Investigation of Efficient Synthetic Routes to Conjugated Thiophene-*S*,*S*-Dioxide-Based Materials

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

Due to their low cost and desirable properties, many recent efforts in the field of semiconductor research have been devoted to the discovery and investigation of organic materials. Within this field, thiophene-based materials make up a large portion of the abundant p-type semiconductors seen in research and commercial devices. All the while, the options for n-type materials are limited due to the restrictive constraints placed on their electronic properties in order to be air stable. Thiophene-*S*,*S*-dioxide-based materials have the potential to be strong contenders with n-type materials currently available. However, they are currently difficult to obtain synthetically, in large part due to the loss of aromaticity that occurs upon oxidation of the thiophene moiety. Typically, long reaction times, and/or harsh reaction conditions, or highly toxic, unstable reagents are required. Herein, two potential synthetic routes to thiophene-*S*,*S*-dioxides are described. The first aimed to take advantage of hydrogen bonding interactions to direct the oxidation of the thiophene, and then use the same directing group as a handle for *ipso*-arylative cross-coupling. This approach would ultimately reduce the need for harsh conditions, and minimize the number of steps required to produce thiophene-*S*,*S*-dioxide-based materials. The second route looked to be the first synthesis of a thiophene-*S*,*S*-dioxide that does not involve the oxidation of a thiophene or thiophene-*S*-oxide, by performing a formal [2+2+1] between two alkynes and sulfur dioxide, provided by an SO_2 surrogate. While the first method was able to produce the desired thiophene-*S*,*S*-dioxide, the oxidation does not seem to be promoted by the intended directing group, and the thiophene-*S*,*S*-dioxides involved have been observed to be unstable to the *ipso*-arylation conditions. Reaction conditions investigated for the second route do not appear to yield

the desired thiophene-*S*,*S*-dioxides, but have produced other materials for which structural elucidation and characterization is ongoing.

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List of Abbreviations

BLA	Bond Length Alternation
CV	Cyclic Voltammetry
DABCO·SO_2, DABSO	1,4-Diazabicyclo[2.2.2]octane bis(sulfur dioxide)
DCM	Dichloromethane
DMDO	Dimethyldioxirane
E_F	Fermi Energy
E_g or ΔE	Electronic Band Gap
EI	Electron Ionization/Electron Impact
HRMS	High Resolution Mass Spectrometry
*m*CPBA	*meta*-Chloroperoxybenzoic acid
MMPP	Magnesium Monoperoxyphthalate
M+	Molecular Ion
*n*BuLi	*n*-Butyllithium
NMR	Nuclear Magnetic Resonance
OFET	Organic Field Effect Transistors
OLED	Organic Light Emitting Diode
OPV	Organic Photovoltaic
OSC	Organic Semiconductor
PCy_3	Tricyclohexylphosphine
TBAHS	Tetrabutylammonium hydrogensulfate

TLC	Thin layer chromatography
UV	Ultraviolet

Chapter 1: Thiophene-*S*,*S*-Dioxides-Based Materials for Organic Electronics

1.1 Organic Electronics and the Electronic Band gap

In recent years, the field of semiconductor research has been largely focused on organic materials. This is due to the fact that, when compared to their inorganic counterparts, devices such as organic light emitting diodes (OLEDs), organic field effect transistors (OFETs), and organic photovoltaics (OPVs) constructed from these materials have the potential to be flexible, lightweight, semitransparent, and tunable, all the while remaining low-cost and capable of being manufactured at lower temperature by lower-cost techniques and higher throughput, while also being more mechanically robust.[1–6] This is made possible, in part, by their solubility in organic solvents, which also enables them to be produced in large quantities by printing techniques.[5] While cost is an important factor in the determination of the practicality of these organic semiconductors (OSCs) in the energy market, it is not the only, nor the most important, consideration that must be taken into account. The efficiencies and lifetimes of these materials are critical factors, and those of currently known OSCs are unable to match those of silicon and other inorganic semiconductor technologies.[6]

When designing an OSC, among the properties that must be taken into consideration for materials being incorporated into electronic devices is the electronic band gap (E_g or ΔE), as many other properties of the semiconductor depend on this. For organic materials, the band gap is related to the HOMO-LUMO gap, which is the energy difference between the lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO), or the amount of

energy required to excite an electron from the HOMO to the LUMO. (Figure 1) For OSCs, this band gap can be modified through chemical modifications of the material, and the target values depend on the desired application. For example, for OPVs, narrowing the band gap of the material allows a larger range of wavelengths to be absorbed, and thus, harnessed for their energy, increasing the efficiency of the devices. However, narrowing the band gap too much can allow for larger amounts of undesirable mechanisms of energy loss, resulting in decreased efficiency of the device. For OSCs, not only is this difference in energy of the HOMO and LUMO important, but the absolute energies of these orbitals also have implications in the properties of the material, as will be discussed further in the following sections.

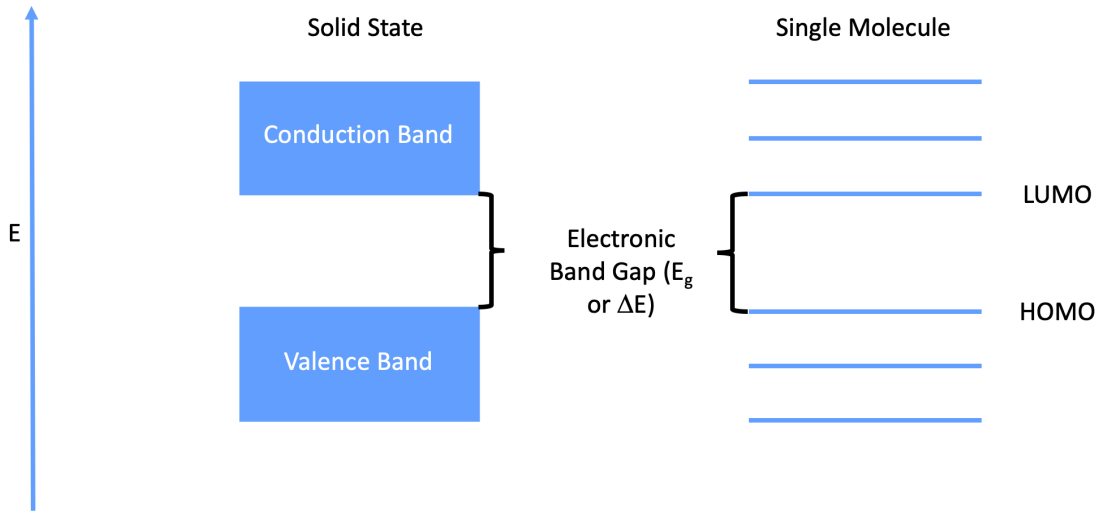


Figure 1: The electronic band gap of bulk solid state materials is related to the HOMO-LUMO gap in single molecules.

1.2 N- and P-Type Organic Semiconductors

One way of categorizing OSCs is by the type of charge carrier that they are able to transport. Those that transport holes are known as p-type semiconductors, and generally have higher energy frontier molecular orbitals. OSCs that transport electrons are known as n-type, and generally have lower energy frontier orbitals. There are also materials, known as ambipolar, which can transport both of the aforementioned charge carriers. (Figure 2)

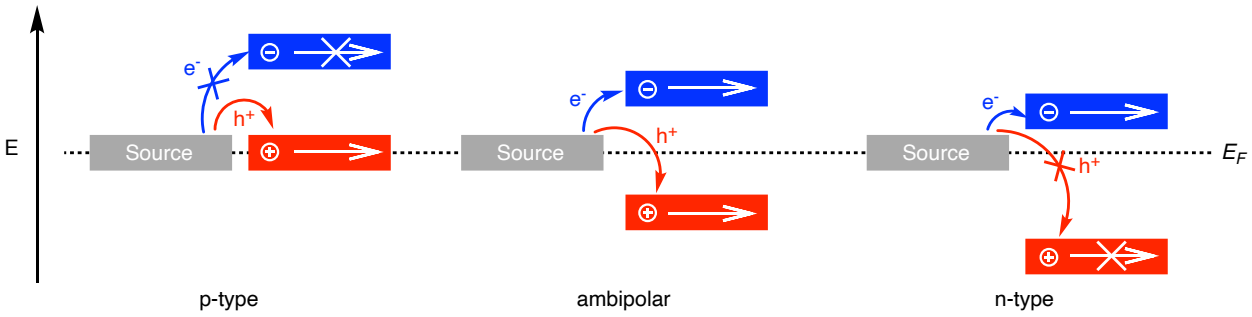


Figure 2: Relative energy levels of p-type, ambipolar, and n-type semiconductors in OFETs. E_F represents the Fermi energy of the source. "X" represents the inhibition of either charge injection or transport.

For organic electronic devices, such as organic field effect transistors, charge carrier mobility is arguably the most important device parameter. Unfortunately, structural disadvantages of OSCs cause charge transport in these materials to be inherently inferior to that of inorganic semiconductors. These disadvantages include the fact that the charge is required to move through longer, weaker intermolecular secondary bonds, such as the van der Waals force, in OSCs, as opposed to the shorter, stronger primary intramolecular bonds, such as ionic and covalent bonds, connecting the atoms or ions in their inorganic counterparts.[1–3] The charge transport in OSCs is further hindered by the complicated geometry of the molecules that results

in inefficient packing of the molecules causes the semiconductors to be disordered relative to their inorganic counterparts.[5] Despite their intrinsic limitations, OSCs have been used to fabricate OFETs with charge carrier mobilities comparable to multi-crystalline silicon. However, these accomplishments of OSCs have mostly been achieved for hole-transporting p-type semiconductors in p-type OFETs. Unfortunately, many electronic applications require electron-transporting n-type OFETs to work alongside the p-type OFETs. To date, far fewer n-type OSCs have been reported, and those that have, have much lower mobilities than their p-type counterparts. This small number of reported n-type OSCs can be attributed the requirements placed on their electronic structure in order to be stable to ambient air and moisture. These constraints arise from the fact that when an electron is injected into the LUMO of an OSC in an OFET, if the energy of this LUMO is too high, the electron is at a high-energy state, which is prone to interact or react with O_2 and H_2O in the air, as well as silanol groups on SiO_2 dielectric surfaces, which either traps or annihilates the electron, thus weakening or entirely inhibiting electron transport. While these undesirable reactions can be partially inhibited by OFET architecture, theoretical and empirical work has shown that a LUMO energy of approximately 4 eV or lower is required in order to achieve air-stable electron transport.[5] Synthesizing an OSC that fits this constraint is not trivially achieved and has thus resulted in a limited selection of commercially viable n-type materials. Lowering the LUMO energy of an n-type OSC also serves to reduce the electron injection barrier height (the energy difference between the LUMO of the OSC and the Fermi energy (E_F) of the source electrode), thus reducing the contact resistance for n-channel OFETs with contacts that have lower Fermi energies, such as Au, thus increasing the electron mobility of the OFET.

1.3 Tuning the Electronic Band gap of Conjugated Polymers

In addition to being able to synthesize an OSC, particularly conjugated polymers, with HOMO and LUMO levels within a desired range, for this material to be broadly applicable, it is best if these energy levels can also be controllably varied, or tuned, so that they can be applicable to a wide range of devices. To understand how to adjust these energy levels, it is first helpful to understand the features of the conjugated polymer that contribute to them. This can be done by looking at the common p-type semiconductor polythiophene, which is a polyaromatic conjugated polymer. As can be seen in Figure 3, there is a series of alternating single and double bonds through the polymer backbone. When these single and double bonds are arranged such that the individual thiophene units maintain their aromaticity and the π-electrons are confined to each individual thiophene, as is shown on the left of Figure 3, the polymer is considered to be in its so-called aromatic form. However, there is another possible resonance structure for ground state polythiophene. In this resonance form, shown on the right of Figure 3, the π-electrons are delocalized across the polymer backbone, and it is referred to as the quinoidal form of the conjugated polymer. Due to the loss of aromatic stabilization, the quinoidal form is higher in energy than the aromatic one, and consequently, also has a small band gap. The bond length alternation (BLA) is a parameter that refers to the ratio of aromatic to quinoidal population in such a system. BLA is defined as the average of the difference in length between adjacent carbon-carbon bonds in a polyene chain. A larger BLA indicates larger contribution of the aromatic form and more contribution of the quinoidal form decreases the BLA.[7] Therefore, the higher the resonance stabilization energy of the aromatic subunit of the polymer, the higher the BLA, as increased aromaticity of said unit makes it less likely that the polymer will adopt the quinoidal

form. This also subsequently raises the band gap of the polymer. Therefore, one major way to control band gap is to either stabilize or destabilize the aromatic form of the polymer, to either increase or decrease the band gap, respectively.

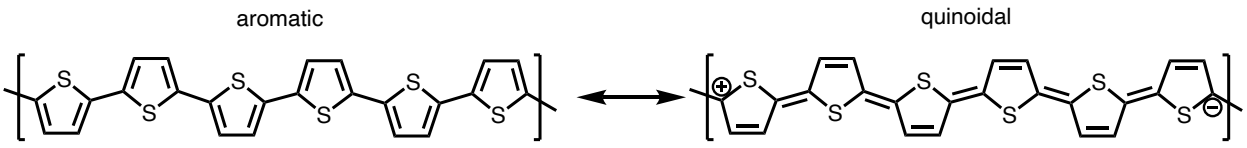


Figure 3: Aromatic and quinoidal resonance structure of polythiophene.

Band gap tuning can also be achieved by exploiting electronic and steric effects through chemical modification techniques such as rigidification of the molecule. Rigidification increases planarization and allows for increased interaction of adjacent p-orbitals, which extends the conjugation, and leads to a decrease in the BLA, and thus, a smaller band gap. In general, as the conjugation length increases, the HOMO-LUMO gap decreases to a certain extent. At a certain length of conjugation, the band gap levels off, and further increase in conjugation length has little to no effect on the band gap. The incorporation of electron-donating or electron-withdrawing groups on the aromatic unit (such as the thiophene of polythiophene) can also modify the band gap through inductive or mesomeric effects. Electron-donating groups add electron density to the system, raising the energy of the HOMO, while electron-withdrawing groups lower the energy of the LUMO, both effectively decreasing the band gap.[8]

1.4 Thiophene-*S*,*S*-Dioxides

1.4.1 Hypervalent Sulfur

Oligo- and polythiophene-based materials are heavily employed in organic electronics due, in part, to their excellent electronic properties such as high electron mobilities, and good on/off ratios.[9] They are also easily synthesized and can be tuned by functionalization at the α and β positions, as well as by changes to the molecular size and/or shape.[10,11] The resulting materials generally fall into the class of p-type materials due to their electron-rich backbone and high-lying HOMO.[9] Additionally, thiophenes contain a sulfur atom that obeys the octet rule. (i.e. it has 8 valence electrons) Since sulfur is known to form a variety of hypervalent species, such as sulfuranes, persulfuranes, sulfoxides, sulfones, and sulfonium ylides, this provides another avenue in which thiophene-based materials can be modified. However, it wasn't until 1998 that Barbarella and coworkers first took advantage of the hypervalent nature of the sulfur atom in the thiophene unit through oxidation to the thiophene-*S*,*S*-dioxide in order to decrease the electron density, as shown in Figure 4.[12]

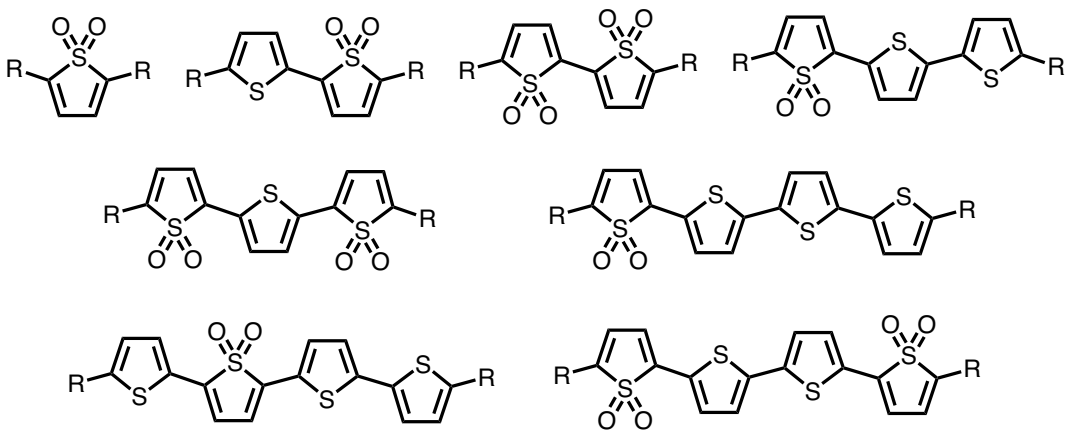


Figure 4: Examples of thiophene-S,S-dioxide molecules and oligomers reported by Barbarella and coworkers.

1.4.2 Non-Aromaticity and Other Properties of Thiophene-*S*,*S*-Dioxides

Thus far, the only reported method for the synthesis of thiophene-*S*,*S*-dioxides is through the oxidation of the thiophene. Oxidation of the thienyl sulfur in thiophene-based materials first generates the sulfoxide, but when this oxidation is carried out with strong oxygen-transfer reagents, such as *meta*-chloroperoxybenzoic acid (*m*CPBA), the resulting thiophene-*S*-oxide is quickly oxidized again, resulting in the thiophene-*S*,*S*-dioxide.[13] The thiophene-*S*,*S*-dioxide holds certain advantages over its singly oxidized counterpart, including stability to ultraviolet (UV) radiation,[13,14] as well as lower HOMO and LUMO energy levels,[15] which makes them more suitable for use as components of n-type materials. Overall, the oxidation of thienyl sulfur results in polarization of the thiophene and reduced electron density of the diene,[16] and thus, a significant decrease in the aromatic character of the thiophene component. This loss of aromaticity is evidenced by X-ray crystallography data of 2,5-diphenylthiophene-*S*-oxide, which showed it to be puckered, such that the sulfur lies 0.278 Å outside of the plane created by the

four thienyl carbons, and the oxygen lies 0.746 Å outside on the opposite side of said plane. (Figure 5)

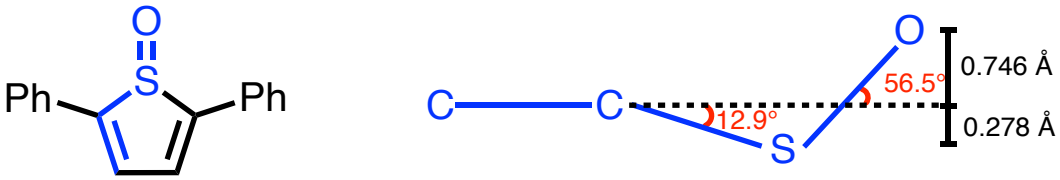


Figure 5: Puckered structure of 2,5-diphenylthiophene-*S*-oxide.

Additionally, in comparison to 2,5-diphenylthiophene, the bond order alterations are considerably more noticeable in the thiophene-*S*-oxide analogue, and these alterations become even more pronounced in the thiophene-*S*,*S*-dioxide analogue, as shown in Table 1.[17,18] Together, the non-planarity upon first oxidation of 2,5-diphenylthiophene, alongside the bond order alteration observed in both of the oxidized products, provide strong evidence for the significant loss of aromaticity that occurs in the oxidation of thiophenes. An additional numeric approach for the evaluation of aromaticity based on bond alternation, known as the Julg-François index (A_j), was defined such that the Kekulé structure of benzene has an A_j value of 0, while a system with all bonds of equal length has a value of 1.[19] The A_j value of the thienyl ring in 2,5-diphenylthiophene is 0.99. Upon oxidation to the sulfoxide, this number decreases to 0.79, and drops to 0.18 once oxidized to the sulfone. These values further support the argument that the thienyl ring of the thiophene system loses a significant amount of aromatic character upon oxidation.[17] (Table 1)

Table 1: Bond orders, ring shapes, and Julg-François indices of thienyl bonds of 2,5-diphenylthiophene, its *S*-oxide and *S*,*S*-dioxide.

		X =		
		S	**SO**	**SO_2**
Bond Order	C(2)-S & C(5)-S	1.53	1.11	1.01
	C(2)-C(3) & C(4)-C(5)	1.94	2.11	2.16
	C(3)-C(4)	1.46	1.23	1.15
Ring Shape		Planar	Puckered	Planar
A_j		0.99	0.79	0.18

The breaking of aromaticity of the thiophene allows for thiophene-*S*-oxides and thiophene-*S*,*S*-dioxides to behave as isolated dienes, as evidenced by their participation in [4+2]-cycloaddition reactions with alkenes. The trapping of thiophene-*S*-oxides with alkenes actually provided some of the strongest preliminary evidence for their existence as intermediates in the peroxide-mediated oxidation of thiophenes before they were able to be isolated.[13,20] In terms of conjugated polymers, the breaking of aromaticity of the thiophene units destabilizes the aromatic form of the material, thus lowering the band gap of the aromatic form, and allowing for increased electron delocalization across the polymer backbone, and a smaller band gap. (Figure 6) This increased conjugation is further enhanced by the removal of the sulfur atom's lone pair from the system that occurs upon oxidation, which makes the thiophene-S,S-dioxide backbone of these materials electron-deficient, thus, lowering the LUMO.[21]

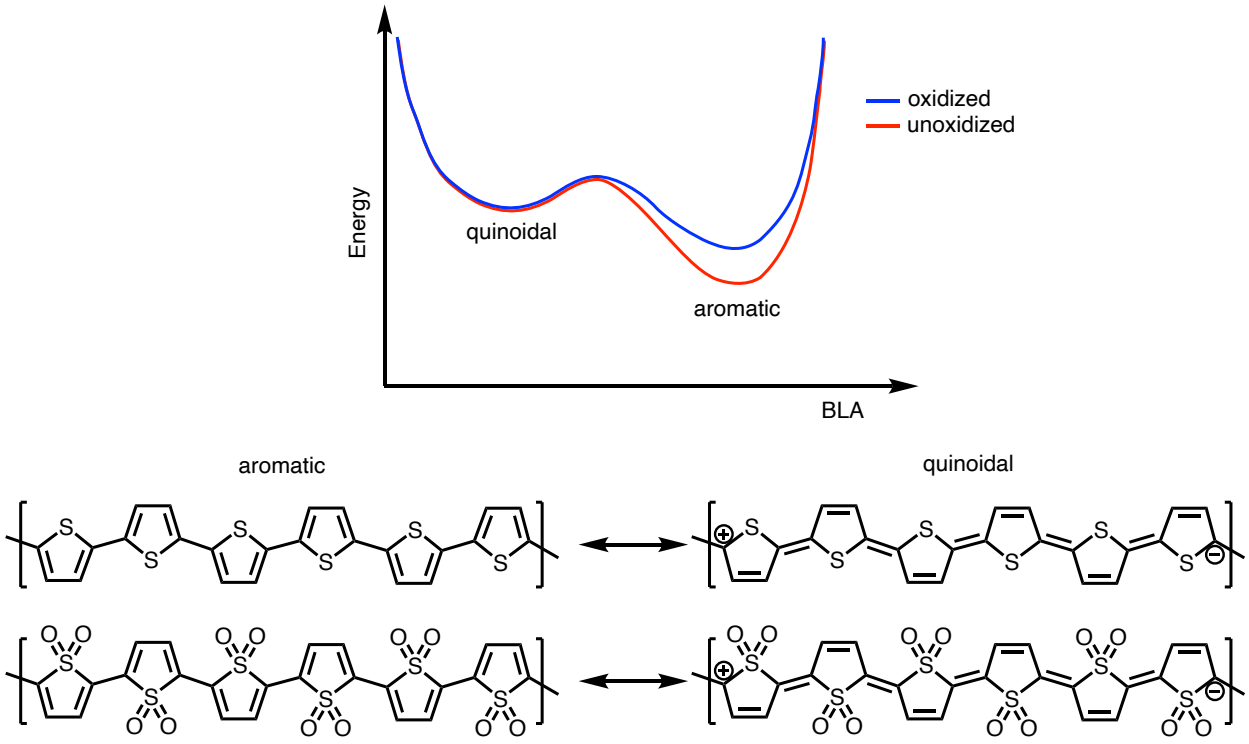


Figure 6: Relative energy vs. bond length alternation for polythiophene and polythiophene-*S*,*S*-dioxide.

Computationally, this oxidation and loss of aromaticity is expected to correspond to a decrease in the HOMO-LUMO gap.[22] Upon the synthesis of some thiophene-S,S-dioxide-containing oligomers by Barbarella and coworkers, these computations were found to be consistent with the 60-110 nm red shift that was observed relative to the non-oxidized counterparts.[23] Cyclic voltammetry (CV) experiments showed that both the HOMO and LUMO energies are lowered upon oxidation of the thienyl sulfur, but the LUMO is more so affected, resulting in the overall decrease in band gap. It is also noteworthy that this shift in reduction potential toward more negative values implies possible n-type behaviour, a rare feat for many OSCs, particularly those based on thiophenes. These electronic effects of oxidation, both predicted computationally and observed experimentally, are illustrated below in Figure 7.

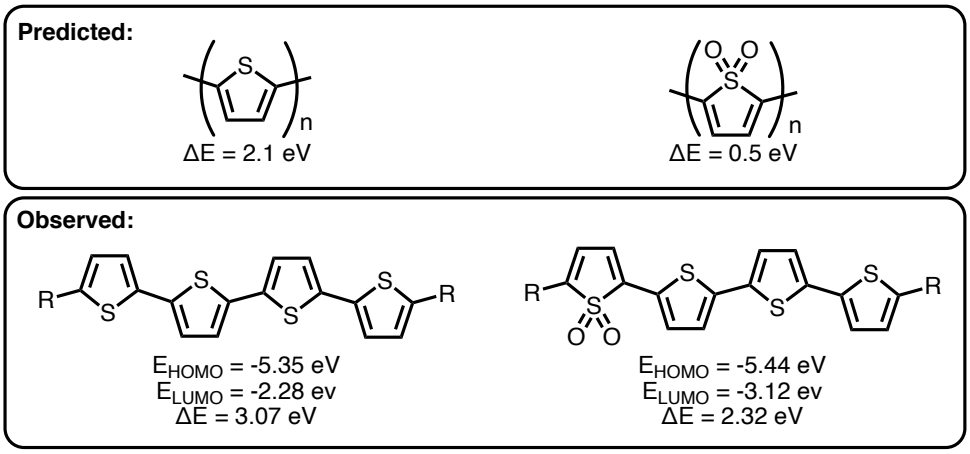
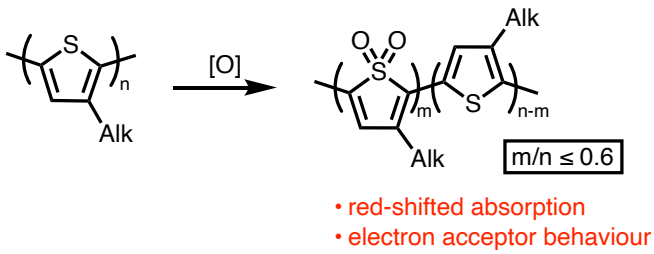


Figure 7: Computationally predicted and experimentally observed differences in electronic properties between poly-/oligothiophenes and poly-/oligothiophenes containing thiophene-*S*,*S*-dioxide units.

In addition to their excellent properties as single molecules, oligothiophene-*S*,*S*-dioxides have favourable bulk properties for electronic application when compared with their non-oxidized counterpart, as they tend to arrange into herringbone motifs in the solid state, resulting in decreased charge transport properties in the direction of the molecular backbone. It has been observed from their crystal structure that oxidized oligothiophenes demonstrate favourable π–π stacking, allowing for increased intermolecular interactions. The fact that these thiophene-S,S-dioxide-based materials are air-stable, as well as tunable (through α and β substitution, as well as chain-modifications), gives these materials the potential to be important additions to the current arsenal of n-type materials.

