Spring 5-9-2020

13C NMR Substituent Effects on para-Substituted Tolans: Using Deuteration to Assign 13C Signals in Methyltolan

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^{13}C NMR Substituent Effects on *para*-Substituted Tolans: Using Deuteration to Assign ^{13}C Signals in Methyltolan

By:

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A thesis submitted to the faculty of The University of Mississippi in partial fulfillment of the requirements of the Sally McDonnell Barksdale Honors College.

Oxford
May 2020

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ACKNOWLEDGEMENTS

I would like to acknowledge everyone who has helped me throughout my undergraduate research career. First of all, I would like to thank Dr. Daniell Mattern for giving me the opportunity to work in his organic chemistry lab. I would also like to thank Dr. Mattern for working patiently with me on this project as well as helping me to become well-versed in organic chemistry. Finally, I would like to thank Dr. Trey Vaughn for helping me in the lab and showing me how to efficiently perform the techniques I have needed so far.

ABSTRACT

Substituents are capable of affecting their molecules via induction, resonance, and field effects. Using the Hammett equation, the effect a range of substituents has on different properties of a molecule can be quantified.[1] Hammett's parameters have been correlated with the substituent effects on ^{1}H NMR chemical shifts in different molecules, including experiments on substituted chalcones (1,3-diarylpropenones).[2] The effect a substituent has on a molecule can also be observed using ^{13}C NMR. The chemical shifts of carbons throughout the molecule may be affected by the substituent. This was shown to be true by Wilson and Zehr in *para*-substituted terphenyls.[3] In order to determine how an alkyne bridge affected the ability of substituents to affect carbons throughout certain molecules, we observed substituent effects in *para*-substituted tolans.

In previous work, substituents were found to affect the chemical shifts of every carbon in the molecule, but there was difficulty in distinguishing certain carbons from one another due to a close proximity in chemical shift.[4] This phenomenon was observed in the ^{13}C NMR spectra for acetyltolan, cyanotolan, and methyltolan. This uncertainty was attempted to be resolved using isotopic substitution. Deuterating one of the ambiguous carbons would theoretically cause this peak to essentially vanish on a ^{13}C NMR spectrum, allowing one to determine that the identity of the remaining peak was the carbon that was not deuterated. The synthesis of methyltolan was attempted using multiple variations of the Sonogashira coupling procedure to test this hypothesis. Once both methyltolan and d_5-methyltolan were synthesized, their resulting ^{13}C

NMR spectra were compared to assign identities to every peak in the original ^{13}C NMR spectrum of methyltolan. The deuterated carbon peaks disappeared in the ^{13}C NMR spectrum of d_5-methyl tolan, which allowed for the determination of the identity of each peak in the ^{13}C NMR spectrum of methyltolan. This technique was found to be a promising method for determining the identities of ambiguous peaks on a ^{13}C NMR spectrum.

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List of Abbreviations and Symbols

σ	Substituent constant
K	Equilibrium constant of substituted benzoic acid
K_0	Equilibrium constant of reference compound
ρ	Slope of regression line
DSP	Dual substituent parameter
^{13}C NMR	^{13}Carbon Nuclear Magnetic Resonance
σ_I	Induction substituent constant
σ_R	Resonance substituent constant
C1-10	Carbons 1-10 of a *para*-substituted tolan
s-$BuNH_2$	*sec*-butylamine
TLC	Thin layer chromatography
DMF	Dimethylformamide
R_f	Retention factor
DCM	Dichloromethane
DEPTQ	Distortionless enhancement by polarization transfer including quaternary nuclei
ppm	Parts per million
D	Deuterium
TMS	Trimethylsilane
EtOH	Ethyl alcohol

MeOH	methyl alcohol
rt	room temperature
AcOH	Acetic acid
ρ_I	Slope of induction regression line
ρ_R	Slope of resonance regression line
p	p-value

List of Tables and Figures

1. Introduction

1.1 Substituent Effects

Substituent effects have been studied heavily in the past and can be used to predict the effects that certain substituents will have on the reactivity of different functional groups. They affect their compounds via field effects, induction, and resonance. One of the most prominent attempts to study substituent effects was conducted by Louis Hammett, who described substituent effects via electron-donating or -withdrawing effects.[1] He did so by comparing the effect of different substituents on the pK_a of benzoic acid.[1] The substituent constant, sigma (σ), is calculated from the log of the ratio of the substituted acid's pK_a to that of benzoic acid, also known as the Hammett equation.[1]

$$\log(K/K_0) = \sigma\rho$$

K refers to the equilibrium constant of the substituted benzoic acid, K_0 refers to that of the reference compound (benzoic acid), and ρ represents the reaction constant.[5]

Sigma values can then be used to determine the effect of a range of substituents on certain processes. This can be accomplished by completing a regression analysis of different compounds with varying substituents. A greater slope of the regression line, or rho (ρ), suggests that substituents have a greater effect on the process in question. Taft developed a more specific quantification of Hammett's sigma constant using dual substituent parameters (DSPs).[6] He

divided the substituent effect sigma into σ_R and σ_I, representing the effect of substituents on resonance and induction, respectively.[6] Using these parameters, a dual regression analysis can be completed, giving the effect substituents have on both resonance and induction.

Substituent effects on ^{13}C NMR chemical shifts can be correlated with their effects on chemical processes, and many experiments showing these correlations have been conducted using both sigma values and DSPs. In the past, substituent effects on *para*-substituted terphenyls have been studied, which showed ^{13}C NMR effects at the most distant carbons.[3]

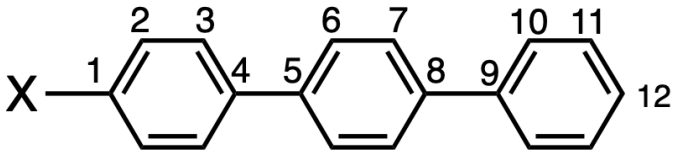


Figure 1: A *para*-substituted terphenyl.

We focused on the ^{13}C NMR spectra of *para*-substituted tolans to determine the effect a substituent would have on the most distant carbons. However, a problem that arises with the synthesis of *para*-substituted tolans is the inability to distinguish between several carbons due to their proximity in chemical shift.[4] When the two nearly-coincident carbons are on different aromatic rings of a *para*-substituted tolan, this issue can potentially be overcome by deuterating one of the aromatic rings. Deuterating an aromatic carbon causes its ^{13}C NMR peak to split into a small triplet and effectively disappear, allowing one to determine which peak from the compound's original ^{13}C NMR spectrum belongs to each carbon. This splitting occurs due to the three spin states found in deuterium, those being -1, 0, and 1. In addition to splitting into a triplet, deuterated ^{13}CNMR signals are also less intense than hydrogenated carbon signals. This phenomenon occurs because of the ability of hydrogen to relax a carbon faster, allowing for the

carbon to absorb again quickly. Deuterium does not have this effect, meaning that deuterated carbon peaks absorb less and are lower in intensity than hydrogenated carbon peaks. Based on these principles, it was theorized that deuterating the unsubstituted aromatic ring of a *para*-substituted tolan would allow the carbons with similar chemical shift values on each ring to be distinguished from one another.

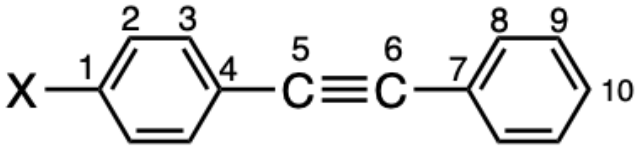


Figure 2: A *para*-substituted tolan. X = any substituent. Carbons 3 and 8 have indistinguishable chemical shifts for both methyltolan and acetyltolan. Deuterating the second aromatic ring should allow the two carbons to be distinguished via ^{13}C NMR.

There are several tolans which have multiple carbons appearing at or near the same chemical shift on their ^{13}C NMR spectra. These include 4-methyltolan, 4-acetyltolan, and 4-cyanotolan.[4] Both methyltolan and acetyltolan have similar chemical shifts for carbons 3 and 8, while cyanotolan has indistinguishable carbons at C2 and C3.[4] Each of these molecules' ambiguous carbons could potentially be distinguished from one another by deuterating one of the carbons in question and not the other. For methyltolan and acetyltolan, this can be accomplished by using a perdeuterated aryl halide in the synthesis of the tolan, leading to a *para*-substituted tolan with one deuterated aromatic ring and one non-deuterated ring. For cyanotolan, a starting material with deuterium at C2 only must be used. We began by experimenting with methyltolan, with acetyltolan and cyanotolan to follow.

