thing” and we realized that any derivative that we were likely to be able to prepare having at least one C_6F_5 group and two CN groups would probably be too acidic to measure by our methods. Nevertheless, the single acidity measurement that we conducted using our tiny but purified sample of 1-cyano-2,3,4-tris(perfluorophenyl)cyclopentadiene allowed us to roughly compare the acidifying power of nitrile groups to our previously measured perfluoroaryl groups. Using a combination of our previous data and Webster’s data, we guessed that 1,2,4-tris(perfluoropyridyl)cyclopentadiene should be close enough to 1-cyano-2,3,4-tris(perfluorophenyl)cyclopentadiene to act as an indicator. To determine what peaks were resolved enough to measure, we compared the preliminary acidity mixture to spectra of the pure components (Figure 26).

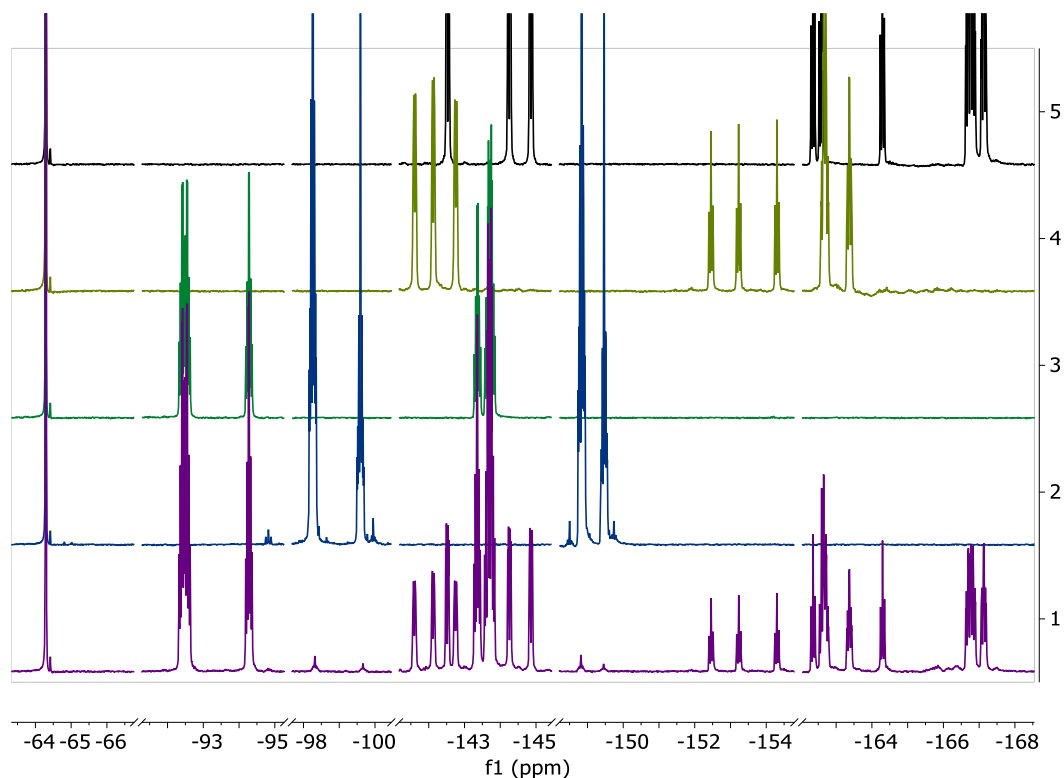


Figure 26. ^{19}F NMR spectra (376 MHz) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm). Spectrum 1: Equilibrium mixture of HA, H-Ind, A^- , and Ind^- generated by reaction of HA and H-Ind with FluoLi; H-Ind = 1,2,4- $\text{C}_5\text{H}_3(\text{C}_5\text{F}_4\text{N})_3$; HA = 2-cyano-1,3,4- $\text{C}_5\text{H}_2(\text{C}_5\text{F}_4\text{N})_3$. Spectrum 2: Ind^- generated from H-Ind and excess FluoLi. Spectrum 3: H-Ind. Spectrum 4: A^- generated from HA and excess FluoLi. Spectrum 5: HA.

Having identified which peaks were available for measuring each component, we then ran a single preliminary acidity test using 1,2,4-tris(perfluoropyridyl)cyclopentadiene as our indicator (Spectrum 1 in Figure 26 is shown again as Figure 27 so that integrations may be included). After integrating all the available peaks for each component, we statistically corrected them for the number of fluorine atoms each peak represented (eq 14). After calculating the ΔpK , we rearranged the ΔpK equation to solve for the pK value of 1-cyano-2,3,4-tris(perfluorophenyl)cyclopentadiene which was found to be -5.64 (eq 19–21,

HA=1-cyano-2,3,4-tris(perfluorophenyl)cyclopentadiene, A^- = 1-cyano-2,3,4-tris(perfluoro-phenyl)cyclopentadienide).

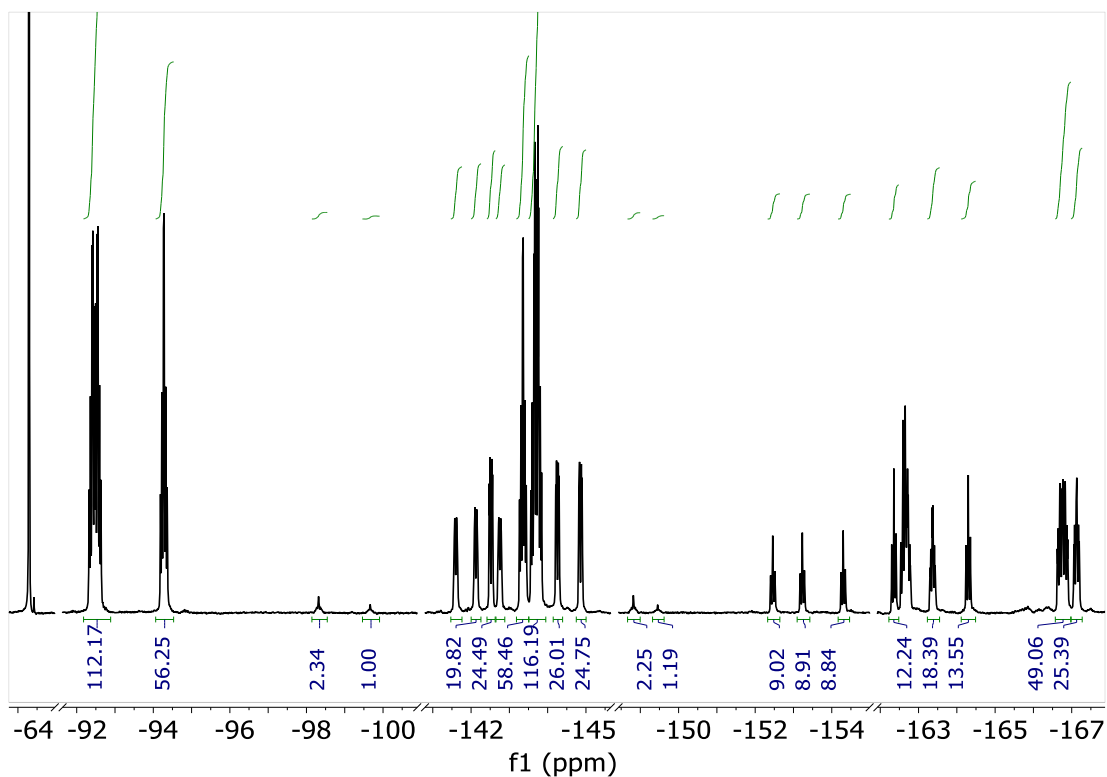


Figure 27. ^{19}F NMR (376 MHz) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm). Acidity measurement of 1-cyano-2,3,4-tris(perfluorophenyl)cyclopentadiene, 1,2,4-tris(perfluoropyridyl)cyclopentadiene, and their respective conjugate bases generated by adding sub-stoichiometric fluorenyllithium.

$$\Delta\text{pK} = \log \left[\frac{[\text{IndH}][\text{A}^-]}{[\text{Ind}^-][\text{HA}]} \right] = \log \left[\frac{[343.07/12][175.49/14]}{[6.78/12][103.07/11]} \right] = 1.83 \quad (19)$$

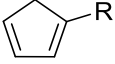
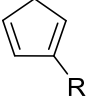
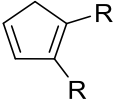
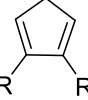

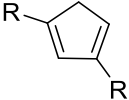
$$\Delta\text{pK} = 1.83 = \text{pK}_{\text{Ind}} - \text{pK}_{\text{HA}} = -3.81 - \text{pK}_{\text{HA}} \quad (20)$$

$$\text{pK}_{\text{HA}} = -3.81 - 1.83 = -5.64 \quad (21)$$

We learn from this measurement that the addition of one nitrile group to 1,2,3-tris(perfluorophenyl)cyclopentadiene results in an increase in acidity corresponding to a decrease of 9.14 pK units (a factor exceeding one billion). Put in another way, by replacing

one perfluorophenyl group of 1,2,3,4-tetra(perfluorophenyl)cyclopentadiene with a nitrile group, we enhanced its acidity by 5.27 pK units. Using this change in acidity we were able to make more refined estimates for the acidities of monocyanocyclopentadiene and dicyanocyclopentadienes by subtracting 5.27 units from their perfluorophenyl analogues, which our group characterized thoroughly in the past (Table 6). This comparison enabled us to determine which of our previous perfluoroaryl cyclopentadienes – already fixed on the SLI scale – could act as a good indicator for our 1-monocyanocyclopentadiene and 1,2-dicyanocyclopentadiene and their respective isomers. Of course, these estimations assume that the replacement of perfluorophenyl groups with nitrile groups is linear.

Table 6. Estimated pK values of mono and dicyanocyclopentadiene compounds

Compounds	pK _{THF} when R= -C ₆ F ₅	Estimated pK _{THF} when R= -CN
	10.82	5.55
	10.25	4.98
	7.68	-2.86
	7.03	-3.51
	6.31	-4.23
	5.88	-4.66

Based on our estimated acidity data, we believed that the best indicators for 1-cyanocyclopentadiene and 2-cyanocyclopentadiene would be 1,2,3-tris(perfluorophenyl)cyclopentadiene and/or 1,3-bis(perfluorophenyl)cyclopentadiene (the 1,3 and 1,4 isomers are inseparable tautomers). In addition, we believed that by measuring against these indicators could help us with a gap that we had been struggling to bridge for a while in our group between 1,4-bis(perfluorophenyl)cyclopentadiene and 1,2,3-tris(perfluorophenyl)cyclopentadiene. We started with 1,2,3-tris(perfluorophenyl)cyclopentadiene as our indicator to validate our hypothesis.

At the outset, we encountered a significant technical problem that we had dreaded for some time: THF as a solvent is not suitable for our ^1H measurements because of the enormous solvent signals; even THF- d_8 , which is already prohibitively expensive for us (\$50 per spectrum), will show residual proton isotopes, and these signals will be in an important region of the spectrum for us – near 3.7 ppm, where we often need to find the CH_2 signals of our neutral cyclopentadienes. For these reasons, we were compelled to find another solvent, and we reasoned that CD_3CN would have appropriate dielectric strength (37.5 vs 7.58 for THF) to prevent the formation of close ion pairs while being also much more practical for the observation of ^1H nuclei. Also it's much less expensive! We had to make a second concession owing to the necessity of isolating and storing the cyano-substituted cyclopentadienes as their potassium salts. Whereas we previously were able to enforce the presence of lithium cation as the sole counterion for all conjugate bases in our equilibrium mixtures, by starting with potassium derivatives of the cyano-substituted cyclopentadienes, we were forced to accept K^+ as our counterion moving forward. Again, our assumption is that acetonitrile is able to solvate K^+ effectively, and we base this assumption on the fact

that the Bordwell acidity scale is based on potassium salts using DMSO as the solvent, and Bordwell claims to have thermodynamic (complete) ion-separation, and the dielectric constants of DMSO (46.7) and acetonitrile are similar. This analysis does ignore an important factor, which is that the oxygen atom of DMSO is probably a stronger ligand for alkali metal cations than the nitrogen atom of acetonitrile, which is consistent with the fact that alkali salts tend to be more soluble in DMSO, although they do tend to have appreciable solubility in MeCN as well. But, in the end, we must accept that we are not making true SLI measurements if we are using CD₃CN as the solvent and potassium ion as the counterion for our carbanions. What follows is a description of a bracketing technique to estimate the unknown acidity – on the SLI scale – using measurements completed in CD₃CN.

In our initial experiment, we first identified what peaks were associated with 1-cyanocyclopentadiene and 2-cyanocyclopentadiene and 1-cyanocyclopentadienide in the equilibrium mixture (Figure 28).

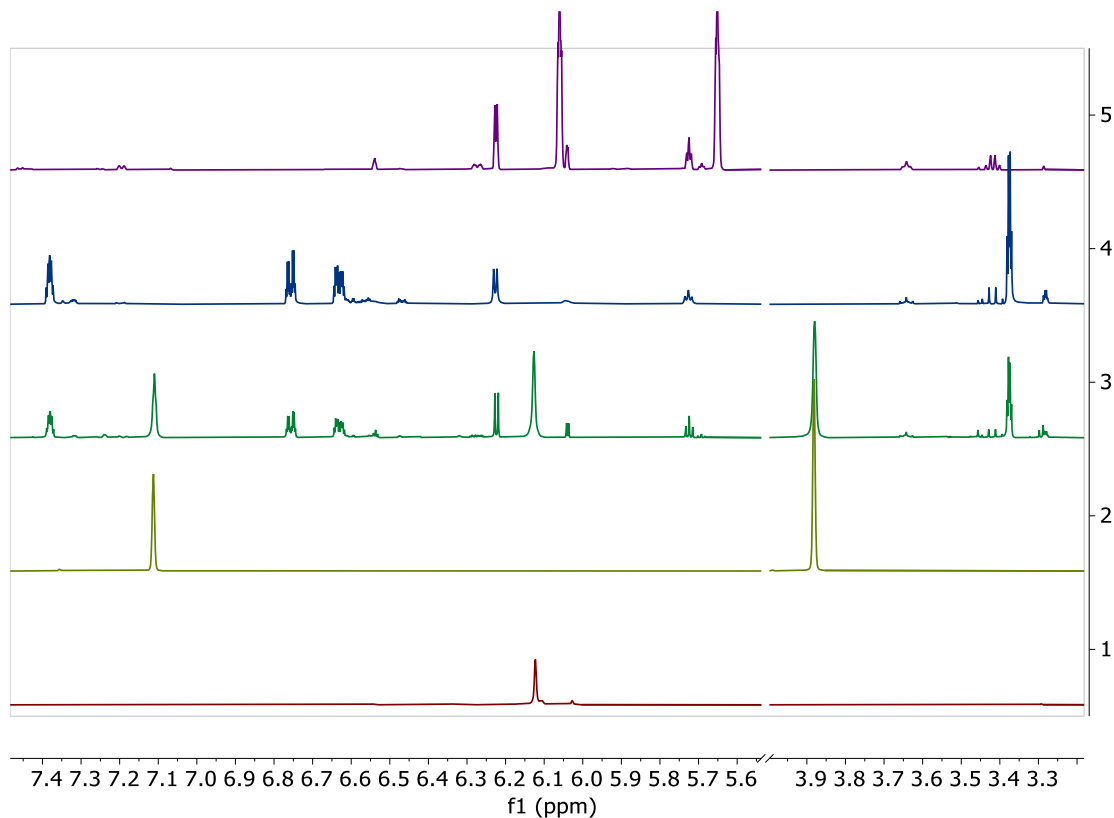


Figure 28. ^1H NMR spectra (400 MHz, CD_3CN). Spectrum 1: pure potassium 1,2,3-tris(perfluorophenyl)cyclopentadienide generated in-situ from the diene and excess KH followed by centrifugation to separate the unreacted KH. Spectrum 2: 1,2,3-tris(perfluorophenyl)cyclopentadiene. Spectrum 3: the equilibrium mixture. Spectrum 4: 1-cyanocyclopentadiene and 2-cyanocyclopentadiene with some 1,3-dicyanocyclopentadienide and 1,2-dicyanocyclopentadienide. Spectrum 5: 1-cyanocyclopentadienide with some 1,3-dicyanocyclopentadienide and 1,2-dicyanocyclopentadienide.

From our comparison of the spectra, it was clear that we would have minor amounts of potassium 1,3-dicyanocyclopentadienide and potassium 1,2-dicyanocyclopentadienide as well as smaller amounts of other impurities such as residual solvents. However, the beauty of method is that as long as we have one well resolved peak of each reactive species, we can conduct the acidity measurement even with these impurities present, so long as they are not, to our knowledge, interfering with the signals we need to integrate.

The most immediate take-home conclusion from Figure 28 is that the equilibrium mixture contains no monocyanocyclopentadienide anion whatsoever, which means that 1,2,3-tris(perfluorophenyl)cyclopentadiene was too acidic to function as an indicator for either of the monocyanocyclopentadiene isomers. This prompted us to try 1,3/1,4-bis(perfluorophenyl)cyclopentadiene (Figure 29). By comparing these spectra, we found that all components were present in the mixture allowing for a preliminary measurement of 1-cyanocyclopentadiene. Unfortunately, 2-cyanocyclopentadiene was present only in minor quantity and we were not able to find useful signals free of interference (from impurities) for integration. Nevertheless, using the equilibrium mixture as our preliminary acidity test (Figure 30, which is the same as Spectrum 1 in Figure 29, but with integrals and chemical shifts displayed), we were able to show that 1-cyanocyclopentadiene is slightly more acidic than 1,4-bis(perfluorophenyl)cyclopentadiene (the major tautomer) by 0.06 pK units in CD₃CN (eq 22–24). This led us to determine the pK_{THF} of 1-cyanocyclopentadiene to be 6.25.