Campos and coworkers have also successfully demonstrated this decrease in band gap through successive controlled oxidations of thiophene units in poly(3-alkylthiophenes). As they increased the thiophene-*S*,*S*-dioxide content of the polymers up to 60%, they observed a significantly red-shifted ultraviolet-visible (UV-Vis) absorption, indicating decreasing band gap. They also

performed photoluminescence-quenching experiments that provided evidence of the electron-accepting behaviour of the 60% oxidized polymer, indicating that these polymers may behave as n-type materials.[24] (Figure 8)



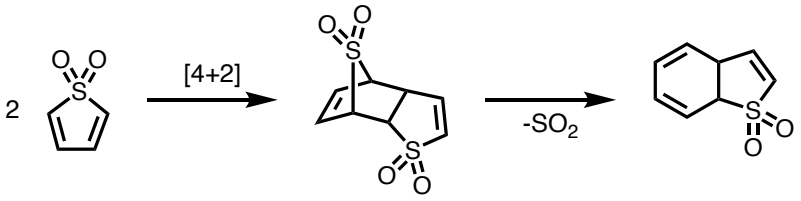
Scheme 1*:* Controlled oxidation of poly(3-alkylthiophenes) up to 60% performed by Campos and coworkers.

Chapter 2: Thiophene-*S*,*S*-Dioxide Materials *via* Directed Oxidation and *ipso*-Arylation

2.1 Synthesis of Thiophene-*S*,*S*-Dioxide-Based Materials Through Thiophene Oxidation

2.1.1 Oxidation of Thiophenes

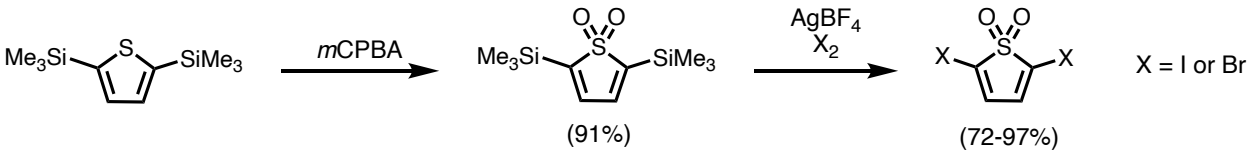
Despite the long list of desirable properties imparted by thiophene-*S*,*S*-dioxide upon their incorporation into organic electronic materials, it may seem strange that these motifs are not ubiquitous in the field of organic electronics. Their absence comes down to the extreme difficulty in the chemistry of thiophene oxidation. Thus far in the literature, long reaction times and high reaction temperatures have typically been employed in order overcome the loss of aromaticity of the thiophene. However, these conditions are known to promote [4+2] cyclodimerization of either the thiophene-S-monoxide or the thiophene-S,S-dioxide (Scheme 2), elimination, or other reactions of the oxidized products including epoxidation of the double bonds.[25,26]



Scheme 2: [4+2] Cyclodimerization of thiophene-S,S-dioxide followed by loss of the bridge sulfonyl group.

Typical thiophene oxidation conditions employ oxygen-transfer reagents including, but not limited to, hydrogen peroxide, *meta*-chloroperoxybenzoic acid (*m*CPBA), and dimethyldioxirane (DMDO). These reagents generally produce the corresponding thiophene-*S*,*S*-dioxide in low yields, that decrease even further as oxidations of more electron-deficient thiophenes are

undertaken.[27] However, with a little synthetic creativity, it has been shown that it is possible to produce electron-deficient thiophene-S,S-dioxides in moderate to good yields by first oxidizing 2,5-bis(trimethylsilyl)thiophene, and then substituting the trimethylsilyl groups to provide the 2,5-iodo- or bromo-thiophene-*S*,*S*-dioxide (Scheme 3).[28] In addition to the activation towards oxidation through the electron donating (ED) nature of the trimethylsilyl groups, their steric bulk is also postulated to aid the oxidation by preventing the Diels-Alder cyclodimerization and other previously mentioned side reactions of the oxidized product.[27,29] While this workaround is able to provide the desired electron-deficient thiophene-S,S-dioxide small molecules in moderate yields, it is not enough to make these viable as commercial n-type materials.



Scheme 3: Synthetic approach used to synthesize electron-deficient thiophene-S,S-dioxides.

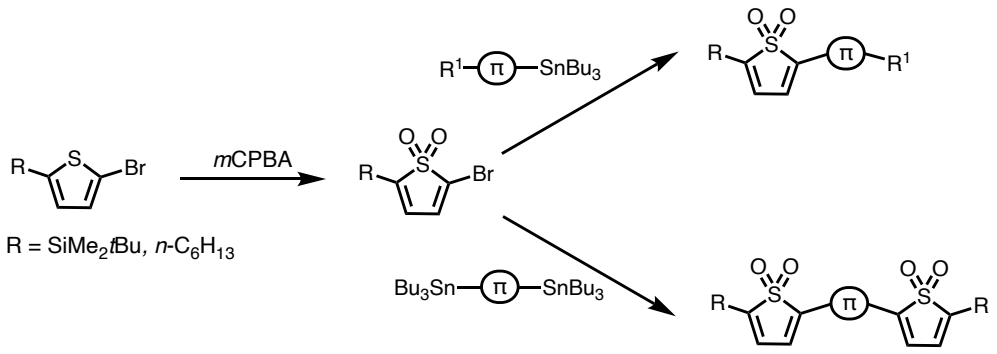
More recently, a major breakthrough in this chemistry occurred when Rozen and coworkers developed an acetonitrile-stabilized hypofluorous acid complex (HOF•CH_3CN), which is considered the most powerful oxygen-transfer reagent currently known.[30] This reagent has been shown to oxidize oligothiophenes to the [all]-S,S-dioxides, in high yields under mild conditions, thereby avoiding the formation of side products, and in much shorter times than the peracids and peroxy compounds used conventionally. In fact, HOF•CH_3CN was able to oxidize oligothiophenes up to 4 repeat units as well as fused and star-shaped thiophenes.[30] In the

previously discussed work of Campos and coworkers, HOF•CH_3CN was used to oxidize the poly(3-alkylthiophenes) up 60%.[24]

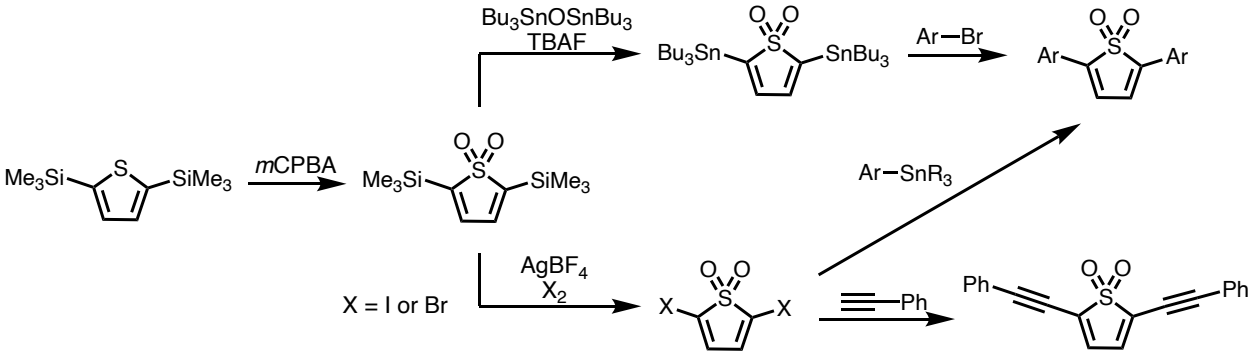
While this reagent has proven to be of great synthetic value, it is also not commercially viable due to its instability and toxicity. Despite the acetonitrile complex being much more stable than hypofluorous acid alone, it must still be prepared *in situ* from fluorine gas and reacted soon after its formation. It is also considered to be just as toxic as its non-complexed counterpart.[31]

2.1.2 Coupling of Oxidized Thiophenes

Since *m*CPBA is not able to oxidize oligo- or polythiophenes in adequate yields, if at all, and HOF•CH_3CN is not easily accessible in the average chemistry laboratory, nor commercially practical, it is unsurprising that the oligothiophenes synthesized by Barbarella and coworkers, shown previously in Figure 4, were assembled via cross-coupling reactions after the oxidation of the applicable thiophene-S,S-dioxide unit(s).[32] (Scheme 4) Others have utilized similar Stille cross-couplings to couple thiophenes with different aryl moieties. Similar to the work of Barbarella and coworkers, 2,5-bis(trimethylsilyl)thiophenes were used in the oxidation before being converted to the dihalogenated or bistributyltin analogues for use in subsequent Stille cross-couplings.[33] Another approach involved using the 2,5-dibromothiophene-S,S-dioxide obtained from the oxidized 2,5-bis(trimethylsilyl)thiophene, and using that directly in a Sonogashira cross-coupling with an arylacetylene.[34] Both of these approaches are illustrated below in Scheme 5.



Scheme 4: General synthetic approach used by Barbarella and coworkers to synthesize thiophene-S,S-dioxide-containing oligomers.



Scheme 5: Alternative synthetic routes used to synthesize cross-coupled thiophene-S,S-dioxides.

2.2 Directed Oxidation

Hydrogen bonding interactions have previously been shown to have promoting effects in the epoxidation of cyclic allylic alcohols with peracids.[35] Using an allylic hydroxyl group, epoxidation proceeded faster than expected, based solely on inductive interactions, and in a stereospecific fashion, such that the resulting epoxy groups were found to always be in a *cis* relationship to the directing hydroxy groups, with none of the *trans* product being detected. This led to the postulation of a favourable hydrogen bonding interaction between the reactants, resulting in a transition state resembling that shown in Figure 9.

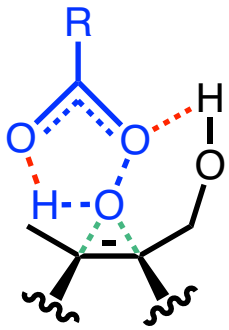
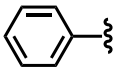
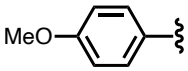
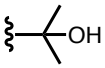
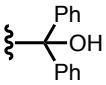


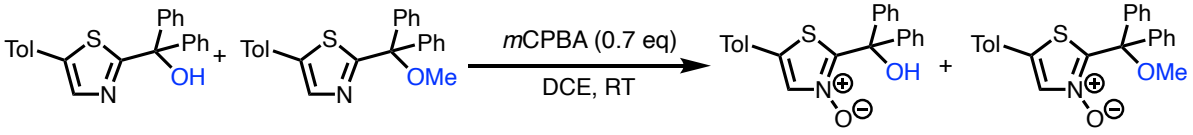
Figure 8: The hydrogen-bonded transition state postulated in the epoxidation of cyclic allylic alcohols. The peracid moiety is shown in blue, while the allylic alcohol is shown in black, the forming epoxide bonds are shown in green and the hydrogen bonding interactions are shown in red.

A similar hydrogen-bonding interaction has been postulated to explain previous results obtained in the Schipper lab in the oxidation of 5-substituted thiozales to the corresponding *N*-oxides with *m*CPBA. In this work, carried out by Geoffrey S. Sinclair, the yields of the oxidations of 5-substituted thizaoles were greatly improved by the incorporation of dimethyl- and diphenylcarbinol groups at the 2-position. This effect is shown in Table 2.

Table 2: Yields of oxidations of various 2- and 5- substituted thiazoles demonstrating the effect of directed oxidation. All work performed by Geoffrey S. Sinclair.

R^1 / R^2		
	10%	28%
	81%	56%
	89%	93%

While the mechanism of these transformations has not been fully investigated, preliminary competition experiments between a carbinol-substituted thiazole and the analogous methyl ether (Scheme 6) indicate that a hydrogen bonding interaction is potentially important for the observed increase in yield upon incorporation of the carbinol groups.[36]

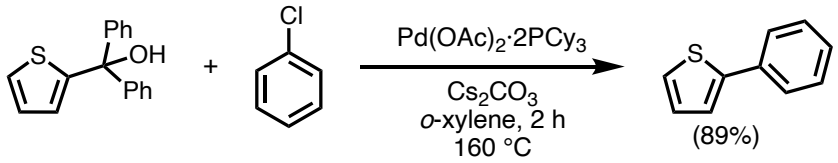


6:1

Scheme 6: Competition oxidation between a carbinol-substituted thiazole and its methyl ether analogue.

2.3 Palladium-Catalyzed ipso-Arylation and Polymerization

These dialkyl and diarylcarbinol groups used in the above directed oxidations were derived from the hydroxymethyl groups used to protect terminal alkynes.[37,38] However, it has also been previously reported that these α,α-disubstituted carbinols allow for further C-C bond formation via two competing palladium-catalyzed processes; C-H bond cleavage at the ortho-position (ortho-arylation), as well as sp^2-sp^3 C-C bond cleavage (β-carbon elimination/*ipso*-arylation).[39] Both routes proceed through arylpalladium(II) alkoxide intermediates, which can allow for selective access to the β-carbon elimination product through *ortho*-substitution of the diarylcarbinol species (if applicable), as well as the use of a bulky phosphine ligand, such as tricyclohexylphosphine (PCy_3).[40] This coupling (*via* β-carbon elimination) has been successful in the allylation and arylation of alkynyl-,[41] phenyl-[39,40,42–44], furanyl-[40], and thienyl-[40,45] systems. It is of even more interest that 2-thienyl(diphenyl)carbinols were found to be very reactive in this transformation (Scheme 7). The reaction proceeds selectively to the *ipso*-arylated thiophene in good yield, in half the time of the corresponding benzene, producing only negligible amounts of biphenyl. The authors postulate that the success of this reaction can possibly be attributed to the coordination ability of the internal sulfur atom.[40]



Scheme 7: The reaction of a carbinol-substituted thiophene in *ipso*-arylative coupling with chlorobenzene.

The mechanism of *ipso*-arylative polymerization is believed to involve four key steps : (I) oxidative addition of an aryl halide to an active Pd(0) catalyst, (II) addition of the carbinol to the aryl palladium halide species resulting in the loss of a hydrogen halide, (III) β-carbon elimination as the carbinol group leaves as a ketone, alongside diaryl palladium species formation, and (IV) reductive elimination of the diaryl with regeneration of the Pd(0) catalyst. This mechanism is shown in Figure 10 for the species involved in Scheme 7. [46,47]

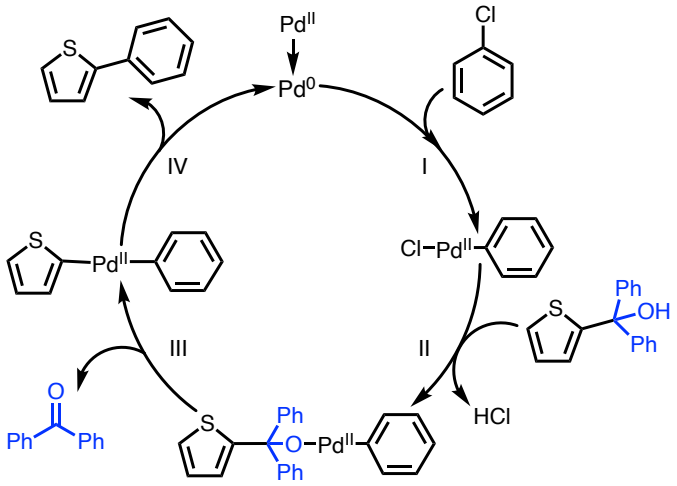


Figure 9: Catalytic cycle for ipso-arylative cross-coupling of a carbinol-substituted thiophene with chlorobenzene

ipso-Arylative polymerization has been found to produce polymers with properties that are indistinguishable from those prepared by more conventional cross-coupling methods, such as Stille cross-coupling, while also avoiding the use of the metal-containing functional groups, such as stannanes, that often accompany the more conventional methods.[46] Upon optimization studies of the *ipso*-arylative polymerization of poly(3-hexylthiophene), it has been found that PCy_3 generates polymers of higher molecular weights than other phosphine ligands. Further

studies of the termination of the reaction determined that the loss of active end-groups via protodehalogenation, protodecabinolation, and/or reductive coupling ends the polymerization, and results in polymer chains that are terminated with protons on both ends.[46] Despite these undesirable side reactions being slower than *ipso*-arylation, they become an issue in the polymerization process at higher molecular weights, and currently limit the use of this method as a way to access conjugated polymers over more traditional cross-coupling methods. However, further optimization efforts may yet be able to achieve more chain-growth character in this reaction, and delay, or eliminate, the termination of polymerization via the aforementioned side reactions.

2.4 Proposed Synthetic Route to Conjugated Thiophene-*S*,*S*-Dioxide-Based Materials

Given all of this previously reported information, it was proposed that a 2,5-bis(diphenylcarbinol)-substituted thiophene would undergo oxidation with peroxyacids, such as *m*CPBA, to give the corresponding thiophene-*S*,*S*-dioxide in good yields. It was then thought that the thiophene-*S*,*S*-dioxide product would then be able to undergo *ipso*-arylation to furnish conjugated thiophene-*S*,*S*-dioxide-based small molecules and polymers. This approach would reduce the number of steps required to synthesize such materials and release only benzophenone as a by-product of the cross-coupling, presenting an attractive alternative to the synthetic methods previously reported and discussed above. (Figure 10)

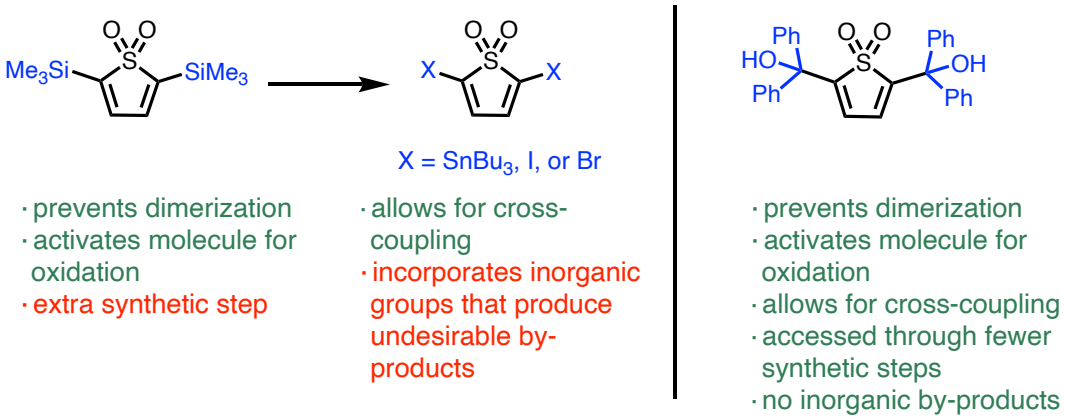
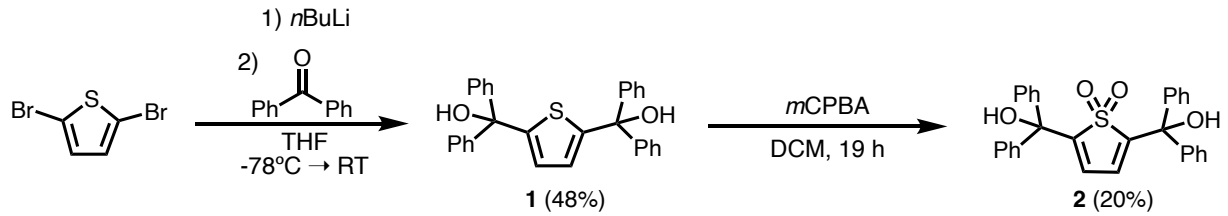


Figure 10: The proposed 2,5-bis(diphenylcarbinol)-substituted thiophene-*S*,*S*-dioxide is proposed to be able to be obtained in high yields and allow for direct *ipso*-arylative coupling to conjugated materials.

2.5 Synthesis of 2,5-bis(hydroxydiphenylmethyl)thiophene and Oxidation with *m*CPBA

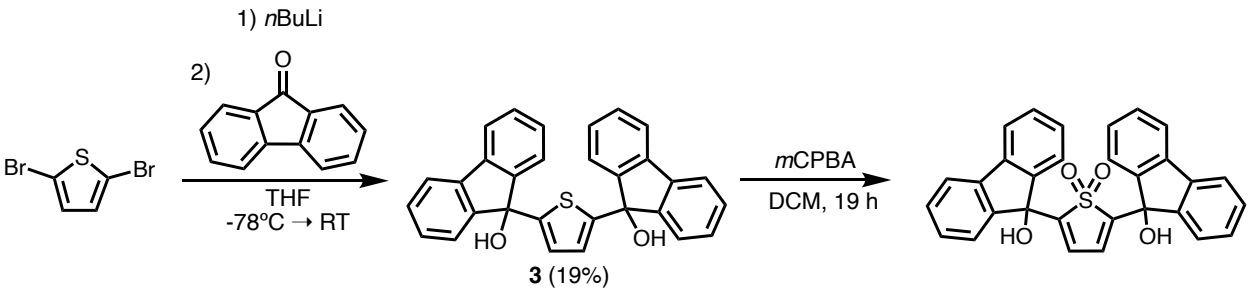
2,5-bis(hydroxydiphenylmethyl)thiophene (**1**) was synthesized from 2,5-dibromothiophene via lithium-halogen exchange, followed by nucleophilic addition to benzophenone and acidic workup. (Scheme 8) This compound was then subject to oxidation with *m*CPBA, as it was initially hypothesized that *m*CPBA, being a peroxy acid, would be able to hydrogen bond with the alcohol of the diphenylcarbinol groups, thus holding the *m*CPBA in close proximity to the sulfur atom of the thiophene, aiding in its oxidation. However, upon treatment of **1** with *m*CPBA and stirring at room temperature for 19 hours, the desired thiophene-*S*,*S*-dioxide **2** was produced in only approximately 20% yield, and could not be purified from a number of other observed products. (Scheme 8) Due to the observation of both these many side products, and significant starting material by thin layer chromatography (TLC), it was concluded that the oxidation reaction was not being aided by the directing effect, as anticipated, and that the substrate may not tolerate acidic conditions.



Scheme 8: Synthesis of 2,5-bis(diphenylcarbinol)-substituted thiophene and its oxidation with *m*CPBA.

In an effort to circumvent this possible acid sensitivity, the oxidation of **1** was performed in the presence of a 0.5 M aqueous solution of sodium bicarbonate. This biphasic system was stirred for 19 hours, and while it did provide a cleaner reaction by TLC, the yield was not improved. This indicated that, while the substrate indeed is likely acid-sensitive, this was not the sole reason for the low yield of the oxidation.

In a separate attempt to overcome this potential acid-sensitivity, the fluorenone analogue of **1** (**3**) was synthesized in a parallel manner and subject to the same oxidation conditions with *m*CPBA (Scheme 9). It was hypothesized that the pseudo-fluorenyl cation resulting from the loss of water would be less likely to form in the presence of acid due to the antiaromatic nature of the fluorenyl cation.[48,49] However, by TLC, this oxidation still produced only a small amount of the desired thiophene-S,S-dioxide product that was not able to be isolated.



Scheme 9: Synthesis of 9,9'-(thiophene-2,5-diyl)bis(9*H*-fluoren-9-ol) and its oxidation with *m*CPBA.

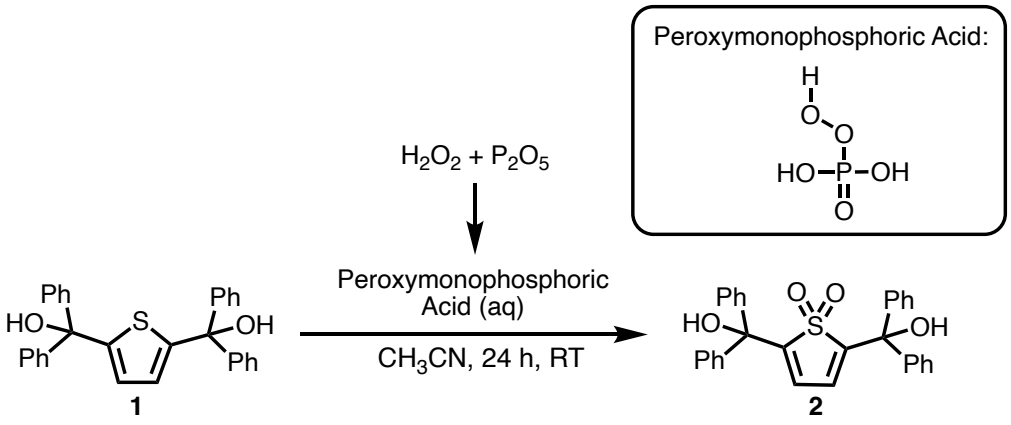
2.6 Oxidation of 2,5-bis(hydroxydiphenylmethyl)thiophene with Other Oxygen Transfer Reagents

2.6.1 Magnesium Monoperoxyphthalate (MMPP)

In an effort to improve the yield and circumvent the acid sensitivity issues encountered with *m*CPBA, other oxygen transfer reagents were considered. MMPP was invesitigated first due to its functional similarity to *m*CPBA. (i.e. that it is an easily handled solid that can simply be added to a stirring solution of the substrate) Therefore, analogously to our *m*CPBA oxidations, 3 equivalents of MMPP·6H_2O were added to a stirring solution of **1** in DCM. After 48 hours at room temperature, TLC indicated a significant amount of **1** remaining, and the formation of miniscule amounts of multiple other products that could not be isolated. Though the desired product was not obtained from this reaction, it was a good indication that the previous hypothesis regarding the acid-sensitivity of **1** was likely correct, and that the oxidation by peroxy acids was not being directed, as had been originally hypothesized.

2.6.2 Peroxymonophosphoric Acid

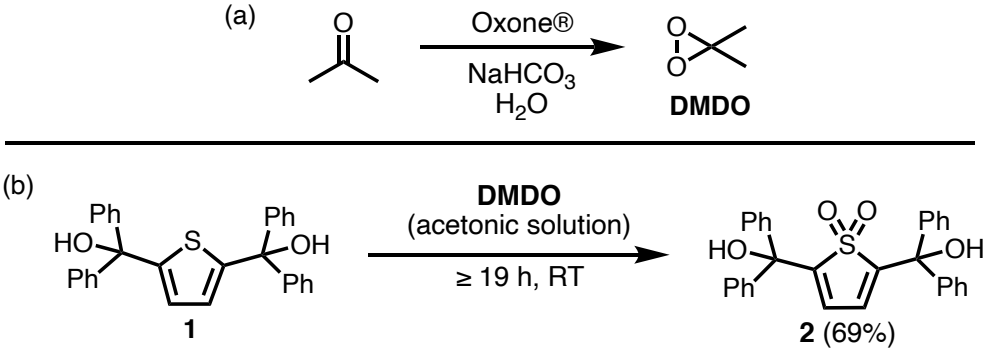
Given the previous results, one last peroxy acid oxidation was attempted to further confirm the working hypothesis. A peroxymonophosphoric acid solution was chosen as our oxygen transfer reagent, as these solutions have previously been shown to be able to efficiently oxidize electron-poor benzo[*b*]thiophenes to the corresponding sulfones.[50] Additionally, solutions of peroxymonophosphoric acid can be easily prepared from 30% hydrogen peroxide and phosphorus pentoxide, and can be stored for up to two weeks.[50] Upon treatment of **1** with 2 equivalents of peroxymonophosphoric acid (Scheme 10), consumption of **3**, along with the formation of three unidentified products was observed after 24 h at room temperature and only a small amount of the desired thiophene-*S*,*S*-dioxide product **2** was observed but was not able to be isolated. Since alongside the peroxy acid in the peroxymonophosphoric solution described above, there also exists a significant amount of phosphoric acid, it was not surprising, given our previous results with *m*CPBA and MMPP, that this oxidation was not successful, and led to the production of multiple side products.