1.2 Sonogashira Coupling Procedure

For the synthesis of tolans, multiple variations of the Sonogashira coupling procedure were attempted. The general procedure involves the coupling of a terminal alkyne to an aryl halide using a palladium catalyst (Figure 3a).[7] A copper co-catalyst has also been used historically, but there have been several successful copper-free Sonogashira couplings reported.[8,9,10,11] In addition to the palladium catalyst, a base is used to help deprotonate the terminal alkyne. A copper-free version was used to synthesize both methyltolan and d_5-methyltolan.[9] The copper-free mechanism involves two connected palladium cycles (Pd^0 and Pd^{II}).[12] The Pd^0 cycle involves the formation of a Pd-aryl halide complex, which then reacts with the palladium bisacetylide formed in the Pd^{II} cycle to give the coupled product (Figure 3d).[12]

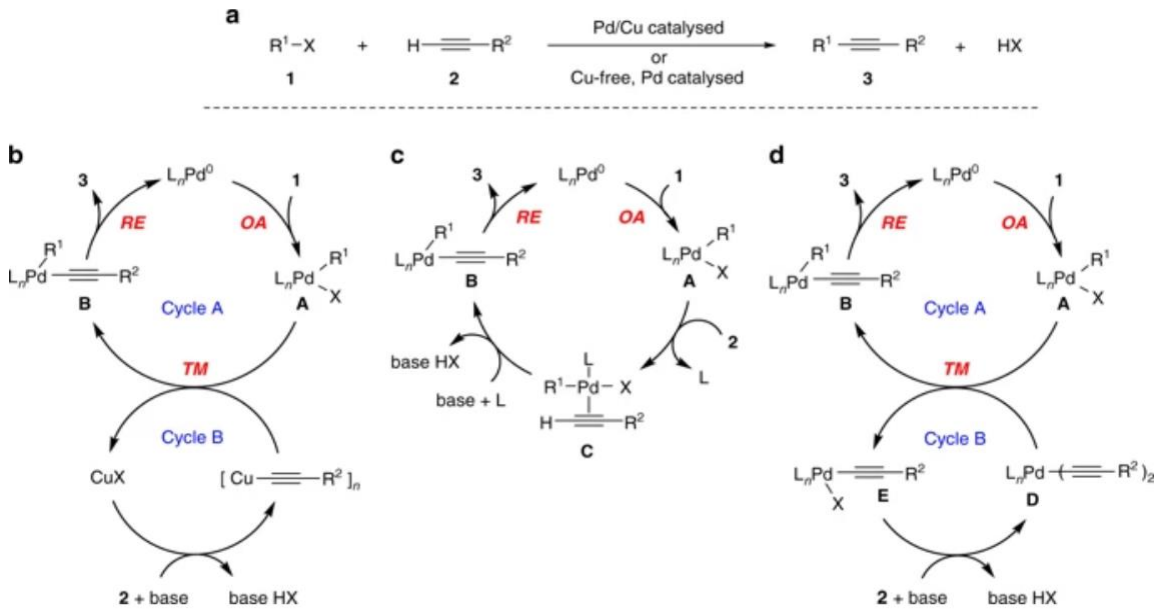
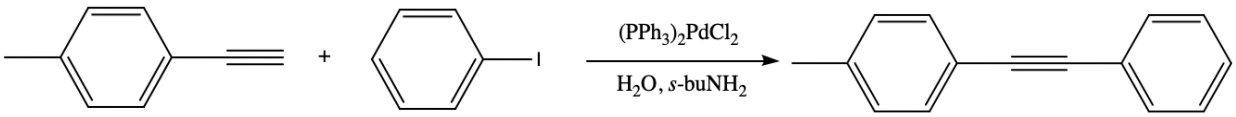


Figure 3: Copper-free Sonogashira coupling procedure mechanism.[12]

2. Results and Discussion

2.1 Synthesis of Methyltolan using Iodobenzene



Scheme 1: Synthesis of methyltolan using iodobenzene.[8]

The goal of this experiment was to synthesize methyltolan using a copper-free Sonogashira reaction. It involved using iodobenzene and 4-ethynyltoluene along with a palladium catalyst in a 1:1 ratio of water and *sec*-butylamine (Scheme 1).[8] A ^{13}C NMR spectrum was taken of the crude product (Figure 4), confirming that the desired product had been formed (Chemical shifts are given in Figure 5). However, a procedure that could synthesize methyltolan starting with bromobenzene was needed due to the fact that commercially-available d_5-bromobenzene would be used to synthesize the deuterated product. Therefore, the product was not further purified.

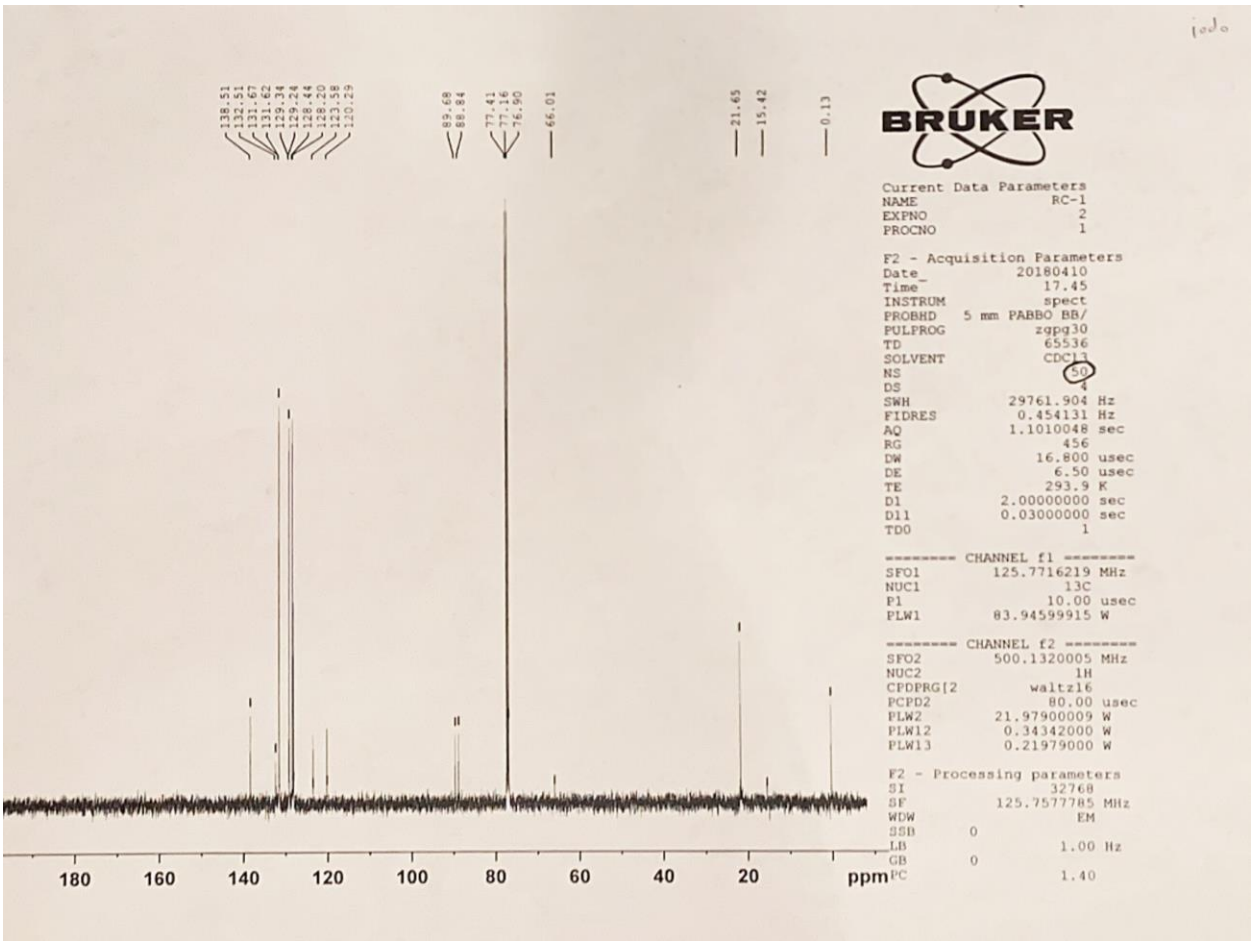


Figure 4: ^{13}C NMR spectrum of methyltolan (crude) synthesized using iodobenzene.