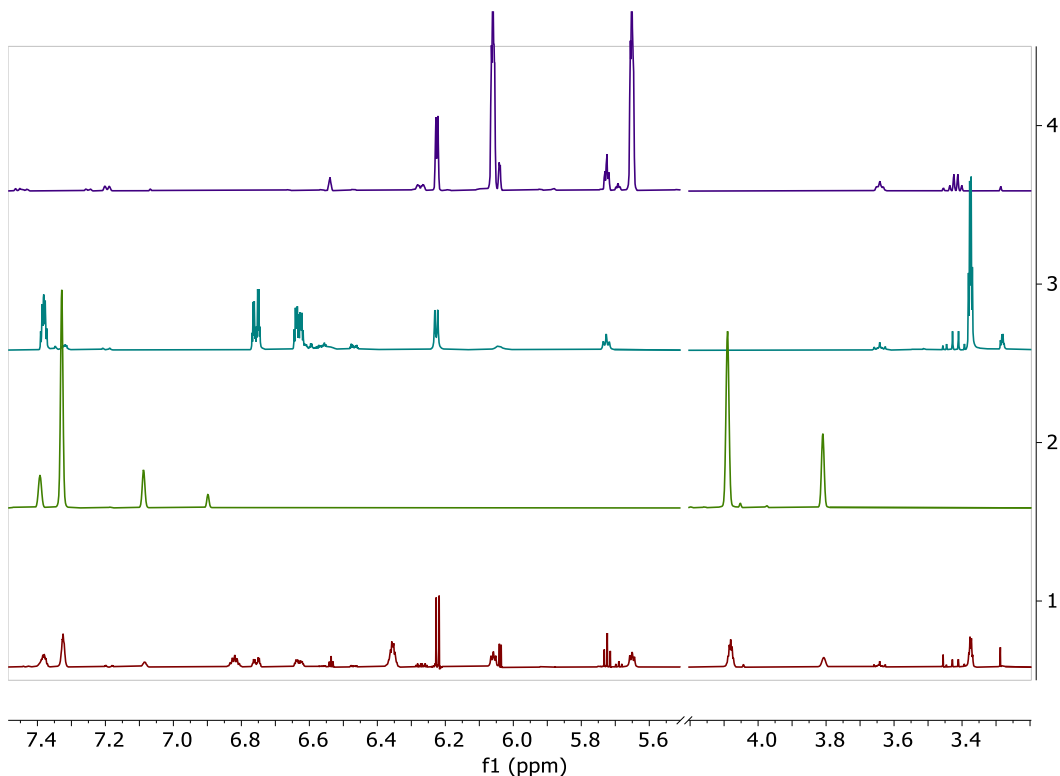


Figure 29. ^1H NMR spectra (400 MHz, CD_3CN). Spectrum 4: monocyanocyclopentadienide (5.6 and 6.1 ppm) with minor amounts of dicyanocyclopentadienide (two isomers; four signals from 5.7 to 6.6 ppm). Spectrum 3: 1-cyanocyclopentadiene (major: 3.4, 6.6, 6.7, and 7.4 ppm) and 2-cyanocyclopentadiene (minor: CH_2 at 3.3 ppm) with small amounts of dicyanocyclopentadienide. Spectrum 2: 1,4-bis(perfluorophenyl)cyclopentadiene and 1,3-bis(perfluorophenyl)cyclopentadiene. Spectrum 1: The equilibrium mixture.

$$\Delta\text{pK} = \log \left[\frac{[\text{IndH}][\text{A}^-]}{[\text{Ind}^-][\text{HA}]} \right] = \log \left[\frac{[4.69/4][1.40/1]}{[4.29/3][2.98/3]} \right] = 0.06 \quad (22)$$

$$\Delta\text{pK} = 0.06 = \text{pK}_{\text{Ind}} - \text{pK}_{\text{HA}} = 6.31 - \text{pK}_{\text{HA}} \quad (23)$$

$$\text{pK}_{\text{HA}} = 6.31 - 0.06 = 6.25 \quad (24)$$

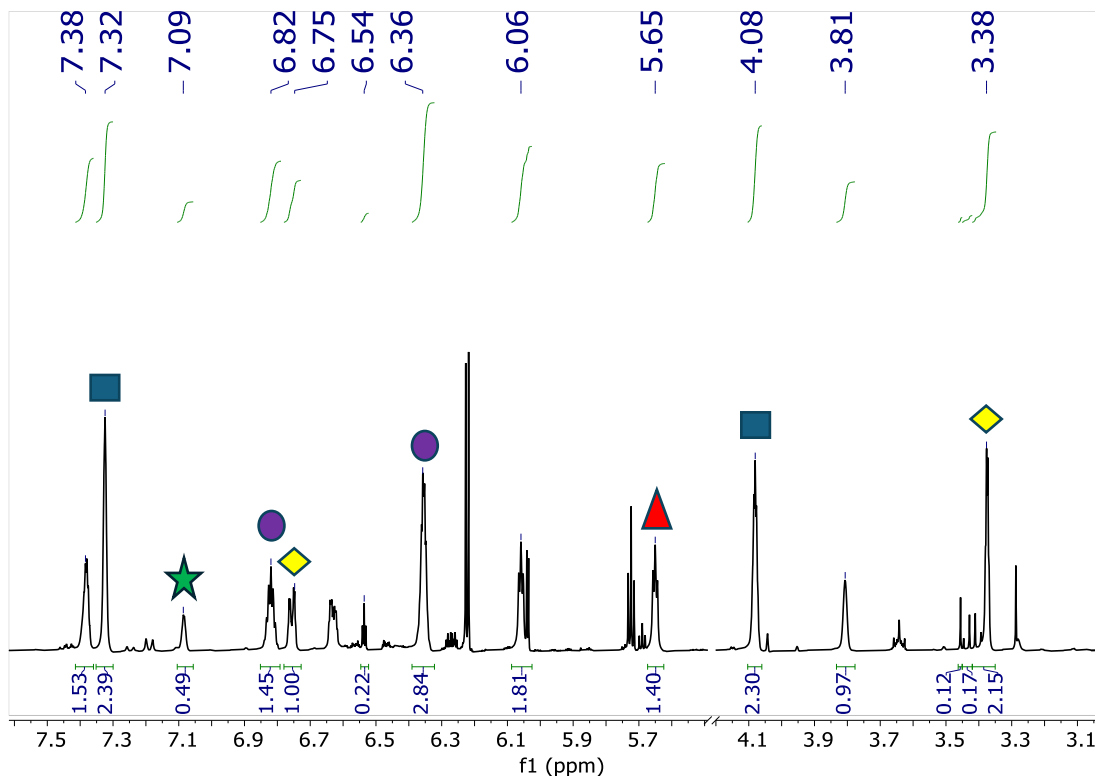


Figure 30. ^1H NMR (400 MHz, CD_3CN) spectrum of the preliminary acidity measurement between 1-cyanocyclopentadiene (yellow diamond), 2-cyanocyclopentadiene, 1,4-bis(perfluorophenyl)cyclopentadiene (blue square), 1,3-bis(perfluoro-phenyl)cyclopentadiene (green star), 1-cyanocyclopentadienide (red triangle), and 1,3-bis(perfluoro-phenyl)cyclopentadienide (purple circle).

We were thrilled to be able to compare a cyano-substituted cyclopentadiene directly to a fluoroaryl-substituted cyclopentadiene for the first time using ^1H NMR as the measurement. Taking a short detour for a moment, we had hoped that we might be able to use 1-cyanocyclopentadiene to help us bridge the “gap” in the data shown in Table 1 (between 5.88 and 3.52) that was left for us by Matt Thornberry in his Dissertation.² However, a pK value of 6.25 for the new cyano derivative is not helpful in this regard. Thus, we had to find an alternative compound to bridge this “gap”. Fortunately, one of our former undergraduate researchers, Stephen Williams, had synthesized 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene by reacting methylcyclopentadienylsodium

with excess sodium hydride and hexafluoro-benzene in THF. According to Matt's previous observations, the addition of an alkyl group to cyclopentadiene decreases the acidity (i.e. higher pK value) by ~ 2 pK units. Using pK value of 1,2,4-tris(perfluorophenyl)cyclopentadiene, we estimated that the acidity of 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene to be ~ 4.89 pK. Thus, we tested it both against 1,2,3-tris(perfluorophenyl)cyclopentadiene and 1,4-bis(pentafluorophenyl)cyclopentadiene and its tautomer (Figures 52-59; Tables 12-13 in the Supporting Information). From these acidity trials, we found that 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene had a pK value of 5.17. Furthermore, we were able to correct the pK value 1,2,3-tris(perfluorophenyl)cyclopentadiene to 3.50, which was 0.02 units off from Matt's original measurement. This correction was then applied to all acids following 1,2,3-tris(perfluorophenyl)cyclopentadiene as shown in Table 1. A corollary conclusion is that even though the "gap" left by Matt was quite large – around 2.3 pK units – his measurement of the "gap" was accurate within his experimental error. Correcting all of our remaining acidities by 0.02 pK units is a trivial adjustment.

Based on our acidity data, we estimated that 1,2,4-tris(perfluoropyridyl)cyclopentadiene would be the best choice for our initial indicator to measure 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, and 1,3-dicyanocyclopentadiene. To confirm this, we first ran a preliminary acidity test using CD_3CN as our solvent (Figure 31). Using NMR spectra of the pure acids and conjugate bases, we identified the peaks corresponding to all the components in the mixture. From this preliminary measurement, we were able to get rough acidity values for the 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, and 1,3-dicyanocyclopentadiene.

Values for 1,2-dicyanocyclopentadiene could not be determined as the acid peaks were obstructed by impurities. Notably, its CH₂ signal is obscured by residual THF in the sample, underscoring the problems that we would have if we had used THF or THF-*d*₈ as the medium for these measurements.

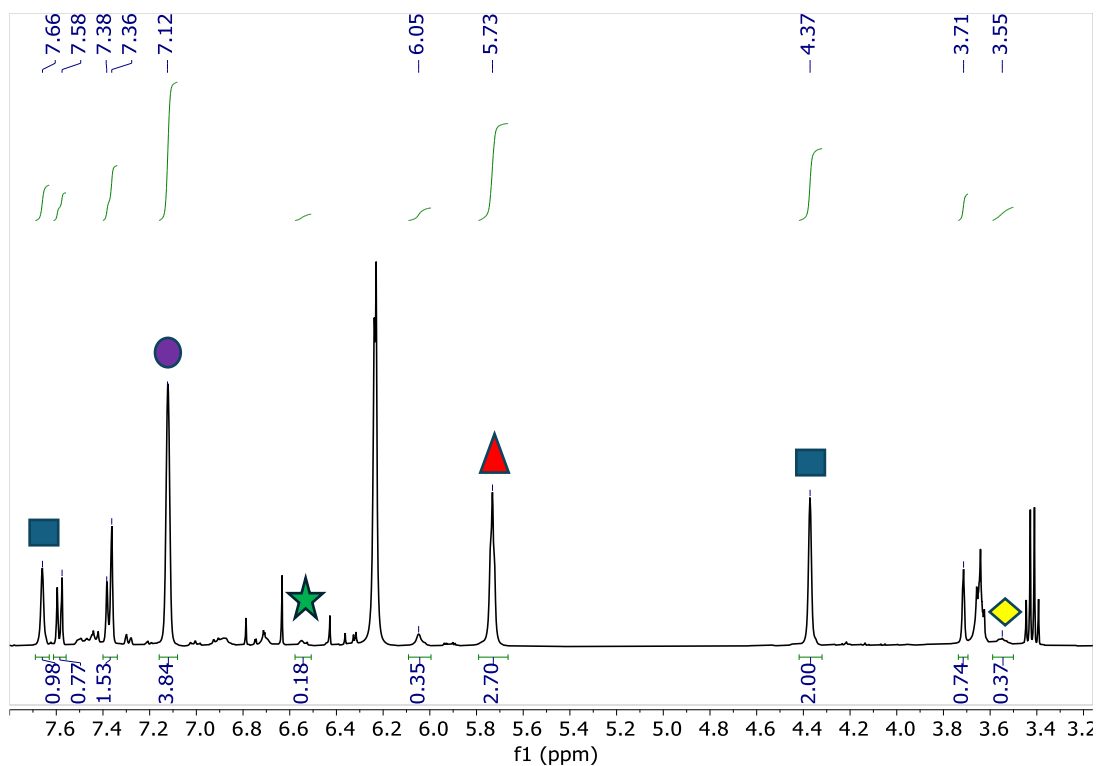


Figure 31. ¹H NMR spectrum (400 MHz, CD₃CN) of the preliminary acidity measurement between 1,2,4-tris(perfluoropyridyl)cyclopentadiene (blue square), 1,2-dicyanocyclopentadiene (green star), 2,3-dicyanocyclopentadiene (yellow diamond), 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, 1,2,4-tris(perfluoropyridyl)cyclopentadienide (purple circle), 1,2-dicyanocyclopentadienide (red triangle), and 1,3-dicyanocyclopentadienide

The preliminary measurement proved our initial indicator choice correct, but it also suggested that a more acidic indicator may need to be used to more accurately determine the acidity of 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene, because these species are partially occluded and also present in very small concentrations, suggesting that

they are too acidic for 1,2,4-tris(perfluoropyridyl)cyclopentadiene. With this in mind, we ran another preliminary acidity test using 1,2,3,4-tetrakis(perfluoro-4-tolyl)cyclopentadiene (Figures 32 & 33). This time, however, we used ^{19}F NMR in addition to ^1H NMR to measure the conjugate base of our indicator with no obstructions. In this test we were able to successfully measure the acidity of both 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene. However, this test resulted in a different pK value for compound 2,3-dicyanocyclopentadiene from the previous test (-4.66 vs -4.20). The confusing result prompted us to measure the two indicators against each other in CD_3CN (Figure 34).

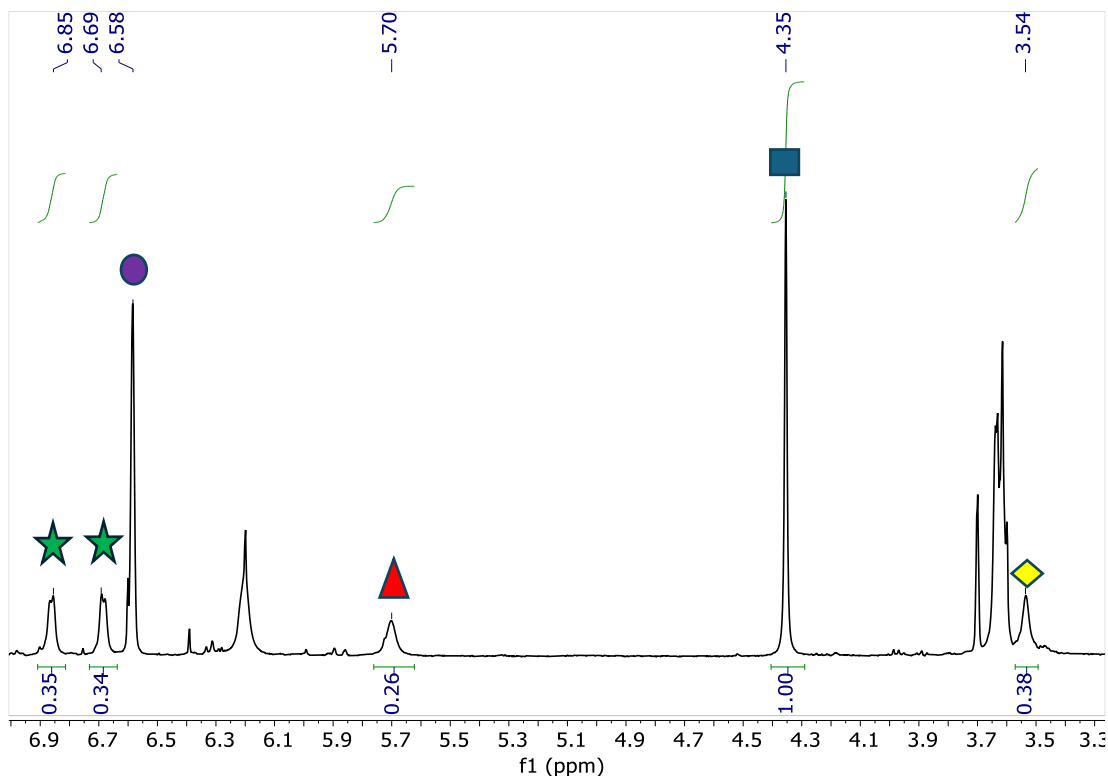


Figure 32. ^1H NMR (400 MHz, CD_3CN) spectrum of acidity test between 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene (blue square), 1,2-dicyanocyclopentadiene (green star), 2,3-dicyanocyclopentadiene (yellow diamond), 1,4-dicyanocyclopentadiene, 1,3-dicyano-cyclopentadiene, and their respective conjugate bases: 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene (purple circle) and 1,2-dicyanocyclopentadiene (red triangle)