Scheme 10: Preparation of peroxymonophosphoric acid solution and its use in the oxidation of the 2,5-bis(diphenylcarbinol)-substituted thiophene.

2.6.3 Dimethyldioxirane (DMDO)

Operating now on the above hypothesis that the thiophene substrate **3** would not tolerate acidic conditions, and that the possible directing effect imparted by the 2,5-dicarbinol groups was not aiding the oxidation, dimethyldioxirane (DMDO) was considered as a possible oxygen transfer reagent. DMDO is known to be a powerful oxygen transfer reagent, and has been reported to have success in the oxidation of thiophenes to the corresponding thiophene-*S*,*S*-dioxides in moderate to good yields.[27] Additionally, since it is not a peroxy acid, and can be prepared as an acetonic solution from a basic solution of water, acetone, and Oxone®, it was promising for use in the oxidation of **1**. The major drawback of this method is the preparation of DMDO, as it is extremely volatile and unstable, it must be used almost immediately upon preparation. Additionally, reported methods for the preparation of DMDO are notoriously low yielding. Nevertheless, acetonic solutions of DMDO were able to be prepared, according to Scheme 11a, in concentrations up to 72 mM, as determined by titration with thioanisole. Upon treatment of **1** with these DMDO solutions (Scheme 11b), compound **2** was obtained in up to 69% isolated yield.



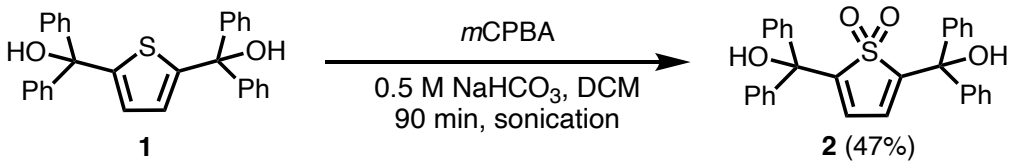
Scheme 11: (a) Preparation of DMDO solution and (b) its use in the oxidation of the 2,5-bis(diphenylcarbinol)-substituted thiophene.

It is also noteworthy that preliminary results seem to indicate that the rate of addition of the DMDO seems to affect the yield of the thiophene-*S*,*S*-dioxide product, and changes how many equivalents of DMDO may be needed. While in theory, only 2 equivalents of DMDO are required for the reaction, due to the instability and volatility of the reagent alongside the difficulty of the oxidation of thiophenes previously reported, it is not surprising that more would be required. When **1** was subject to 5.5 equivalents of DMDO all at once, and stirred overnight at room temperature, consumption of the thiophene starting material **1** was observed by TLC, but the desired product **1** was obtained in only 40% yield. However, when the reaction was scaled up and larger amounts of DMDO were required, size limitations of the available equipment made it such that several batches of DMDO had to be prepared over several days. Therefore the individual DMDO solutions were added to the oxidation of **1** in uneven time increments over these several days. This slow addition of the DMDO was able to yield the desired product **2** in 69% yield using only 1.4 equivalents of DMDO, suggesting that a slower, portion wise addition of DMDO may result in smaller amounts being required. However, at this point, a significant amount of our thiophene-*S*,*S*-dioxide product had been obtained, and the oxidation was not further optimized.

2.6.4 Return to *m*CPBA

While the DMDO route is tedious and lengthy, it was able to provide enough of the desired product for the rest of the investigation detailed below. However, late in the investigation, following the example of Barbarella and coworkers,[51] ultrasound assistance was employed in the oxidation of thiophene substrate 1 with *m*CPBA. The biphasic system containing 0.5 M sodium bicarbonate was once again employed in an effort to minimize the degradation of the substrate

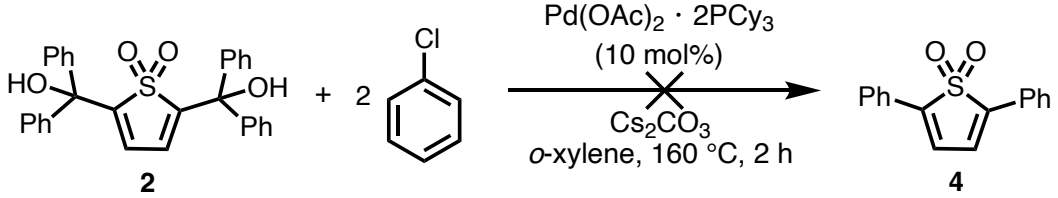
in the presence of acid. Excitingly, when this biphasic solution was sonicated for 90 minutes, the yield of the oxidation with *m*CPBA more than doubled, compared to the same system stirred for 19 hours, to 47%. (Scheme 12)



Scheme 12: Buffered oxidation of 2,5-bis(diphenylcarbinol)-substituted thiophene with *m*CPBA and ultrasound assistance.

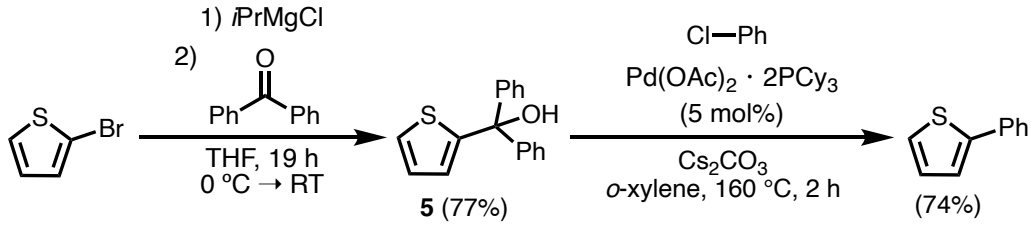
2.7 *ipso*-Arylative Cross-Couplings of 2,5-Bis(hydroxydiphenylmethyl)thiophene-*S*,*S*-Dioxide

Now that a significant amount of pure thiophene-*S*,*S*-dioxide **2** had been produced, a preliminary *ipso*-arylative cross-coupling of the compound was attempted (Scheme 13) in order to determine its suitability for the reaction, and some slightly optimized reaction conditions. Unfortunately, despite being able to observe consumption of **2** by TLC, and isolate a significant amount of benzophenone, (the byproduct of the desired reaction) none of the desired cross-coupled product **4** was observed.



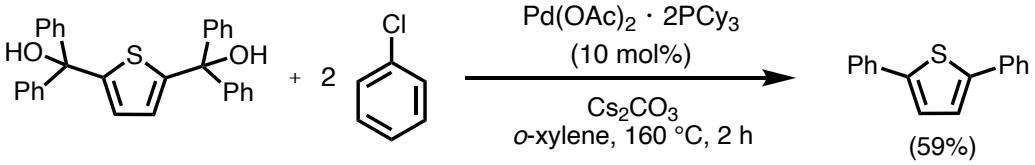
Scheme 13: Preliminary unsuccessful *ipso*-arylation reaction of a thiophene-*S*,*S*-dioxide with chlorobenzene.

In order to verify that the *ipso*-arylation conditions were being properly reproduced, the previously reported *ipso*-arylation of the 2-diphenylcarbinol-substituted thiophene **5** was performed. (Scheme 14) 2-Phenylthiophene was obtained in 74% yield, which was comparable to that previously reported,[40] indicating that the nonsuccess of the *ipso*-arylation of **2** was not an issue with the reproduction of the required conditions.



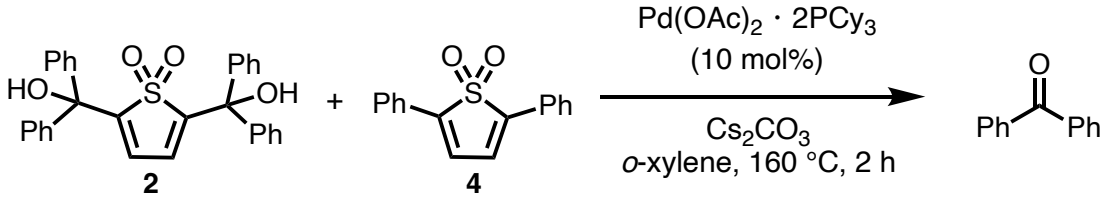
Scheme 14: Synthesis of diphenyl(thiophen-2-yl)methanol and its *ipso*-arylation with chlorobenzene.

These conditions were also applied to the unoxidized thiophene **1** and stoichiometry was optimized for the double *ipso*-arylation. (Scheme 15) It was found that the optimal conditions that afforded 59% of the desired 2,5-diphenylthiopene were the same as those previously applied in the *ipso*-arylation of **2**, once again indicating that its nonsuccess was not an issue with the *ipso*-arylation conditions.



Scheme 15: Double *ipso*-arylation of the 2,5-bis(diphenylcarbinol)-substituted thiophene with chlorobenzene.

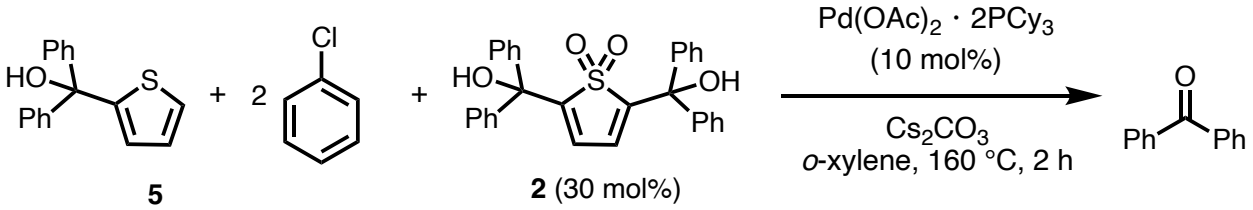
Curious about the consumption of **2** that occurred, two possible scenarios were investigated. The first, was that **2** was not stable to the *ipso*-arylation conditions and its consumption was caused by degradation. The second scenario considered was that the cross-coupled product **4** was similarly unstable to the reaction conditions and was subject to degradation before observation or isolation could take place. In order to investigate if either of these scenarios were likely, a sample of **2** and a sample of **4** were, together, subject to the *ipso*-arylation conditions in the absence of chlorobenzene. (Scheme 16) After 2 hours, neither **2** nor **4** were observed by TLC, but benzophenone was present.



Scheme 16: The 2,5-bis(diphenylcarbinol)-substituted thiophene-*S*,*S*-dioxide and 2,5-diphenylthophene-*S*,*S*-dioxide degrade under *ipso*-arylation conditions.

From these results, it was very possible that the thiophene-*S*,*S*-dioxide starting material and product were unable to tolerate the *ipso*-arylation conditions. However, another scenario was considered in which, due to the non-aromatic nature of the thiophene-*S*,*S*-dioxides, it was possible that they were behaving as isolated alkenes and interfering with the desired reactivity. In order to determine if this was the case, the *ipso*-arylation of **5** was performed in the presence of 30 mol% of **2**. (Scheme 17) The observation of benzophenone as the only new product formed after 2 hours allowed for the conclusion that the thiophene-*S*,*S*-dioxides are likely not amenable

to *ipso*-arylative coupling. Therefore, this route to thiophene-*S*,*S*-dioxide-based materials was abandoned in favour of others more promising.



5 **2** (30 mol%)

Scheme 17: The *ipso*-arylation of diphenyl(thiophen-2-yl)methanol in the presence of a thiophene-*S*,*S*-dioxide.

Chapter 3: Thiophene-S,S-Dioxide *via* Formal [2+2+1] Reaction of Alkynes with SO_2

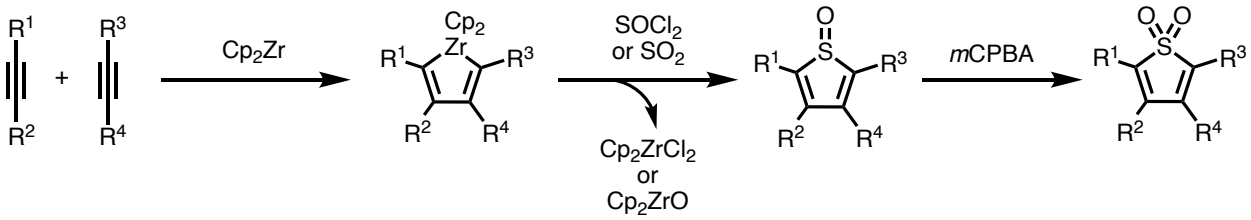
3.1 Synthesis of Thiophene-*S*,*S*-Dioxide-Based Materials Through Reactions with SO_2

3.1.1 Zirconocene Coupling of Alkynes and Reaction with SO_2

There are several accounts from the 1990s of the synthesis of substituted thiophene-*S*-oxides from alkynes and SO sources *via* a zirconacyclopentadiene intermediate. These zirconacyclopentadienes are prepared by reduction of Cp_2ZrCl_2, with *n*BuLi or magnesium turnings to produce the Negishi reagent (Cp_2Zr), which in turn reacts with two alkynes to afford the zirconocene metallacycle intermediate. This zirconacyclopentadiene is then reacted with thionyl chloride or sulfur dioxide to produce the corresponding thiophene-*S*-oxide in moderate to excellent yields.[52–55] The reactions with sulfur dioxide generally proceed in significantly higher yields than the analogous ones with thionyl chloride. This has been attributed to the more efficient oxo-transfer from the sulfur dioxide to the zirconacene in the formation of the Cp_2ZrO byproduct, as opposed the analogous process in the formation of the Cp_2ZrCl_2 from thionyl chloride.[54]

It is important to note that these methods described produce only the thiophene-*S*-oxides, with small amounts of the thiophene sometimes observed. In order to access the thiophene-*S*,*S*-dioxides, oxidation of the *S*-oxide with a peracid or peroxy compound is once again required. The advantage of the oxidation beginning with the *S*-oxide, as opposed to the thiophene, is that the initial oxidation (and corresponding loss of aromaticity) is the most challenging of the two oxidations. Therefore, oxidation beginning with the *S*-oxide to the *S*,*S*-dioxide is much higher

yielding than the double oxidation of the thiophene, and even allows for selective oxidation of thiophene-*S*-oxides in the presence of thiophenes.[54] This synthetic approach has been employed to the synthesis of molecularly defined thiophene-*S*-oxide- and thiophene-*S*,*S*-dioxide-containing oligomers.[55] (Scheme 18)



Scheme 18: Synthesis of thiophene-S-oxides and -S,S-dioxides via a zirconacyclopentadiene.

3.1.2 SO_2 Insertions

Sulfur dioxide insertion reactions have recently attracted significant attention in the field of organic synthesis due to their ability to install sulfonyl moieties in an atom- and step-economical fashion, using readily available sources.[56] This chemistry has made significant advances in the last decade by the utilization of bench-stable SO_2 surrogates, which allow for the circumvention of the use of corrosive, environmentally-harmful, and toxic SO_2 gas. These surrogates include, but are not limited to: metal sulfite/disulfite salts (M_nSO_3/$M_nS_2O_5$), thionyl chloride and water, sodium formaldehyde sulfoxylate (rongalite), and 1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) (DABCO·SO_2, DABSO). (Figure 11) In addition to their advantages with respect to health and the environment, SO_2 surrogates also allow for increased control over the equivalents of SO_2 added to the reactions. This is particularly advantageous for transition metal catalyzed reactions,

as unlike carbon monoxide insertion chemistry, their use with sulfur dioxide had previously been limited as large excesses of SO_2 gas would poison the catalyst.[56]

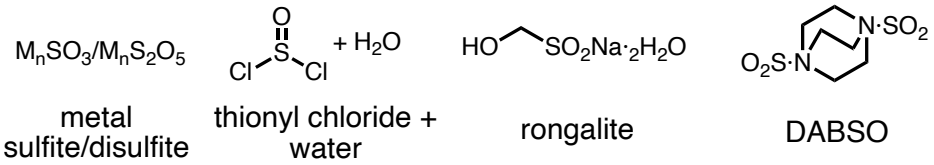
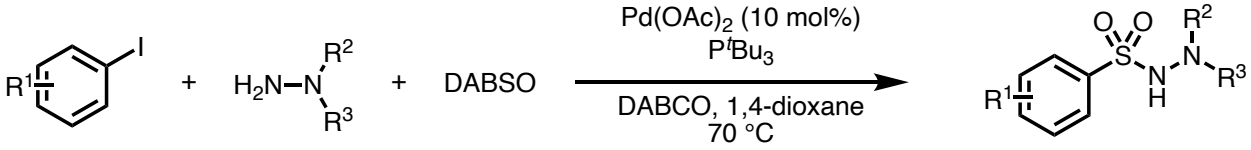


Figure 11: Selected sulfur dioxide surrogates.

The first report of a sulfur dioxide surrogate was provided by the Willis group from Oxford University when they reported the three-component palladium-catalyzed coupling of aryl iodides, sulfur dioxide, and hydrazines to the corresponding *N*-aminosulfonamides in good to excellent yields. (Scheme 19) After having no success in the desired coupling using sulfur dioxide gas, which they attributed to the multiple binding modes and amphoteric nature of sulfur dioxide, the group thought to employ an amine-SO_2 adduct, namely DABSO, as their source of sulfur dioxide. To their delight, this was the key to success for the reaction.[57] Though the DABSO compound had been reported previous to this paper, this was the first time it had been used as a source of sulfur dioxide.



Scheme 19: First report of DABSO as an SO_2 surrogate in the palladium-catalyzed coupling of aryl iodides, hydrazines, and sulfur dioxide.

The unique structure of sulfur dioxide allows for a variety of reactivities. It is amphoteric, as its lone pair in its high-lying σ-based HOMO allows it to react as a nucleophile, while the low-lying LUMO concentrated on the sulfur give it its electrophilic properties. In SO_2 insertion, these properties generally translate to four types of reactions: nucleophilic addition of organometallic reagents, transition metal catalysis, free radical reactions, and pericyclic reactions. These procedures have been successfully employed for the synthesis of sulfonamides, sulfamides, sulfonyl chlorides and fluorides, sulfoxides, and sulfones.[56] (Figure 12)

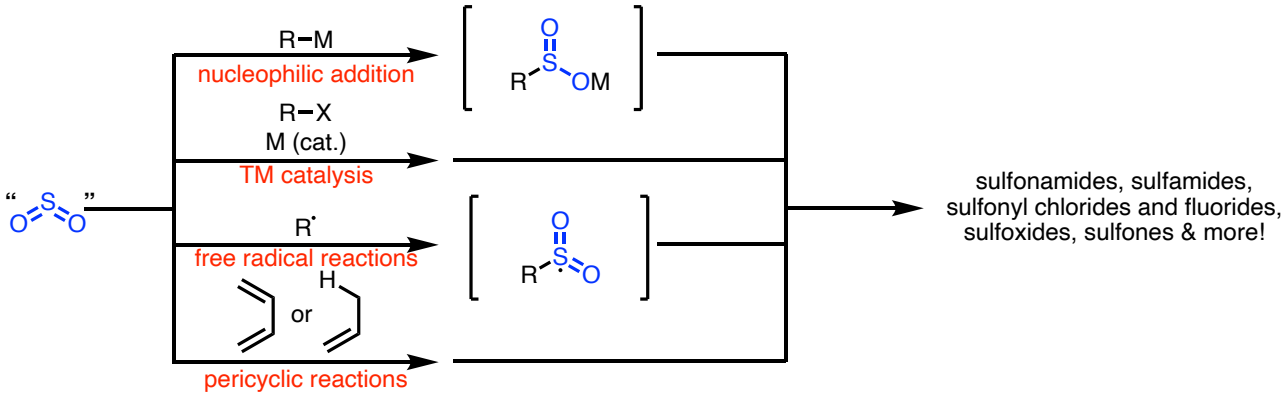
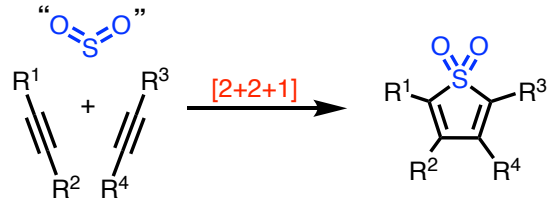


Figure 12: Four types of SO_2 insertion reactions.

3.2 Proposed Research

Given the rapid growth of the field of SO_2 insertion chemistry, it was only natural at this point to investigate whether this chemistry could be applied to the first ever synthesis of a thiophene-*S*,*S*-dioxide that does not involve the oxidation of the thiophene, and could therefore tolerate the presence of oxidation-sensitive function groups. This method would also be significantly more step- and atom-economical than those previously known. There are many different ways to go about such a reaction, but, for a method that would be easily amenable to polymerization in the interest of thiophene-*S*,*S*-dioxides for electronic applications, a two or three component reaction

that would form a new C-C bond would be most useful. A formal [2+2+1] reaction between two alkynes (or a suitable diyne) and SO_2 (or surrogate) was envisioned. (Scheme 20)



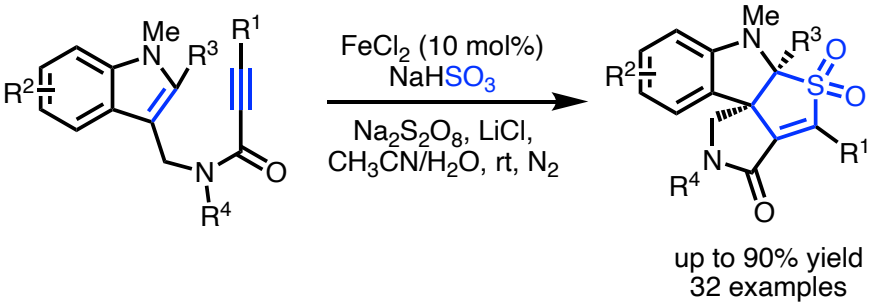
Scheme 20: Envisioned formal [2+2+1] with two alkynes and sulfur dioxide (*via* an SO_2 surrogate) for the synthesis of a thiophene-*S*,*S*-dioxide.

In an effort to facilitate such a reaction, a 1,7-diarylhepta-1,6-diyne motif was chosen to minimize the number of components required for the reaction. In addition to this, disubstitution at the 4-position of the diyne was desirable, as this was expected to increase the rate of a cyclization reaction via the Thorpe-Ingold effect.[58] Finally, as the SO_2 surrogate, a metal disulfite, specifically, sodium metabisulfite, was chosen, as these metal sulfite and disulfite salts are more easily accessible and environmentally benign than other sulfur dioxide surrogates.

3.3 Screening of Transition Metals

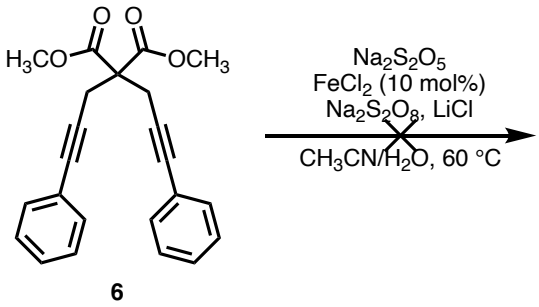
3.3.1 Iron

Yin and coworkers have recently reported the formal [2+2+1] of an enyne system with sodium bisulfite to produce a 5-membered cyclic sulfone under iron catalysis.[59] (Scheme 21) Since this was similar to the reactivity envisioned for the diyne systems chosen, iron was used as the starting point for these investigations.



Scheme 21: Formal [2+2+1] of enyne system with sodium bisulfite as the SO_2 surrogate to produce 5-membered cyclic sulfones.

Scheme 22 shows the reaction conditions employed with 1,7-diarylhepta-1,6-diyne **7**. Unfortunately, however, even after 48 hours, no new compounds could be observed by TLC.



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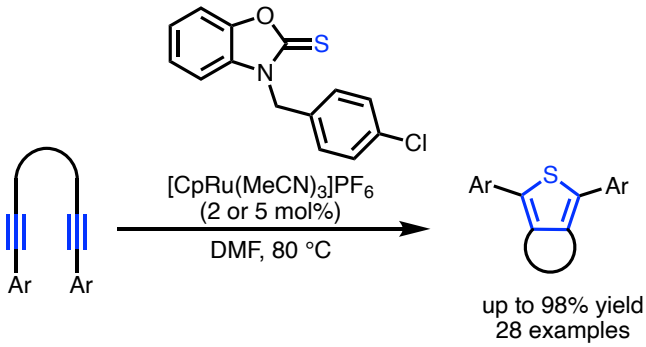
Scheme 22: Conditions employed for the unsuccessful formal [2+2+1] reaction attempt with iron.

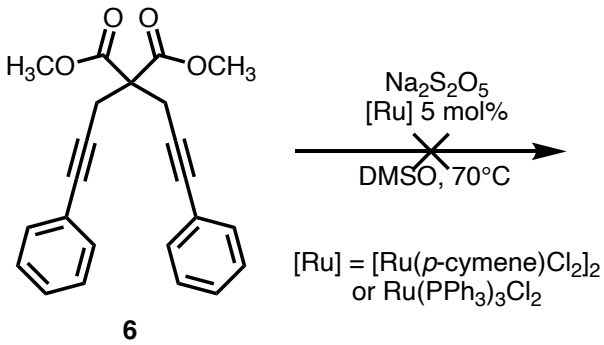
3.3.2 Ruthenium

Next, ruthenium was investigated, as Yamamoto and coworkers have reported its use in the production of fused thiophenes in a catalytic formal [2+2+1] from similar 1,7-diarylhepta-1,6-diyne systems through a proposed cationic ruthenacycle intermediate.[60] (Scheme 23)



Scheme 23: Synthesis of fused thiophenes *via* a catalytic formal [2+2+1] reaction.

It was questioned whether an SO_2 surrogate in a catalytic ruthenium system would allow for similar reactivity. Unfortunately, again, after subjecting **7** to the conditions shown in Scheme 24 for 24 hours, no new compounds could be observed by TLC.

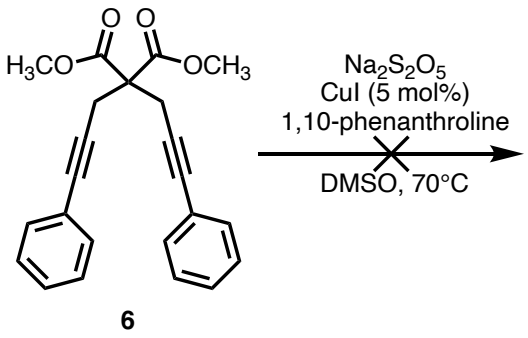


Scheme 24: Conditions employed for the unsuccessful formal [2+2+1] reaction attempt with ruthenium.

3.3.3 Copper and Palladium

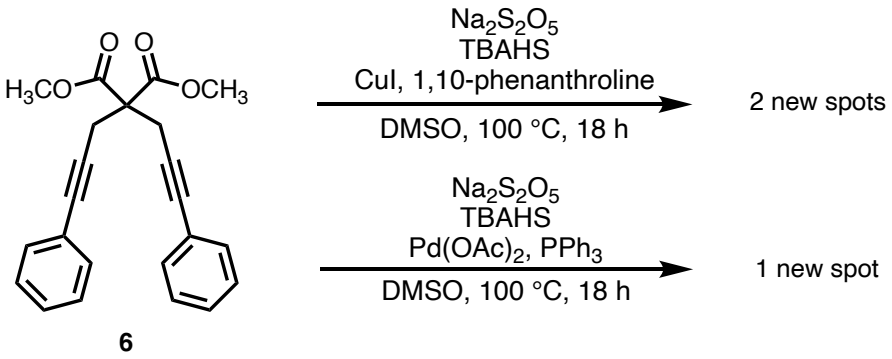
Copper and palladium are common metals used in transition metal catalyzed SO_2 insertion reactions.[56] Therefore, investigation of their potential role in these reactions was a natural next step in our efforts toward the synthesis of a thiophene-*S*,*S*-dioxide from an SO_2 source. Beginning

with copper, under the conditions shown in Scheme 25, no new compounds were observed. However, upon the addition of 1.75 equivalents tetrabutylammonium hydrogensulfate (TBAHS) as a phase transfer catalyst, and an increase in temperature to 100 °C, (Scheme 26) along with remaining starting material, the formation of two new compounds was observed by TLC. Small amounts of these compounds were isolated but ^{1}H nuclear magnetic resonance (NMR) spectra of these isolates did not appear to be those of pure single compounds, even after repeated column chromatography. Additionally, due to the small amounts of the compounds recovered, phthalate contamination from either the plastic tubing of the automatic flash columns, and/or the wash-grade solvents used in the purification appeared to be an issue.