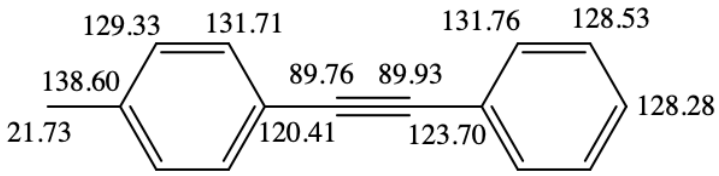
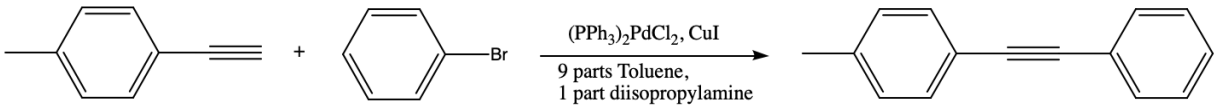


Figure 5: ^{13}C-NMR chemical shifts for methyltolan.

After synthesizing methyltolan using iodobenzene, a method for synthesizing it with bromobenzene was needed. In order to accomplish this, the same procedure was used, substituting bromobenzene for iodobenzene. The ^{13}C NMR spectrum of the crude product showed only starting materials (Figure 6A), so the reaction was conducted again, this time using heat. After being stirred and heated at 60 degrees C overnight, a ^{13}C NMR was taken of the crude product (Figure 6B). The spectrum showed similar results as the previous experiment, indicating that the desired product was not formed.

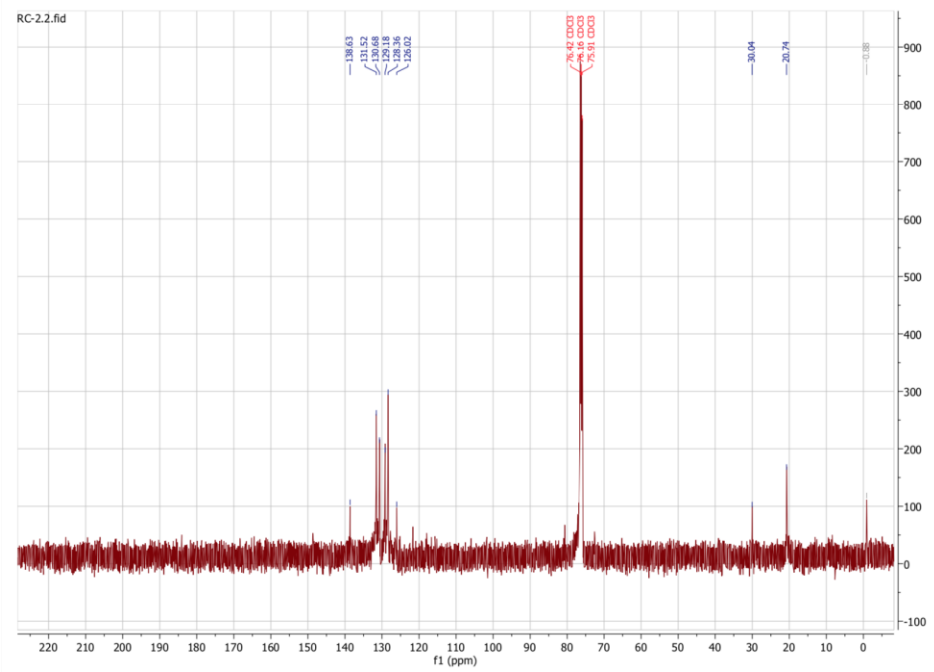
2.2 Attempted Synthesis of Methyltolan using Palladium and Copper Catalysts



Scheme 2: Synthesis of methyltolan using both palladium and copper catalysts.[13]

In an effort to synthesize methyltolan starting from bromobenzene, a procedure using copper(I) iodide and bis(triphenylphosphine)-palladium(II) chloride as co-catalysts was used.[13] The starting materials were bromobenzene and 4-ethynyltoluene in nine parts toluene and one part diisopropylamine.[13] After stirring overnight at room temperature, the crude product was isolated and thin layer chromatography (TLC) using hexanes as the developing solvent was used to determine if the desired product had formed. The TLC plate appeared to show the formation of a new spot in the product lane, so column chromatography was thought to be the best method of purification.

A)



B)

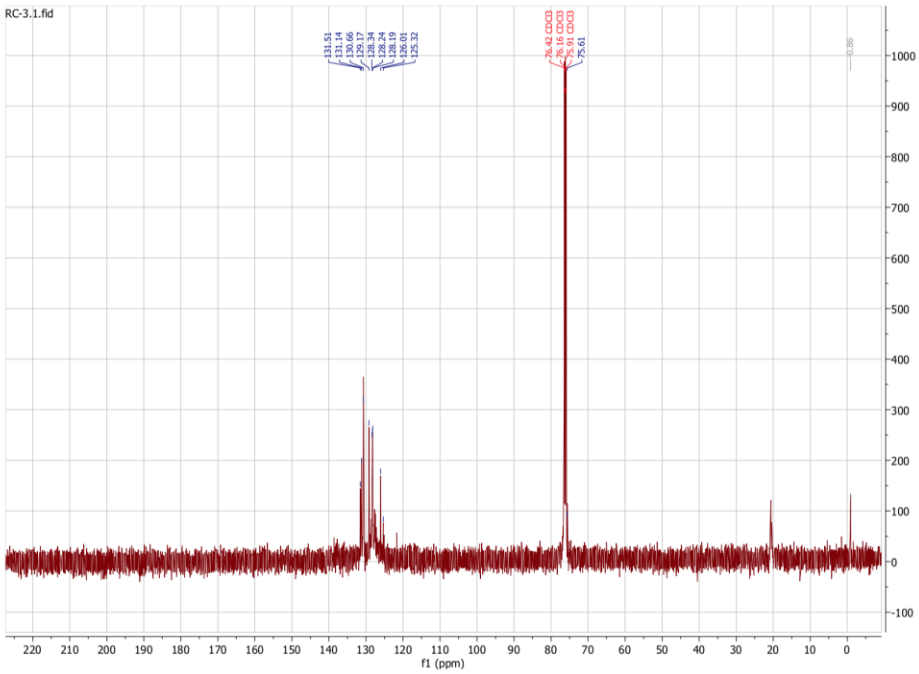


Figure 6: ^{13}C NMR spectra of attempted syntheses using bromobenzene. (A) ^{13}C NMR spectrum for the reaction of bromobenzene and 4-ethynyltoluene at room temperature. (B) ^{13}C NMR spectrum of the same reaction at 60℃.

However, the product would not dissolve in hexanes at room temperature, so it was theorized that recrystallization from hexanes might be possible. Recrystallization was attempted by dissolving the product in hot hexanes and then using gravity filtration to remove any impurities. The solution was then allowed to cool overnight, and upon examination the next morning, several crystals had formed. A ^{13}C NMR spectrum was then taken of the pure product (Figure 7). However, this showed that the crystals were pure 4-ethynyltoluene, meaning that the isolated solid was primarily starting materials.