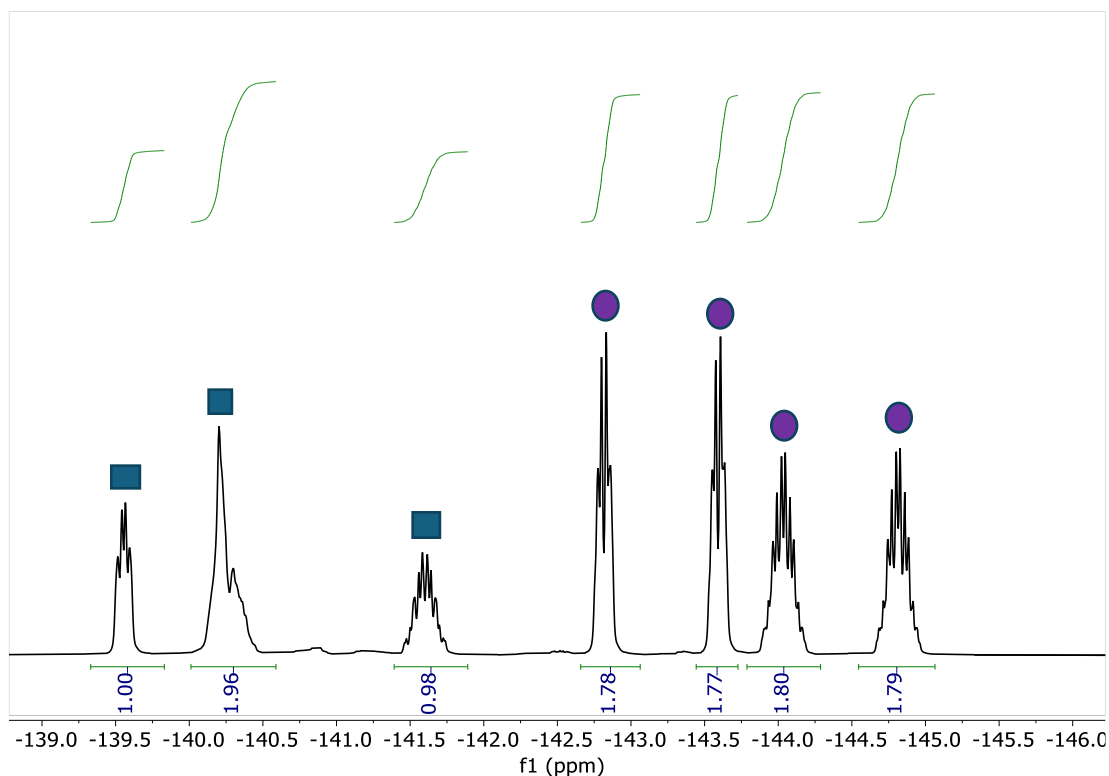


Figure 33. ^{19}F NMR (376 MHz, CD_3CN) spectrum of acidity measurements between 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene (blue square), 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadienide (purple circle), 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

Our hypothesis was that the ΔpK of the two indicators had changed with the change in solvent and thus resulted in two different values for 2,3-dicyanocyclopentadiene. Using previous NMR spectra to identify the corresponding peaks, we measured the ΔpK between 1,2,4-tris(perfluoropyridyl)cyclopentadiene and 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene to be 0.87. This is a different gap compared to the ΔpK in THF (1.28). Having identified the difference in ΔpK , we ran two full (triplicate) sets of trials on dicyanocyclopentadienides using 1,2,4-tris(perfluoropyridyl)cyclopentadiene in one set of trials, and 1,2,3,4-tetra(perfluorotolyl)cyclopentadiene in the second set of trials.

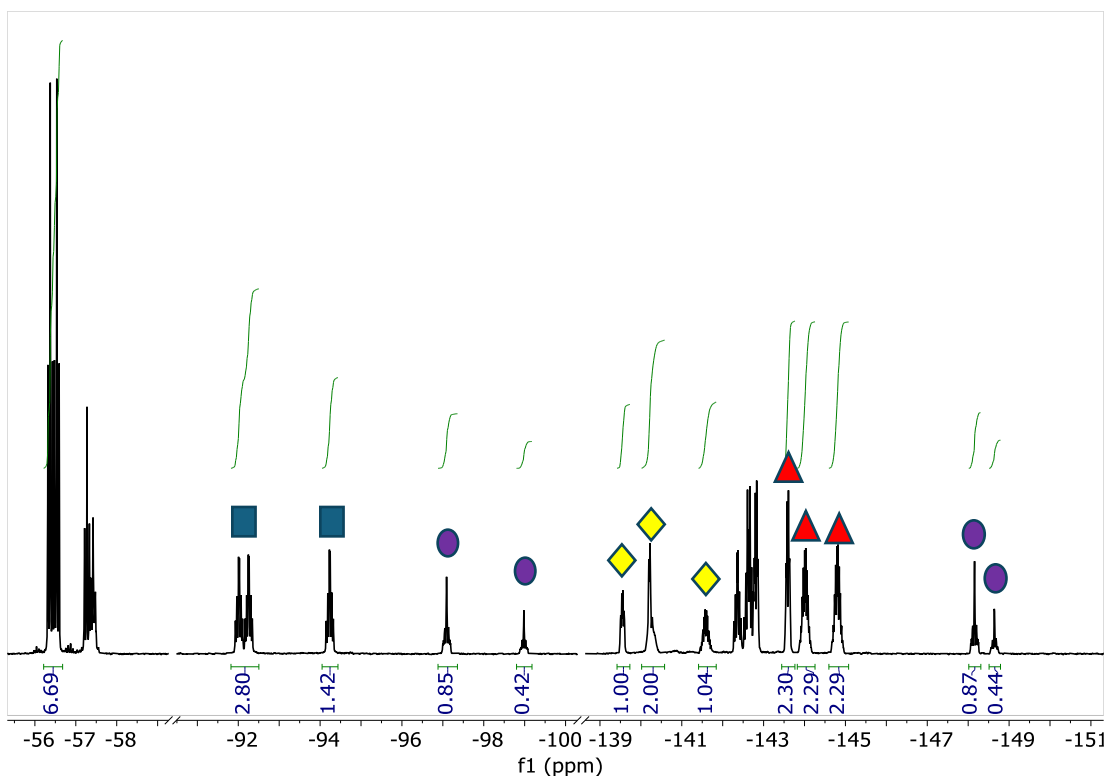


Figure 34. ^{19}F NMR (376 MHz, CD_3CN) spectrum of acidity measurement Trial 1 (HAR-2-153-1) between 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene (yellow diamond), 1,2,4-tris(perfluoropyridyl)cyclopentadiene (blue square), 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadienide (red triangle), and 1,2,4-tris(perfluoropyridyl)cyclopentadienide (purple circle)

In these sets of trials, the conjugate base of 1,4-dicyanocyclopentadiene and 1,3-dicyanocyclopentadiene could not be accurately integrated, so we lost the ability to estimate their acidities. However, compounds 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene had peaks that were well resolved and allowed precise measurement. This was a lucky break because these compounds are the only species in Webster's scale that have pK values in both water and MeCN. Thus, if pK_{THF} could be obtained for 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene, we could adjust the SLI scale to give calculated pK_a values in water for the first time.

While we could have claimed victory at this point, we noticed bothersome internal inconsistencies in our data. Because we are on the verge of unifying the SLI and aqueous acidity scales, we wanted to ensure that our data was the highest quality possible. The ΔpK_{MeCN} for our dicyanocyclopentadienes and our two indicators did not add up to the ΔpK_{MeCN} between the two indicators themselves. This failure prompted us to employ multipoint baseline corrections to our ^1H NMR acidity test spectra. Previously, it was thought that a baseline correction was unnecessary for our ^1H NMR acidity tests. However, after applying the baseline correction, the results were firstly more reproducible overall, and more importantly the ΔpK_{MeCN} for our dicyanocyclopentadienes and our two indicators finally added up (within error) to the ΔpK_{MeCN} between the two indicators themselves (Figure 35).

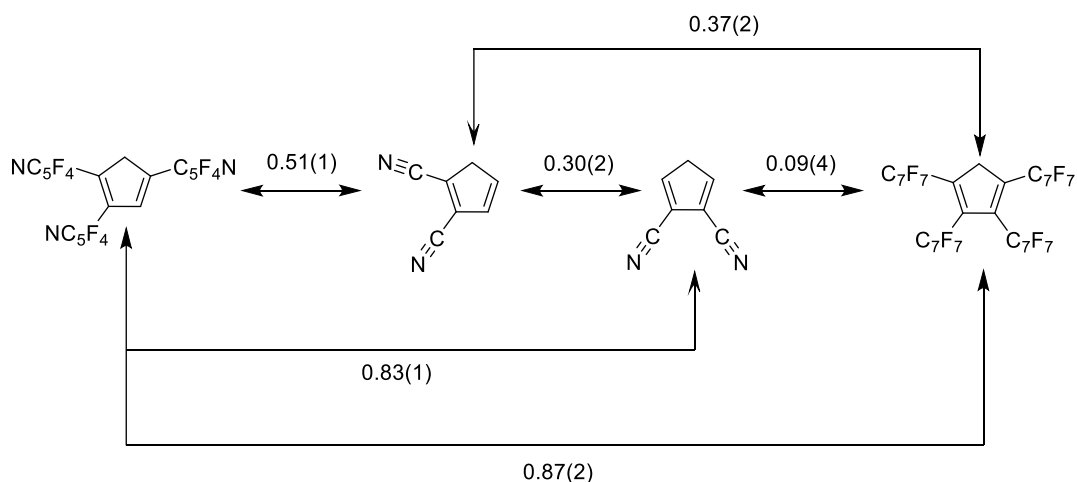


Figure 35. ΔpK_{MeCN} values between 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,2,4-tris(perfluoropyridyl)cyclopentadiene, and 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene relative to each other.

Having fixed the ΔpK_{MeCN} issues, we began to calculate what the ΔpK_{THF} values would be for 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene. To achieve this, we first

had to calculate the individual pK_{MeCN} and pK_{a} values of 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene. At this point we found a discrepancy with Webster's original data. In the end, this issue is unlikely to make a wholesale change in the alignment of the two acidity scales, but again we are at a point where we are trying to step carefully. Webster had calculated the pK_{a} values of these two compounds and claimed that they have the same value ($pK_{\text{a}} = 0.81$ for both the 1,2 and 2,3-dicyanocyclopentadiene tautomers). We found that these pK_{a} values differ by 0.30 (Figure 35). Reviewing Webster's work carefully, we conclude that he had attempted to split an unresolved UV-vis spectrum into two tautomers, and his calculations resulted in equal pK_{a} values for both (0.81). We believe this part of his result is flawed, but his approach should have given an accurate result for the "observed" or "averaged" acidity value for the pair of tautomers, and he reported this value as $pK_{\text{a}}(\text{obs}) = 1.11$. Our spectra are resolved, so we were able to establish the *difference* using our NMR methods, albeit in CD_3CN . And considering the structural differences between the two tautomers, the acidity difference of 0.30 pK units is reasonable. Now we can combine Webster's aqueous "observed" value for the unresolved tautomers with our assessment of the acidity difference to obtain the true aqueous pK_{a} values of the two tautomers that Webster was not able to resolve.

This problem has been encountered before in our lab. The indene derivative 1-phenyl-3-(2',3',5',6'-tetrafluorophenyl)indene was originally reported by Streitwieser as having an "observed" acidity but he was likewise, using UV-vis, not able to determine the two individual tautomers' acidities.⁴⁶ Dr. Matthew Thornberry had managed to determine the pK_{THF} values of 1-phenyl-3-(2',3',5',6'-tetrafluorophenyl)indene and its tautomer (interconverting the 1- and 3-substituents) by using his own ΔpK_{THF} data and the observed

pK_{THF} value of the equilibrium mixture of the two tautomers as reported by Streitwieser (these two indene derivatives are the first two compounds listed in Table 1).^{2,46} Using Dr. Thornberry's method and Webster's pK values in water, we first defined the acid dissociation of compounds 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene (eq 25). This equation represents the "observed" acidity of the mixture, so there are two acid concentrations summed in the denominator but only one (common) conjugate base concentration in the numerator. In exchange measurements, H^+ does not really exist but these are theoretical arguments based on thermodynamic acidity definitions.

$$K_a = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{[1,2-(CN)_2CpH] + [2,3-(CN)_2CpH]} = 0.08 \quad (25)$$

We then defined the ΔpK between 1,2-dicyanocyclopentadiene and its isomer before rearranging the equation to give us two expressions for the two independent acid concentrations (eq 26-29). The two expressions (eqs 28 and 29) are equivalent but useful.

$$\Delta pK = pK_{1,2-(CN)_2CpH} - pK_{2,3-(CN)_2CpH} = \log \frac{[1,2-(CN)_2CpH]}{[2,3-(CN)_2CpH]} = 0.30 \quad (26)$$

$$\frac{[1,2-(CN)_2CpH]}{[2,3-(CN)_2CpH]} = 10^{0.30} = 1.99 \quad (27)$$

$$[1,2-(CN)_2CpH] = 1.99[2,3-(CN)_2CpH] \quad (28)$$

$$[2,3-(CN)_2CpH] = 0.50[1,2-(CN)_2CpH] \quad (29)$$

These two expressions could then be substituted into our original acid dissociation equation to solve for the pK_a value of 2,3-dicyanocyclopentadiene (eq 30-33).

$$K_a = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{[1,2-(CN)_2CpH] + [2,3-(CN)_2CpH]} = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{1.99[2,3-(CN)_2CpH] + [2,3-(CN)_2CpH]} = 0.08 \quad (30)$$

$$K_a = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{2.99[2,3-(CN)_2CpH]} = 0.08 \quad (31)$$

$$K_a = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{[2,3-(CN)_2CpH]} = 0.08 \times 2.99 = 0.24 \quad (32)$$

$$pK_a(2,3-(CN)_2CpH) = -\log(0.24) = 0.62 \quad (33)$$

We then repeat this again to find the pK_a value of 1,2-dicyanocyclopentadiene (eq 34-37).

$$K_a = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{[1,2-(CN)_2CpH] + [2,3-DCCp]} = \frac{[H^+][1,2-(CN)_2CpH(cb)]}{[1,2-(CN)_2CpH] + 0.5[1,2-(CN)_2CpH]} = 0.15 \quad (34)$$

$$K_a = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{1.50[1,2-(CN)_2CpH]} = 0.08 \quad (35)$$

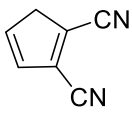
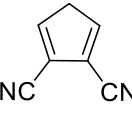
$$K_a = \frac{[H^+][1,2-(CN)_2Cp(cb)]}{[1,2-(CN)_2CpH]} = 0.08 \times 1.50 = 0.12 \quad (36)$$

$$pK_a(1,2-(CN)_2CpH) = -\log(0.12) = 0.92 \quad (37)$$

This formal approach gives the two acidity constants in beautifully symmetrical fashion, but starting from eq 33, we could have taken a short cut to the result shown in eq 37, just by recognizing that the pK_a of the 1,2-isomer is 0.30 units higher than that of the 2,3-isomer. With these acidity constants in hand, we can now connect the aqueous scale to other scales. Because 1,2-dicyanocyclopentadiene is the one compound that Webster characterized in both water and acetonitrile, he was able to estimate (using the “observed” acidity constants in each solvent) that the acetonitrile scale was offset from the aqueous scale by 9.06 units.¹ In Table 7, we likewise added 9.06 to the acidity constants for the individual tautomers to arrive at pK_{MeCN} values for each. With the pK_{MeCN} and pK_a values

determined, we could work on back-calculating the pK_{THF} values of our compounds. To tackle this problem, we needed to deal with a small discrepancy that we mentioned only briefly above. Figure 35 is reproduced and further developed as Figure 36. We had measured the acidity difference between the two bracketing perfluoroaryl-substituted cyclopentadienes in both CD_3CN (difference = 0.87) and in THF (difference = 1.28).

Table 7. pK values of 1,2-dicyanocyclopentadiene and its isomer in water, THF, and CH_3CN .

	pK_a	pK_{THF}	pK_{MeCN}
	0.92	-4.56	9.98
	0.62	-5.00	9.68

These kinds of “random” fluctuations are common when comparing any two acidity scales and are likely due to variations in solvation. At this point, we can be reasonably sure that because the acidities of the two dicyanocyclopentadiene tautomers are between the acidities of these two bracketing cyclopentadiene derivatives as measured in CD_3CN , then their acidities, on the SLI scale, should be between -3.81 and -5.09. To make further progress, however, we assumed that the differences among the compounds shown in Figure 36 “expanded” in proportion to the difference between the bracketing indicators. This “expansion ratio” of 1.47 is meant to apply only to this small section of our acidity scale and should not be interpreted to extrapolate beyond its boundaries. In the end, assuming that the setup remains “proportional” allows us to estimate the two acidities much more

closely, but we recognize that this approach is based on assumptions that we have not tested.