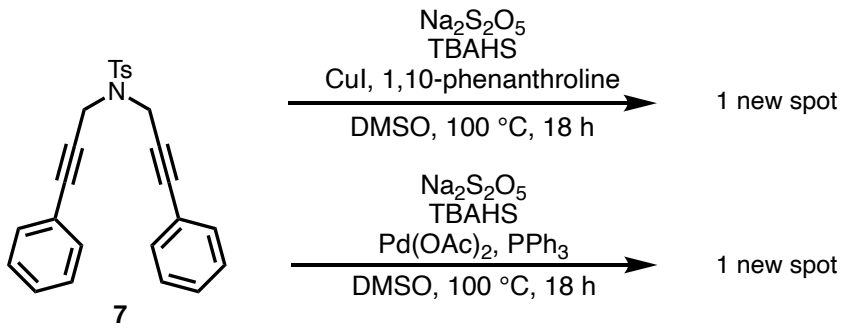
Scheme 25: Conditions employed for the unsuccessful formal [2+2+1] reaction attempt with copper.

Similar conditions were then employed switching out copper for palladium and 1,10-phenanthroline for triphenylphosphine. (Scheme 26) Unlike in the reaction with copper, the reaction with palladium produced only one new compound by TLC. Though similar to the case with copper, only small amounts of the diyne appear to have reacted, resulting in small amounts of this new compound that did not appear pure by ^{1}H NMR.



Scheme 26: Conditions employed for formal [2+2+1] reaction attempt with copper and palladium that showed partial conversion of the diyne staring material.

Nevertheless, encouraged by seeing some kind of reaction, the same conditions were applied to diyne **8**, in an effort to take advantage of the tosyl group for the crystallization of the new products in order to determine their identity by x-ray crystallography, as well as avoid the observed decarboxylation of the malonate diyne that was observed with that substrate. (Scheme 27) In the reaction with copper, along with starting material, one other compound was observed, while, under the palladium conditions, a different single product was observed by TLC. Upon isolation of these products by column chromatography (this time done manually in a glass column and using HPLC-grade solvents to avoid phthalate contamination), despite appearing pure by TLC using an ethyl acetate/hexanes mobile phase, these compounds still appeared to be quite impure by ^{1}H NMR, though did appear to be free of characteristic phthalate peaks.



Scheme 27: Employment of a second diyne starting material in the previously explored conditions.

In an effort to elucidate the structure of these impure compounds, gas chromatography-mass spectrometry (GC-MS) was performed. The chromatograms appeared to show that both of the materials contained mixtures, but had one obvious major component. Obtaining the electron ionization/electron impact (EI) mass spectra for the major components of each of the materials, molecular ion (M+) peaks for the for the components are 213.06 for the product of the copper reaction, and 201.95 for that of the reaction with palladium. While these masses do not correspond to the originally sought-after thiophene-*S*,*S*-dioxides, they may still be synthetically interesting, and therefore, further isolation and structural elucidation efforts were undertaken.

3.4 Isolation and Structural Elucidation Efforts for Products of Reactions with Copper and Palladium

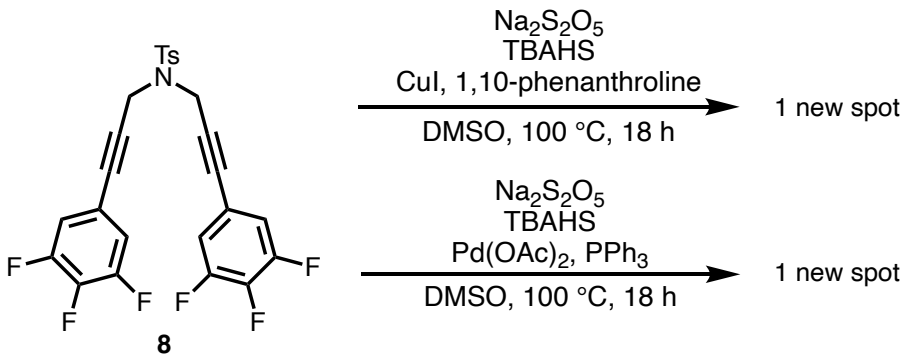
Upon further experimentation with different TLC mobile phases, a dichloromethane (DCM)/hexanes mobile phase revealed that the previously isolated material from the reaction with copper was actually a mixture three different components, while the material from the palladium reaction separated into two components. Isolation of the compounds from the

reaction with copper by column chromatography using a more suitable mobile phase provided two of the 3 compounds pure by ^{1}H NMR. For the material produced in the palladium reaction, only one of the two components have thus far been successfully isolated. Further structure elucidation and characterization of pure products including ^{13}C NMR, high resolution mass spectrometry (HRMS), and x-ray crystallography are ongoing.

In yet a further effort to elucidate the structures of the products of these reactions, the reactions were performed using a slightly derivatized version of **8**. Diyne **9** was chosen as it was anticipated that it could provide an easy way to identify some of the mass fragments from the EI mass spectra when compared to those previously obtained, while the trifluoro substitution on the diyne would help to "clean up" the aromatic region of the ^{1}H NMR spectra by reducing the number of aromatic protons, while also shielding the remaining aromatic protons on the attached benzene rings, moving them upfield from potentially important new or changed aromatic peaks of the products.

Upon subjection of **9** to the copper reaction conditions, (Scheme 28) along with the expected unreacted starting material, a single compound was isolated as a white solid after only a single column chromatographic separation that was pure by ^{1}H NMR. Next steps for this product include obtaining the ^{13}C NMR and HRMS spectra and, if possible, x-ray crystallography.

As for the reaction with palladium, (Scheme 28) three new products were observed by TLC. However, they have thus far not been able to be isolated due to difficulties with coelution.

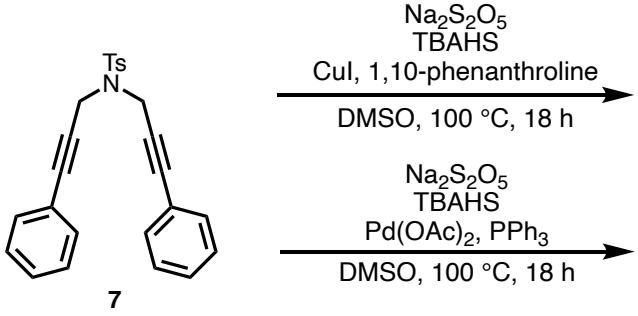


Scheme 28: Employment of a third diyne starting material in the previously explored conditions.

3.5 Investigation of Copper and Palladium Reaction Conditions

In an effort to gain insight into these observed reactions, small scale control reactions of **8** were run excluding any of: the metal, ligand, or sodium metabisulfite. Upon the completion of the reaction time, the reaction mixture was analyzed by TLC using an ethyl acetate/hexanes mobile phase and compared to that of the previous analogous reaction. The results of these comparisons are presented in Table 3.

Table 3: Results of systematic omission of the metal, ligand, and sodium metabisulfite in the reaction conditions under investigation. E_{Cu} is the expected product of the reaction with copper, E_{Pd} is the expected product of the reaction with palladium, and A & B are unknown products not previously observed.



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	Copper	**Palladium**
No Metal	E_{Cu}	B
No Ligand	E_{Cu} + A	E_{Pd} + B
No Sodium Metabisulfite	A	B

These results indicate that for the reaction with copper, the metal may not be necessary in the reaction, as the previously obtained product forms in its absence. As for the ligand in this reaction, when it is omitted, the previously obtained product still forms indicating that its presence may also not be necessary. Though it must also be noted that though the expected product forms in the absence of these two reaction components, they may still have an effect on the yield, as the products of these control reactions were not isolated. Additionally, the absence of the ligand appears to allow for the formation of a different product that is not observed in the initial reaction indicates that its presence may suppress the formation of this product. Finally, the fact that none of the previously obtained product from the reaction with copper forms in the absence of the sodium metabisulfite is an indication that the sodium metabisulfite is involved, and possibly even incorporated into the aforementioned product. It can also be noted that the product that does form in the absence of sodium metabisulfite appears to be the same as the

second product formed in the reaction when the ligand is omitted, indicating that this cannot include an SO_2 moiety or any other involvement from the sodium metabisulfite.

Moving on to the reaction with palladium, it does appear as though the metal is required for this reaction, as none of the previously obtained product forms in its absence. Instead, a new product that was not previously observed forms. The results for the ligand in the palladium reaction appear to be similar to that of the copper reaction; in the absence of the ligand, the expected product still forms, but another product is also allowed to form that isn't observed when the ligand is present. And once again, the sodium metabisulfite appears to be required for the formation of the previously obtained product, as none of said product forms in its absence. Finally, only the unexpected product from the previous two controls forms in the absence of the sodium metabisulfite, once again indicating that, like the analogous product from the copper reactions, this product does not incorporate SO_2, nor does it require any other feature of the metabisulfite in order to form.

3.6 Future Considerations

While it can be fairly concluded that this investigation did not yield the intended results, as is often the case in scientific research, there is still lots of potential for the detection of new and exciting chemistry. The first steps towards exploring this potential include the completion of the structural elucidation of at least the products that have been isolated thus far. Even better, would be to isolate the remaining observed products, and identify them as well. Any further work would

depend on the structures of these products, which will be treated as novel until proven otherwise.

Conclusion

The investigation into two potential new routes for the synthesis of thiophene-*S*,*S*-dioxide-based materials was undertaken. The first aimed to used 2,5-bis(diphenylcarbinol) substitution of the thiophene in order to both direct the oxidation and provide a handle for cross-coupling. Unfortunately, the oxidations showed no improvement in yield compared to previously reported techniques. Nevertheless, the desired thiophene-*S*,*S*-dioxide was able to be synthesized in sufficient amounts to allows for an attempt at the first *ipso*-arylative polymerization of a thiophene-*S*,*S*-dioxide. Disappointingly, none of the desired *ipso*-arylation product was detected in preliminary couplings, and control experiments gave strong evidence that thiophene-*S*,*S*-dioxides are unstable to the *ipso*-arylation conditions as they have been previously reported. From here, it may be worthwhile to investigate whether the *ipso*-arylation can be performed under milder conditions that would tolerate these thiophene-*S*,*S*-dioxides, as well as other sensitive substrates.

The second route proposed for the synthesis of thiophene-*S*,*S*-dioxides differs from those known previously, as it does not involve the oxidation of a thiophene or a thiophene-*S*-oxide. It looked to amend some of the SO_2 surrogate and SO_2 insertion chemistry that has accelerated in the last decade to the synthesis of thiophene-*S*,*S*-dioxides through a formal [2+2+1] between two alkynes and sulfur dioxide (*via* an SO_2 surrogate). Reactions of a 1,7-diarylhepta-1,6-diyne system with sodium metabisulfite in the presence of iron and ruthenium showed no conversion of the diyne. When copper was used, a similar situation was encountered, but upon the addition of a phase-transfer catalyst, some conversion of the diyne was observed. Similar conditions were applied to

a reaction in the presence of palladium, and conversion of the diyne was also observed. Difficulties with purification of the products and degradation of the diyne substrate led to the extension of these reactions to other diyne systems. Structural elucidation is ongoing, but the data collected thus far indicates that these products are not the desired thiophene-*S*,*S*-dioxides. Nonetheless, efforts to identify these products continue in the Schipper Group, as it is still unknown whether or not they indicate known reactivity.

Supporting Information

1 General Considerations

1.1 Materials & Instrumentation

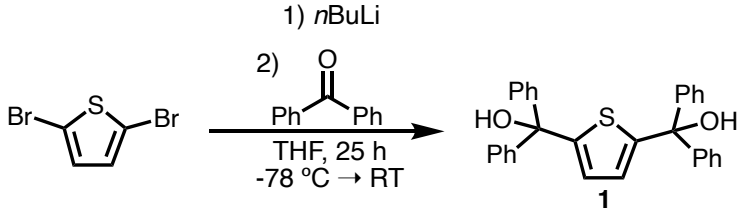
Dry tetrahydrofuran and triethylamine were obtained from a JC Meyer Solvent Systems' Pheonix Solvent Drying System. 4 Å molecular sieves were activated by heating at approximately 200 °C under vacuum overnight. *o*-Xylene was dried by treatment with these activated molecular sieves and then degassed by placing under dynamic vacuum until bubbling had ceased. *m*CPBA was purchased from Sigma-Aldrich in ≤ 77% purity and used without further purification.

^{1}H NMR spectra were recorded at room temperature on a Brüker AVANCE300 (300 MHz) δ or Brüker AC300 (300 MHz) δ spectrometer. ^{13}C NMR spectra were broad band decoupled and recorded on a Brüker AVANCE300 (75.5 MHz) δ or Brüker AC300 (75.5 MHz) δ spectrometer. Chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in $CDCl_3$ (δ 7.26), acetone-d_6 (δ 2.05), or DMSO-d_6 (δ 2.50) in ^{1}H NMR or the carbon signal of the deuterated solvent ($CDCl_3$, δ 77.0) in ^{13}C NMR. High resolution mass spectra (HRMS) were obtained by electrospray ionization recorded on a Thermo Scientific Q ExactiveTM Plus Hybrid Quadrupole-OrbitrapTM. Gas chromatography-mass spectrometry (GC-MS) was performed and recorded on an Agilent 5975B GC/MS.

2 Experimental procedures

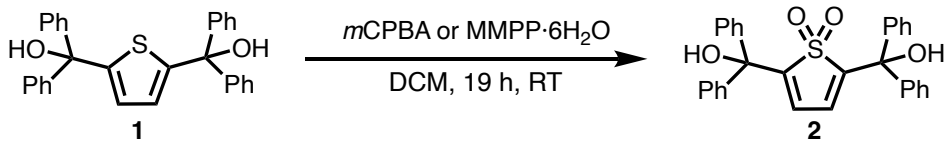
2.1 Synthesis and Oxidation of 2,5-bis(hydroxydiphenylmethyl)thiophene

2.1.1 Synthesis of 2,5-bis(hydroxydiphenylmethyl)thiophene (**1**)



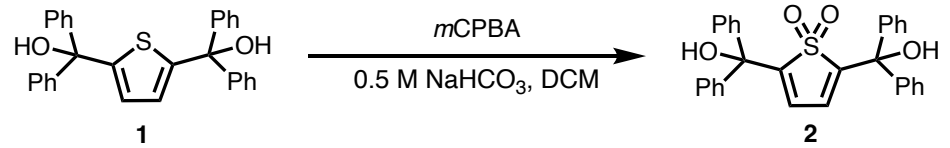
To an argon-purged oven-dried vial containing 50 mL of dry tetrahydrofuran, were added 0.5 mL (4.4 mmol) of 2,5-dibromothiophene. This mixture was then stirred and cooled in a -78 °C bath. 6.0 mL (9.6 mmol, 2.2 eq) of a 1.6 M solution of *n*-butyllithium in hexanes were then added, dropwise, to the stirring solution. The resulting pale-yellow solution was then stirred at -78 °C for 1 h. After this time, 1.786 g (9.8 mmol, 2.2 eq) of benzophenone were added in one portion and the solution was then stirred and warmed to room temperature over 25 hours. The reaction was quenched with sat. NH_4Cl. The product was extracted with 3 times with dichloromethane. The combined organic fractions were washed with brine and dried over $MgSO_4$ and then concentrated *in vacuo*. The product was purified by column chromatography using a gradient of 0 to 35% ethyl acetate in hexanes resulting in an off-white powder. 0.961 g (48%); R_f = 0.65 (30% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.39-7.27 (m, 20H), 6.55 (s, 2H), 2.89 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 152.1, 146.3, 128.0, 127.6, 127.2, 126.3, 80.1; HRMS calculated for $C_{30}H_{23}OS$ $[M\text{-}OH]^+$ 431.1464 and $NaC_{30}H_{24}O_2S$ $[M+Na]^+$ 471.1389; Found: 431.1465 and 471.1388.

2.1.2 Oxidations of 2,5-bis(hydroxydiphenylmethyl)thiophene with mCPBA and MMPP



In a dark environment, 100 mg (0.22 mmol) of **1** were dissolved in 8 mL of dichloromethane in an opaque vessel. 168 mg (0.75 mmol, 3.4 eq) of *m*CPBA were added to this stirring solution in three portions over 40 minutes or 426 mg (3.0 eq) of MMPP·$6H_2O$ were added all in one portion. The reaction vessel was capped and stirred for 19 hours at room temperature. In the case of the *m*CPBA oxidations, the reaction solution was concentrated *in vacuo*. The resulting solid was purified by column chromatography using a gradient of 0 to 50% ethyl acetate in hexanes. The resulting slightly impure product was recovered in approximately 20% yield.

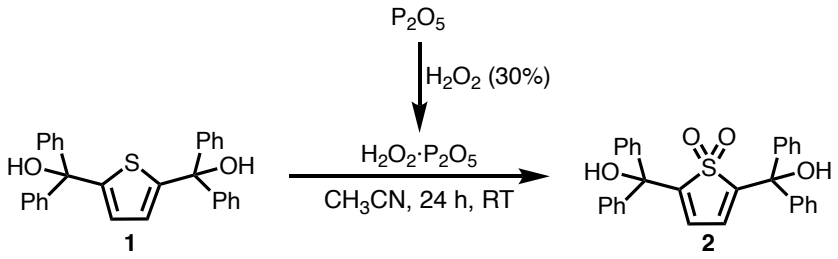
2.1.3 Buffered Oxidations 2,5-bis(hydroxydiphenylmethyl)thiophene with mCPBA



To a solution of 448 mg (1.0 mmol) of **1** in 35 mL of dichloromethane and 17 mL of a 0.5 M aqueous solution of $NaHCO_3$ were added 453 mg (2.0 mmol, 2.0 eq) of *m*CPBA in a single portion. The reaction vessel was capped and either stirred for 19 hours, or sonicated for 90 minutes at room temperature, venting the vessel every 10 minutes of the last 30 minutes of sonication to prevent pressure buildup. The phases of the resulting solution were separated, and the organic phase was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The resulting solid

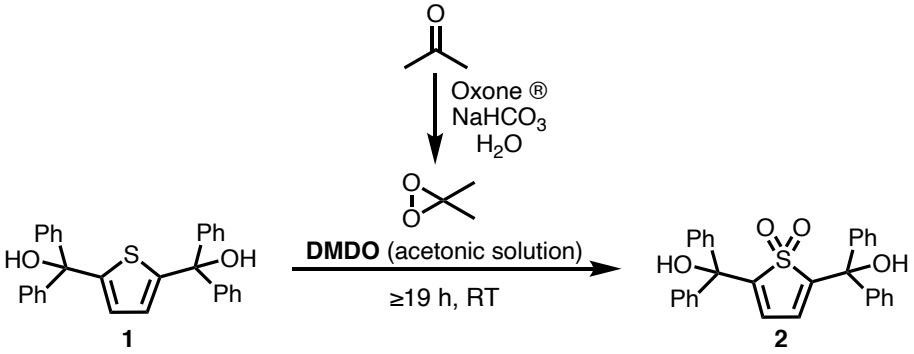
was purified by column chromatography using a gradient of 0 to 40% ethyl acetate in hexanes to give the off-white solid product. Stirring: 0.098 g (21%), Sonication: 0.220g (47%).

2.1.4 Oxidations of 2,5-bis(hydroxydiphenylmethyl)thiophene with Peroxymonophosphoric Acid

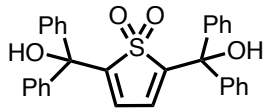


A solution of $H_2O_2{\cdot}P_2O_5$ was prepared according to a modified literature procedure.[50] To a flask of 20.02 g of phosphorus pentoxide, in an ice bath, was added 90 mL of cold 30% H_2O_2, dropwise with intermittent stirring and scraping of the bottom of the flask to break up large chunks of solid. The solution was then transferred to a 100 mL volumetric flask, and the volume was completed with the cold H_2O_2 solution. The concentration of peroxymonophosphoric acid was titrated by addition of 0.10 mL of the solution to a solution of 0.05 mL of thioanisole in 1.0 mL of CD_3CN. After 5 minutes, the ^1H NMR of this solution was obtained, and the ratio of the oxidized thioanisole to the non-oxidized was used to determine the concentration the solution to be 0.72 M. This solution was then stored in a refrigerator at approximately 5 °C and used in the oxidation of 2,5-bis(hydroxydiphenylmethyl)thiophene within two weeks of preparation by addition of 0.95 mL of the 0.72 M (0.68 mmol, 2 eq) peroxymonophosporic acid solution to a stirring solution of 160 mg (0.36 mmol) of **1** in 4 mL of acetonitrile. The resulting solution was stirred for 24 h at room temperature and monitored by TLC using 30% ethyl acetate in hexanes. The observed product was observed as a faint spot by TLC, but could not be isolated from the reaction mixture.

2.1.5 Oxidations of 2,5-bis(hydroxydiphenylmethyl)thiophene with DMDO



DMDO was prepared by adding 25 g of Oxone®, monopersulfate compound to a stirring solution of 24 g of sodium bicarbonate in 30 mL of acetone and 20 mL of water at 0 °C. The resulting slurry was then subject to vacuum distillation using an aspirator at -78°C until the stirring reaction solution ceased foaming (approximately 1.5 h). The resulting distillate, an acetonic solution of DMDO, was titrated by addition of 1.0 mL of this solution to a solution of 0.03 mL of thioanisole in 0.4 mL of acetone-d_6. After sitting for at least 5 minutes, the ^{1}H NMR of this solution was obtained, and the ratio of the oxidized to the non-oxidized thioanisole was used to determine the concentration of DMDO in the distillate. Typical concentrations were in the range of 20-40 mM. The remainder of the distillate was then used immediately in the oxidation of 2,5-bis(hydroxydiphenylmethyl)thiophene by direct addition of the solution to solid 2,5-bis(hydroxydiphenylmethyl)thiophene in a 1:1.4 ratio of compound **1** to DMDO, and stirring at room temperature for at least 19 hours. If large quantities of oxidized product **2** were needed, multiple batches of DMDO were added sequentially in 1.5 h increments. After addition of the final batch, the reaction solution was stirred for an additional 19 h. After this time, the reaction solution was concentrated *in vacuo* and then purified by column chromatography using a gradient of 0 to 50% ethyl acetate in hexanes. The resulting solid was then washed twice with small amounts of cold hexanes to yield the off-white solid product in up to 69% yield.

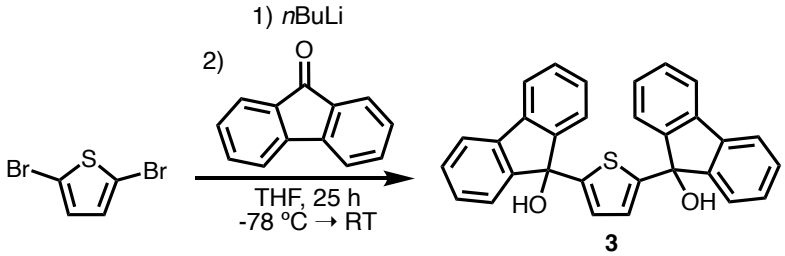


2

2,5-bis(hydroxydiphenylmethyl)thiophene-*S,S*-dioxide (**2**): R_f = 0.40 (30% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.45-7.31, (m, 20H), 6.14 (s, 2H), 3.76 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 147.9, 142.5, 128.3, 128.3, 127.1, 126.4, 79.7; HRMS calculated for $C_{30}H_{23}O_3S$ $[M\text{-}OH]^+$ 463.1362; Found: 463.1361.

2.2 Synthesis and Oxidation of 9,9'-(thiophene-2,5-diyl)bis(9H-fluoren-9-ol)

*2.2.1 Synthesis of 9,9'-(thiophene-2,5-diyl)bis(9H-fluoren-9-ol) (**3**)*

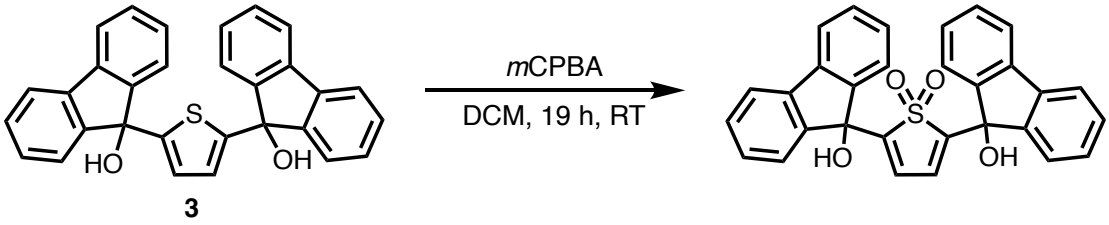


3

In an analogous method to the preparation of compound **1**, 1.0 mL (8.8 mmol) of 2,5-dibromothiophene were added to an argon-purged, oven-dried vial containing 50 mL of dry tetrahydrofuran. This mixture was then stirred and cooled to -78 °C. 12.0 mL (19.2 mmol, 2.2 eq) of a 1.6 M of *n*-butyllithium in hexanes were then added, dropwise, to the stirring solution. The resulting pale-yellow solution was then stirred at -78 °C for 1 h. After this time, 3.682 g (9.8 mmol, 2.2 eq) of 9-fluorenone were then added in one portion and the resulting solution was then stirred and warmed to room temperature over 25 hours. After this time, the reaction was quenched with sat. NH_4Cl. The product was extracted 3 times with dichloromethane. The

combined organic fractions were washed with brine and dried over $MgSO_4$, and then concentrated *in vacuo*. The product was purified by column chromatography using a gradient of 0 to 50% ethyl acetate in hexanes. 0.768 g (19%); R_f = 0.40 (30% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.63 (d, *J* = 7.3 Hz, 4H), 7.58 (d, *J* = 7.1 Hz, 4H), 7.39-7.27 (m, 8H), 6.45 (s, 2H), 2.60 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 148.7, 146.9, 139.2, 129.4, 128.3, 124.9, 123.6, 120.1, 82.19; HRMS calculated for $C_{30}H_{19}OS$ $[M\text{-}OH]^+$ 427.1151; Found: 427.1154.

2.2.2 Oxidation of 2,5-bis(9H-fluoren-9-ol)thiophene with mCPBA

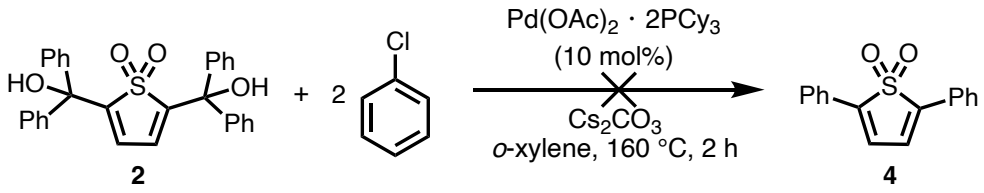


3

83 mg (0.37 mmol, 3.1 eq) of *m*CPBA were added to a stirring solution of 53 mg (0.12 mmol) of **3** in 8 mL of dichloromethane. The resulting solution was stirred at room temperature for 19 hours. After this time, the reaction mixture was analyzed by TLC (30% ethyl acetate in hexanes) and a potential product spot, along with several other unknown spots, was observed, but was not able to be isolated by column chromatography.