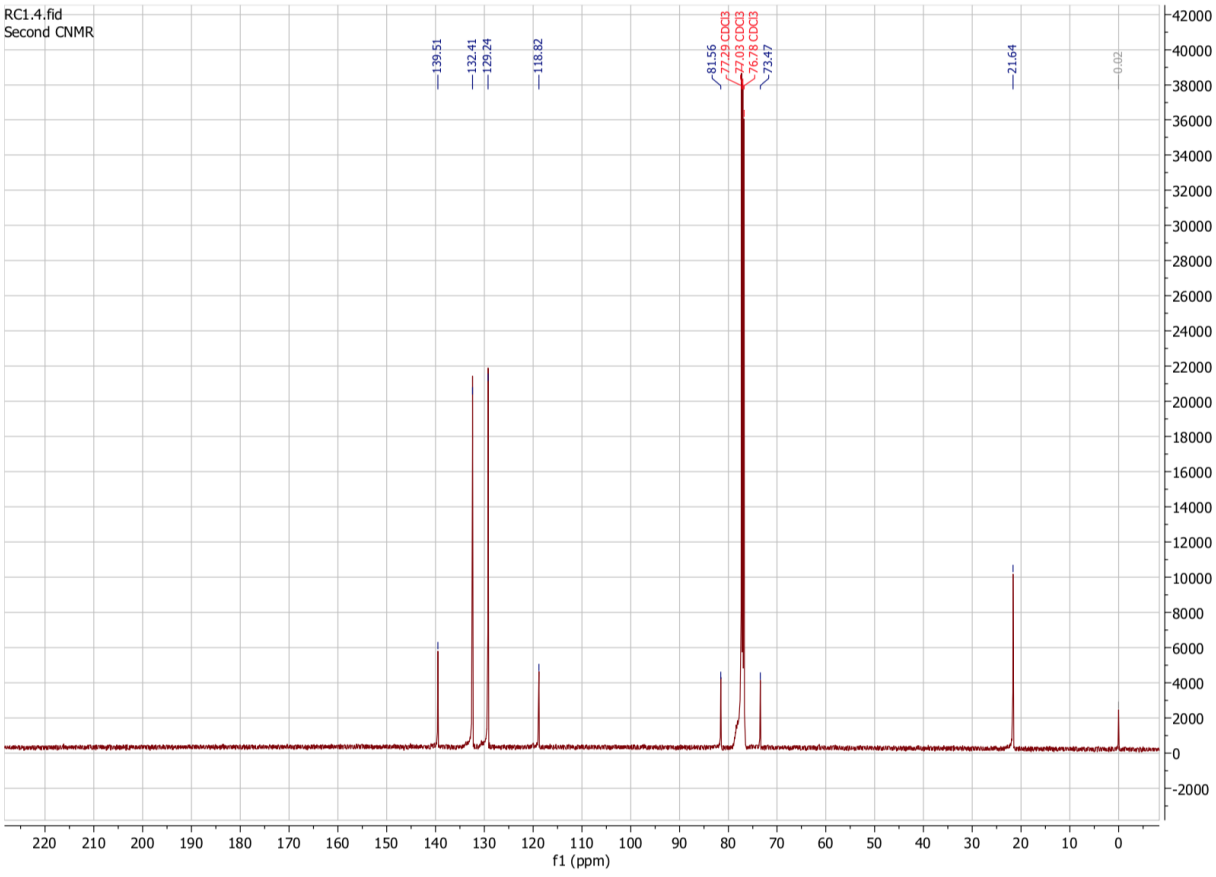
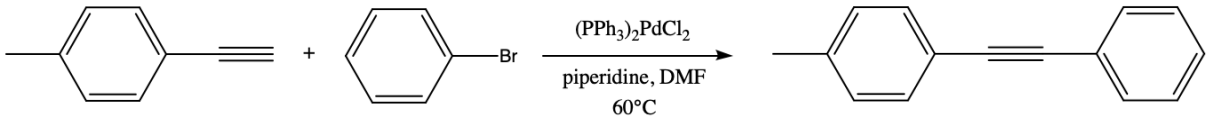


Figure 7: ^{13}C NMR spectrum of purified 4-ethynyltoluene. This was the starting material of the reaction, showing that the synthesis was unsuccessful.

2.3 Attempted Synthesis of Methyltolan using Copper-Free Sonogashira Procedure



Scheme 3: Copper-free synthesis of methyltolan.[9]

After failing to synthesize methyltolan using a copper co-catalyst, a copper-free procedure that was specific for aryl bromides was attempted (Scheme 3).[9] DMF and piperidine were used along with 4-ethynyltoluene and bromobenzene, and the mixture was stirred at 60°C under argon.[9] After the reaction was complete, the crude product was isolated. A ^{13}C NMR spectrum of the crude product showed several impurities, but confirmed that the desired product had been synthesized. TLC using hexanes as the developing solvent showed two different spots for the starting material and product; however, they were very close in R_f value. The product was then further purified via column chromatography using hexanes as the eluent. ^{13}C NMR analysis of the pure product (Figure 8) showed two extra peaks in the alkyne region as well as extra aromatic peaks, suggesting that the product still contained starting materials in addition to the desired product.

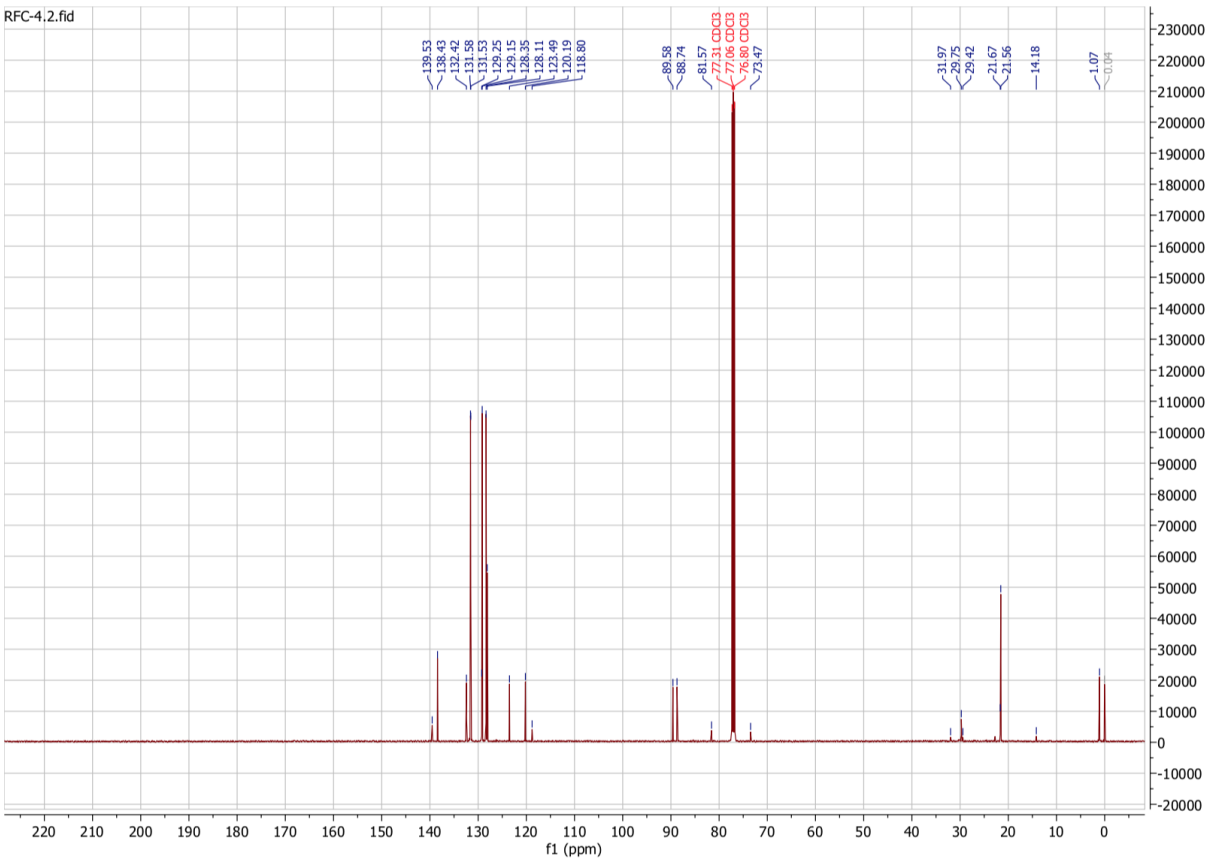


Figure 8: ^{13}C NMR spectrum of methyltolan after column chromatography purification. Hexanes were used as the eluent. The spectrum still shows two excess alkyne peaks, suggesting that the starting material was still present.