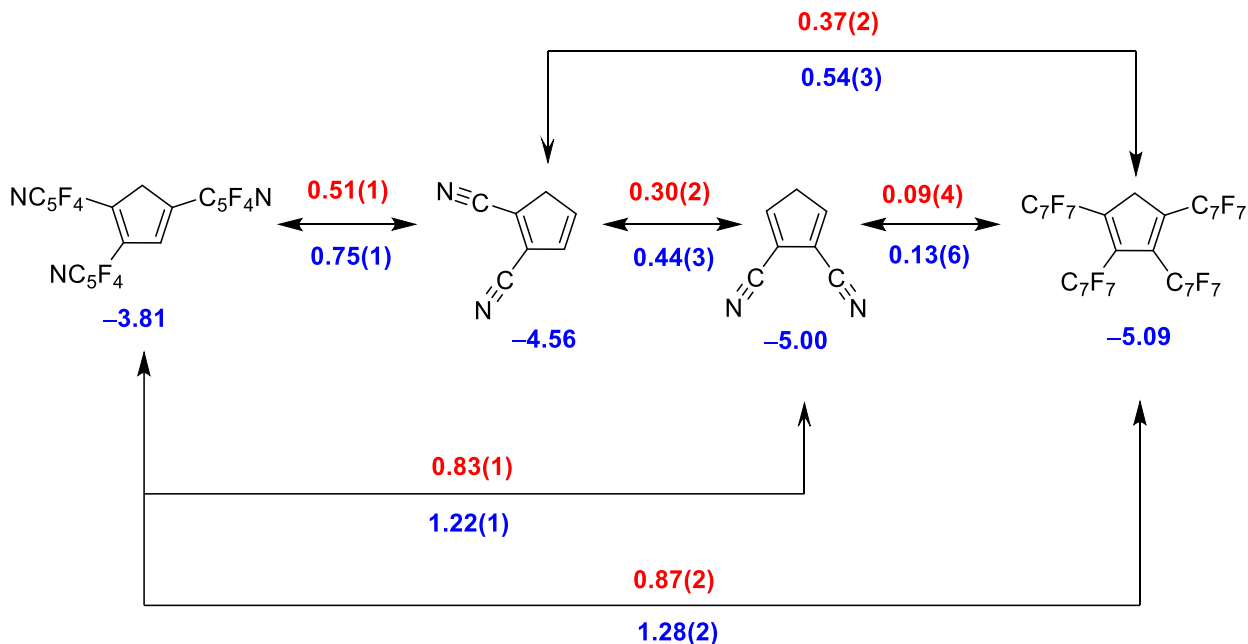


Figure 36. ΔpK values among 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,2,4-tris(perfluoropyridyl)cyclopentadiene, and 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene. Red: differences measured in CD_3CN . Blue: SLI values interpolated between the established acidities of the bracketing acids using a proportional method described in the text.

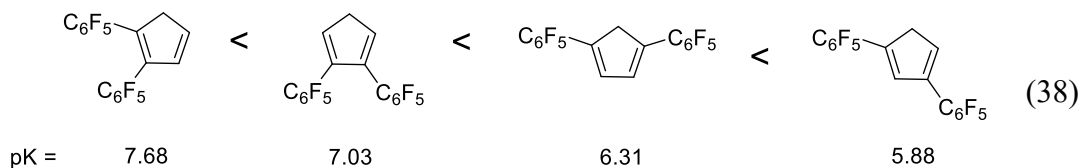
Now by comparing the aqueous and interpolated SLI values for the two cyano tautomers we can estimate an offset value to finally align the aqueous and SLI scales. We were, at last, able adjust the entire SLI scale by adding 5.48 to all the pK_{THF} values to give pK_a values (Table 8). Of course, the meaning of these aqueous acidities can always be called into question by noting that only two of the compounds in Table 8 are soluble in water.

Table 8. Aqueous pK_a values for carbon acids obtained by offsetting the SLI scale by 5.48 pK units. Compounds in bold are the dicyanocyclopentadienes measured in this work. Asterisk denotes a measured aqueous pK_a value. Estimation of the pK_a of its tautomer (brackets) is explained in the text.

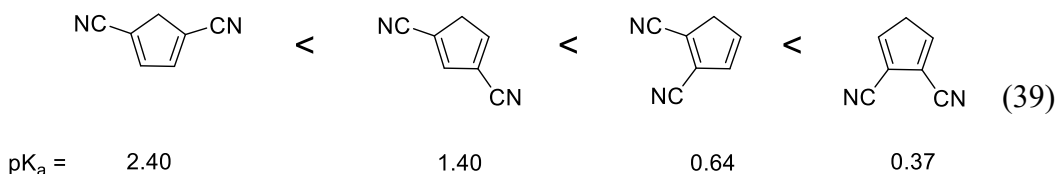
Compound	pK _a
1,2,4-tris(perfluoropyridyl)-3-perfluorophenylcyclopentadiene	-0.53
1,2,3-tris(perfluoropyridyl)-4-perfluorophenylcyclopentadiene	-0.40
1,2,3,4-tetra(perfluorotolyl)cyclopentadiene	0.39
2,3-dicyanocyclopentadiene	0.62*
1,2-dicyanocyclopentadiene	[0.92]
1,3-bis(perfluoropyridyl)-2,4-bis(perfluorophenyl)cyclopentadiene	1.31
2,3-bis(perfluoropyridyl)-1,4-bis(perfluorophenyl)cyclopentadiene	1.47
1,2,3-tris(perfluorotolyl)-4-perfluorophenylcyclopentadiene	1.53
1,2,4-tris(perfluoropyridyl)cyclopentadiene	1.67
1-perfluoropyridyl-2,3,4-tris(perfluorophenyl)cyclopentadiene	3.00
2-perfluoropyridyl-1,3,4-tris(perfluorophenyl)cyclopentadiene	3.28
1-perfluorotolyl-2,3,4-tris(perfluorophenyl)cyclopentadiene	3.83
2-perfluorotolyl-1,3,4-tris(perfluorophenyl)cyclopentadiene	3.94
1,2,3,4-tetra(perfluorophenyl)cyclopentadiene	5.11
1,3-bis(perfluoropyridyl)cyclopentadiene	5.45
1,4-bis(perfluoropyridyl)cyclopentadiene	6.10
2,3-bis(perfluoropyridyl)cyclopentadiene	6.90
1,2-bis(perfluoropyridyl)cyclopentadiene	7.45
1,2,4-tris(perfluorophenyl)cyclopentadiene	8.37
1,2,3-tris(perfluorophenyl)cyclopentadiene	8.98
1,3-bis(perfluorophenyl)cyclopentadiene	11.36
1,4-bis(perfluorophenyl)cyclopentadiene	11.79
2-perfluoropyridylcyclopentadiene	12.21
2,3-bis(perfluorophenyl)cyclopentadiene	12.51
1,2-bis(perfluorophenyl)cyclopentadiene	13.16
1-perfluoropyridylcyclopentadiene	13.19
1-Phenyl-3-(2',3',5',6'-tetrafluorophenyl)indene	14.62
3-Phenyl-1-(2',3',5',6'-tetrafluorophenyl)indene	14.98

1,1,3,3-Bis(biphenylene)propene	15.86
1,2,3,4,5-Pentaphenyl-1,3-cyclopentadiene	16.55
1,3-Diphenylindene	17.80
9-(2',3',5',6'-Tetrafluorophenyl)-fluorene	19.60
1,12-(<i>o</i> -Phenylene)-7,12-dihydropleiadene	19.92
1,2,3-Triphenylindene	20.17
9-Phenyl-3,4-benzofluorene	20.32
9-Biphenylfluorene	22.47
9-Phenyl-1,2-benzofluorene	22.86
9-Phenylfluorene	23.08
9-Phenyl-2,3-benzofluorene	23.32
9-(<i>p</i> -Dimethylaminophenyl)fluorene	24.50
3,4-Benzofluorene	24.77
1,2-Benzofluorene	25.18
Benzanthrene	25.61
9-Benzyl-9H-benzo[<i>def</i>]fluorene	26.83
9-Benzylfluorene	26.84
9-Isopropylidene fluorene	27.81
9-Butylfluorene	27.88
9-Methylfluorene	27.94
2:3,6:7-Dibenzofluorene	28.16
Fluorene	28.38
2,3-Benzofluorene	28.43
9- <i>tert</i> -Butylfluorene	29.89
Biphenyldithiane	34.78

From the acidity data of our dicyanocyclopentadiene compounds, we notice an important change in the acidifying trend from our previous (perfluoroaryl)cyclopentadiene data. In our previous work, we had established that the order of least acidic to most acidic between isomers was as follows for bis(perfluorophenyl)cyclopentadienes (eq 38).



This trend held for all forms of perfluoroaryl groups attached. In both our work and Webster's work, however, we see a reversal of the trend as follows (eq 39).



This reversal in the observed trend points to the 1,2-dicyanocyclopentadienide being a more stable conjugate base than the 1,3-dicyanocyclopentadienide. This reversal does not come to us completely by surprise. Webster had previously commented on this trend in his original work. He postulated that the use of highly acidic titrants such as TFA and H₂SO₄ was *kinetically selective*, favoring formation of more cross conjugated (less stable) isomers of the cyanocyclopentadienes. However, even in his original work, this hypothesis faces challenges, as the tricyanocyclopentadienes were separated into pure isomers and tested individually, and this trend reversal was still observed. One way of validating this hypothesis would be to use titrant acid only marginally more acidic (say, by 2 pK units) than the mixtures being titrated. While Webster was unable to do this, we have achieved this in our work (Figure 36) and the trend reversal holds. The trend reversal holding proves that it is driven thermodynamically not kinetically, because we are confident that our NMR measurements reflect processes at equilibrium.

To understand why this trend is reversed in eq 39, we must first establish why we see our original trend in eq 38. In our previous work, we originally hypothesized that perfluoroaryl groups that were proximal to each other experienced increased steric hinderance between each other. This steric hinderance between perfluoroaryl groups would prevent either group from achieving coplanarity with the cyclopentadiene body needed to form the highly stable resonance structure depicted in Figure 37.

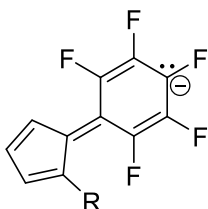


Figure 37. Resonance structure of 1,2-bis(perfluorophenyl)cyclopentadienide. R = $-\text{C}_6\text{F}_5$

In this case, the inability to form this resonance structure would cause a destabilizing effect to the 1,2-bis(perfluorophenyl)cyclopentadienide relative to its distal isomer 1,3-bis(perfluorophenyl)cyclopentadienide, which does not experience this steric hinderance. Any instability to the conjugate base makes the acidic form of that conjugate base more stable by comparison. This is reflected in a less acidic pK value than their distal isomers as we observed in Eq. 38.

The switch to nitrile groups results in no steric bulk hindering either group when they are proximal to each other. Furthermore, the nitrile groups start off coplanar to the cyclopentadiene body. Thus, they can achieve the highly stable resonance structure depicted in Figure 38.

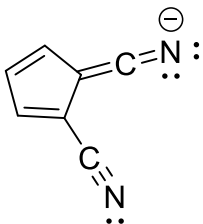


Figure 38. Resonance structure of 1,2-dicyanocyclopentadienide.

These factors provide an increased stabilization effect to 1,2-dicyanocyclopentadienide relative to its distal isomer 1,3-dicyanocyclopentadienide. This increased stabilization of 1,2-dicyanocyclopentadienide leads to an increased acidifying effect to 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene relative to their distal isomers. Thus, we see the trend we observed between dicyanocyclopentadiene isomers in eq 39.

To validate our hypothesis, we first conducted computational geometry optimization studies of 1,2-bis(perfluorophenyl)cyclopentadienide and 1,3-bis(perfluorophenyl)cyclopentadienide (Figure 39).

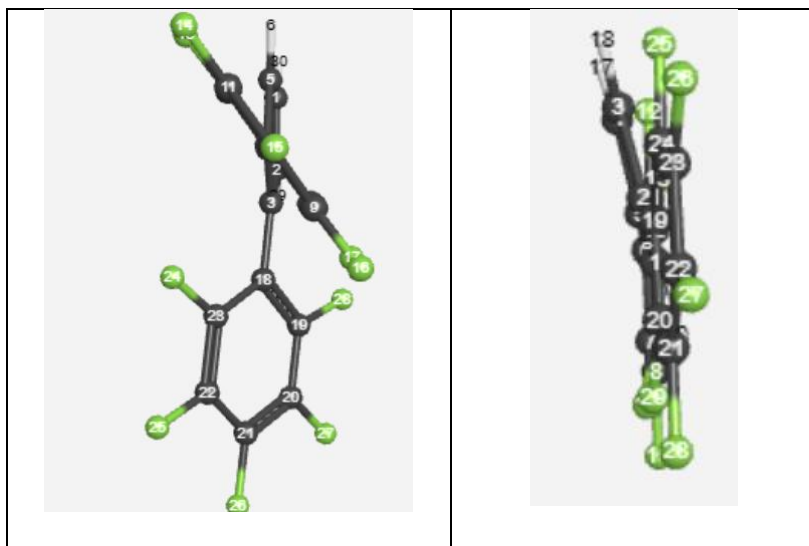


Figure 39. Computational comparison of the dihedral angle between 1,2-bis(perfluorophenyl)cyclopentadienide (Left) and 1,3-bis(perfluorophenyl)cyclopentadienide (Right). Calculations used Gaussian B3LYP with 6-31G(d) basis set in WebMO.

These computational studies showed that the dihedral angle between the $-C_6F_5$ groups on 1,2-bis(perfluorophenyl)cyclopentadienide was more substantial than they were on 1,3-bis(perfluorophenyl)cyclopentadienide (37.174° vs 13.211°). This difference in dihedral angle confirmed that 1,2-bis(perfluorophenyl)cyclopentadienide experiences more steric hindrance between its $-C_6F_5$ groups. We then compared the dipole moments between 1,2-dicyanocyclopentadiene, 1,2-dicyanocyclopentadienide, 1,3-dicyanocyclopentadiene, and 1,3-dicyanocyclopentadienide to establish the stabilizing effect the resonance structure in Figure 38 has on the 1,2-dicyanocyclopentadienide relative to 1,3-dicyanocyclopentadienide (Figure 40).

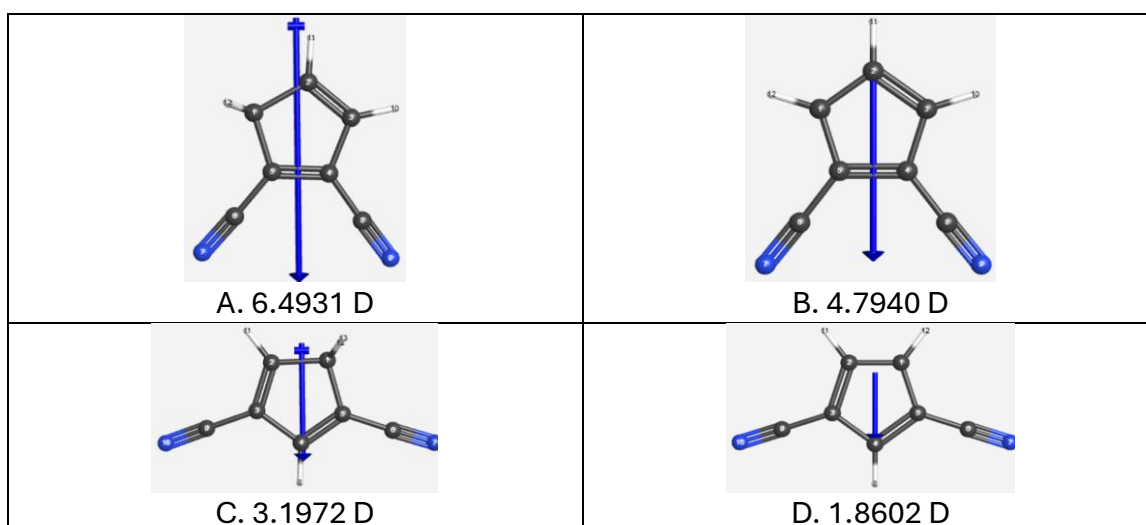


Figure 40. Dipole moments of 1,2-dicyanocyclopentadiene (A), 1,3-dicyanocyclopentadiene (C), and their conjugate bases (B and D, respectively). Calculations used Gaussian B3LYP with 6-31G(d) basis set in WebMO.

From Figure 40, we were able to determine that the change in dipole moment between 1,2-dicyanocyclopentadiene and 1,2-dicyanocyclopentadienide was larger than the change in dipole moment between 1,3-dicyanocyclopentadiene and 1,3-dicyanocyclopentadienide (1.6991 Debye vs 1.3370 Debye). These results would seem to validate our hypothesis that the lack of steric hindrance between proximal nitrile groups provides a more stabilizing

effect to 1,2-dicyanocyclopentadienide relative to 1,3-dicyanocyclopentadienide and thus makes its respective acid forms more acidic than their distal counterparts. However, these conclusions are still speculative, and additional studies will need to be conducted to better understand this underlying correlation.

Conclusions for Chapter 3

Using a combination of ^1H and ^{19}F NMR spectroscopy, we successfully measured and calculated the pK_a , pK_{THF} , and pK_{MeCN} of 1,2-dicyanocyclopentadiene and 2,3-dicyanocyclopentadiene. Using these compounds as reference points, we then calculated the true pK_a values of all acids on the SLI scale. Along the way, we confirmed that the previously observed “switch” in acidity trends between isomers with proximal nitrile groups and isomers with distal nitrile groups was thermodynamically driven. Finally, using computational chemistry, we were able to determine the cause of the “switch” was rooted in the lack of steric bulk around the nitrile groups contributed to a more stable conjugate base than either their proximal counterparts or their perfluoroaryl analogs.

General Acidity Measurements

An NMR tube is charged with 1,2,3,4-tetrakis(perfluorotolyl)cyclopentadiene (13 mg, 14 μmol) and about 2.0 mg (14 μmol) of potassium 1,2-dicyanocyclopentadienide. Using a Schlenk adapter, CD_3CN was added anaerobically using a syringe. After equilibrating 24 h, the sample was submitted to the Analytical Services Center for analysis using ^1H NMR (64 scans, 15 s relaxation delay) and ^{19}F NMR (64 scans, 15 s relaxation delay, 15° pulse angle).

“Standard Solvent” for ^{19}F NMR acidity studies Preparation.