2.3 *ipso*-Arylation

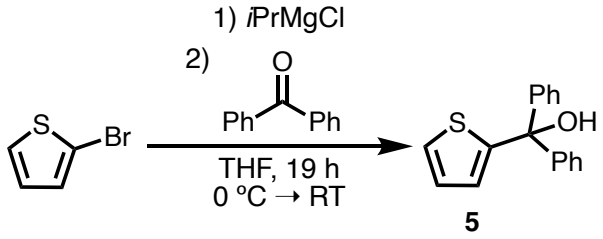
2.3.1 ipso-Arylation Procedure



A microwave vial containing a stir bar and 653 mg (2.0 mmol, 4 eq) of anhydrous Cs_2CO_3 was dried in a vacuum oven at 150 °C for 2 hours. After this time, the vial was removed from the oven and cooled slightly before 241 mg (0.50 mmol) of compound **2**, 12 mg (0.05 mmol, 0.1 eq) of $Pd(OAc)_2$, and 40 mg (0.1 mmol, 0.2 eq) of $PCy_3{\cdot}HBF_4$ were added. The vial was then sealed, purged with argon, and allowed to cool to room temperature. 10 mL of dry, degassed *o*-xylene was then syringed in, followed by 0.20 mL (2.0 mmol, 4 eq) of chlorobenzene. The reaction solution was stirred and heated to 160 °C for 2 hours and then cooled to room temperature. 30 mL of water was added to the reaction mixture, which was then extracted 3 times with dichloromethane, washed with brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The resulting brown oil was purified by column chromatography using a gradient of 0 to 30% ethyl acetate in hexanes. 117 mg (64%) of benzophenone were recovered.

2.3.2 ipso-Arylation Control Experiments

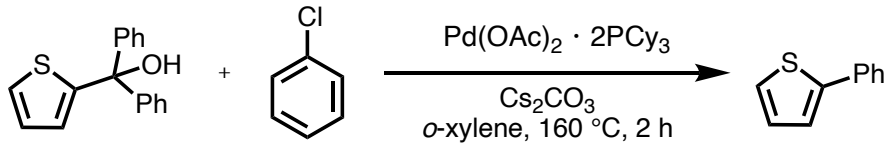
2.3.2.1 Synthesis of 2-(hydroxydiphenylmethyl)thiophene (**5**)



5

To a sealed argon-purged oven-dried vial containing 8 mL of dry tetrahydrofuran, were added 0.48 mL (5.0 mmol) of 2-bromothiophene. This solution was stirred and cooled in a 0 °C bath. 3.0 mL (6.0 mmol, 1.2 eq) of a 2.0 M solution of *i*PrMgCl were then added, dropwise, to the stirring solution. The ice-water bath was then removed and the resulting solution was stirred at room temperature for 30 minutes. After this time, the solution was once again cooled in an ice-water bath, and 1.051 g (5.8 mmol, 1.2 eq) of benzophenone were added. The resulting solution was removed from the ice-water bath and stirred at room temperature for 19 hours. After this time, the reaction was quenched with sat. NH_4Cl. The product was extracted 3 times with dichloromethane. The combined organic fractions were washed with brine and dried over $MgSO_4$ and then concentrated *in vacuo*. The product was purified by column chromatography using a gradient of 0 to 5% ethyl acetate in hexanes. 1.022 g (77%); R_f = 0.65 (20% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.30-7.16 (m, 11H), 6.85 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.63 (dd, *J* = 3.6, 1.3 Hz, 1H), 2.86 (s, 1H). Recorded data is consistent with that previously reported.[61]

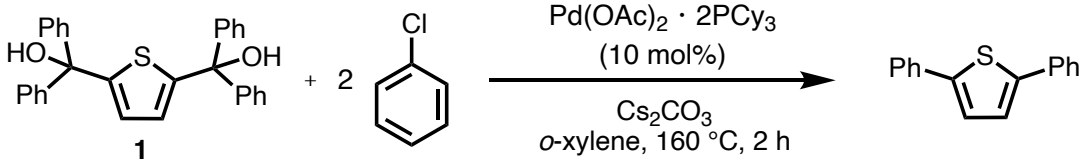
2.3.2.2 *ipso*-Arylation of 2-(hydroxydiphenylmethyl)thiophene



5

A microwave vial containing a stir bar and 326 mg (1.0 mmol, 1.9 eq) of anhydrous Cs_2CO_3 was dried in a vacuum oven at 150 °C for 2 hours. After this time, the vial was removed from the oven and cooled slightly before 135 mg (0.51 mmol) of **5**, 6 mg (0.003 mmol, 0.05 eq) of $Pd(OAc)_2$, and 19 mg (0.05 mmol, 0.1 eq) of $PCy_3{\cdot}HBF_4$ were added. The vial was then sealed, purged with argon, and allowed to cool to room temperature. 5 mL of dry, degassed *o*-xylene was then syringed in, followed by 0.10 mL (1.0 mmol, 1.9 eq) of chlorobenzene. The reaction solution was stirred and heated to 160 °C for 2 hours, and then cooled to room temperature. 15 mL of water was added to the reaction mixture, which was then extracted with 3 times with dichloromethane, washed with brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The resulting brown oil was purified by column chromatography using a gradient of 0 to 15% ethyl acetate in hexanes. 61 mg (74%) of 2-phenylthiophene and 74 mg (79%) of benzophenone were recovered.

2.3.2.3 *ipso*-Arylation of 2,5-bis(hydroxydiphenylmethyl)thiophene



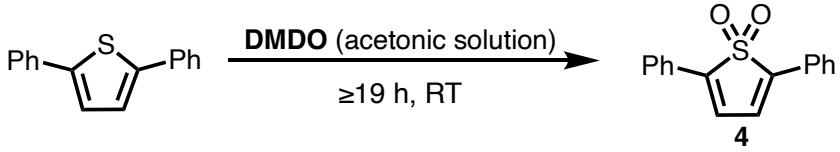
1

A microwave vial containing a stir bar and 660 mg (2.0 mmol, 4 eq) of anhydrous Cs_2CO_3 was dried in a vacuum oven at 150 °C for 2 h. After this time, the vial was removed from the oven and cooled slightly before 227 mg (0.50 mmol) of compound **1**, 12 mg (0.05 mmol, 0.1 eq) of $Pd(OAc)_2$, and 38 mg (0.1 mmol, 0.2 eq) of $PCy_3{\cdot}HBF_4$ were added. The vial was then sealed, purged with

argon, and allowed to cool to room temperature. 10 mL of dry, degassed *o*-xylene was then syringed in, followed by 0.20 mL (2.0 mmol, 4 eq) of chlorobenzene. The reaction solution was stirred and heated to 160 °C for 2 h and then cooled to room temperature. 30 mL of water was added to the reaction mixture, which was then extracted 3 times with dichloromethane, washed with brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The resulting brown oil was purified by column chromatography using a gradient of 0 to 30% ethyl acetate in hexanes. 69 mg (59%) of 2,5-diphenylthiophene and 182 mg (100%) of benzophenone were recovered.

2.3.2.4 Exposure of Thiophene-*S*,*S*-Dioxides to *ipso*-Arylation Conditions

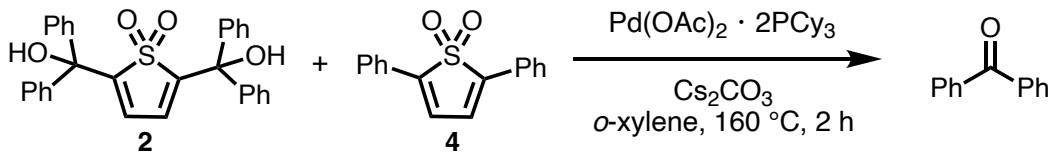
2.3.2.4.1 Synthesis of 2,5-diphenylthiophene-*S*,*S*-dioxide (**4**)



4

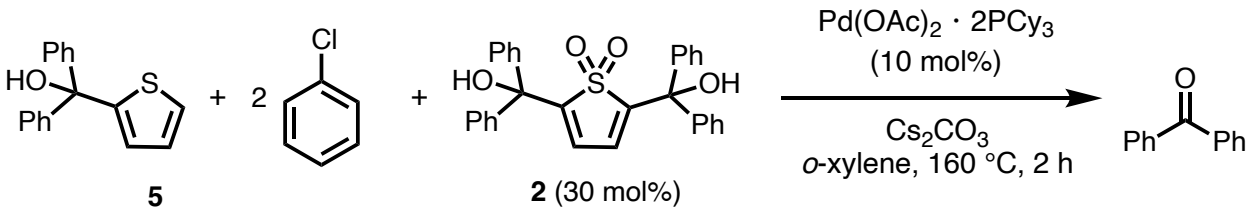
To a stirring solution of 236 mg of **1** in dichloromethane was added 11 mL of a 0.72 M (0.79 mmol, 3.9 eq) of a DMDO solution in acetone. The reaction flask was capped and stirred at room temperature for 19 hours. The solvent was then removed *in vacuo* and the resulting yellow solid was purified by column chromatography using a gradient of 0 to 50% ethyl acetate in hexanes. R_f = 0.60 (30% ethyl acetate in hexanes) ^{1}H NMR data was collected in DMSO-d_6 and was consistent with that previously reported.[33] Data is reported in $CDCl_3$ for consistency between substrates presented here. ^{1}H NMR (300 MHz, $CDCl_3$) 7.81-7.77 (m, 4H), 7.51-7.41 (m, 6H), 7.03 (s, 2H).

2.3.2.4.2 Exposure of Thiophene-*S*,*S*-Dioxides to *ipso*-Arylation Conditions



A microwave vial containing a stir bar and 66 mg (0.20 mmol, 4 eq) of anhydrous Cs_2CO_3 was dried in a vacuum oven at 150 °C for 2 h. After this time, the vial was removed from the oven and cooled slightly before 24 mg (0.05 mmol) of compound **2**, 15 mg (0.05 mmol) of compound **4**, 1 mg (0.005 mmol, 0.1 eq) of $Pd(OAc)_2$, and 4 mg (0.2 mmol, 0.2 eq) of $PCy_3{\cdot}HBF_4$ were added. The vial was then sealed, purged with argon, and allowed to cool to room temperature. 1 mL of dry, degassed *o*-xylene was then syringed in. The reaction solution was stirred and heated to 160 °C for 2 h and then cooled to room temperature. TLC using a mobile phase 20% ethyl acetate in hexanes showed no indication of the presence of compounds **2** or **4** but did show the presence of benzophenone.

2.3.2.4.3 Poisoning of *ipso*-Arylation of 2-(hydroxydiphenylmethyl)thiophene

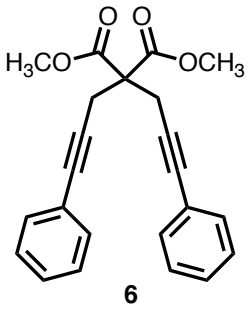


A microwave vial containing a stir bar and 326 mg (1.0 mmol, 1.9 eq) of anhydrous Cs_2CO_3 was dried in a vacuum oven at 150 °C for 2 hours. After this time, the vial was removed from the oven and cooled slightly before 135 mg (0.51 mmol) of **5**, 73 mg (0.15 mmol, 0.30 eq) of **2**, 6 mg (0.003 mmol, 0.05 eq) of $Pd(OAc)_2$, and 19 mg (0.05 mmol, 0.1 eq) of $PCy_3{\cdot}HBF_4$ were added. The vial was then sealed, purged with argon, and allowed to cool to room temperature. 5 mL of dry,

degassed *o*-xylene was then syringed in, followed by 0.10 mL (1.0 mmol, 1.9 eq) of chlorobenzene. The reaction solution was stirred and heated to 160 °C for 2 hours, and then cooled to room temperature. The reaction mixture was analyzed by TLC using a mobile phase of 10% ethyl acetate in hexanes.

2.4 Synthesis of Diynes

2.4.1 Dimethyl 2,2-bis(3-phenylprop-2-yn-1-yl)malonate (**6**)

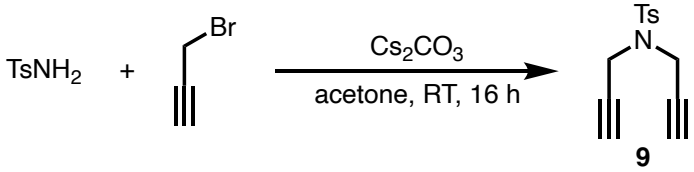


6

Dimethyl 2,2-bis(3-phenylprop-2-yn-1-yl)malonate was prepared by Ruihao Li according to a previously reported literature procedure from the Schipper Group[62] and used as received.

2.4.2 4-Methyl-N,N-di(prop-2-yn-1-yl)benzenesulfonamide-Based Diynes

2.4.2.1 Synthesis of 4-methyl-N,N-di(prop-2-yn-1-yl)benzenesulfonamide (**9**)



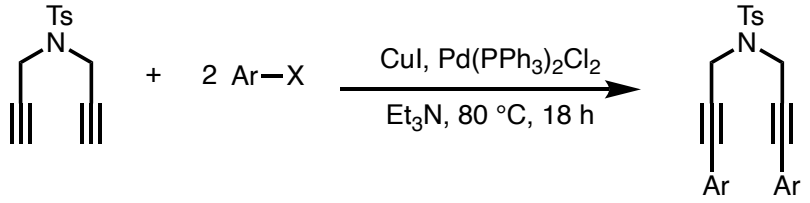
9

4-Methyl-*N*,*N*-di(prop-2-yn-1-yl)benzenesulfonamide was prepared according to a modified literature procedure.[63] 2.5 mL of propargyl chloride (35 mmol, 3.0 eq) were added to a stirring solution of 2.0 g (12 mmol) of *p*-toluenesulfonamide and 11.5 g (35 mmol, 3.0 eq) of Cs_2CO_3 in 50

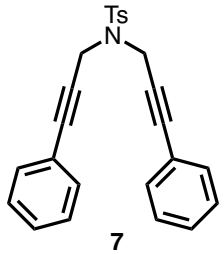
mL of acetone. After stirring at room temperature for 19 hours, the acetone was removed *in vacuo*. The resulting solid was dissolved in 50 mL of distilled water and extracted twice with dichloromethane. The combined dichloromethane fractions were washed with brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The orange oil was purified by column chromatography using a gradient of 0 to 35% ethyl acetate in hexanes resulting in a white crystalline solid. 2.485 g (86%); R_f = 0.60 (30% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.72 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.17 (d, *J* = 2.4 Hz, 4H), 2.43 (s, 3H), 2.15 (t, *J* = 2.4 Hz, 2H). Recorded data is consistent with that previously reported.[63]

2.4.2.2 Sonogashira Reactions of 4-methyl-N,N-di(prop-2-yn-1-yl)benzenesulfonamide

General Sonogashira Reaction Procedure (GP1):

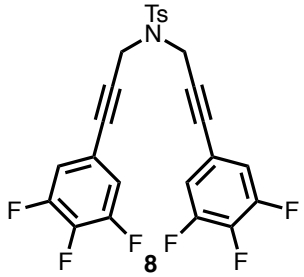


The sonogashira reactions of the diynes was adapted from a literature procedure.[62] $Pd(PPh_3)_2Cl_2$ (88 mg, 0.12 mmol, 0.05 eq), CuI (48 mg, 0.25 mmol, 0.10 eq), and **9** (618 mg, 2.5 mmol) were added to a flame-dried round bottom flask, which was then capped with a rubber septum and purged with argon. 25 mL of dry triethylamine were then syringed in, followed by the aryl halide (6.25 mmol, 2.5 eq). The reaction mixture was stirred at 80 °C for 18 h. After cooling to room temperature, the reaction mixture was filtered through celite and rinsed with 25 mL of diethyl ether. The solvent was then removed *in vacuo* and the resulting material was purified by column chromatography to afford pure compounds **7** and **8**.



7

4-methyl-*N*,*N*-bis(3-phenylprop-2-yn-1-yl)benzenesulfonamide (**7**): Prepared according to GP1 using 1.4 mL of iodobenzene. Column chromatography performed with a gradient of 0 to 20% ethyl acetate in hexanes to afford an off-white crystalline solid. 998 mg (50%); R_f = 0.60 (30% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.80 (d, *J* = 8.3 Hz, 2H), 7.28-7.21 (m, 12H), 4.05 (s, 4H), 2.32 (s, 3H). Recorded data is consistent with that previously reported.[64]



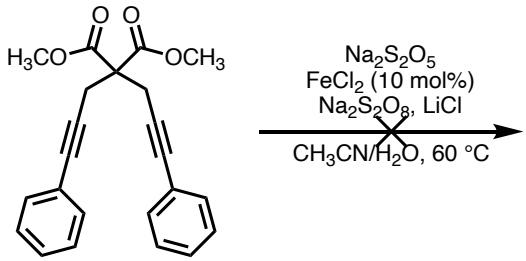
8

4-methyl-*N*,*N*-bis(3-(3,4,5-trifluorophenyl)prop-2-yn-1-yl)benzenesulfonamide (**8**): Prepared according to GP1 with the removal of the argon balloon after purging to prevent the evaporation of the 0.75 mL of 5-bromo-1,2,3,-trifluorobenzene. Column chromatography performed with a gradient of 0 to 40% ethyl acetate in hexanes to afford an off-white crystalline solid. 0.486 g (38%); R_f = 0.75 (30% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.79 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.84-6.73 (m, 4H), 4.41 (s, 4H), 2.42 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 150.8 (ddd, $^1J_{CF}$ = 251.1 Hz, $^2J_{CF}$ = 10.3 Hz, $^3J_{CF}$ = 4.4 Hz), 144.2, 140.5 (dt, $^1J_{CF}$ = 256.0 Hz, $^2J_{CF}$ = 15.2

Hz), 135.4, 129.7, 128.0, 117.8 (td, , $^{3}J_{CF}$ = 10.2 Hz, $^{4}J_{CF}$ = 5.2 Hz), 116.3-115.7 (m), 83.4 (d, $^{5}J_{CF}$ = 2.2 Hz), 82.9 ($^{4}J_{CF}$ = 6.2 Hz, $^{5}J_{CF}$ = 3.0 Hz) HRMS calculated for $C_{25}H_{16}F_6NO_2S$ $[M+H]^+$: 508.0800; Found: 508.0799.

2.5 Screening of Transition Metals for Proposed Formal [2+2+1]

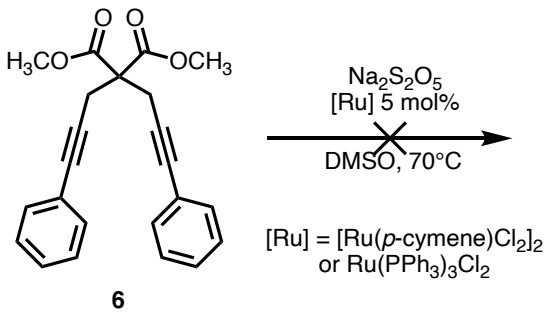
2.5.1 Iron



6

In a microwave vial containing 68 mg (0.2 mmol) of **6**, 4 mg (0.03 mmol, 0.1 eq) of $FeCl_2$, 112 mg (0.6 mmol, 3 eq) of $Na_2S_2O_5$, 97 mg (0.4 mmol, 2 eq) of $Na_2S_2O_8$, and 19 mg (0.4 mmol, 2 eq) of LiCl, were added 0.5 mL of water and 1.5 mL of acetonitrile. The vial was capped and stirred at 60 °C for 48 hours. The reaction was monitored by TLC using a 10% ethyl acetate in hexanes mobile phase, but no new compounds were observed.

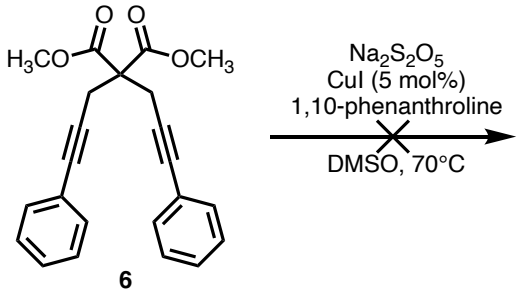
2.5.2 Ruthenium



In a microwave vial containing 109 mg (0.3 mmol) of **6**, 230 mg (1.2 mmol, 4 eq) of $Na_2S_2O_5$, and 9 mg (0.015 mmol, 0.05 eq) of $[Ru(p\text{-cymene})Cl_2]_2$ or 14 mg (0.015 mmol, 0.05 eq) of $Ru(PPh_3)_3Cl_2$, were added 2 mL of dimethyl sulfoxide. The resulting solution was stirred at 70 °C for 24 hours. The reaction was monitored by TLC using a 10% ethyl acetate in hexanes mobile phase, but no new compounds were observed.

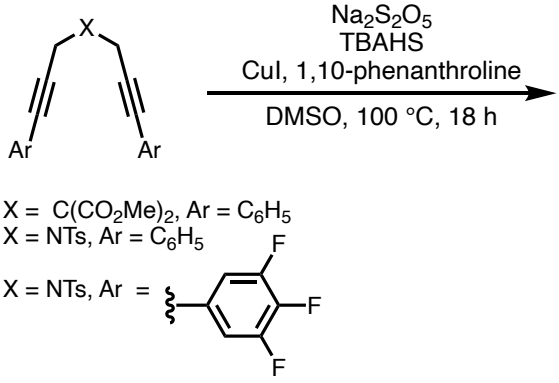
2.5.3 Copper

Without TBAHS:



In a microwave vial containing 109 mg (0.3 mmol) of **6**, 230 mg (1.2 mmol, 4 eq) of $Na_2S_2O_5$, 3 mg (0.015 mmol, 0.05 eq) of CuI, and 8 mg (0.045 mmol, 0.15 eq) of 1,10-phenanthroline, were added 2 mL of dimethyl sulfoxide. The resulting solution was stirred at 70 °C for 24 hours. The reaction was monitored by TLC using a 10% ethyl acetate in hexanes mobile phase, but no new compounds were observed.

General Procedure with TBAHS (GP2):



In a microwave vial containing 1.00 mmol of the diyne, 595 mg (1.75 mmol, 1.75 eq) of tetrabutylammonium hydrogensulfate, 3334 mg (1.75 mmol, 1.75 eq) of $Na_2S_2O_5$, 10 mg (0.05 mmol, 0.05 eq) of CuI, and 36 mg (0.20 mmol, 0.20 eq) of 1,10-phenanthroline, were added 5 mL of dimethyl sulfoxide. The vial was capped and the solution within was stirred at 100 °C for 18 hours. After this time, 30 mL of water were added to the reaction solution. The resulting solution was extracted 5 times with ethyl acetate. The combined organic fractions were then washed 4 times with water. The combined aqueous fractions were back extracted with ethyl acetate. All organic fractions were then combined and washed with brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The resulting crude yellow oil was purified by column chromatography using a gradient of 0 to 30% ethyl acetate in hexanes.

Reaction with **6**:

The reaction was run according to GP2 using 361 mg of **6**. Two new species were recovered from the column; 0.046 g and 0.026 g of two distinct orange oils were obtained; ^{1}H NMR spectra of these oils are available in section 3 but were not clean.

Reaction with **7**:

The reaction was run according to GP2 using 400 mg of **7**. 0.107 g of a yellow oily solid were obtained. R_f = 0.45 (30% ethyl acetate in hexanes); The resulting material from this column was then subject to GC-MS in an effort to determine the identity. (M^+ = 213.06) The remaining material from the first column was once again subject to column chromatography using 70% DCM in hexanes. 3 components were recovered from this column:

0.031 g of a yellow solid; R_f = 0.65 (80% DCM in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.84 (s, 1H), 7.77 (s, 1H), 7.74 (s, 1H), 7.61-7.54 (m, 3H), 7.51-7.29 (m, 7H), 7.09 (dd, *J* = 8.1 , 1.6 Hz), (4.68 (s, 2H), 2.49 (s, 3H).

0.011 g of a yellow solid; R_f = 0.55 (80% DCM in hexanes); ^{1}H NMR spectrum available in section 3 but was not clean.

0.071 g of a yellow oil; R_f = 0.65 (80% DCM in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.68 (d, *J* = 7.8 Hz, 4H), 7.51 (d, *J* = 13.9 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.30-7.20 (m, integration unclear due to residual $CDCl_3$), 7.11 (d, *J* = 6.6 Hz, 2H), 2.36 (s, 3H), 2.19 (s, 3H).

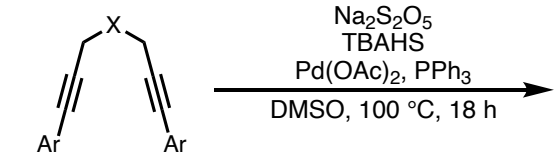
Reaction with **8**:

The reaction was run according to GP2 using 507 mg of **8**. 0.041 g of an off-white solid were obtained. R_f = 0.40 (30% ethyl acetate in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) 7.74 (d, *J* = 8.3 Hz,

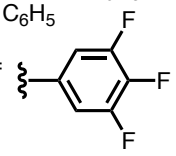
2H), 7.61 (s, 1H), 7.45-7.30 (m, 3H), 6.85 (dd, *J* = 7.5, 6.2 Hz, 2H), 4.76 (s, 2H), 4.35 (s, 2H), 2.41 (s, 3H).

2.5.4 Palladium

General Procedure for Diynes Reactions with Palladium (GP3):



6: X = $C(CO_2Me)_2$, Ar = C_6H_5
7: X = NTs, Ar = C_6H_5
8: X = NTs, Ar =



To a microwave vial containing 1.00 mmol of the diyne, 595 mg (1.75 mmol, 1.75 eq) of tetrabutylammonium hydrogensulfate, 3334 mg (1.75 mmol, 1.75 eq) of $Na_2S_2O_5$, 11 mg (0.05 mmol, 0.05 eq) of $Pd(OAc)_2$, and 39 mg (0.15 mmol, 0.15 eq) of triphenylphosphine, were added 5 mL of dimethyl sulfoxide. The vial was capped and the solution within was stirred at 100 °C for 18 hours. After this time, 30 mL of water were added to the reaction solution. The resulting solution was extracted 5 times with ethyl acetate. The combined organic fractions were then washed 4 times with water. The combined aqueous fractions were back extracted with ethyl acetate. All organic fractions were then combined and washed with brine and then dried over $MgSO_4$ and concentrated *in vacuo*. The resulting crude yellow oil was purified by column chromatography using a gradient of 0 to 30% ethyl acetate in hexanes.

Reaction with **6**:

The reaction was run according to GP3 using 361 mg of **6**. 0.004 g of a clear oil were obtained; ^{1}H NMR spectrum available in section 3 but was not clean.