The product mixture was then attempted to be further purified using preparative TLC with hexanes as the developing solvent. The mixture was dissolved in DCM and then plated across the base of the TLC plate. After developing the plate, examination under UV light showed one broad band with an R_f value of 0.35. Based on the R_f values of the starting materials and product on the original TLC plate, it was theorized that the lower portion of the band would contain only the desired product. This lower portion was removed and a ^{13}C NMR spectrum was taken (Figure 9). The spectrum still showed excess peaks in the alkyne region, although some of

the extra aromatic peaks were removed. It was then theorized that recrystallization could be used to purify the methyltolan, but a larger sample would be needed to do so.

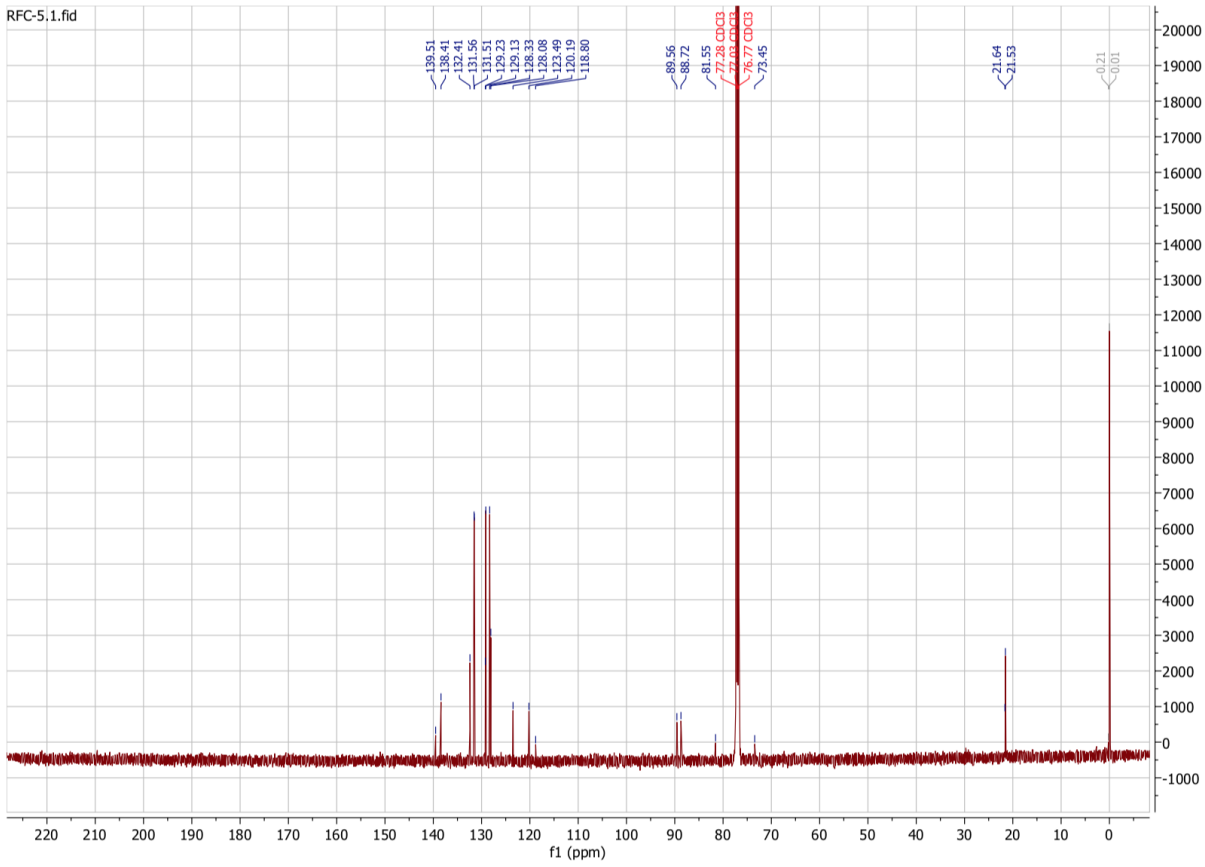


Figure 9: ^{13}C NMR spectrum of methyltolan after preparative TLC purification.

The same procedure was conducted again, with an increase in scale by a factor of five. After obtaining the crude product, recrystallization from hexanes was attempted. Once the mixture cooled overnight, no crystals formed. Recrystallization with methanol and water was then attempted but was unsuccessful. A small amount of hexanes (15 mL) was then used to recrystallize the product. Several small crystals appeared to form, but after vacuum filtration, nothing remained on the filter paper. Based on these findings, it was assumed that a smaller

amount of solvent and a greater amount of product would produce the best recrystallization results.

The same procedure for the synthesis of methyltolan was conducted again. Recrystallization was attempted with the crude product and 2 mL of hexanes. After dissolving the product in hot hexanes, the solution was filtered using a long-stem glass pipet packed with glass wool. The resulting solution was then allowed to cool and then placed in the freezer, and small crystals appeared overnight. However, the crystals and remaining solvent formed a coagulated substance, making it difficult to isolate the crystals. A small amount of the substance was then scraped onto filter paper to allow the solvent to evaporate. A ^{13}C NMR DEPTQ spectrum was taken of the substance (Figure 11). Similar to those of previous experiments, this spectrum showed four peaks in the alkyne region. However, it also showed that these alkynes were not terminal, which indicated that 4-ethynyltoluene, the previously believed chief contaminant, was not present in the product mixture. Instead, it showed two extra alkyne peaks that were not terminal, suggesting that an alkyne-to-alkyne coupling byproduct (Figure 10) had formed.

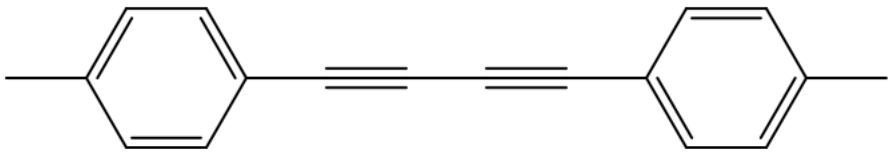


Figure 10: Proposed alkyne-to-alkyne coupling byproduct.