A 100-mL glass bulb (of known mass when fitted with its J-Young valve) was connected to a diffusion-pumped vacuum line and flamed under vacuum ($P < 2 \times 10^{-5}$ Torr) to ensure that the bulb was completely dry. Then, about 50 mL of rigorously degassed THF was vacuum-transferred from NaK₂ alloy using dry-ice cooling. The bulb was refilled with argon and the solvent was warmed to room temperature under argon. Knowing the initial and final masses of the bulb allowed us to determine the total volume of THF that was transferred. Then, the bulb was connected to a Schlenk line and opened under a nitrogen counter-stream. C₆D₆ (used as received from CIL) and benzotrifluoride (used as received from Millipore Sigma) were then added in sufficient volume to reach final overall concentrations of 5% C₆D₆ and 0.2% of PhCF₃ by volume. C₆D₆ is needed for lock and homogeneity (shimming) adjustments; PhCF₃ is used as a chemical shift standard. A concentric NMR tube was prepared containing PhCF₃ dissolved in THF containing 5% of THF in the outer portion and C₆F₆ dissolved in CDCl₃ in the narrow insert. The resulting ¹⁹F NMR spectrum (376 MHz) showed a singlet upfield, which was assigned to C₆F₆ and set to -163.00 ppm, and a triplet downfield, which was assigned to PhCF₃ at a chemical shift of -64.29 ppm. Thereafter, all of our NMR spectra recorded in “standard solvent” were referenced to PhCF₃ at -64.29 ppm, which is equivalent to the standard reference of -163.00 ppm for C₆F₆ in CDCl₃.

Chapter 4: Supplemental Information

Table 9. Acidity measurement between 1,2-dicyanocyclopentadiene (2a), its' isomer (2b), and 1,2,4-tris(perfluoropyridyl)cyclopentadiene indicator (3) and their respective conjugate bases (2(cb) and 3(cb) respectively) measured in d-MeCN

<i>Spectra</i> HAR-2- 147-1	2(cb)	+	3	\rightleftharpoons	2a	+	2b	+	3(cb)	ΔpK (2a)	ΔpK (2b)
<i>Vinyl</i> ¹ H(1)										0.50	0.83
<i>Vinyl</i> ¹ H(2)											
<i>Vinyl</i> ¹ H(3)			1.00		0.26						
<i>Vinyl</i> ¹ H(4)					0.31						
<i>Aliphatic</i> ¹ H(5)			1.96			0.26					
<i>Aromatic</i> ¹ H(1)											
<i>Aromatic</i> ¹ H(2)											
<i>Aromatic</i> ¹ H(3)								1.82			
<i>Aromatic</i> ¹ H(4)	0.82										
<i>Aromatic</i> ¹ H(5)											
# of eq. ¹ H (1)											
# of eq. ¹ H (2)											
# of eq. ¹ H (3)			1		1				2		
# of eq. ¹ H (4)	1				1						
# of eq. ¹ H (5)			2			2					
<i>Relative</i> <i>Integral</i>	0.82		0.98		0.28	0.13		0.91			
<i>Mole</i> <i>Fraction</i>	0.26		0.31		0.09	0.04		0.29			
<i>Spectra</i> HAR-2- 147-2	2(cb)	+	3	\rightleftharpoons	2a	+	2b	+	3(cb)	ΔpK (2a)	ΔpK (2b)
<i>Vinyl</i> ¹ H(1)										0.50	0.82
<i>Vinyl</i> ¹ H(2)											
<i>Vinyl</i> ¹ H(3)			1.00		0.23						

<i>Vinyl</i> ¹ H(4)					0.27								
<i>Aliphatic</i> ¹ H(5)			1.97				0.24						
<i>Aromatic</i> ¹ H(1)													
<i>Aromatic</i> ¹ H(2)													
<i>Aromatic</i> ¹ H(3)											1.54		
<i>Aromatic</i> ¹ H(4)	0.62												
<i>Aromatic</i> ¹ H(5)													
# of eq. ¹ H (1)													
# of eq. ¹ H (2)													
# of eq. ¹ H (3)			1		1						2		
# of eq. ¹ H (4)	1				1								
# of eq. ¹ H (5)			2				2						
<i>Relative Integral</i>	0.62		0.99		0.25		0.12				0.77		
<i>Mole Fraction</i>	0.22		0.36		0.09		0.04				0.28		
<i>Spectra HAR-2-147-3</i>	2(cb)	+	3	\rightleftharpoons	2a	+	2b	+	3(cb)	ΔpK (2a)			ΔpK (2b)
<i>Vinyl</i> ¹ H(1)										0.52			0.83
<i>Vinyl</i> ¹ H(2)													
<i>Vinyl</i> ¹ H(3)			1.00		0.23								
<i>Vinyl</i> ¹ H(4)					0.27								
<i>Aliphatic</i> ¹ H(5)			1.99				0.25						
<i>Aromatic</i> ¹ H(1)													
<i>Aromatic</i> ¹ H(2)													
<i>Aromatic</i> ¹ H(3)											1.57		
<i>Aromatic</i> ¹ H(4)	0.64												
<i>Aromatic</i> ¹ H(5)													

# of eq. ¹ H (1)									
# of eq. ¹ H (2)									
# of eq. ¹ H (3)		1		1				2	
# of eq. ¹ H (4)	1			1					
# of eq. ¹ H (5)		2				2			
<i>Relative Integral</i>	0.64	1.00		0.25		0.12		0.78	
<i>Mole Fraction</i>	0.23	0.36		0.09		0.04		0.28	
<i>Average</i>								0.51 (1)	0.83 (1)

Table 10. Acidity measurement between 1,2-dicyanocyclopentadiene (2a), its' isomer (2b), and 1,2,3,4-tetra(perfluorotolyl)cyclopentadiene indicator (4) and their respective conjugate bases (2(cb) and 4(cb) respectively) measured in d-MeCN

<i>Spectra</i> <i>HAR-2-155-1</i>	2(cb)	+	4	\rightleftharpoons	2a	+	2b	+	4(cb)	ΔpK (2a)	ΔpK (2b)
<i>Vinyl</i> $^1H(1)$										-0.39	-0.11
<i>Vinyl</i> $^1H(2)$					0.40						
<i>Vinyl</i> $^1H(3)$					0.41						
<i>Vinyl</i> $^1H(4)$											
<i>Aliphatic</i> $^1H(5)$			1.00				0.43				
<i>Aromatic</i> $^1H(1)$											
<i>Aromatic</i> $^1H(2)$											
<i>Aromatic</i> $^1H(3)$	0.34										
<i>Aromatic</i> $^1H(4)$											
<i>Aromatic</i> $^1H(5)$											
<i>Ortho</i> (T1)			1.00						2.08		
<i>Ortho</i> (T2)											
<i>Ortho</i> (T3)			1.00						2.07		
<i>Ortho</i> (T4)											
<i>Meta</i> (T1)			1.01						2.10		
<i>Meta</i> (T2)											
<i>Meta</i> (T3)			1.03						2.09		
<i>Meta</i> (T4)											
<i>-CF₃</i> (T1)											
<i>-CF₃</i> (T2)											
<i>-CF₃</i> (T3)											
<i>-CF₃</i> (T4)											
# of eq. 1H (1)											

# of eq. ¹ H (2)					1							
# of eq. ¹ H (3)	1				1							
# of eq. ¹ H (4)	1											
# of eq. ¹ H (5)			2				2					
# of eq. rings (T1)			2									2
# of eq. rings (T2)												
# of eq. rings (T3)			2									2
# of eq. rings (T4)												
Relative Integral	0.34		0.25		0.40		0.21					0.52
Mole Fraction	0.20		0.14		0.23		0.12					0.30
Spectra HAR-2-155-2	2(cb)	+	4	\rightleftharpoons	2a	+	2b	+	4(cb)		ΔpK (2a)	ΔpK (2b)
Vinyl ¹ H(1)											-0.37	-0.05
Vinyl ¹ H(2)					0.62							
Vinyl ¹ H(3)					0.65							
Vinyl ¹ H(4)												
Aliphatic ¹ H(5)			1.00				0.60					
Aromatic ¹ H(1)												
Aromatic ¹ H(2)												
Aromatic ¹ H(3)	0.94											
Aromatic ¹ H(4)												
Aromatic ¹ H(5)												
Ortho (T1)			1.00									3.51
Ortho (T2)												
Ortho (T3)			1.00									3.51
Ortho (T4)												
Meta(T1)			1.00									3.57
Meta(T2)												
Meta(T3)			1.03									3.53
Meta(T4)												

-CF ₃ (T1)																				
-CF ₃ (T2)																				
-CF ₃ (T3)																				
-CF ₃ (T4)																				
# of eq. ¹ H (1)																				
# of eq. ¹ H (2)						1														
# of eq. ¹ H (3)	1					1														
# of eq. ¹ H (4)	1																			
# of eq. ¹ H (5)			2							2										
# of eq. rings (T1)			2																2	
# of eq. rings (T2)																				
# of eq. rings (T3)			2																2	
# of eq. rings (T4)																				
Relative Integral	0.94		0.25			0.63				0.30									0.88	
Mole Fraction	0.20		0.14			0.23				0.12									0.30	
Spectra HAR-2-155-3	2(cb)	+	4		↔	2a	+	2b	+	4(cb)									ΔpK (2a)	ΔpK (2b)
Vinyl ¹ H(1)																			-0.36	-0.11
Vinyl ¹ H(2)						0.56														
Vinyl ¹ H(3)						0.59														
Vinyl ¹ H(4)																				
Aliphatic ¹ H(5)			1.00							0.65										
Aromatic ¹ H(1)																				
Aromatic ¹ H(2)																				
Aromatic ¹ H(3)	0.80																			
Aromatic ¹ H(4)																				
Aromatic ¹ H(5)																				
Ortho (T1)			1.00																	3.16
Ortho (T2)																				
Ortho (T3)			1.00																	3.14

<i>Ortho (T4)</i>											
<i>Meta(T1)</i>		1.00								3.23	
<i>Meta(T2)</i>											
<i>Meta(T3)</i>		1.03								3.21	
<i>Meta(T4)</i>											
<i>-CF₃(T1)</i>											
<i>-CF₃(T2)</i>											
<i>-CF₃(T3)</i>											
<i>-CF₃(T4)</i>											
# of eq. ¹ H (1)											
# of eq. ¹ H (2)				1							
# of eq. ¹ H (3)	1			1							
# of eq. ¹ H (4)	1										
# of eq. ¹ H (5)		2				2					
# of eq. rings (T1)		2								2	
# of eq. rings (T2)											
# of eq. rings (T3)		2								2	
# of eq. rings (T4)											
<i>Relative Integral</i>	0.80	0.25		0.58		0.32				0.80	
<i>Mole Fraction</i>	0.20	0.14		0.23		0.12				0.30	
<i>Average</i>											-0.37(2) -0.09(4)

Table 11. Indicator acidity measurement between 1,2,4-tris(perfluoropyridyl)-cyclopentadiene (3), 1,2,3,4-tetra(perfluorotolyl)cyclopentadiene indicator (4) and their respective conjugate bases (2(cb) and 4(cb) respectively) measured in d-MeCN

Spectra=HAR-2-155-1	3	+	4(cb)	\rightleftharpoons	3(cb)	+	4	ΔpK_{MeCN} (3-4)
Ortho(T1)							1.00	0.88
Ortho(T2)								
Ortho(T3)			2.30				1.00	
Ortho(T4)								
Ortho(P1)					0.87			
Ortho(P2)								
Ortho(P4)					0.44			
Meta(T1)			2.29				1.00	

Meta(T2)							
Meta(T3)			2.29				1.04
Meta(T4)							
Meta(P1)	2.80				0.85		
Meta(P2)							
Meta(P4)	1.42				0.42		
-CF ₃ (T1)							
-CF ₃ (T2)							
-CF ₃ (T3)							
-CF ₃ (T4)							
# of eq. rings (P1)	2				2		
# of eq. rings (P2)							
# of eq. rings (P4)	1				1		
# of eq. rings (T1)			2				2
# of eq. rings (T2)							
# of eq. rings (T3)			2				2
# of eq. rings (T4)							
Relative Integral	0.70		0.57		0.21		0.25
Mole Fraction	0.40		0.33		0.12		0.14
Spectra=HAR-1-155-2	3	+	4(cb)	\rightleftharpoons	3(cb)	+	4
Ortho(T1)							1.00
Ortho(T2)							
Ortho(T3)			2.01				1.00
Ortho(T4)							
Ortho(P1)					0.74		
Ortho(P2)							
Ortho(P4)					0.38		
Meta(T1)			2.03				0.94
Meta(T2)							
Meta(T3)			2.02				1.01
Meta(T4)							
Meta(P1)	2.58				0.72		
Meta(P2)							
Meta(P4)	1.29				0.36		
-CF ₃ (T1)							
-CF ₃ (T2)							
-CF ₃ (T3)							
-CF ₃ (T4)							
# of eq. rings (P1)	2				2		
# of eq. rings (P2)							
# of eq. rings (P3)	1				1		
# of eq. rings (T1)			2				2
# of eq. rings (T2)							
# of eq. rings (T3)			2				2

# of eq. rings (T4)							
Relative Integral	0.64		0.50		0.18		0.25
Mole Fraction	<i>0.41</i>		<i>0.32</i>		<i>0.11</i>		<i>0.16</i>
Spectra=HAR-1-155-3	3	+	4(cb)	\rightleftharpoons	3(cb)	+	4
							ΔpK_{MeCN} (3-4)
Ortho(T1)							1.00
Ortho(T2)							
Ortho(T3)			1.94				1.00
Ortho(T4)							
Ortho(P1)					0.68		
Ortho(P2)							
Ortho(P4)					0.35		
Meta(T1)			1.96				0.99
Meta(T2)							
Meta(T3)			1.94				1.01
Meta(T4)							
Meta(P1)	2.56				0.66		
Meta(P2)							
Meta(P4)	1.30				0.34		
-CF ₃ (T1)							
-CF ₃ (T2)							
-CF ₃ (T3)							
-CF ₃ (T4)							
# of eq. rings (P1)	2				2		
# of eq. rings (P2)							
# of eq. rings (P3)	1				1		
# of eq. rings (T1)			2				2
# of eq. rings (T2)							
# of eq. rings (T3)			2				2
# of eq. rings (T4)							
Relative Integral	0.64		0.49		0.17		0.25
Mole Fraction	<i>0.41</i>		<i>0.32</i>		<i>0.11</i>		<i>0.16</i>
Average							0.87(2)

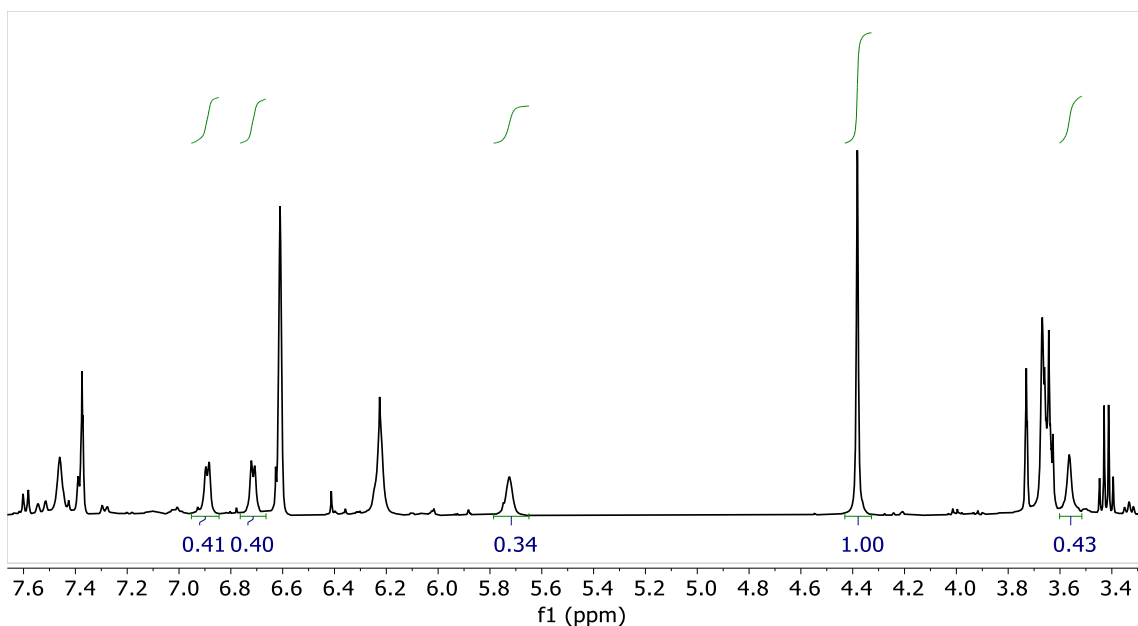


Figure 41: ^1H NMR spectrum (400 MHz, CD_3CN) of Trial 1 (HAR-2-155-1) Acidity Test between between 1,2,3,4-tetra(perfluoro-4-tolyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