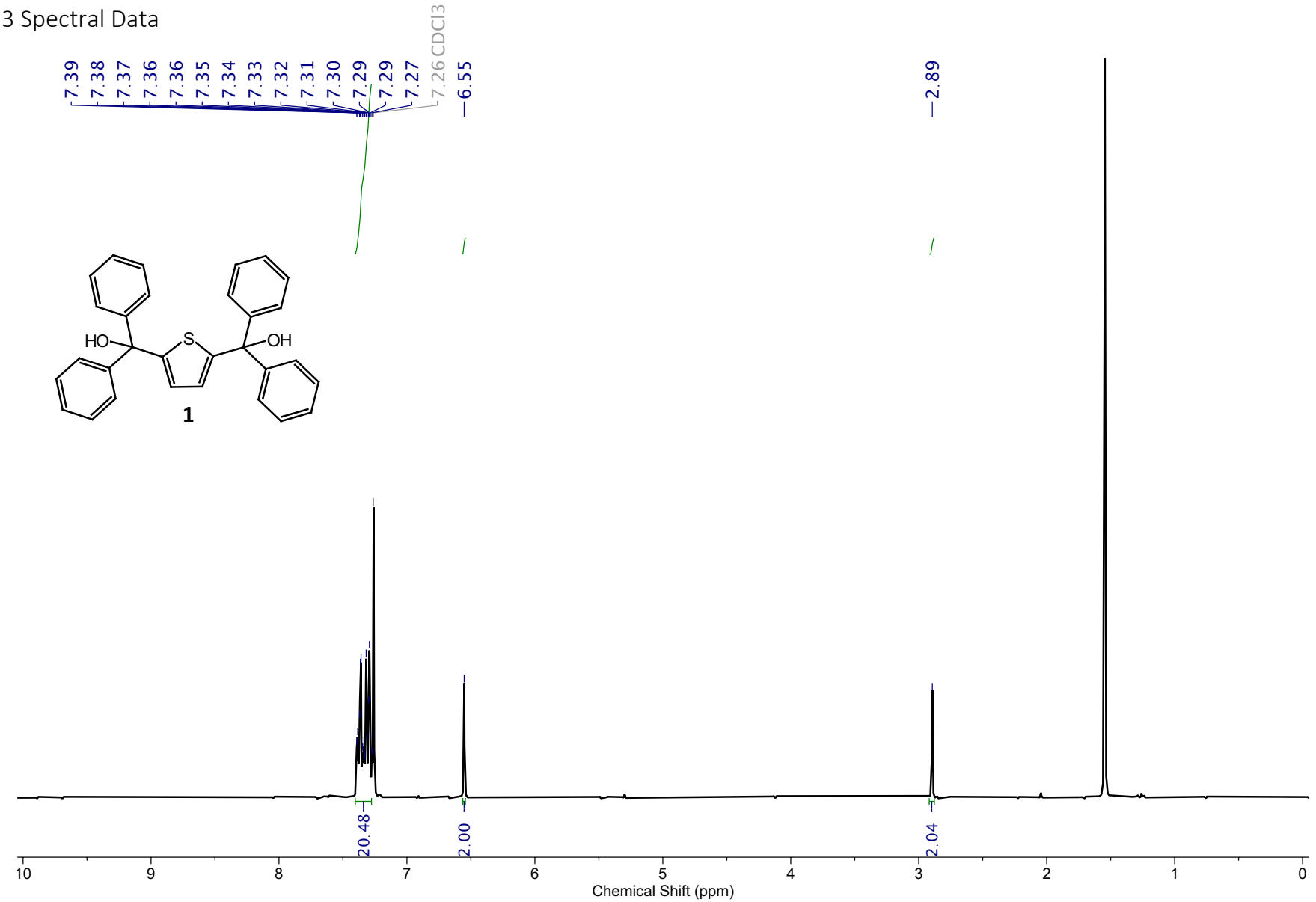
Reaction with **7**:

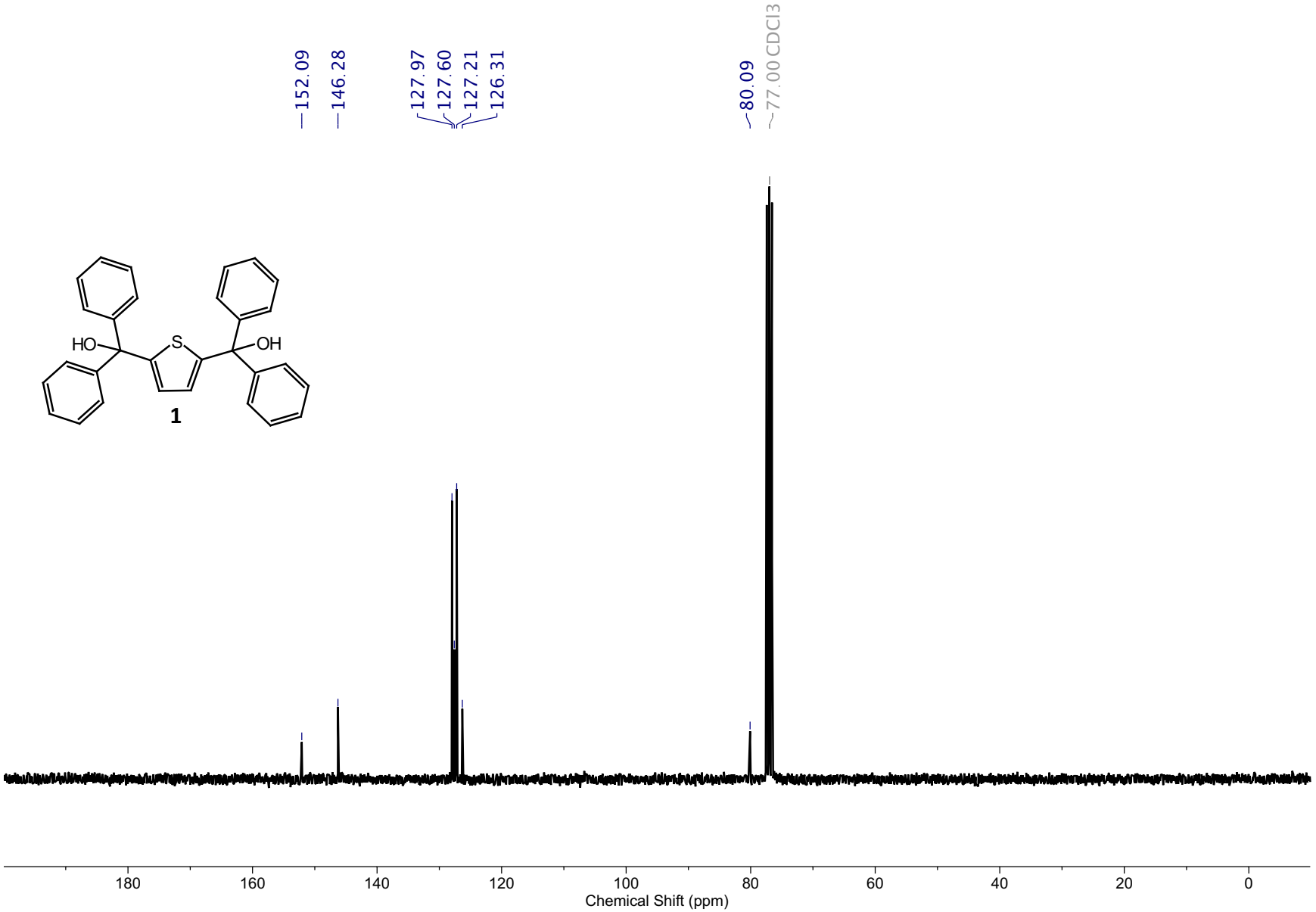
The reaction was run according to GP3 using 400 mg of **7**. 0.072 g of a yellow oily solid were obtained; R_f = 0.35 (30% ethyl acetate in hexanes); The resulting material from this column was then subject to GC-MS in an effort to determine the identity. (M^+ = 201.95) The remaining material from the first column was once again subject to column chromatography using 80% DCM in hexanes. One of two components observed by TLC was recovered from this column. 0.085 g of a yellow oil were obtained; R_f = 0.50 (100% DCM); ^{1}H NMR (300 MHz, $CDCl_3$) 7.66 (d, *J* = 7.9 Hz, 2H), 7.45 (d, *J* = 7.4 Hz, 3H), 7.32 (dd, *J* = 7.9, 4.0 Hz, 4H), 7.17-7.08 (m, 8H), 7.08-6.99 (m, 4H), 6.88 (t, *J* = 6.3 Hz, 4H), 6.69 (d, *J* = 7.5 Hz, 2H), 4.40 (s, 4H), 4.23 (s, 2H), 3.15 (s, 2H), 2.43 (s, 3H), 2.43 (s, 3H), 2.13 (s, 3H).

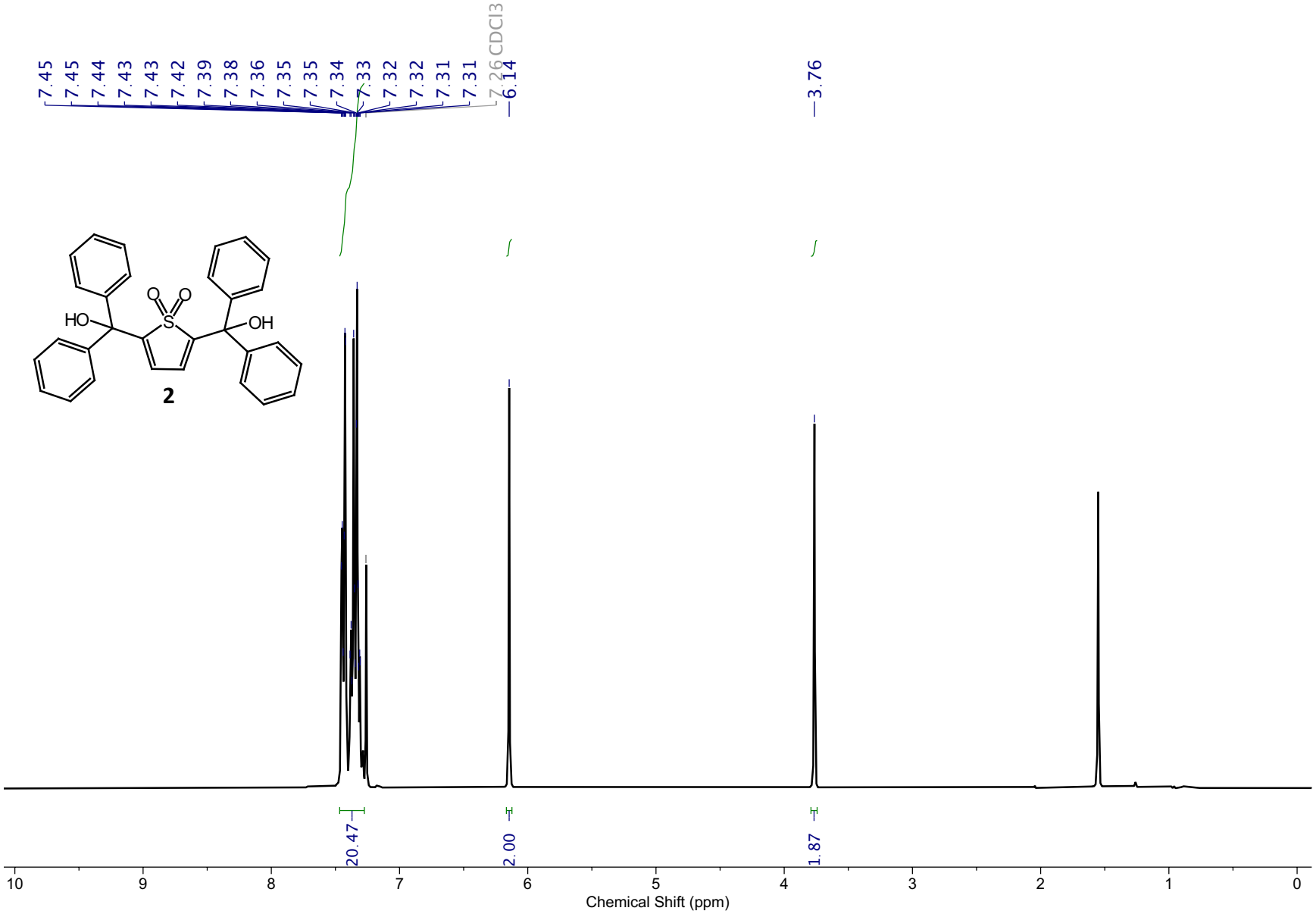
Reaction with **8**:

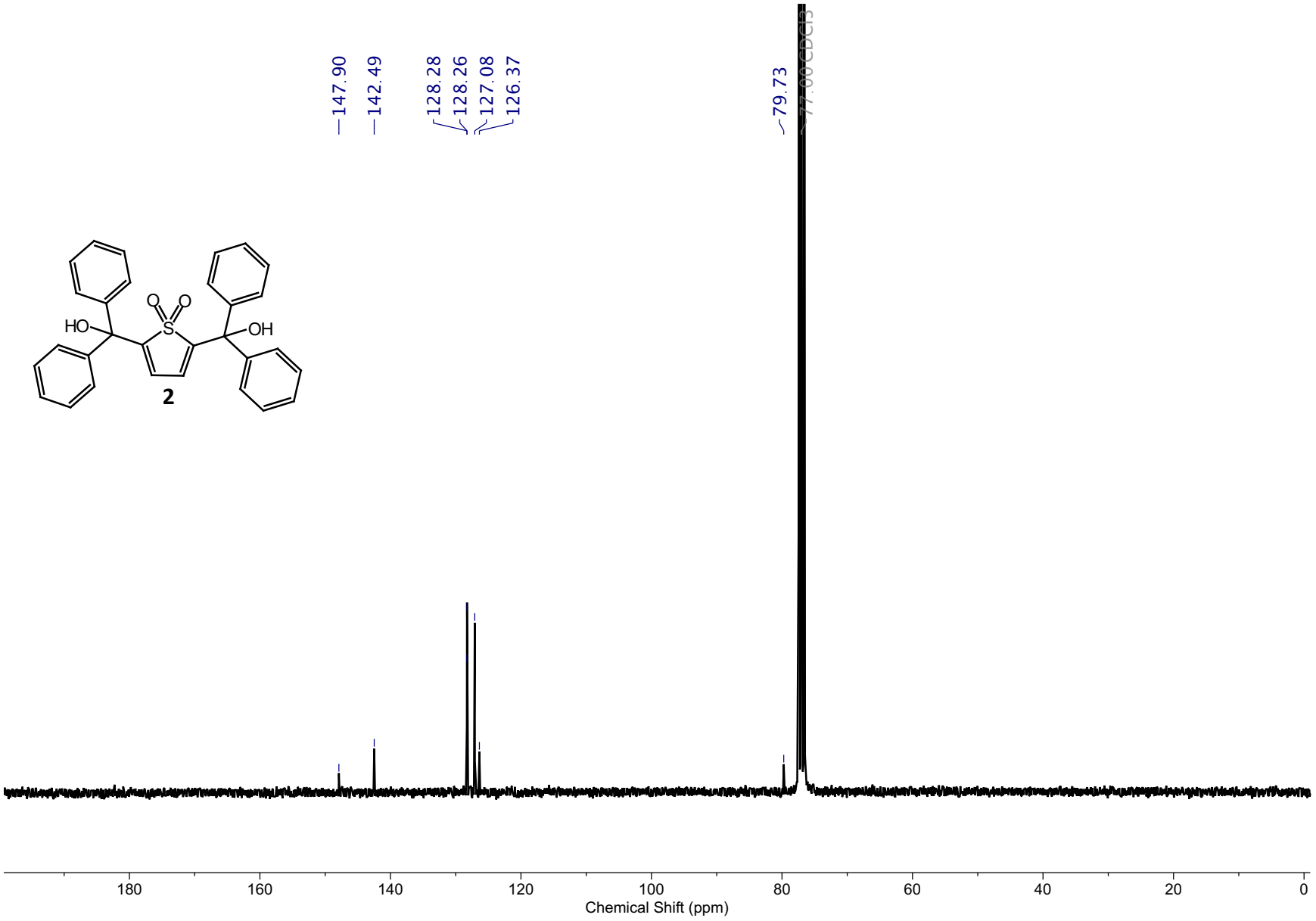
The reaction was run according to GP3 using 507 mg of **8**. The formation of 3 new species was observed by TLC, R_f = 0.30, 0.40, 0.45 (30% ethyl acetate in hexanes). Purification is ongoing.

3 Spectral Data




152.09
146.28
127.97
127.60
127.21
126.31
80.09
77.00 CDCl3
HO
S
OH
1
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


7.45
7.45
7.44
7.43
7.43
7.42
7.39
7.38
7.36
7.35
7.35
7.34
7.33
7.32
7.32
7.31
7.31
7.26 CDCl3
6.14
3.76
HO
OH
O
O
S
2
20.47
2.00
1.87
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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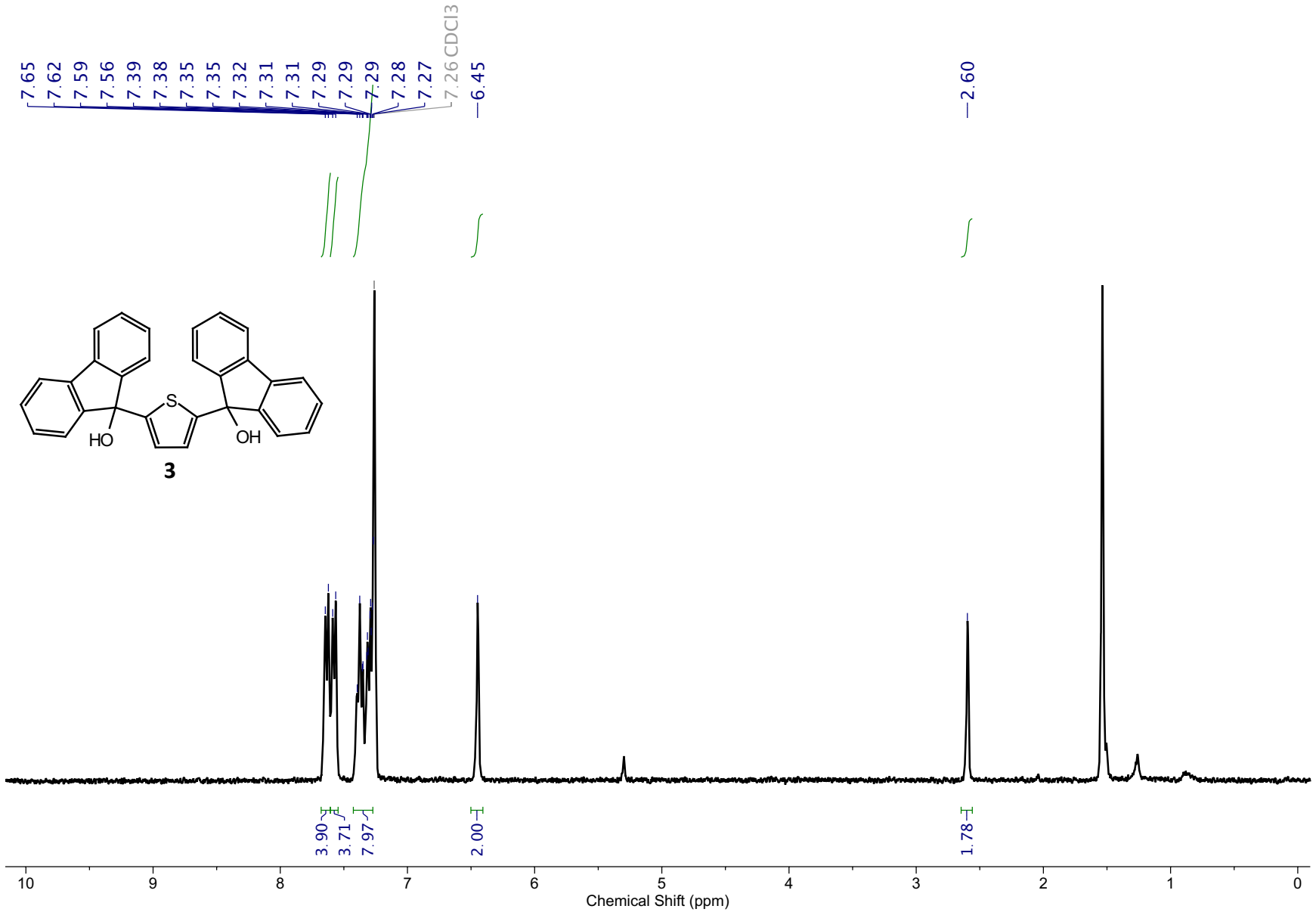
142.49
128.28
128.26
127.08
126.37
79.73
77.00 CDCl3
HO
OH
O
O
S
2
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)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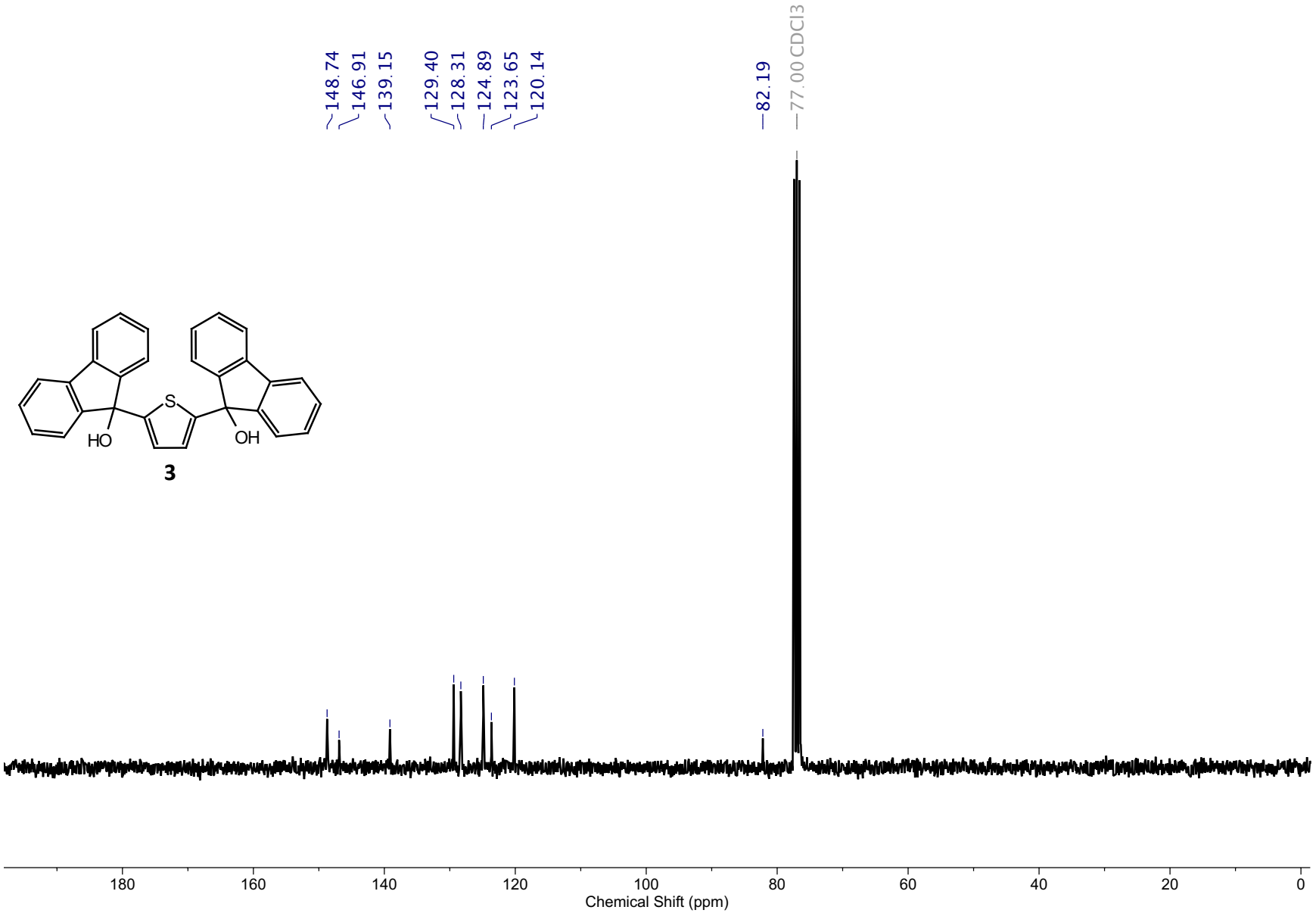
7.62
7.59
7.56
7.39
7.38
7.35
7.35
7.32
7.31
7.31
7.29
7.29
7.29
7.28
7.27
7.26 CDCl3
6.45
2.60
HO
OH
S
3
3.90
3.71
7.97
2.00
1.78
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


148.74
146.91
139.15
129.40
128.31
124.89
123.65
120.14
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77.00 CDCl3
S
HO
OH
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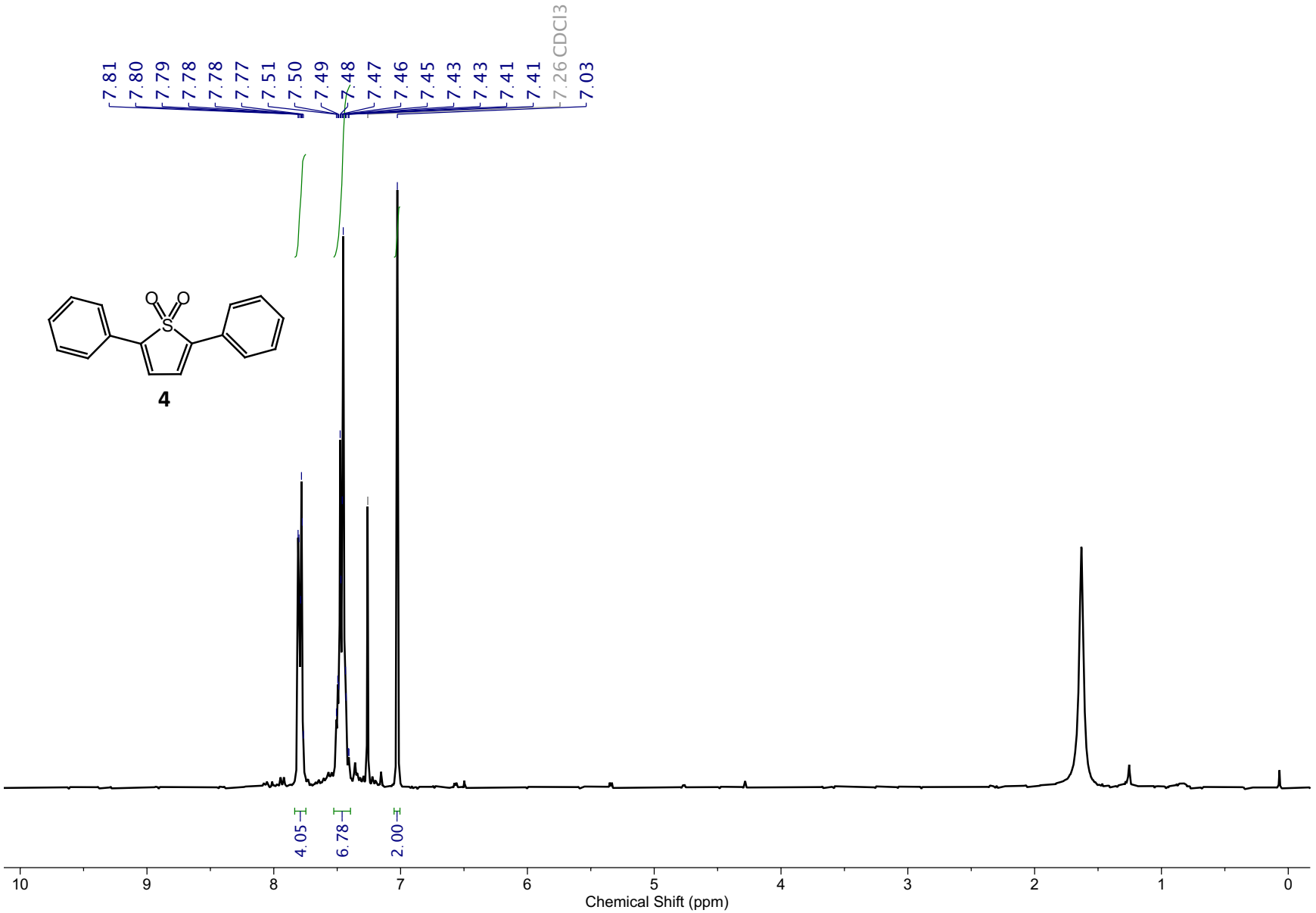
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