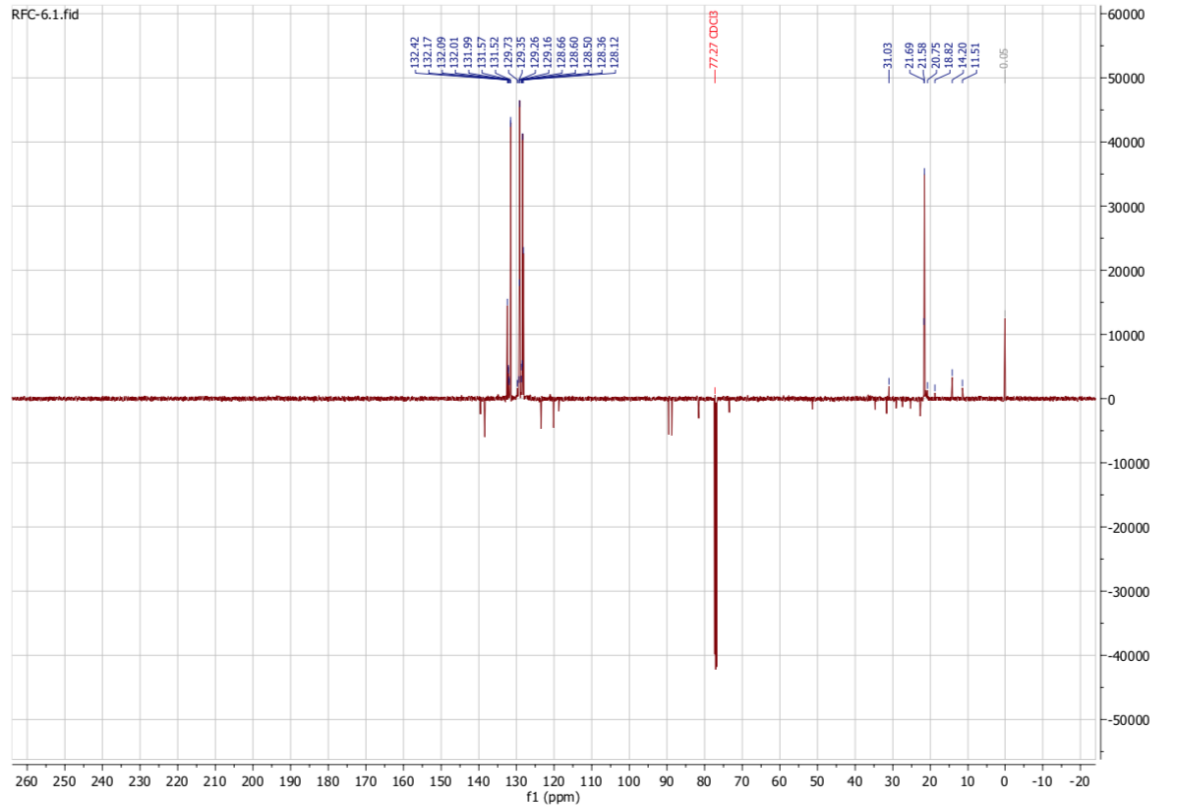


Figure 11: DEPTQ spectrum of methyl tolan after attempted recrystallization. All four alkyne peaks are shown to have an even number (zero) of hydrogens, meaning that the terminal alkyne of 4-ethynyltoluene could not be the main contaminant.

In an effort to prevent the alkyne-to-alkyne product from forming, methyltolan was synthesized again, this time using a 10:1 ratio of aryl bromide to alkyne. After the crude product was obtained, a silver-impregnated column was used for further purification. The column material was prepared by mixing silver nitrate and silica in ethanol and then heating it in the oven to activate the silver. The silver-impregnated column was used so that any alkyne-to-alkyne coupling product that formed would be retarded by the silver in the column. The extra pi bonds present in the alkyne-to-alkyne coupled product would interact with the silver to a greater extent than the desired product would, causing the impurities to elute at a slower rate than the desired

product. After the product was run through the column, a ^{13}C NMR spectrum was taken (Figure 12). The spectrum showed that the excess alkyne peaks had been removed; however, two extra aromatic peaks remained. The two targeted ambiguous peaks were both near 131.5 ppm and correspond to carbons 3 and 8 of methyltolan.

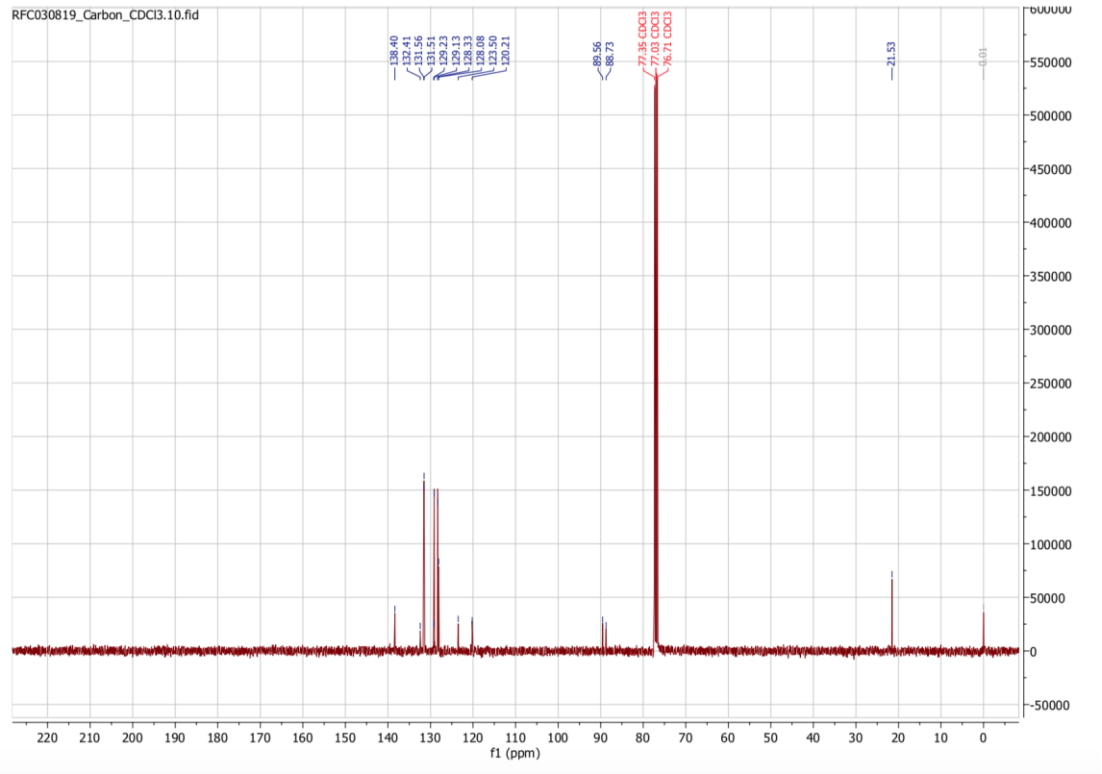
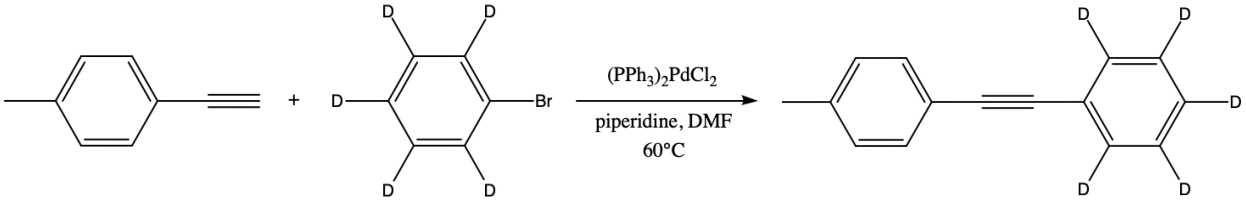


Figure 12: ^{13}C NMR spectrum of methyltolan. The peaks at 131.56 ppm and 131.51 ppm belong to carbons 3 and 8.

2.4 Synthesis of d_5-methyltolan



Scheme 4: The synthesis of d_5-methyltolan.[9]

Due to the fact that each carbon in methyltolan was present in the ^{13}C NMR spectrum, d_5-methyl tolan was synthesized in an attempt to assign identities to each peak. d_5-Bromobenzene and 4-ethynyltoluene were used as starting materials. The resulting crude product was then purified via column chromatography. The purified product showed all expected peaks along with two excess aromatic peaks at 129 and 132 ppm (Figure 13).