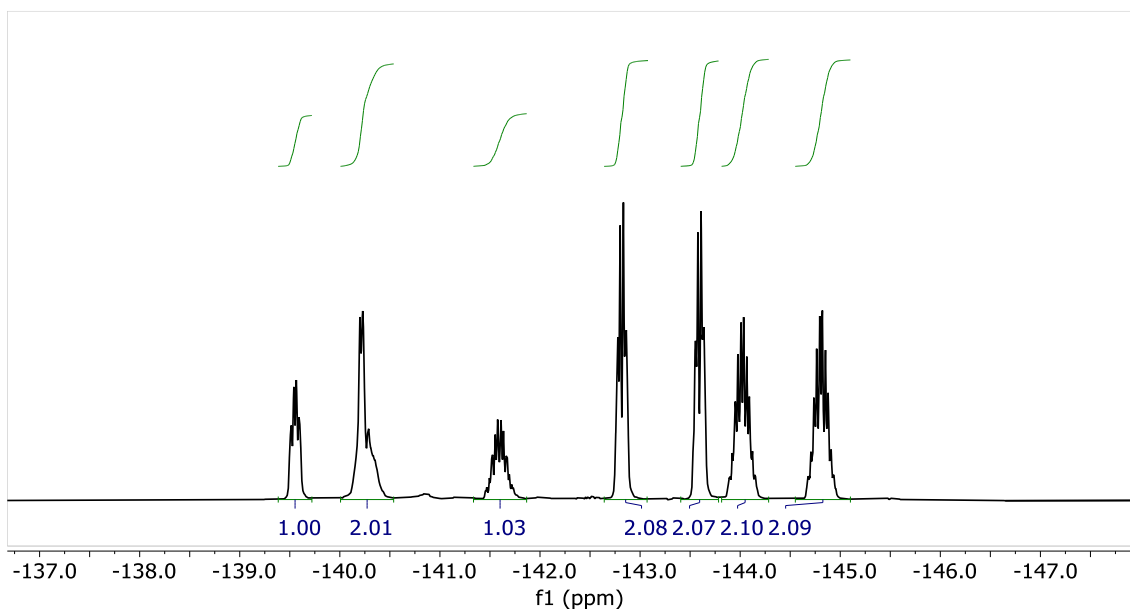


Figure 42. ^{19}F NMR spectrum (376 MHz, CD_3CN) of Trial 1 (HAR-2-155-1) Acidity Test between between 1,2,3,4-tetra(perfluoro-4-tolyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

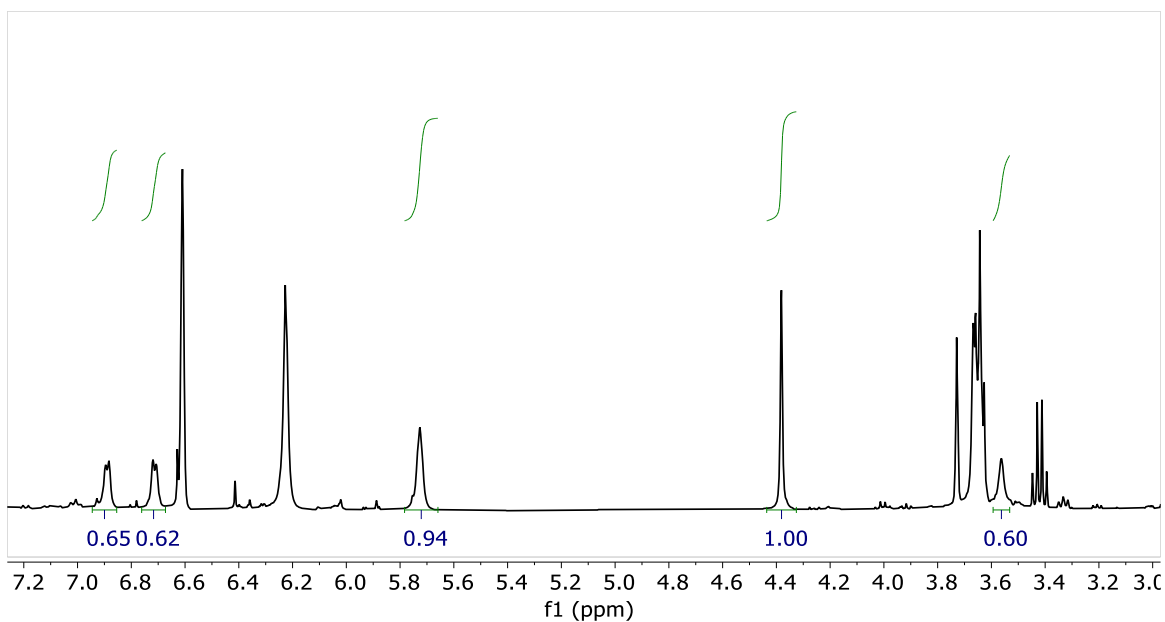


Figure 43. ^1H NMR spectrum (400 MHz, CD_3CN) of Trial 2 (HAR-2-155-2) Acidity Test between between 1,2,3,4-tetra(perfluoro-4-tolyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

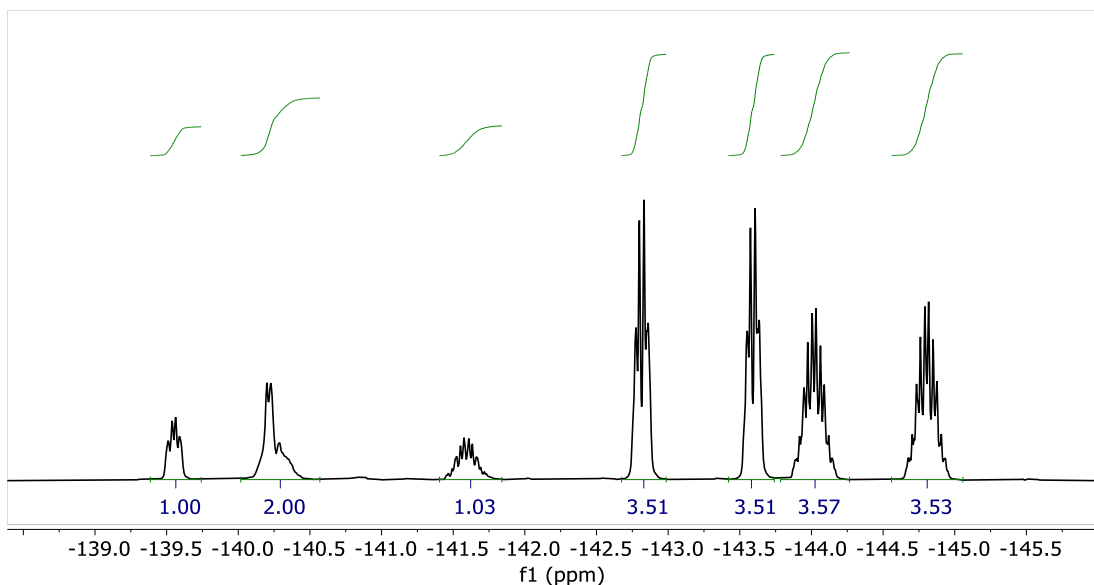


Figure 44. ^{19}F NMR spectrum (376 MHz, CD_3CN) of Trial 2 (HAR-2-155-2) Acidity Test between between 1,2,3,4-tetra(perfluoro-4-tolyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

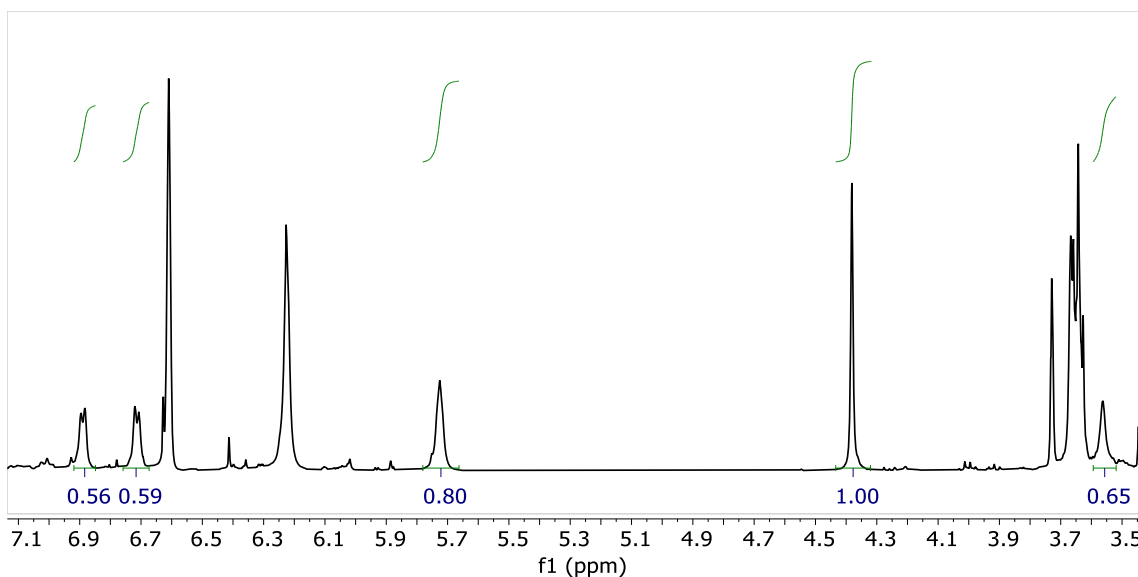


Figure 45. ^1H NMR spectrum (400 MHz, CD_3CN) of Trial 3 (HAR-2-155-3) Acidity Test between between 1,2,3,4-tetra(perfluorotolyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

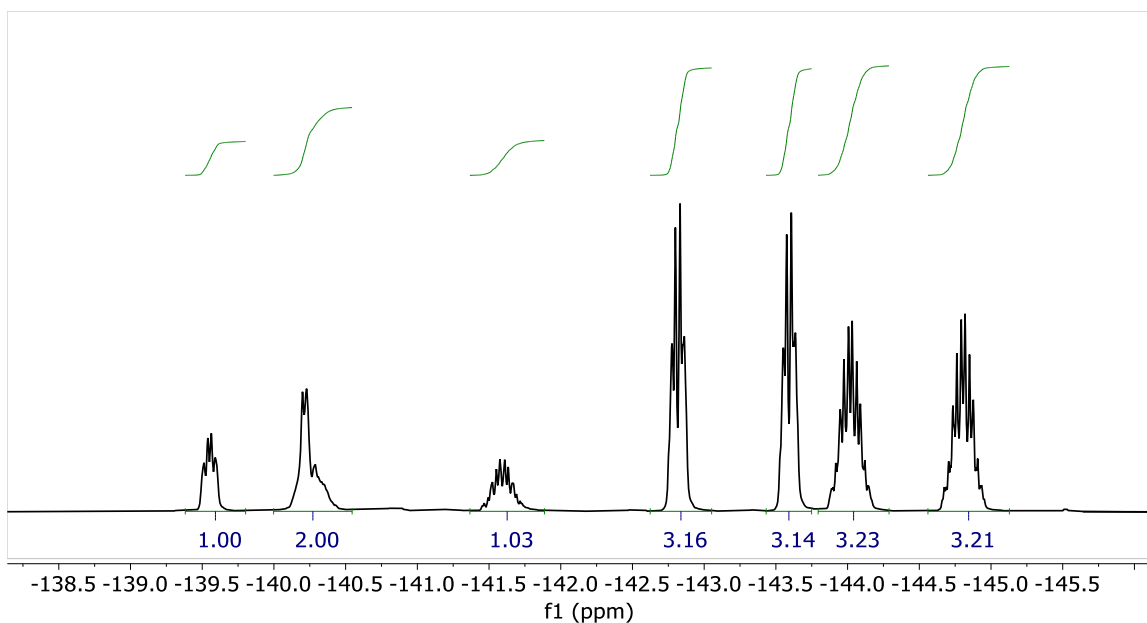


Figure 46. ^{19}F NMR spectrum (376 MHz, CD_3CN) of Trial 3 (HAR-2-155-3) Acidity Test between between 1,2,3,4-tetra(perfluorotolyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

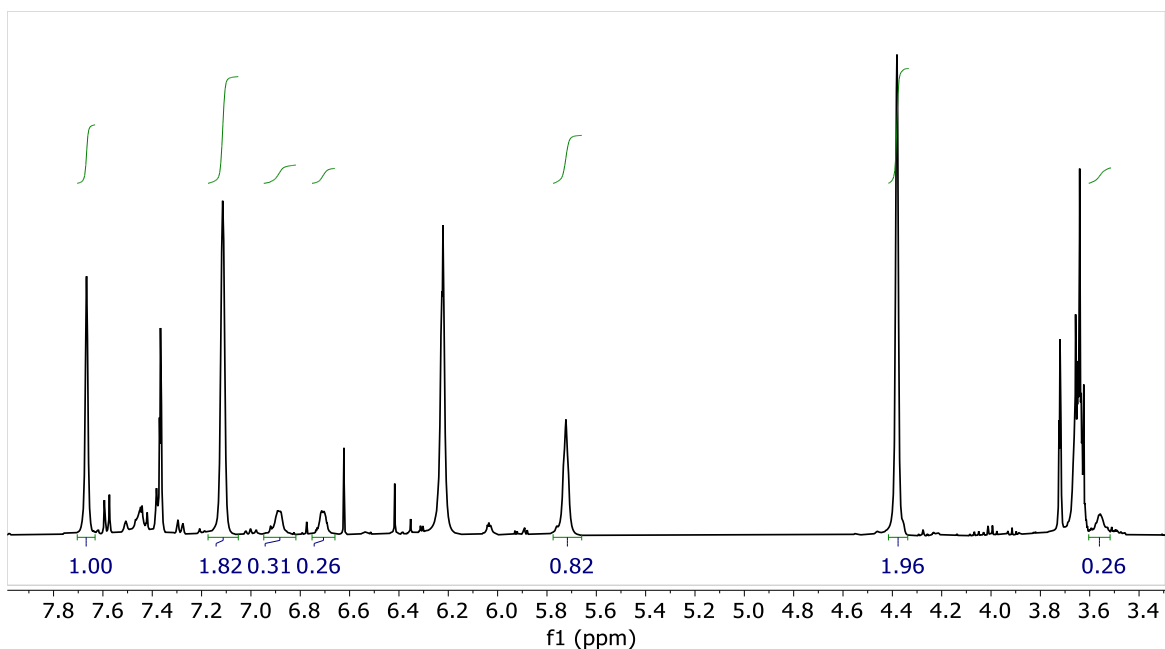


Figure 47. ¹H NMR spectrum (400 MHz, CD₃CN) of Trial 1 (HAR-2-147-1) Acidity Test between 1,2,4-tris(perfluoropyridyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

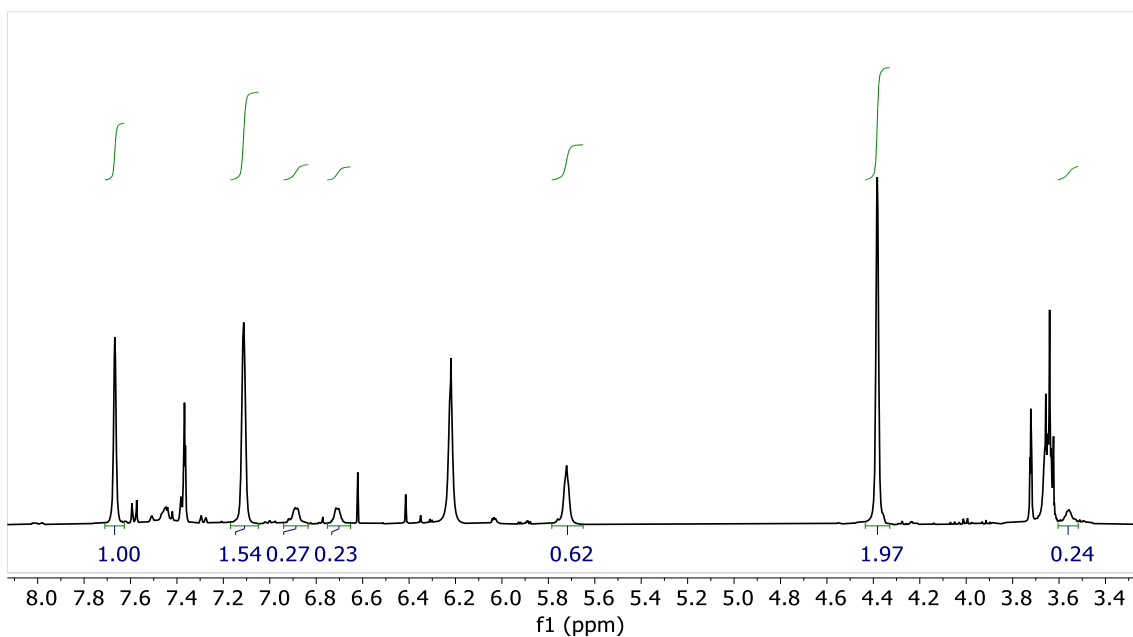


Figure 48. ¹H NMR spectrum (400 MHz, CD₃CN) of Trial 2 (HAR-2-147-2) Acidity Test between 1,2,4-tris(perfluoropyridyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

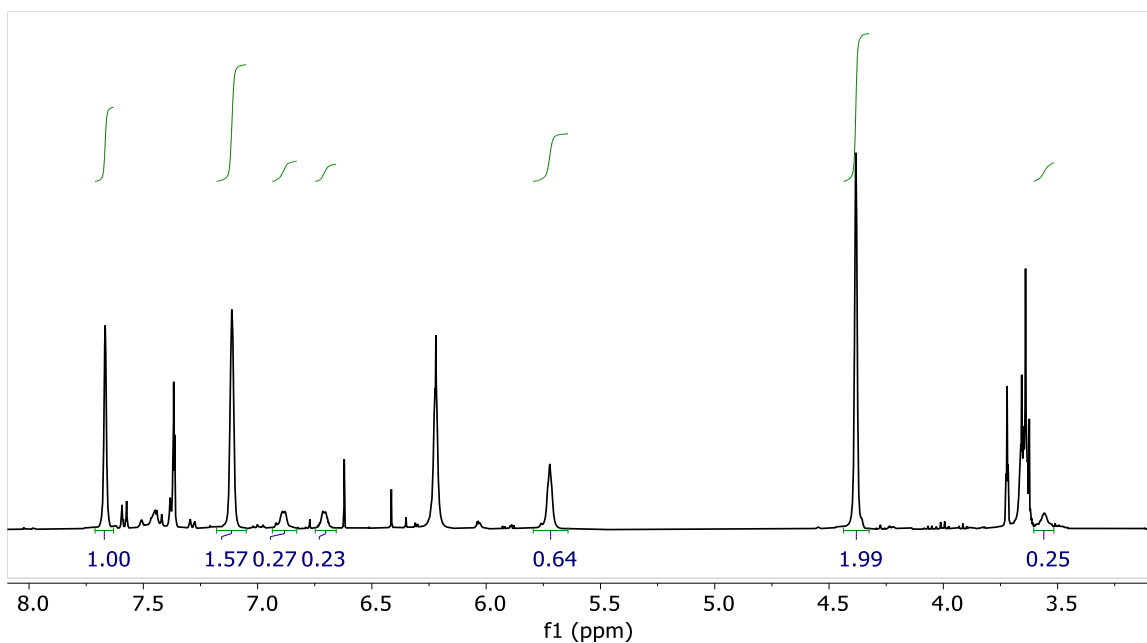


Figure 49. ^1H NMR spectrum (400 MHz, CD_3CN) of Trial 3 (HAR-2-147-3) Acidity Test between 1,2,4-tris(perfluoropyridyl)cyclopentadiene, 1,2-dicyanocyclopentadiene, 2,3-dicyanocyclopentadiene, 1,4-dicyanocyclopentadiene, 1,3-dicyanocyclopentadiene, and their respective conjugate bases.