7.81
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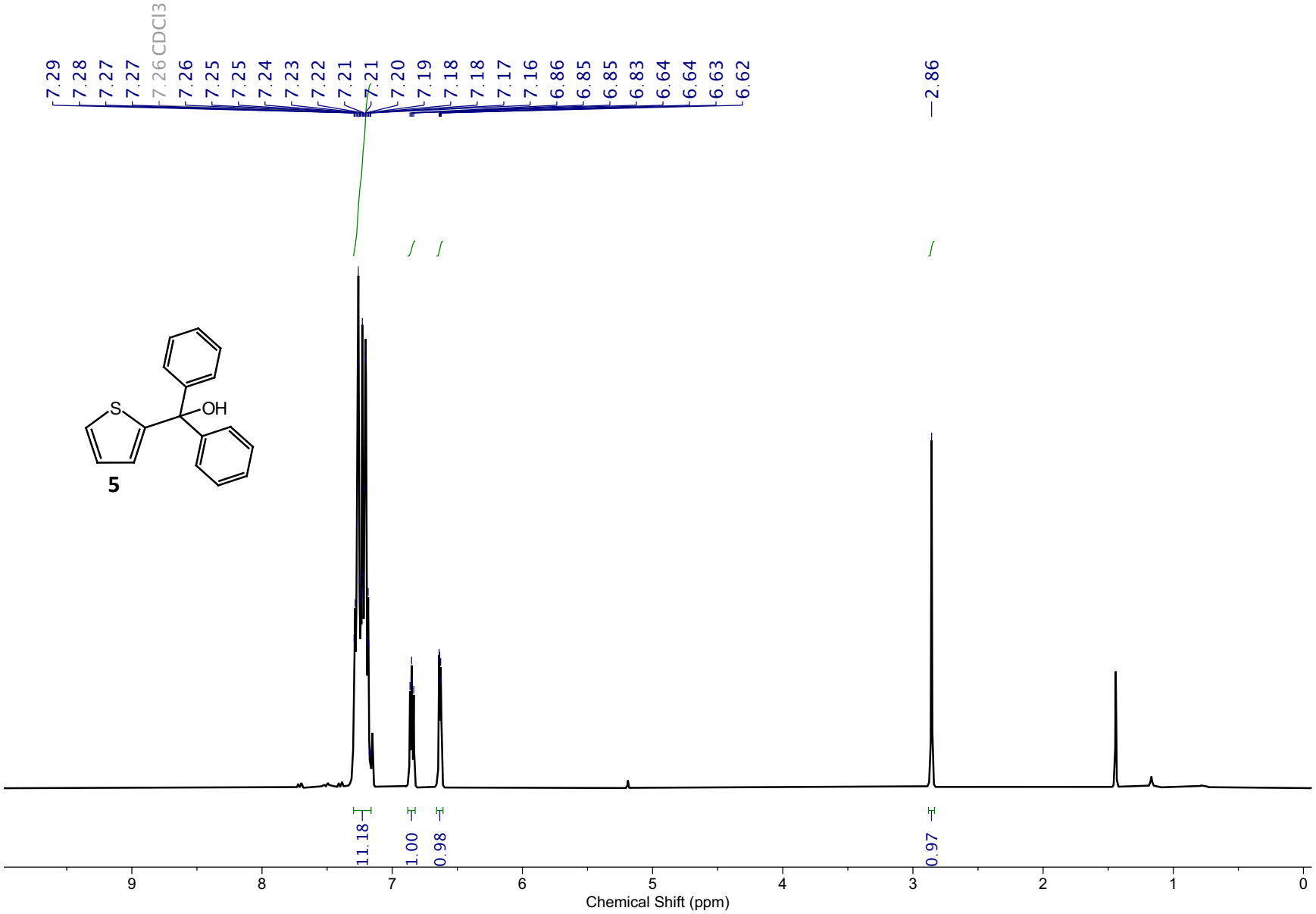
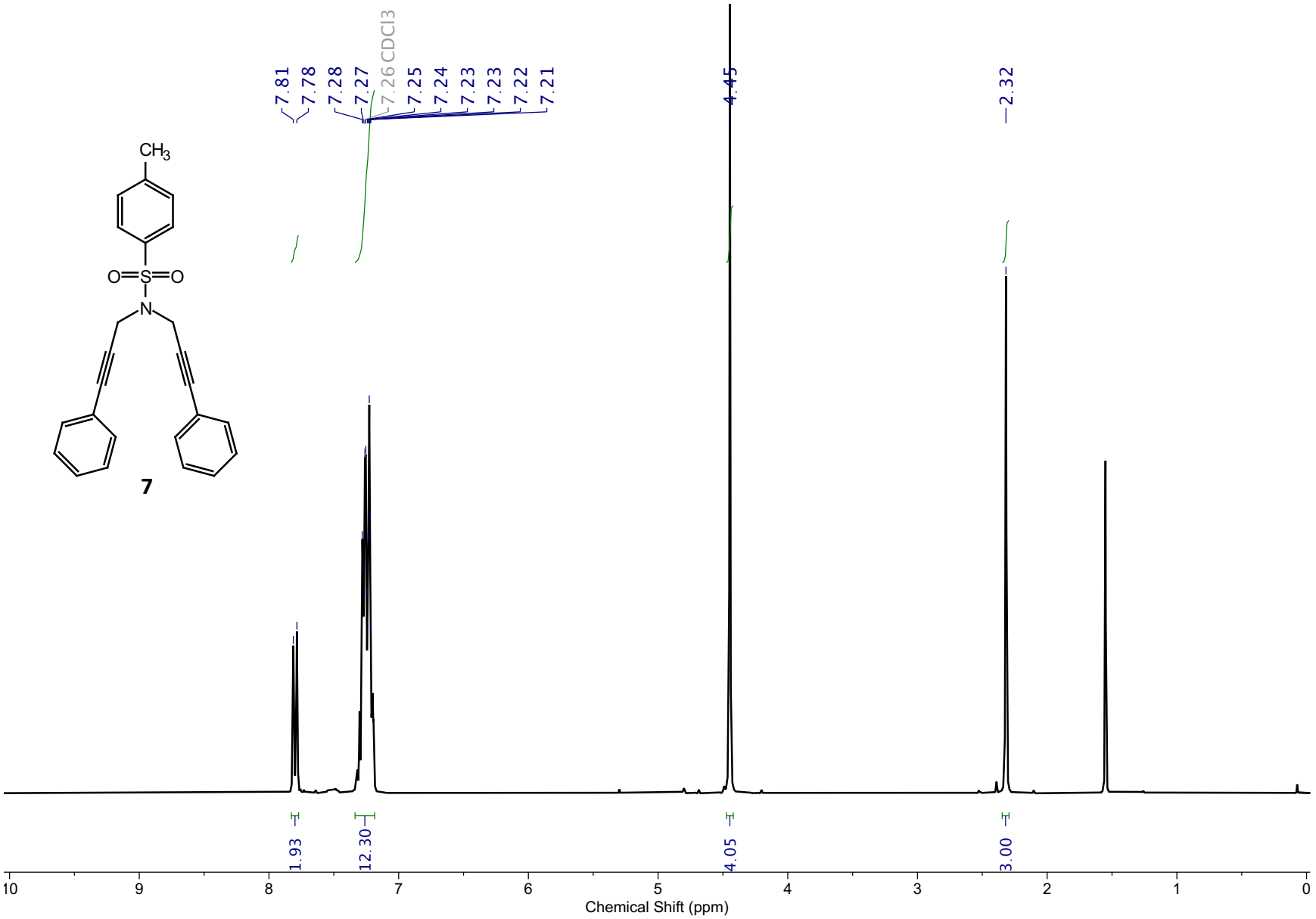
7.79
7.78
7.78
7.77
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.43
7.43
7.41
7.41
7.26 CDCl3
7.03
O
O
S
4
4.05
6.78
2.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


7.29
7.28
7.27
7.27
7.26 CDCl3
7.26
7.25
7.25
7.24
7.23
7.22
7.21
7.21
7.20
7.19
7.18
7.18
7.17
7.16
6.86
6.85
6.85
6.83
6.64
6.64
6.63
6.62
2.86
S
OH
5
11.18
1.00
0.98
0.97
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


7.81
7.78
7.28
7.27
7.26 CDCl3
7.25
7.24
7.23
7.23
7.22
7.21
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2.32
CH3
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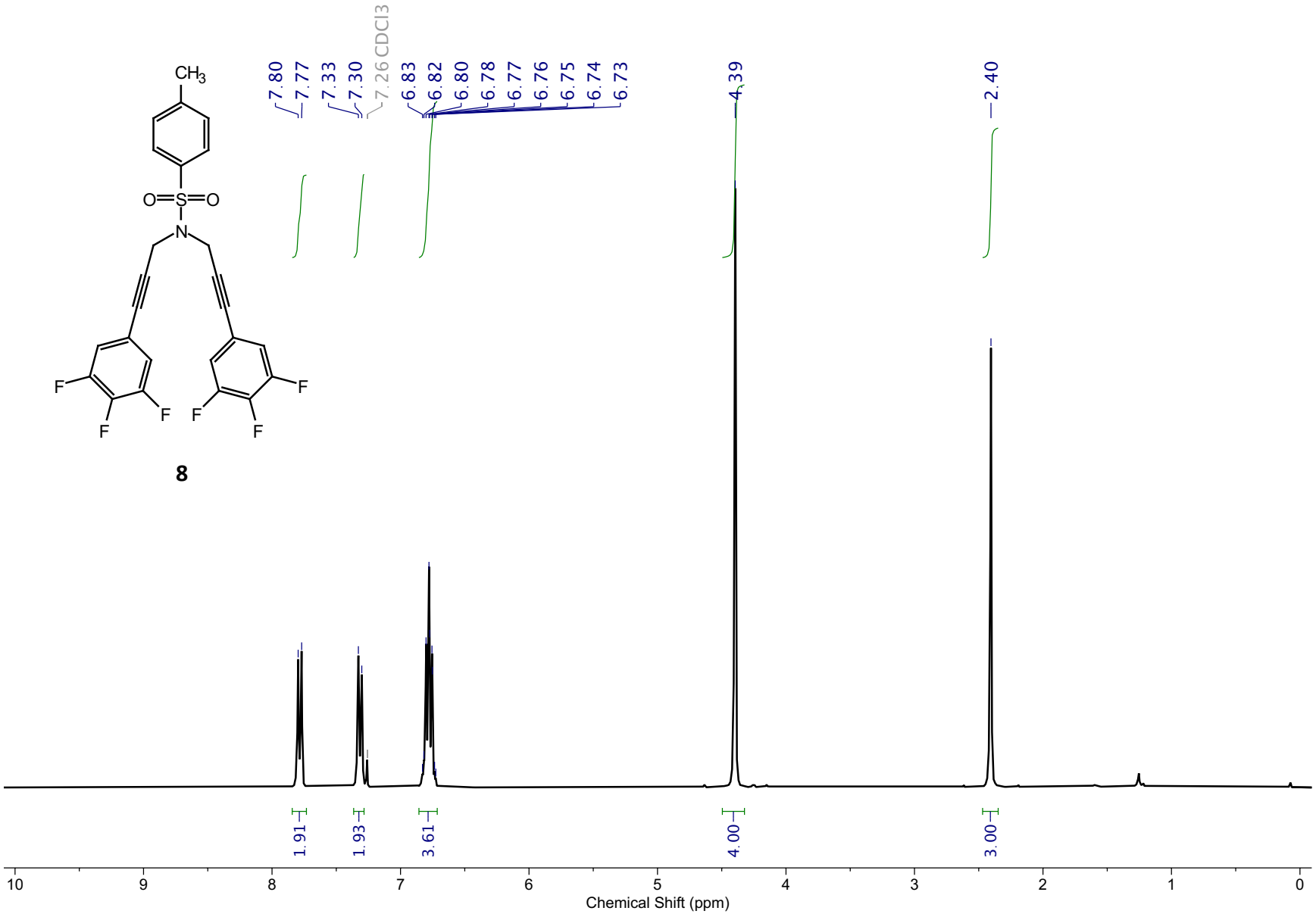
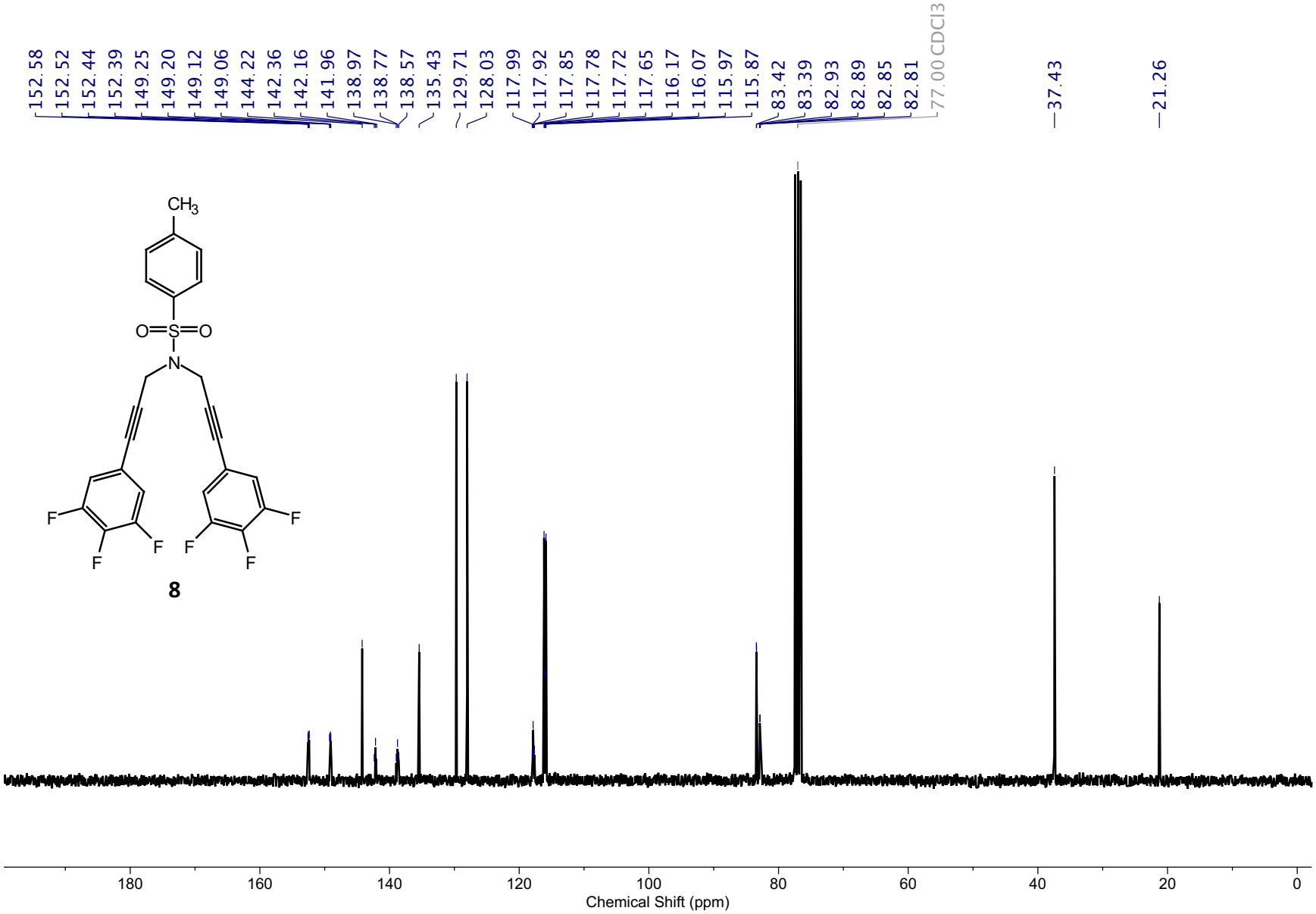
N
7
1.93
12.30
4.05
3.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


CH3
O=S=O
N
F
F
F
F
F
8
7.80
7.77
7.33
7.30
7.26 CDCl3
6.83
6.82
6.80
6.78
6.77
6.76
6.75
6.74
6.73
4.39
2.40
1.91
1.93
3.61
4.00
3.00
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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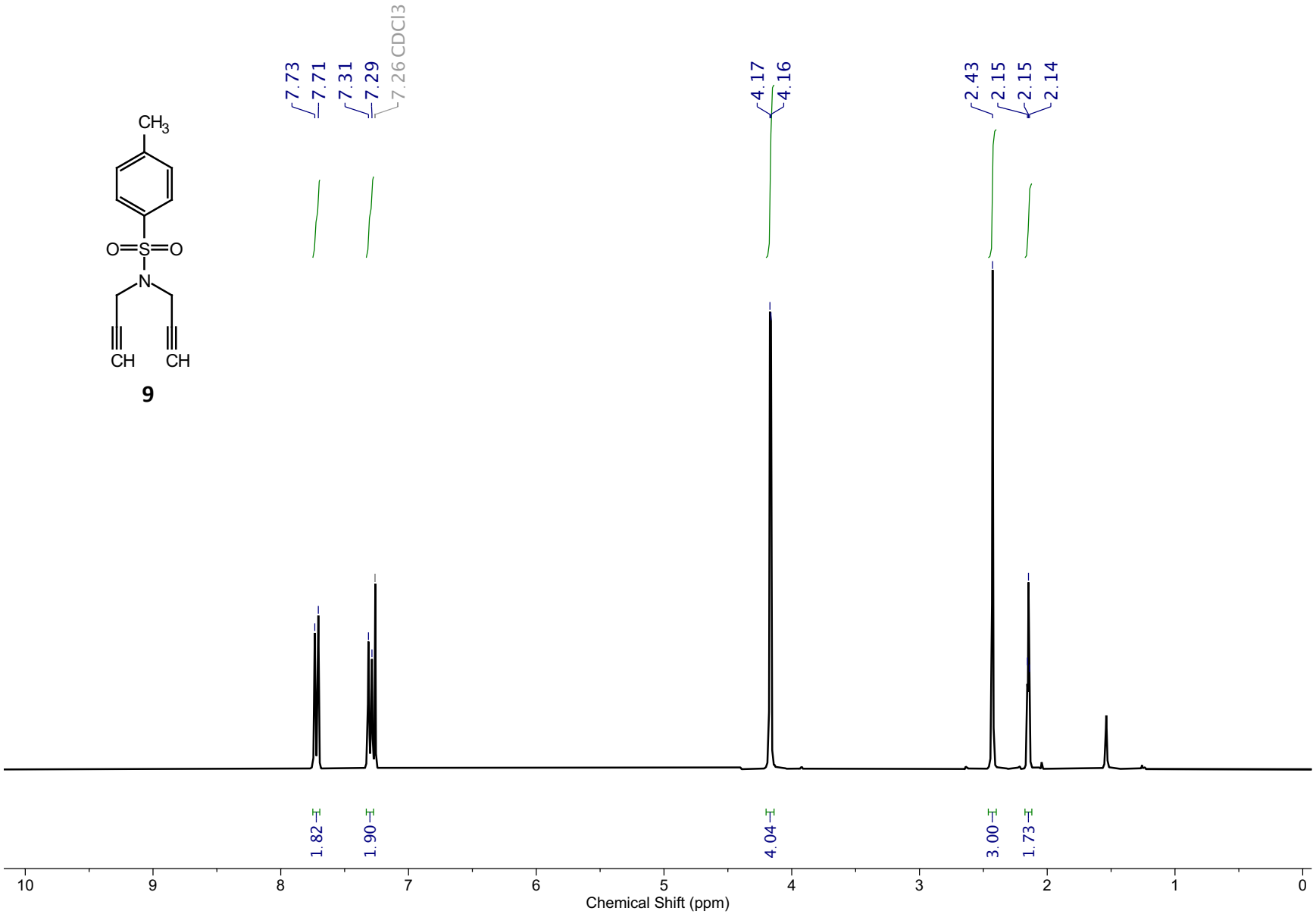
152.52
152.44
152.39
149.25
149.20
149.12
149.06
144.22
142.36
142.16
141.96
138.97
138.77
138.57
135.43
129.71
128.03
117.99
117.92
117.85
117.78
117.72
117.65
116.17
116.07
115.97
115.87
83.42
83.39
82.93
82.89
82.85
82.81
77.00 CDCl3
37.43
21.26
CH3
O=S=O
N
F
F
F
F
F
F
8
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