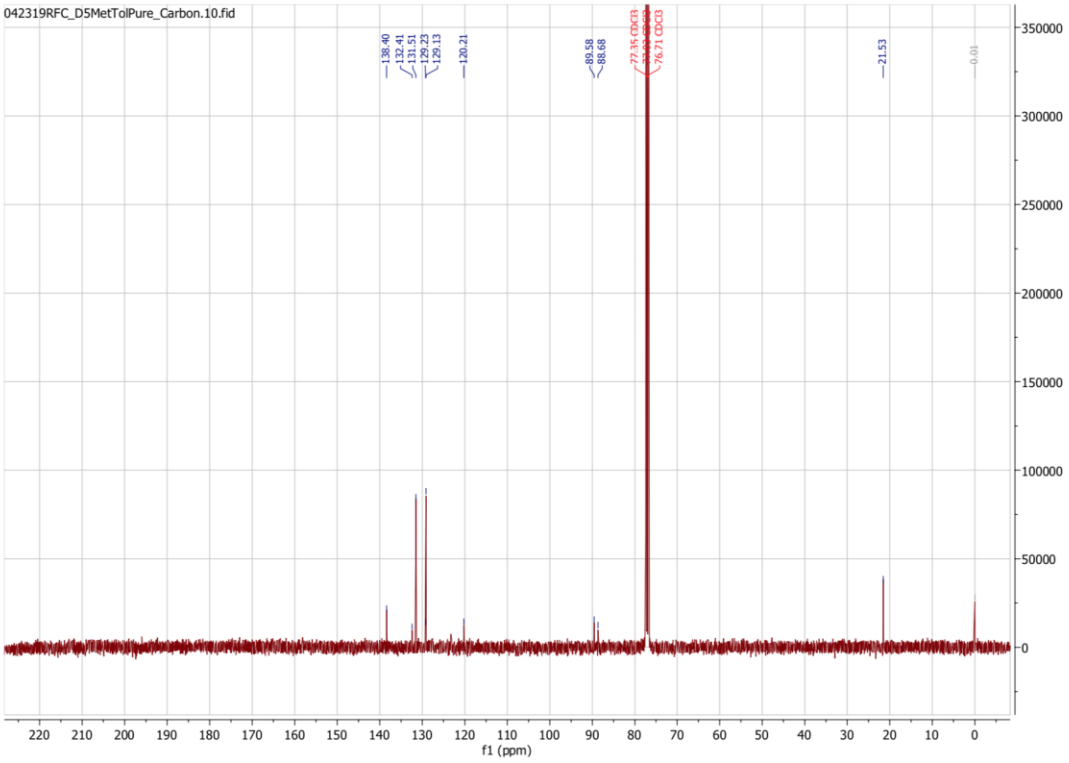


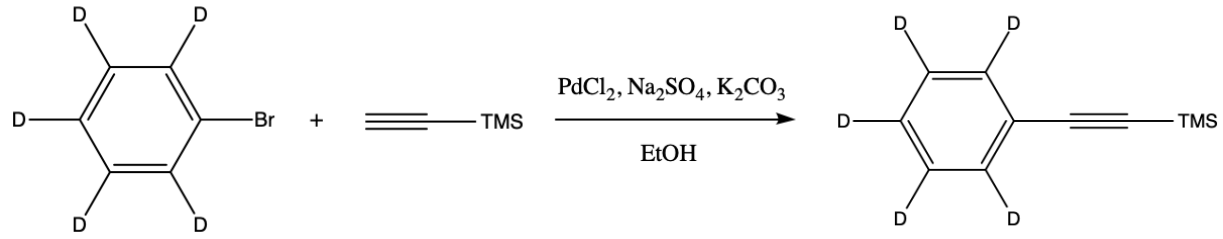
Figure 13: ^{13}C NMR spectrum of d_5-methyltolan. The peak at 131.56 ppm disappeared compared to the nondeuterated sample, meaning that this was the deuterated carbon, C8. The peaks at 129 ppm and 132.41 ppm are extraneous.

After comparing the spectra for methyltolan and d_5-methyltolan (Figures 12 and 13), identities could be assigned to each peak on the ^{13}C NMR spectrum for methyltolan. The spectrum for d_5-methyltolan showed an absence of four aromatic peaks when compared to the spectrum for methyltolan. Therefore, the deuterated carbons of d_5-methyltolan (C8, C9, C10) as well as C7 were not present on the spectrum. These carbons were not present on the spectrum because of the three spin states present in the deuterium atom of each carbon as well as the inability of deuterium to quickly relax a carbon. The number of spin states of the deuterium atoms caused the signals of the aromatic ring carbons to split into triplets and effectively

disappear. Comparing the two spectra shows that the peak at 131.51 ppm was present in the spectrum for d_5-methyltolan while the peak at 131.55 ppm disappeared. Based on these results, it was concluded that the peak at 131.51 ppm corresponded to carbon 3, which was not deuterated when d_5-methyl tolan was synthesized. The peak at 131.55 ppm corresponded to carbon 8 since this carbon was deuterated and therefore would not be present in the spectrum for d_5-methyl tolan.

2.5 Attempted Synthesis of Acetyltolan

A)



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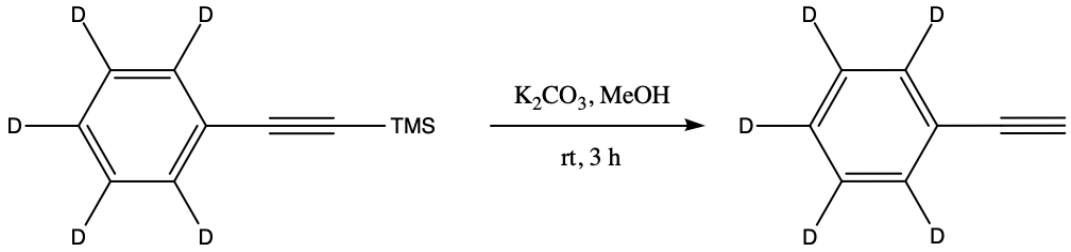
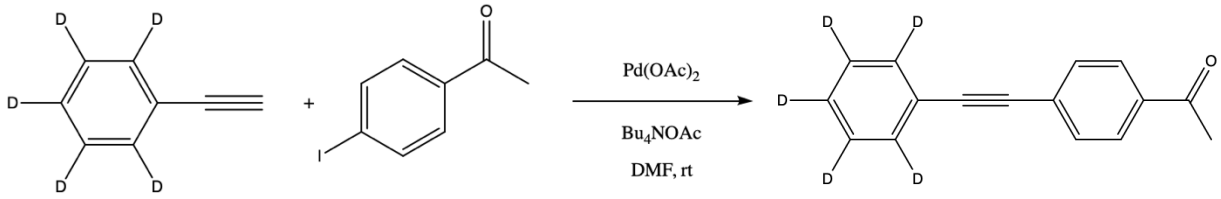


C)



Scheme 5: Synthesis of d_5-acetyltolan. (A): The synthesis of the protected d_5-acetylene to be used in the synthesis of acetyltolan.[10] (B): The deprotection of d_5-acetylene.[14] (C) The synthesis of acetyltolan using the deprotected d_5-acetylene and *p*-iodoacetophenone.[11]

In order to synthesize acetyltolan, the starting material for the reaction, d_5-phenylacetylene, would need to be synthesized first. This would then be reacted with *p*-iodoacetophenone to synthesize acetyltolan.[11] Synthesizing d_5-phenylacetylene involved treating trimethylsilylacetylene with d_5-bromobenzene. Trimethylsilylacetylene was used so that only one terminal alkyne carbon would react with the aryl halide, meaning that the resulting product would need to be deprotected before using it to synthesize acetyltolan.

The first attempt at synthesizing d_5-phenylacetylene involved using a variation of the Sonogashira coupling procedure to couple d_5-bromobenzene to trimethylsilylacetylene.[10] The product was worked up after the reaction was allowed to stir overnight. The resulting material was a waxy, translucent yellow substance. After obtaining the crude product from this reaction, a ^{13}CNMR was taken. The spectrum showed no peaks in the aromatic region but only showed several hydrocarbon peaks. The reaction was attempted again resulting in the same outcome.

2.6 Dual Substituent Parameter Analysis for the Series of *para*-substituted Tolans

Table 1: ^{13}C NMR chemical shifts for the series of *para*-substituted tolans. The data, aside from that of methyltolan, was obtained from previous research.[4]

Substituent	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**
CH_3O	158.60	113.98	133.03	115.37	89.35	88.05	123.58	131.43	128.29	127.91
NHOAc	137.82	119.30	132.41	118.88	89.03	89.03	123.26	131.40	128.33	128.17
CH_3	138.60	129.33	131.71	120.41	89.76	89.93	123.70	131.76	128.53	128.28
H	128.24	128.32	131.57	123.20	89.32	89.32	123.20	131.57	128.32	128.24
Cl	134.66	128.68	132.79	121.77	88.22	90.33	122.92	131.58	128.38	128.47
OAc	136.19	128.26	131.70	128.20	88.59	92.70	122.64	131.70	128.43	128.80
CN	111.44	132.00	132.00	128.21	87.69	93.75	122.19	131.76	128.48	129.10
N_2O	146.96	123.62	132.25	130.24	87.53	94.69	122.08	131.82	128.52	129.26

Table 2: The induction and resonance parameters for the series of para-substituted tolans. Both resonance and induction are shown to have an effect, even at the most distant carbons.