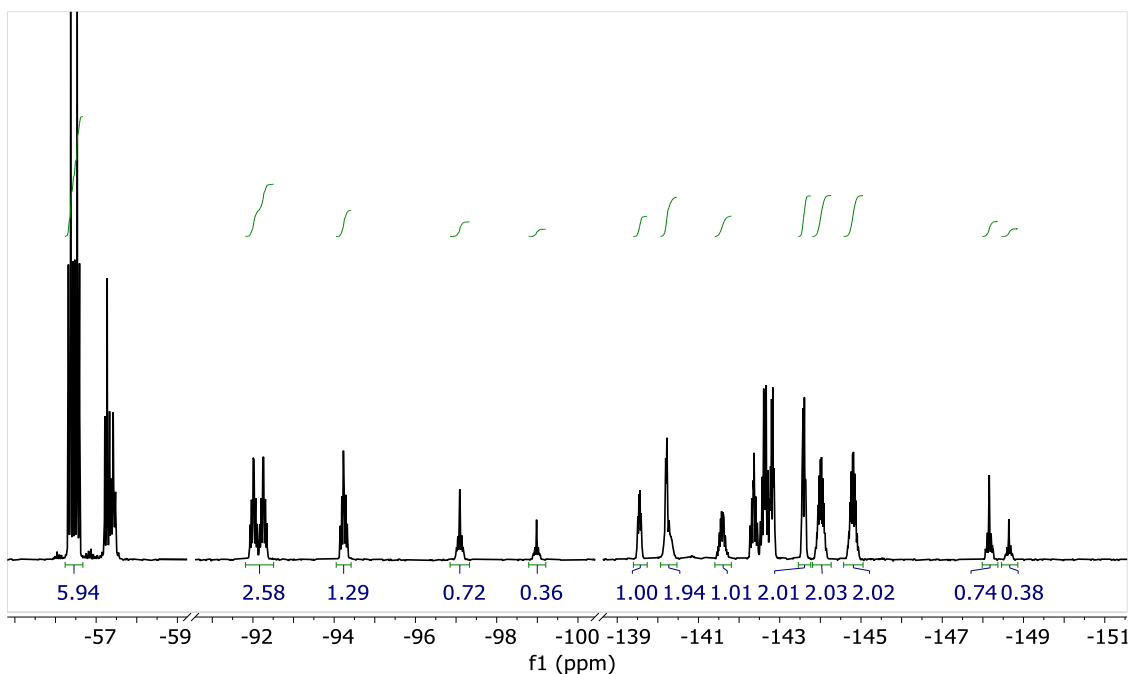


Figure 50. ^{19}F NMR (376 MHz, CD_3CN) spectrum of acidity measurement Trial 2 (HAR-2-153-2) between 1,2,3,4-tetra(perfluorotolyl)cyclopentadiene, 1,2,4-tris(perfluoropyridyl)cyclopentadiene, and their respective conjugate bases.

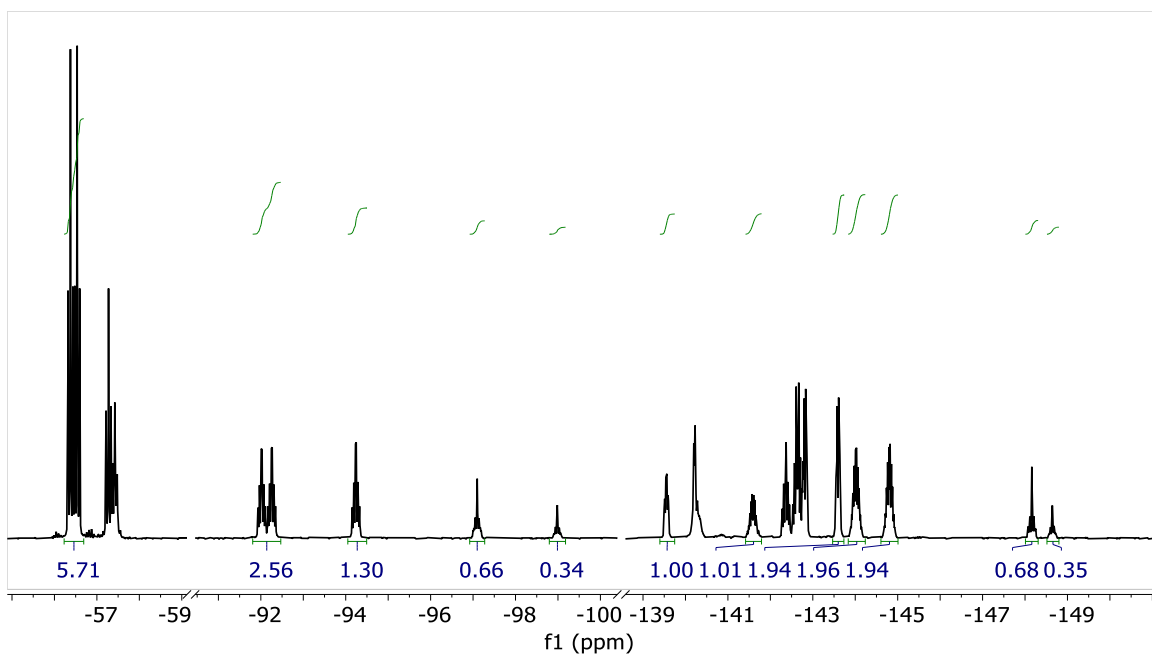


Figure 51. ^{19}F NMR (376 MHz, CD_3CN) spectrum of acidity measurement Trial 3 (HAR-2-153-3) between 1,2,3,4-tetra(perfluorotolyl)cyclopentadiene, 1,2,4-tris(perfluoropyridyl)cyclopentadiene, and their respective conjugate bases.

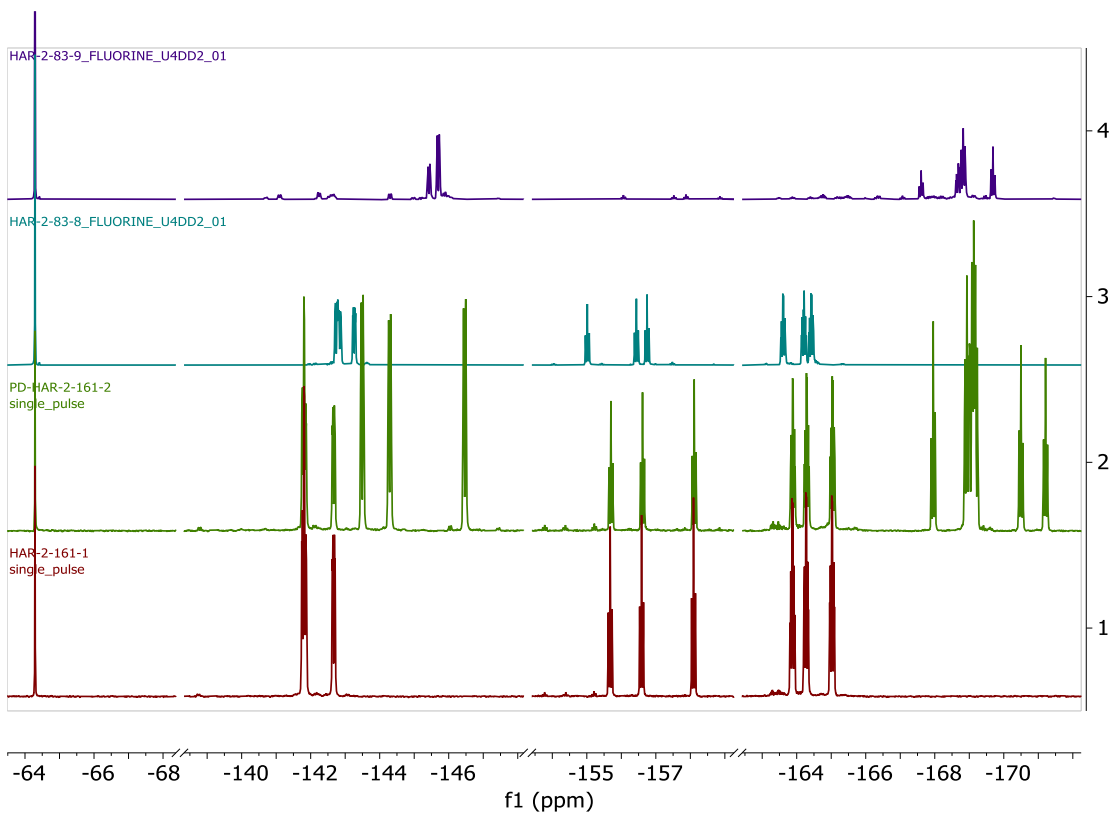


Figure 52. ^{19}F NMR spectra (376 MHz) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm). Spectrum 1: 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene. Spectrum 2: Equilibrium mixture of 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene and its' conjugate base. Spectrum 3: 1,2,3-tris(perfluorophenyl)cyclopentadiene. Spectrum 4: lithium 1,2,3-tris(perfluorophenyl)cyclopentadienide

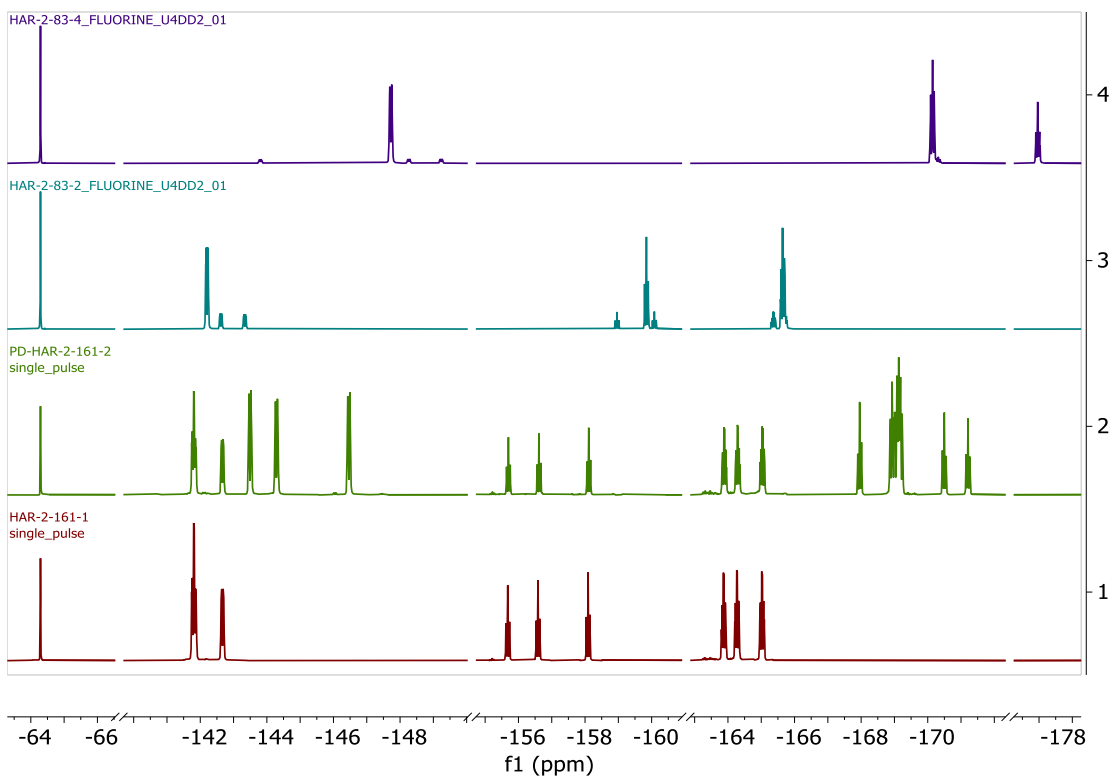


Figure 53. ^{19}F NMR spectra (400 MHz) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm). Spectrum 1: 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene. Spectrum 2: Equilibrium Mixture of 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene and its' conjugate base. Spectrum 3: 1,4-bis(perfluorophenyl)cyclopentadiene and its' tautomer. Spectrum 4: lithium 1,3-bis(perfluorophenyl)cyclopentadienide

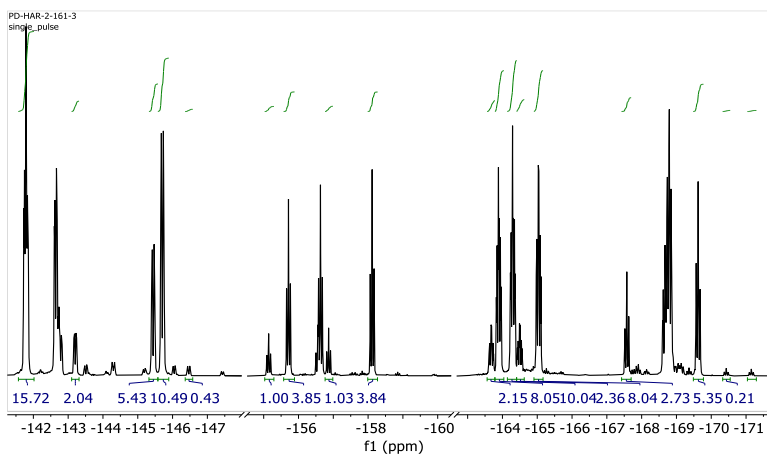


Figure 54. ^{19}F NMR spectrum (400 MHz) of acidity measurement between 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene, 1,2,3-tris(perfluorophenyl)cyclopentadiene, and their conjugate bases Trial 1 (HAR-2-161-3) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm).

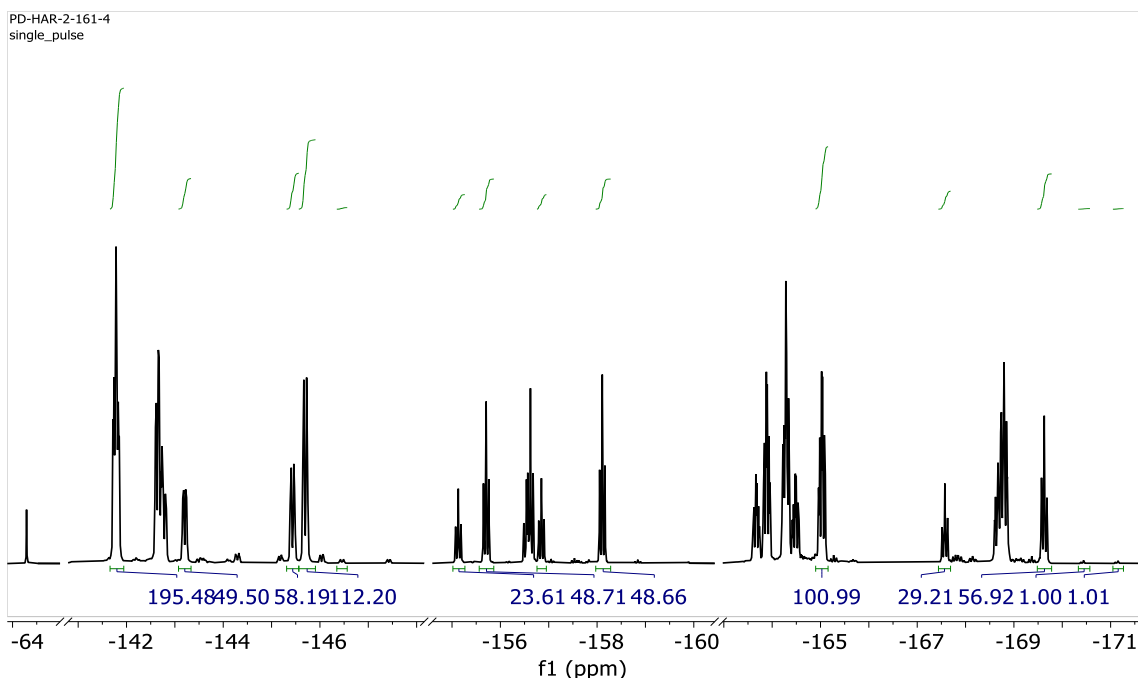


Figure 55. ^{19}F NMR spectrum (376 MHz) of acidity measurement between 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene, 1,2,3-tris(perfluorophenyl)cyclopentadiene, and their conjugate bases Trial 2 (HAR-2-161-4) (400 MHz) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm).