	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**	**C10**
ρ_I	3.243	-4.702	1.365	7.206	-2.870	5.385	-1.714	0.0884	0.0629	1.112
p	0.883	0.55	0.0017	0.00014	<0.0001	0.0035	0.0001	0.58	0.66	0.0013
ρ_R	-29.54	17.841	-1.804	17.133	-1.033	6.425	-1.307	0.3959	0.2060	1.244
p	0.191	0.047	0.0003	<0.0001	0.0062	0.0011	0.0003	0.036	0.16	0.0005
R^2	0.0426	0.410	0.930	0.993	0.964	0.926	0.97	0.518	0.164	0.95
p	0.385	0.12	0.0006	<0.0001	0.0001	0.0007	<0.0001	0.070	0.28	0.0003

^{13}CNMR chemical shift values for the series of *para*-substituted tolans were correlated with Charton's σ_I and σ_R parameters.[4,15] Each tolan used consists of three pi systems, those being a proximal substituted ring, a distal unsubstituted ring, and a triple bond linking the two rings. Based on Table 1, the strongest resonance effects are seen at the *ortho* and *para* positions on the substituted ring. The distant ring also shows moderate resonance effects. This suggests that the tolans are mostly planar and are able to transmit resonance effects throughout the entirety of the molecule. The induction parameters tend to be negative for carbons closer to either the substituent or the linking system, and positive for carbons that are further away from these areas. From the data in Table 1, it can be concluded that ^{13}C chemical shifts experience substituent effects that are correlated with both induction and resonance parameters.

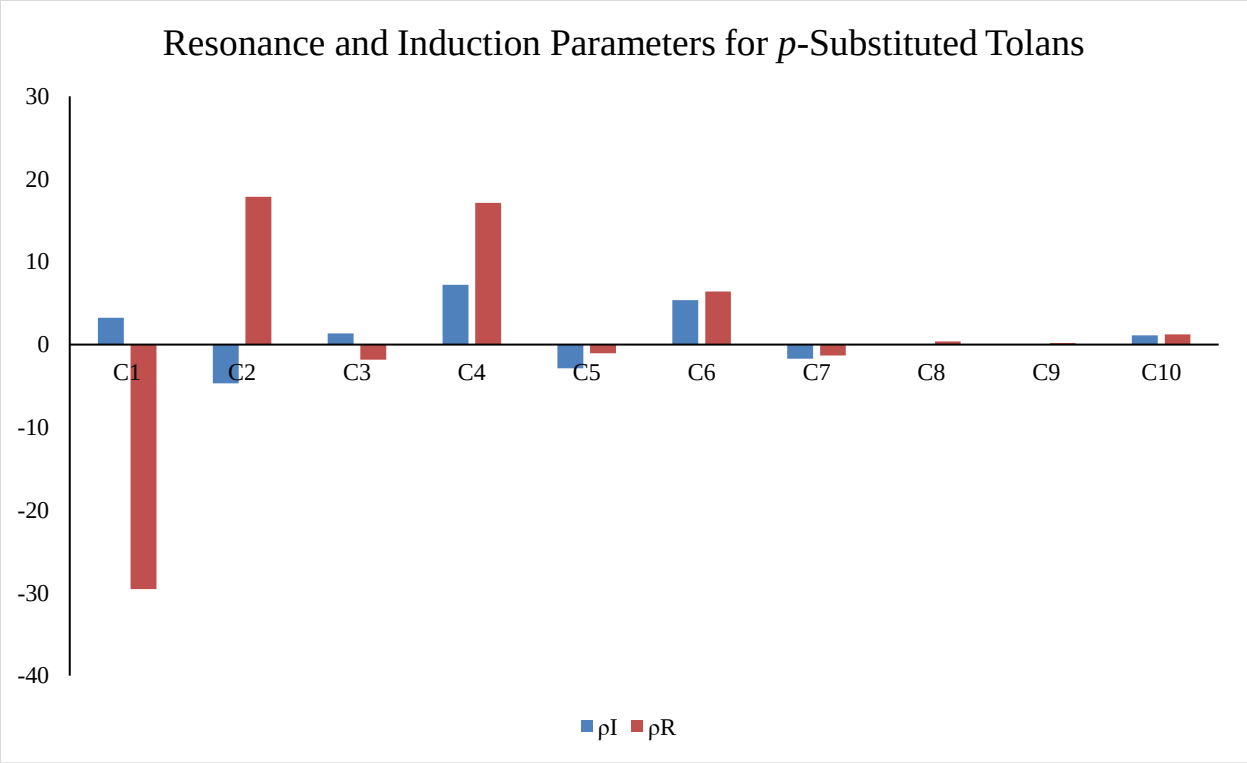


Figure 14: Graph of DSP analysis of the *para*-substituted tolan series. While the greatest correlations for resonance and induction are closer to the substituent, there were significant correlations shown for all carbons.

3. Future Work

Being able to obtain completely pure spectra of both methyltolan and d_5-methyltolan would be helpful. Other ways of purifying these compounds should be explored. Recrystallization using different solvents or column chromatography using a longer stationary phase could be potential avenues to pursue. In addition to purifying methyltolan, distinguishing between the ambiguous carbons present in both acetyltolan and cyanotolan still needs to be accomplished. For acetyltolan, this could potentially be accomplished in a similar way to the methods used for methyltolan due to the fact that C3 and C8 are also indistinguishable on the ^{13}C NMR spectrum of acetyltolan. The current synthetic process used for acetyltolan did not seem very promising, so different methods should be explored. For cyanotolan, the ambiguous carbons (C2 and C3) exist on the same ring. This means that a different approach than what was used for methyltolan and acetyltolan would have to be used in order to deuterate one carbon on the ring and leave the other alone.

4. Conclusion

The process of using isotopic labeling to distinguish between ambiguous carbon signals was proven to be a valid research technique. Although both methyltolan and d5-methyltolan were unable to be completely purified, the results clearly showed differentiation between the ambiguous carbons in question. It would be useful to determine if this technique worked on other molecules, but for now it is a promising method for distinguishing between similar carbon signals.

5. Experimental

5.1 Synthesis of Methyltolan

For the synthesis of methyltolan, 4-ethynyltoluene (254 mg, 2.20 mmol), bromobenzene (2.32 g, 15.0 mmol), piperidine (254 mg, 3.00 mmol), and 47 mg of bis(triphenylphosphine) palladium(II) chloride were added to a 25 mL round-bottom flask along with 3.7 mL of DMF. The reaction mixture was heated to 60°C and allowed to stir under argon overnight. The reaction was then diluted with 30 mL of diethyl ether and washed twice with 5% aqueous HCl, twice with water, and once with a 1:1 mixture of water and brine in a separatory funnel. The product was then dried with $MgSO_4$, and the ether was removed via rotary evaporation. A crude product mass of 330 mg (1.72 mmol) remained. The product was then further purified using silver-impregnated silica gel column chromatography and hexanes as the eluent. This resulted in 94 mg (0.49 mmol) of methyltolan, giving a 22% yield.

5.2 Synthesis of d_5-methyltolan

For the synthesis of d_5-methyl tolan, 4-ethynyltoluene (140 mg, 1.2 mmol), d_5-bromobenzene (246 mg, 1.5 mmol), and piperidine (125 mg, 1.5 mmol) were added to a 10 mL round-bottom flask along with 30 mg of bis(triphyenylphosphine) palladium(II) chloride and 1.8 mL of DMF. The reaction mixture turned from transparent yellow to dark brown after approximately 30 minutes of heating. The reaction was stirred under argon at 60°C overnight.

After stirring, the product was dissolved in diethyl ether and then washed twice with 5% aqueous HCl, twice with water, and once with a 1:1 mixture of water and brine in a separatory funnel. The resulting product was then dried with magnesium sulfate and the ether removed via rotary evaporation. The crude product (130 mg, 0.66 mmol) was a dark reddish-brown solid and a 55% yield was obtained. This was purified via column chromatography, giving a mass of 60 mg (0.3 mmol) and a 25% yield.

5.3 DSP Analysis of *para*-substituted Tolans

In order to complete the DSP analysis of the series of *para*-substituted tolans, the program R Studio was used. The ^{13}C NMR values from the series of substituents for each carbon (Table 1) as well as Charton's σ_I and σ_R values were uploaded into the software.[15] A dual regression analysis was then conducted for each carbon. The slopes of the regression lines, ρ_I and ρ_R, were then determined for carbons 1-10. This data was then used to create the graph seen in Figure 13.

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