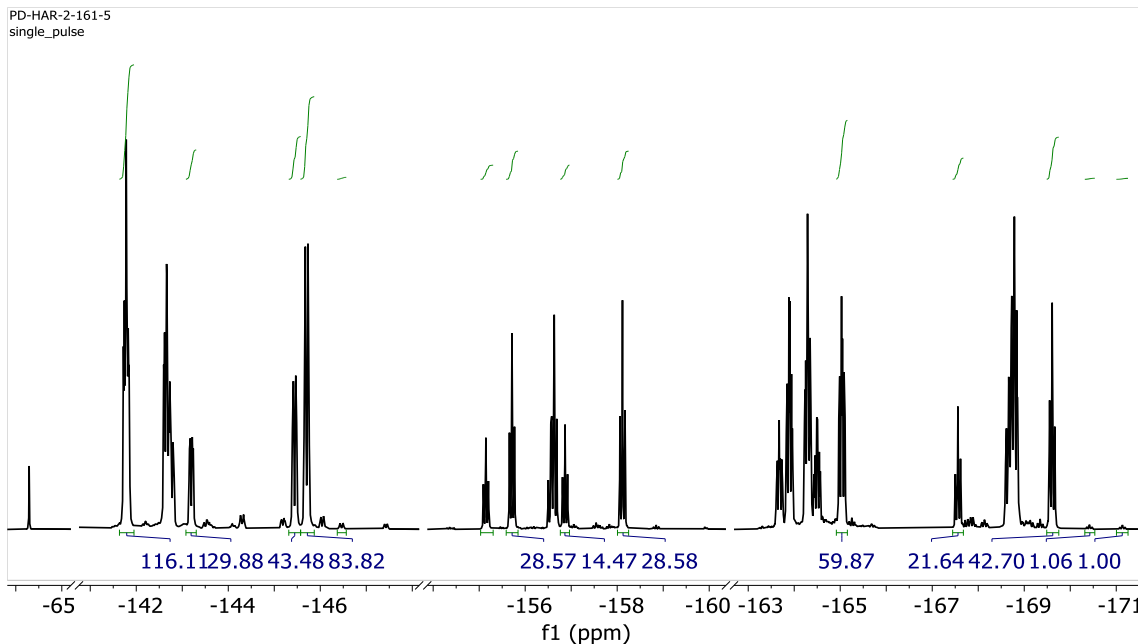


Figure 56. ^{19}F NMR spectrum (376 MHz) of acidity measurement between 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene, 1,2,3-tris(perfluorophenyl)cyclopentadiene, and their conjugate bases Trial 3 (HAR-2-161-5) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm).

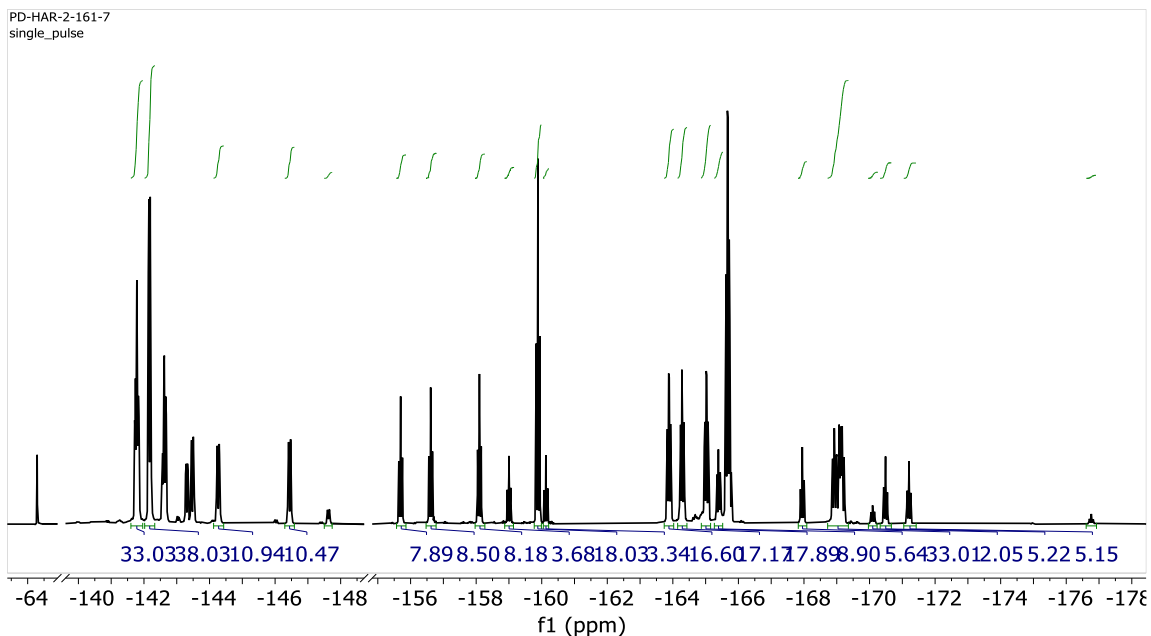


Figure 57. ^{19}F NMR spectrum (376 MHz) of acidity measurement between 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene, 1,3-bis(perfluorophenyl)cyclopentadiene and its tautomer, and their conjugate bases Trial 1 (HAR-2-161-7) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm).

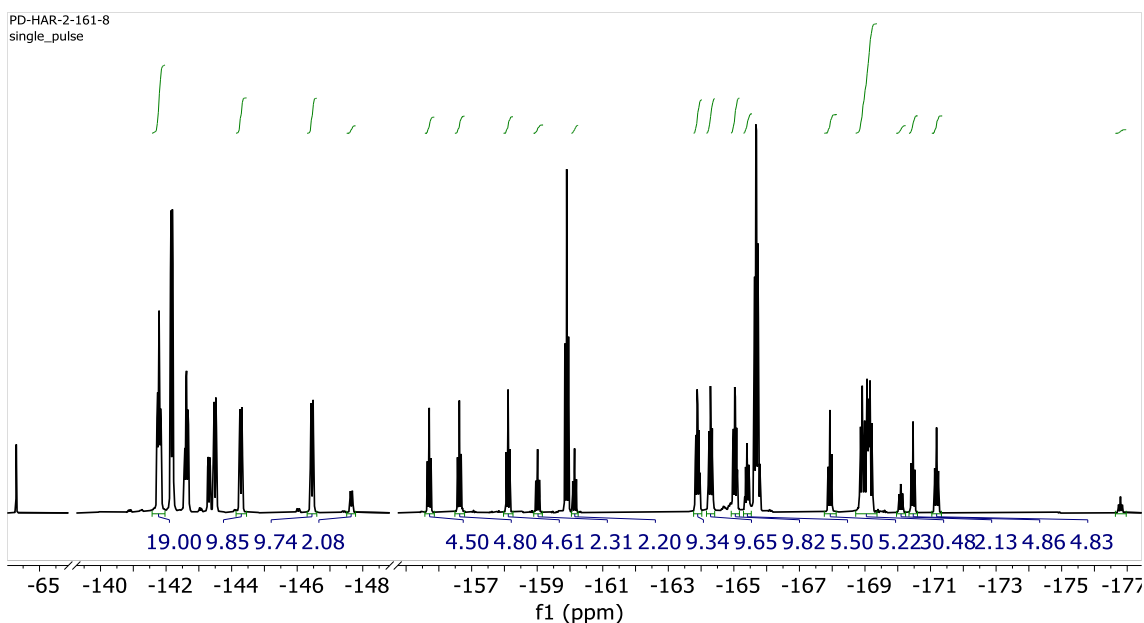


Figure 58. ^{19}F NMR spectrum (376 MHz) of acidity measurement between 1,2,4-tris(perfluoro-phenyl)-3-methylcyclopentadiene, 1,3-bis(perfluorophenyl)cyclopentadiene and its tautomer, and their conjugate bases Trial 2 (HAR-2-161-8) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm).

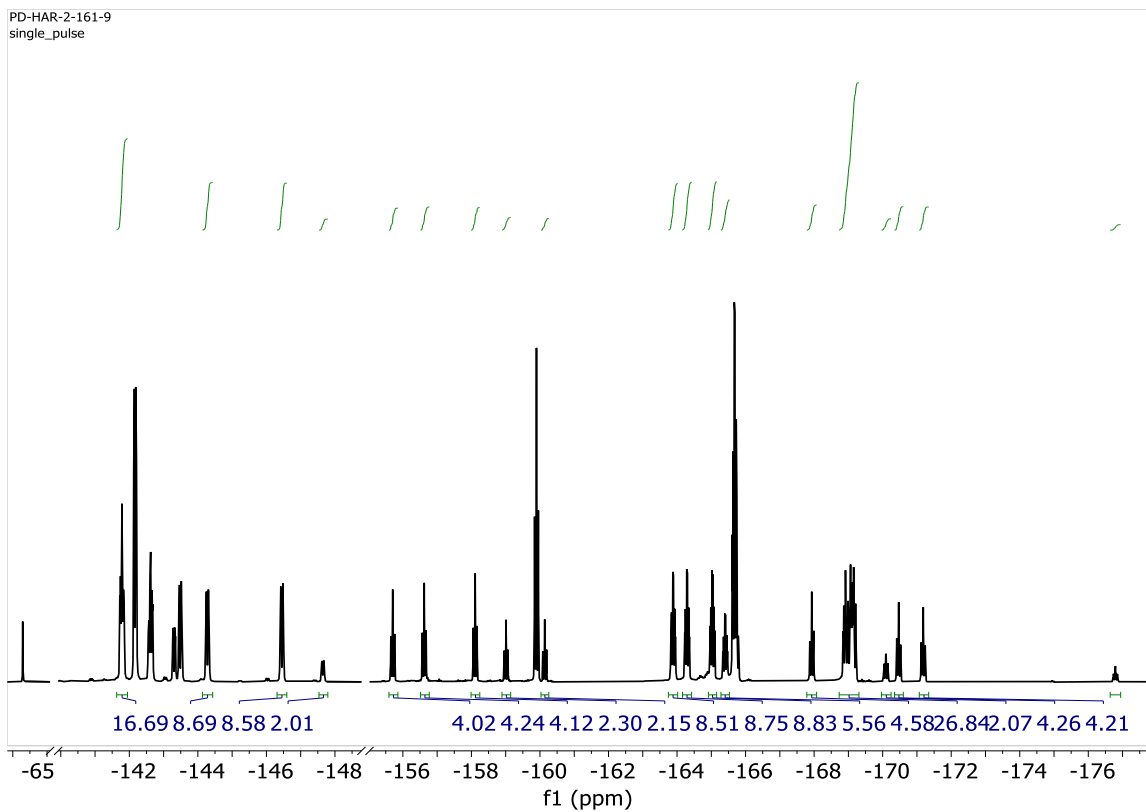


Figure 59. ^{19}F NMR spectrum (376 MHz) of acidity measurement between 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene, 1,3-bis(perfluorophenyl)cyclopentadiene and its tautomer, and their conjugate bases Trial 3 (HAR-2-161-9) in THF containing 5% of C_6D_6 for lock/shim and 0.1% PhCF_3 as a shift standard (64.24 ppm).

Table 12: Acidity measurements between 1,2,3-tris(perfluorophenyl)cyclopentadiene (5), 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene (6) and their respective conjugate bases (5(cb) and 6(cb) respectively) measured in THF containing 5% of C₆D₆ for lock/shim and 0.1% PhCF₃ as a shift standard (64.24 ppm).

Spectra=HAR-2-161-3	5	+	6(cb)	\rightleftharpoons	5(cb)	+	6	$\Delta pK_{\text{THF}}(5-6)$
Ortho(1)	2.04				5.43		15.72	1.69
Ortho(2)					10.49			
Ortho(3)								
Ortho(4)			0.43					
Para(1)	1.00				2.73		3.85	
Para(2)			0.21					
Para(3)	1.03				5.35			
Para(4)			0.21				3.84	
Meta(1)	2.15						8.04	
Meta(2)								
Meta(3)	2.36							
Meta(4)							8.05	
# of eq. rings (1)	1		1		1		1	
# of eq. rings (2)	1		1		2		1	
# of eq. rings (3)	1							
# of eq. rings (4)			1				1	
Relative Integral	1.12		0.21		2.67		3.95	
Mole Fraction	0.13		0.03		0.34		0.50	
Spectra=HAR-2-161-4	5	+	6(cb)	\rightleftharpoons	5(cb)	+	6	$\Delta pK_{\text{THF}}(5-6)$
Ortho(1)	49.50				58.19		195.48	1.70
Ortho(2)					112.2			
Ortho(3)								
Ortho(4)			2.59					
Para(1)	23.61				29.21		48.71	
Para(2)			1.00					
Para(3)	23.60				56.92			
Para(4)			1.01				48.66	
Meta(1)	50.18						102.52	
Meta(2)								
Meta(3)	51.22							
Meta(4)							100.99	
# of eq. rings (1)	1		1		1		1	
# of eq. rings (2)	1		1		2		1	
# of eq. rings (3)	1							
# of eq. rings (4)			1				1	
Relative Integral	24.76		1.15		28.50		49.64	
Mole Fraction	0.23		0.01		0.28		0.48	

Spectra=HAR-2-161-5	5	+	6(cb)	\rightleftharpoons	5(cb)	+	6	ΔpK_{THF} (5-6)
Ortho(1)	29.88				43.48		116.11	1.62
Ortho(2)					83.82			
Ortho(3)								
Ortho(4)			1.98					
Para(1)	14.35				21.64		28.57	
Para(2)			1.06					
Para(3)	14.47				42.70			
Para(4)			1.00				28.58	
Meta(1)	29.65						61.39	
Meta(2)								
Meta(3)	31.85							
Meta(4)							59.87	
# of eq. rings (1)	1		1		1		1	
# of eq. rings (2)	1		1		2		1	
# of eq. rings (3)	1							
# of eq. rings (4)			1				1	
Relative Integral	15.02		1.01		21.29		29.45	
Mole Fraction	0.23		0.01		0.28		0.48	
Average								1.67(4)

Table 13. Acidity measurements between 1,2,4-tris(perfluorophenyl)-3-methylcyclopentadiene (6), 1,4-bis(perfluorophenyl)cyclopentadiene (7a) and its tautomer (7a), and their respective conjugate bases (6(cb) and 7(cb) respectively) measured in THF containing 5% of C₆D₆ for lock/shim and 0.1% PhCF₃ as a shift standard (64.24 ppm).

Spectra=HAR-2-161-7	6	+	7(cb)	=	6(cb)	+	7a	+	7b	ΔpK_{THF} (6-7a)	ΔpK_{THF} (6-7b)
Ortho(1)	33.03		1.98				38.03			1.08	0.71
Ortho(2)					10.94						
Ortho(3)											
Ortho(4)					10.47						
Para(1)	7.89		1.00		5.64		18.03		3.68		
Para(2)	8.50				5.22						
Para(3)								3.34			
Para(4)	8.18				5.15						
Meta(1)	16.60		2.05		33.01				8.90		
Meta(2)	17.17										
Meta(3)											
Meta(4)	17.89										
# of eq. rings (1)	1		2		1		1		1		
# of eq. rings (2)	1				1						

# of eq. rings (3)	1						1		
# of eq. rings (4)				1		1			
Relative Integral	8.40	0.50		5.42		9.34		3.98	
Mole Fraction	0.30	0.02		0.20		0.34		0.14	
Spectra=HAR -2-161-8	6	+ 7(cb)	\rightleftharpoons	6(cb)	+ 7a	+ 7b	ΔpK_{THF} (6-7a)	ΔpK_{THF} (6-7b)	
Ortho(1)	19.00	2.08				24.79	1.09	0.70	
Ortho(2)				9.85					
Ortho(3)									
Ortho(4)				9.74					
Para(1)	4.50	1.00		5.22		11.78		2.31	
Para(2)	4.80			4.86					
Para(3)								2.20	
Para(4)	4.61			4.83					
Meta(1)	9.34	2.13		30.48				5.50	
Meta(2)	9.65								
Meta(3)									
Meta(4)	9.82								
# of eq. rings (1)	1	2		1		1		1	
# of eq. rings (2)	1			1					
# of eq. rings (3)	1							1	
# of eq. rings (4)				1		1			
Relative Integral	4.75	0.52		5.00		6.09		2.50	
Mole Fraction	0.25	0.03		0.27		0.32		0.13	
Spectra=HAR -2-161-9	6	+ 7(cb)	\rightleftharpoons	6(cb)	+ 7a	+ 7b	ΔpK_{THF} (6-7a)	ΔpK_{THF} (6-7b)	
Ortho(1)	16.69	2.01				24.09	1.08	0.71	
Ortho(2)				8.69					
Ortho(3)									
Ortho(4)				8.58					
Para(1)	4.02	1.00		4.58		11.58		2.30	
Para(2)	4.24			4.26					
Para(3)								2.15	
Para(4)	4.12			4.21					
Meta(1)	8.51	2.07		26.84				5.56	
Meta(2)	8.75								
Meta(3)									

Meta(4)	8.83									
# of eq. rings (1)	1		1		1		1		1	
# of eq. rings (2)	1		1		2		1		1	
# of eq. rings (3)	1									
# of eq. rings (4)			1				1		1	
Relative Integral	4.24		0.51		4.40		5.94		2.50	
Mole Fraction	0.24		0.03		0.25		0.34		0.14	
Average										1.08(1) 0.71(1)

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