CH3
O=S=O
N
CH
CH
9
7.73
7.71
7.31
7.29
7.26 CDCl3
4.17
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2.43
2.15
2.15
2.14
1.82
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9
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4
3
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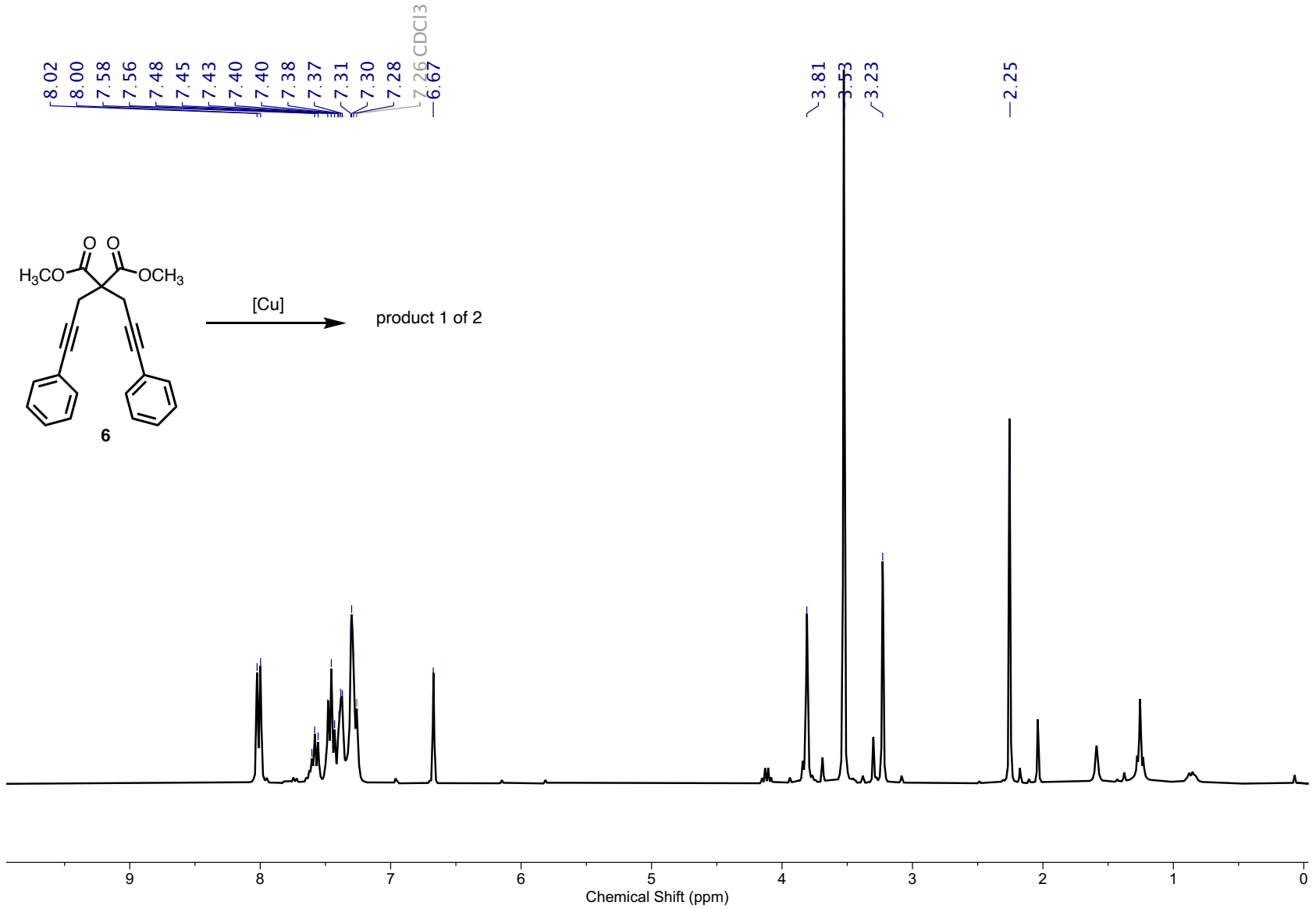
0
Chemical Shift (ppm)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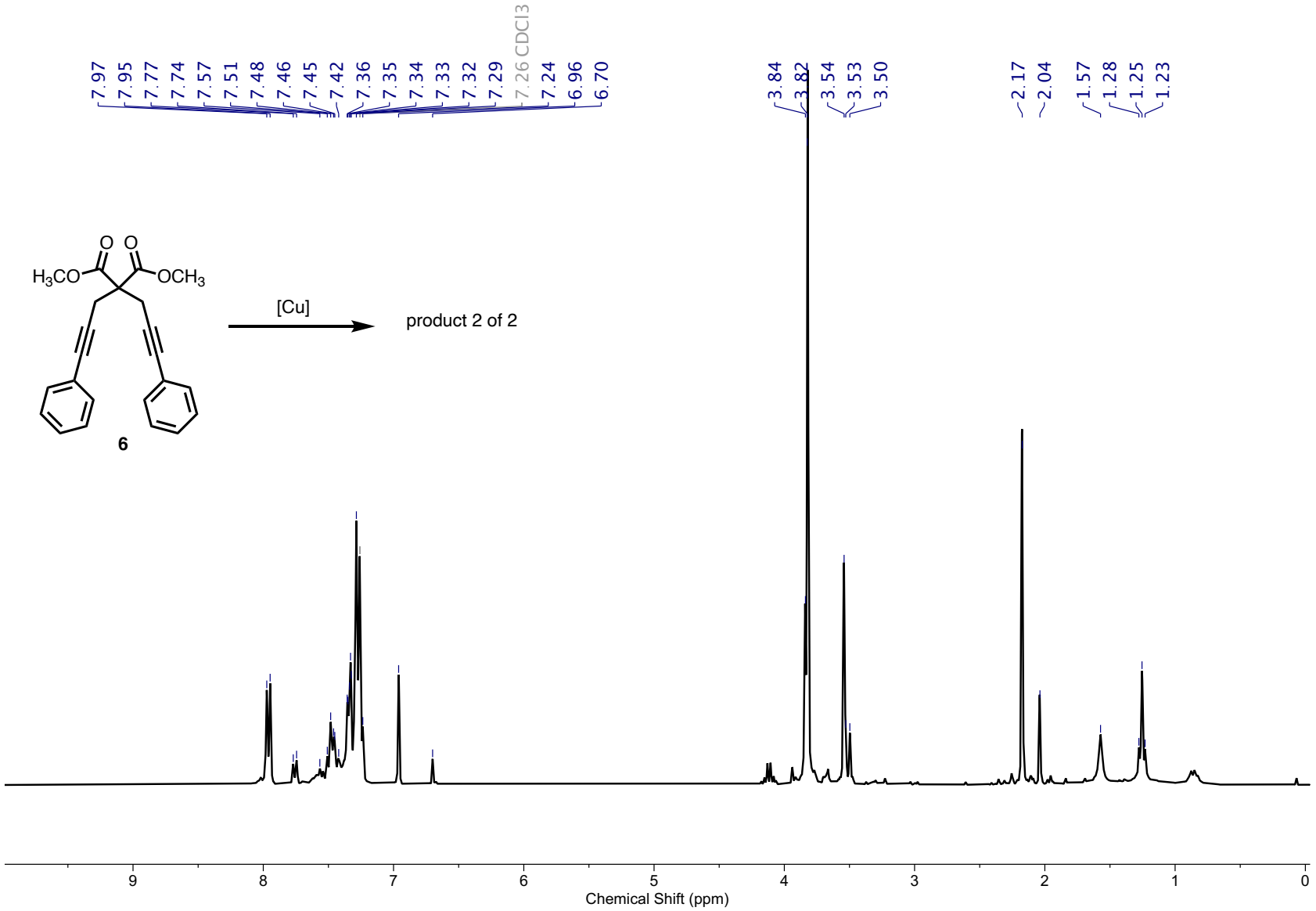
2.25
O
O
H3CO
OCH3
[Cu]
product 1 of 2
6
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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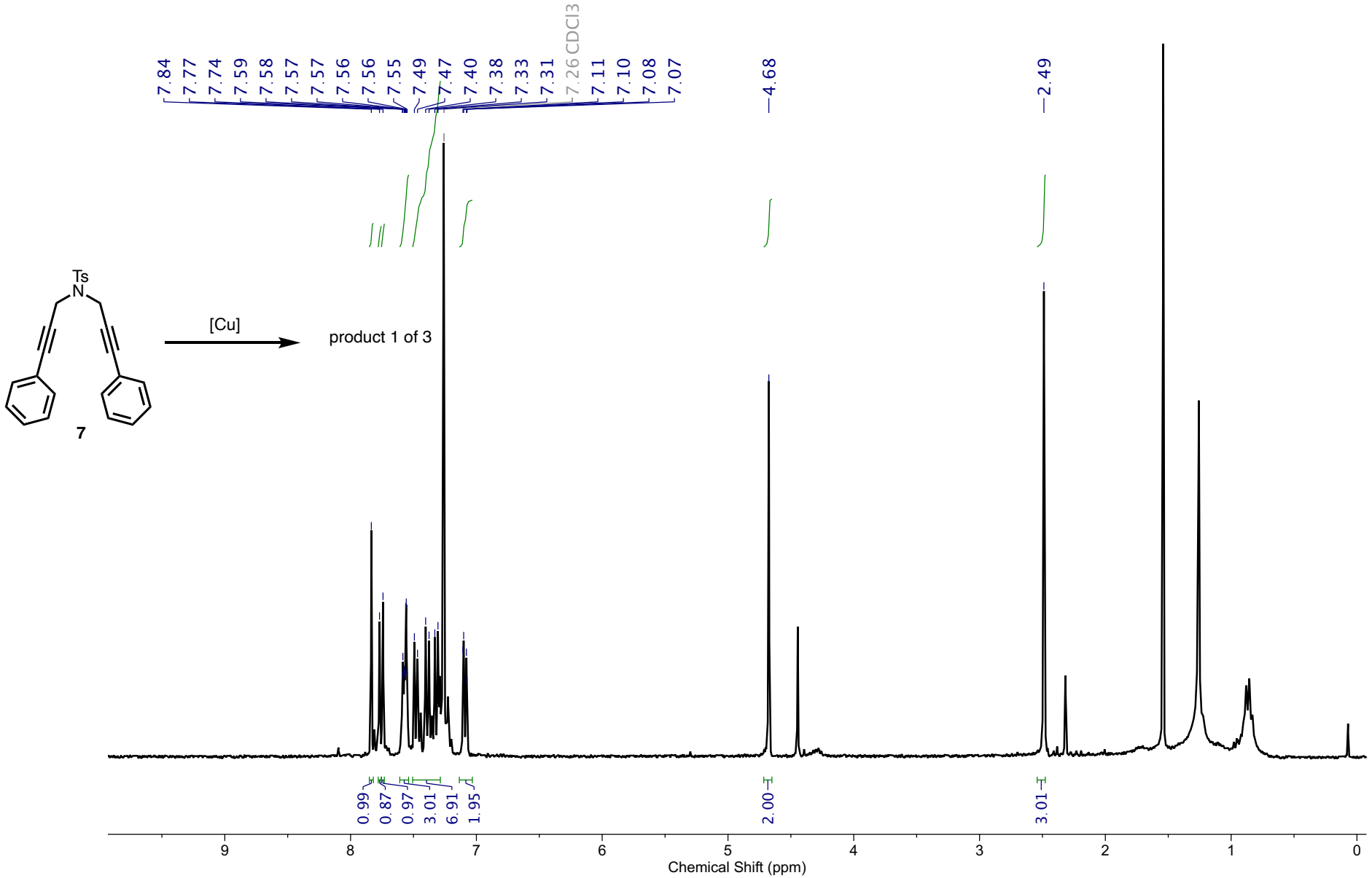
7.34
7.33
7.32
7.29
7.26 CDCl3
7.24
6.96
6.70
3.84
3.82
3.54
3.53
3.50
2.17
2.04
1.57
1.28
1.25
1.23
O
O
H3CO
OCH3
[Cu]
product 2 of 2
6
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)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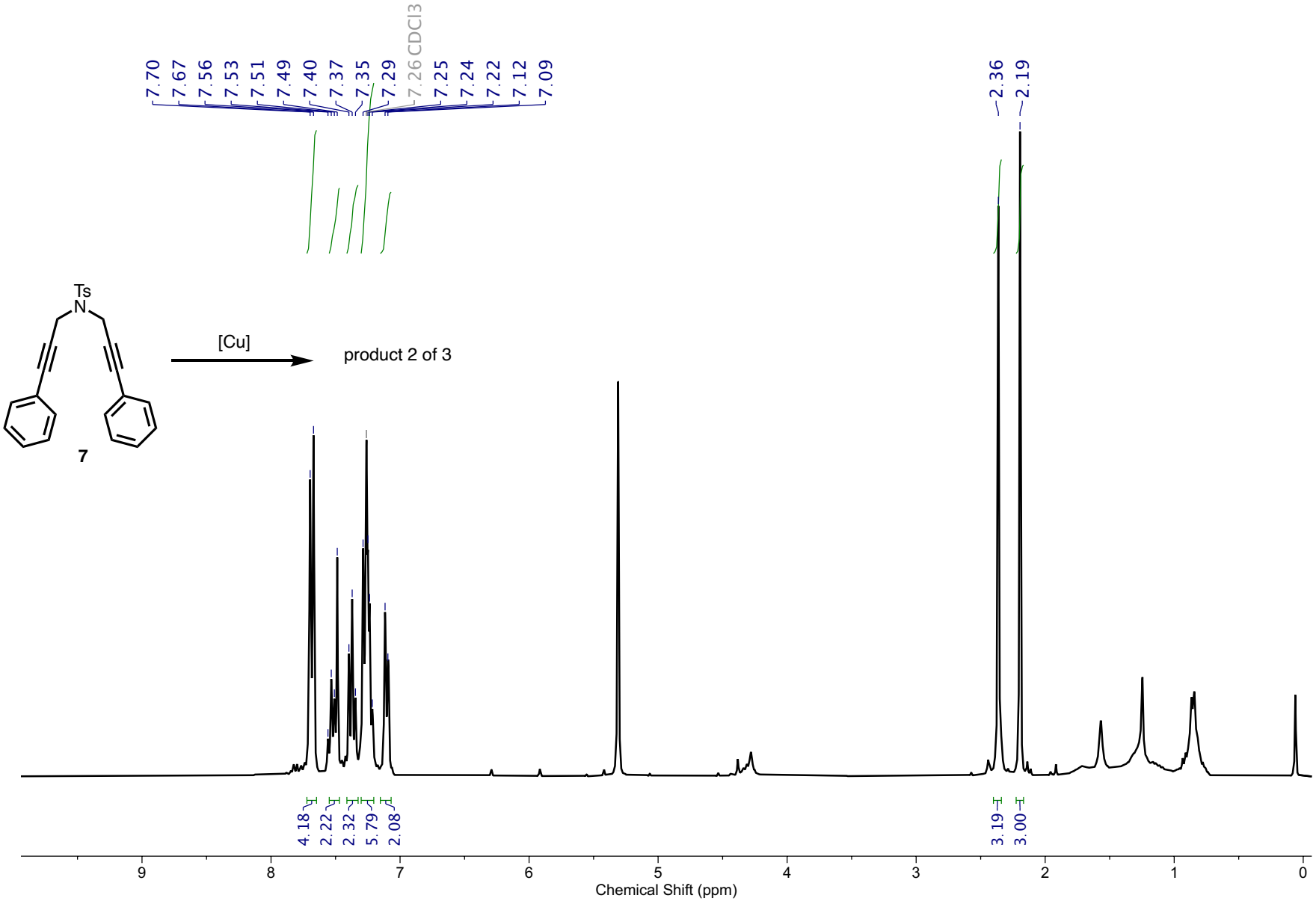
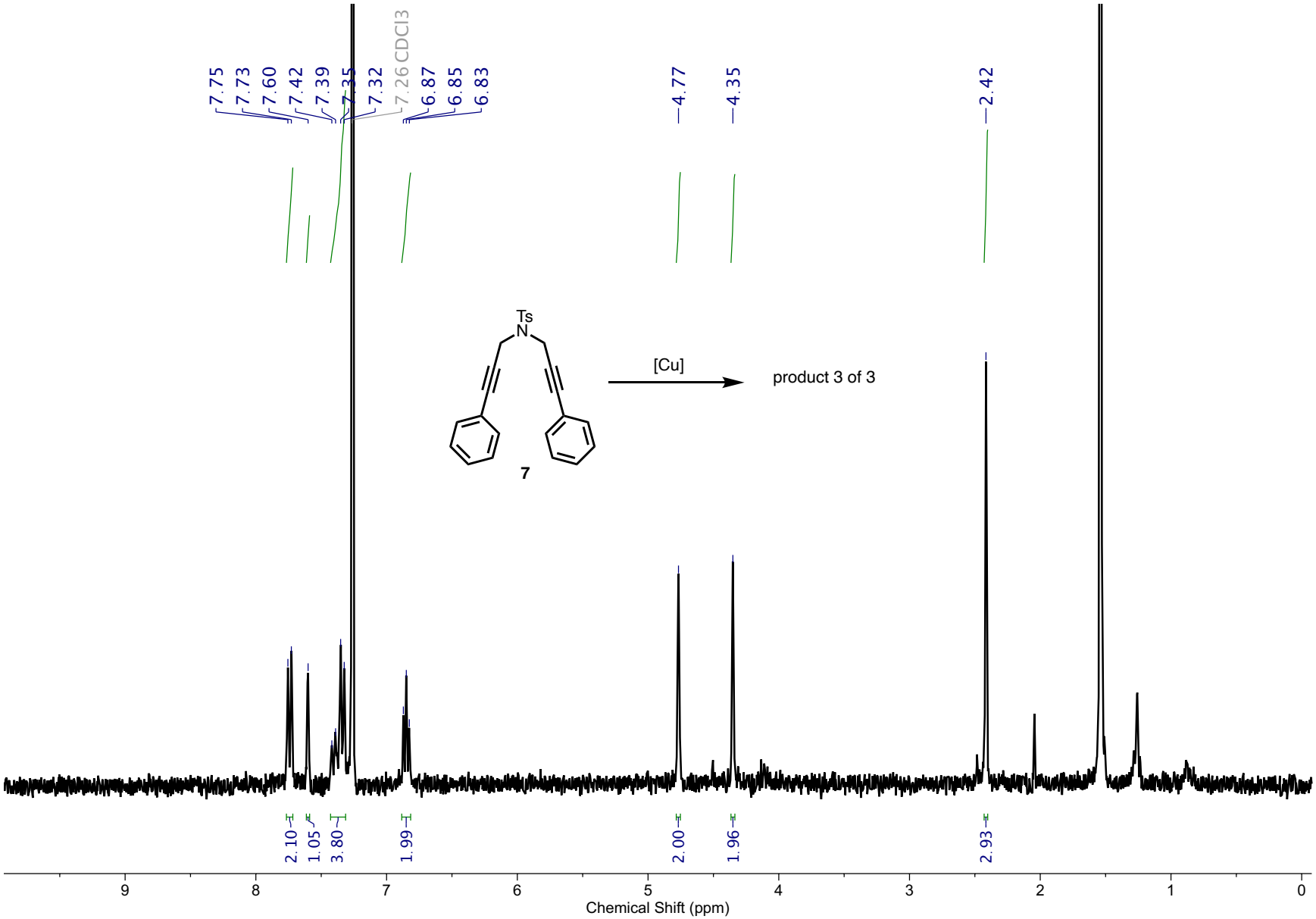
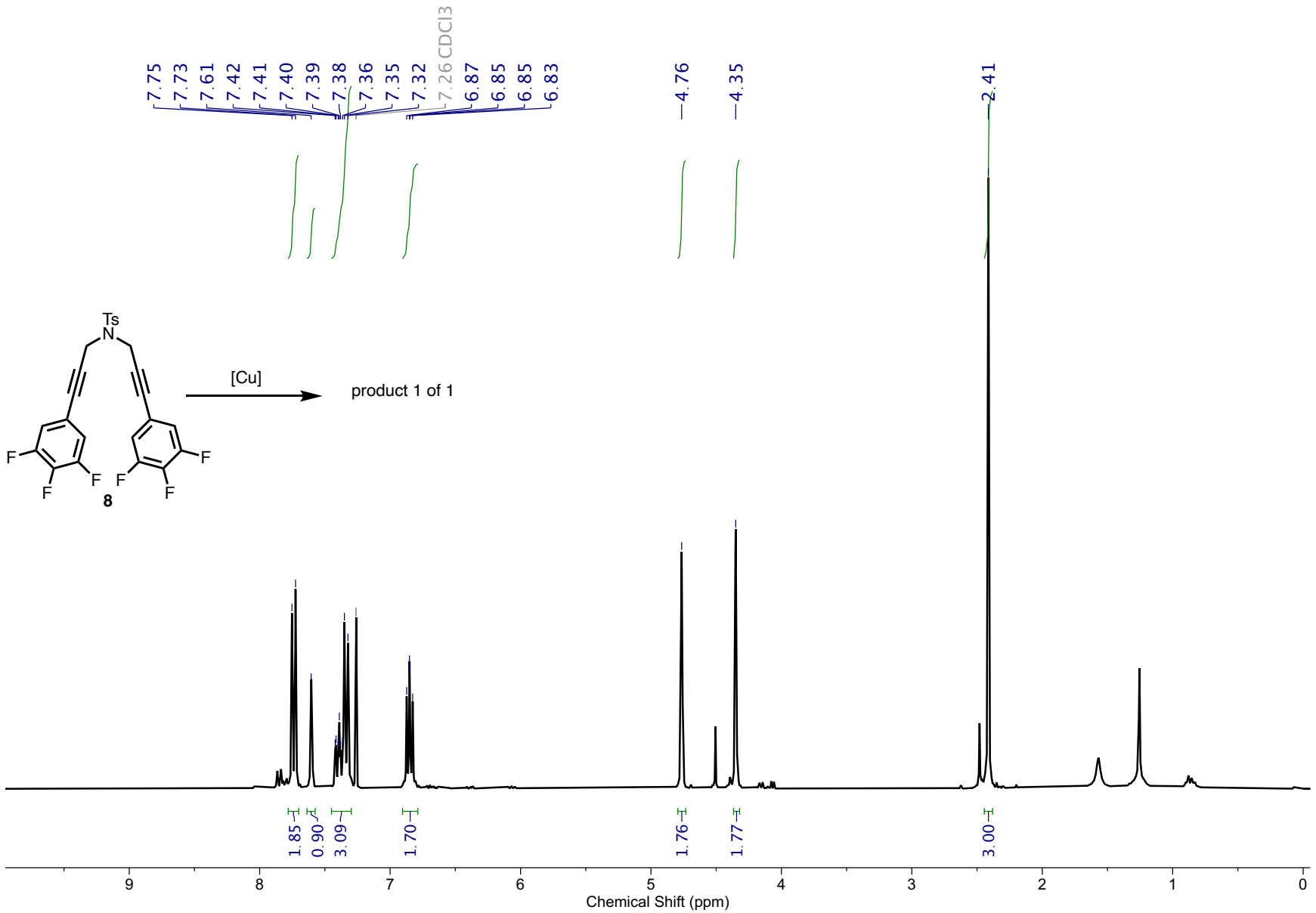
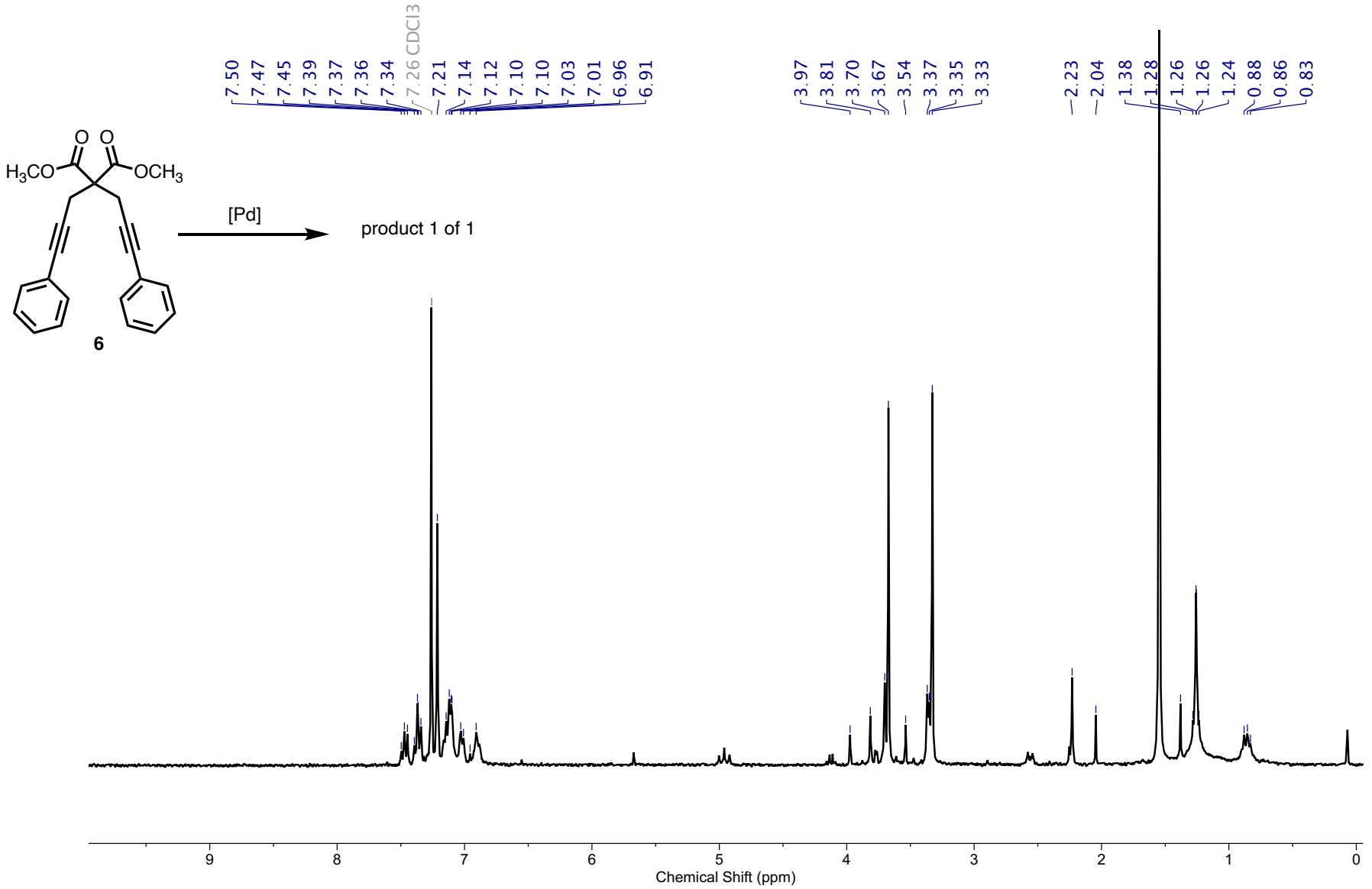
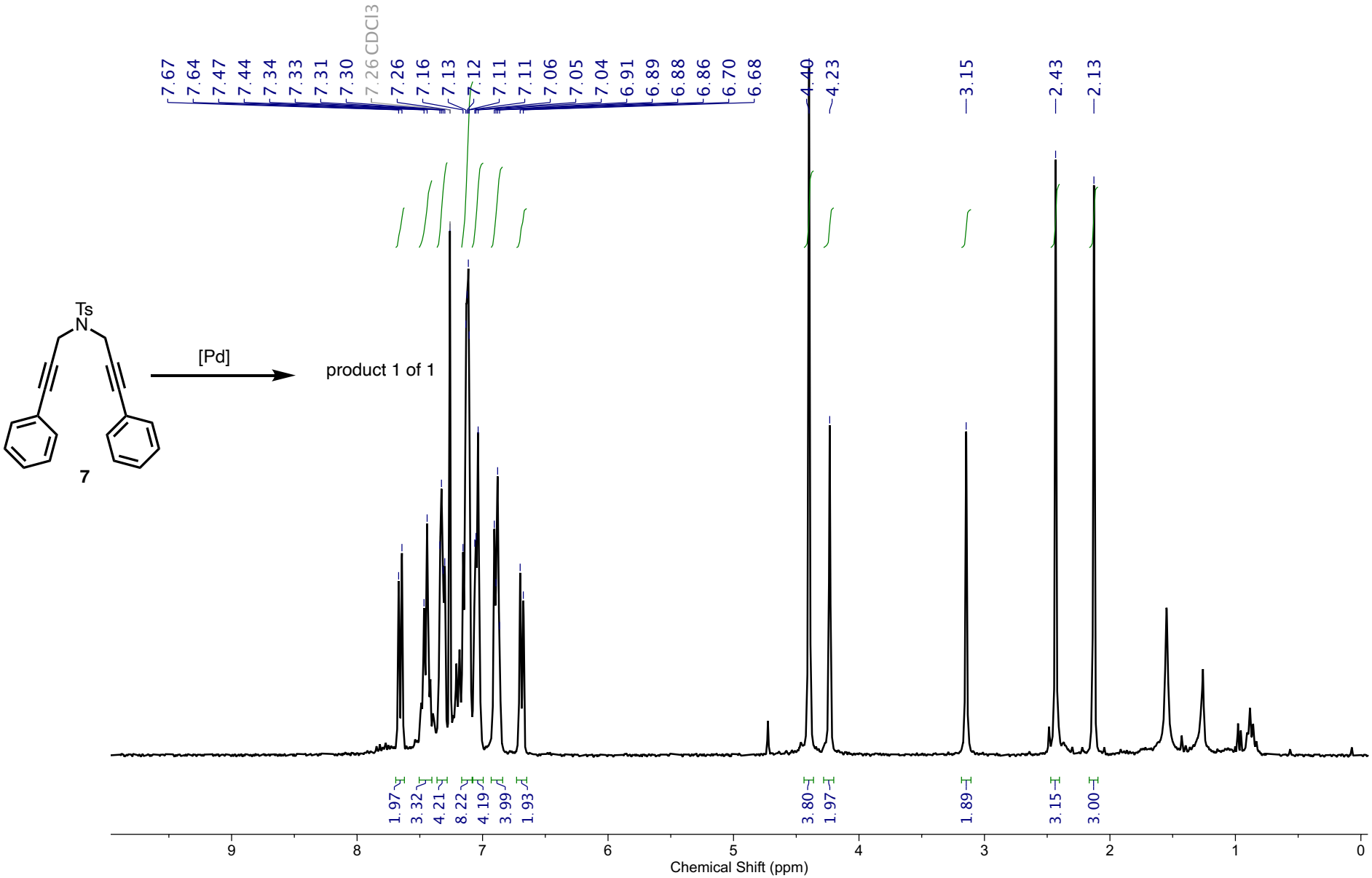
7.59
7.58
7.57
7.57
7.56
7.56
7.55
7.49
7.47
7.40
7.38
7.33
7.31
7.26 CDCl3
7.11
7.10
7.08
7.07
4.68
2.49
Ts
N
[Cu]
product 1 of 3
7
0.99
0.87
0.97
3.01
6.91
1.95
2.00
3.01
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


7.70
7.67
7.56
7.53
7.51
7.49
7.40
7.37
7.35
7.29
7.26 CDCl3
7.25
7.24
7.22
7.12
7.09
2.36
2.19
Ts
N
[Cu]
product 2 of 3
7
4.18
2.22
2.32
5.79
2.08
3.19
3.00
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

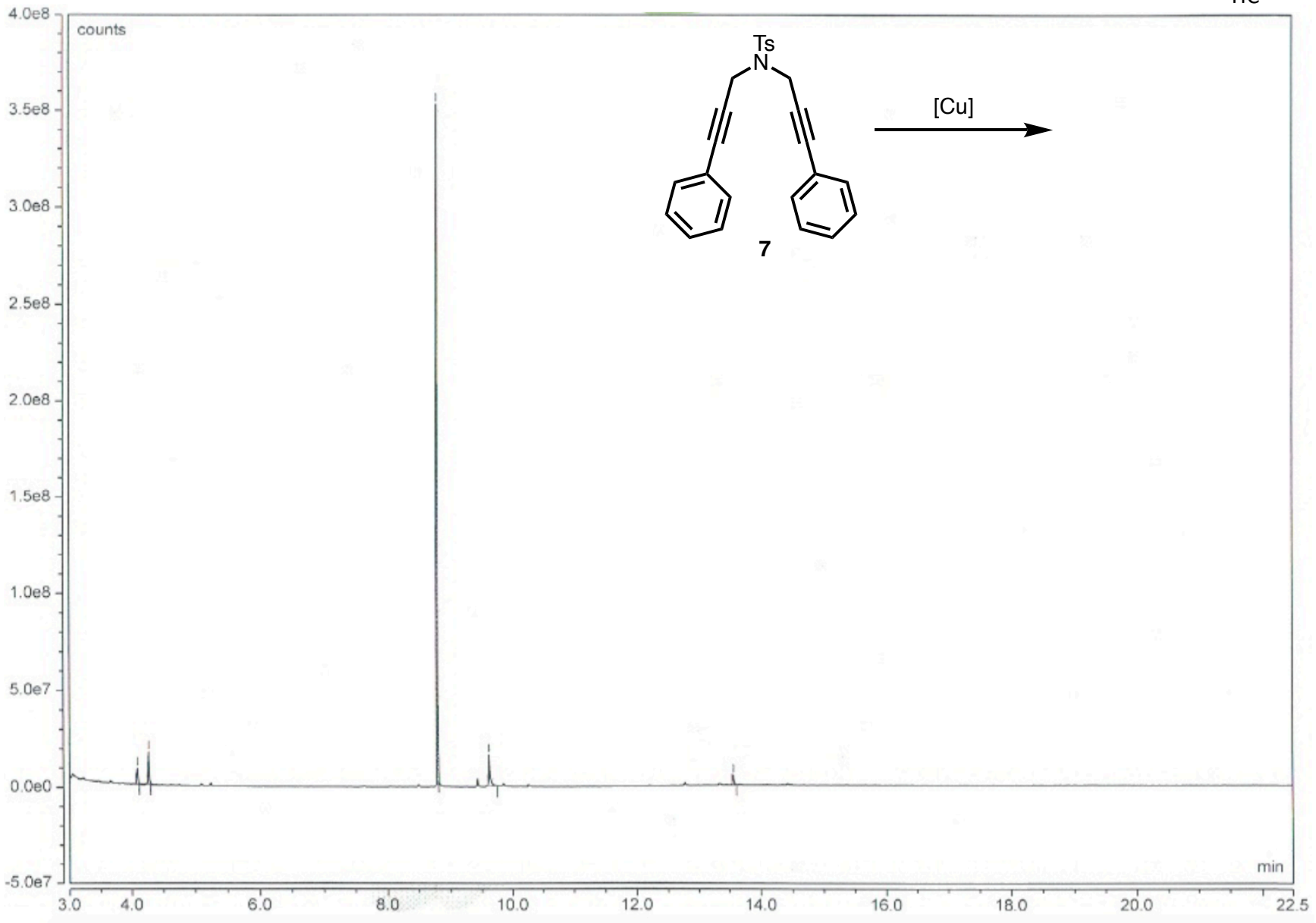

7.75
7.73
7.60
7.42
7.39
7.35
7.32
7.26 CDCl3
6.87
6.85
6.83
4.77
4.35
2.42
Ts
N
[Cu]
product 3 of 3
7
2.10
1.05
3.80
1.99
2.00
1.96
2.93
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

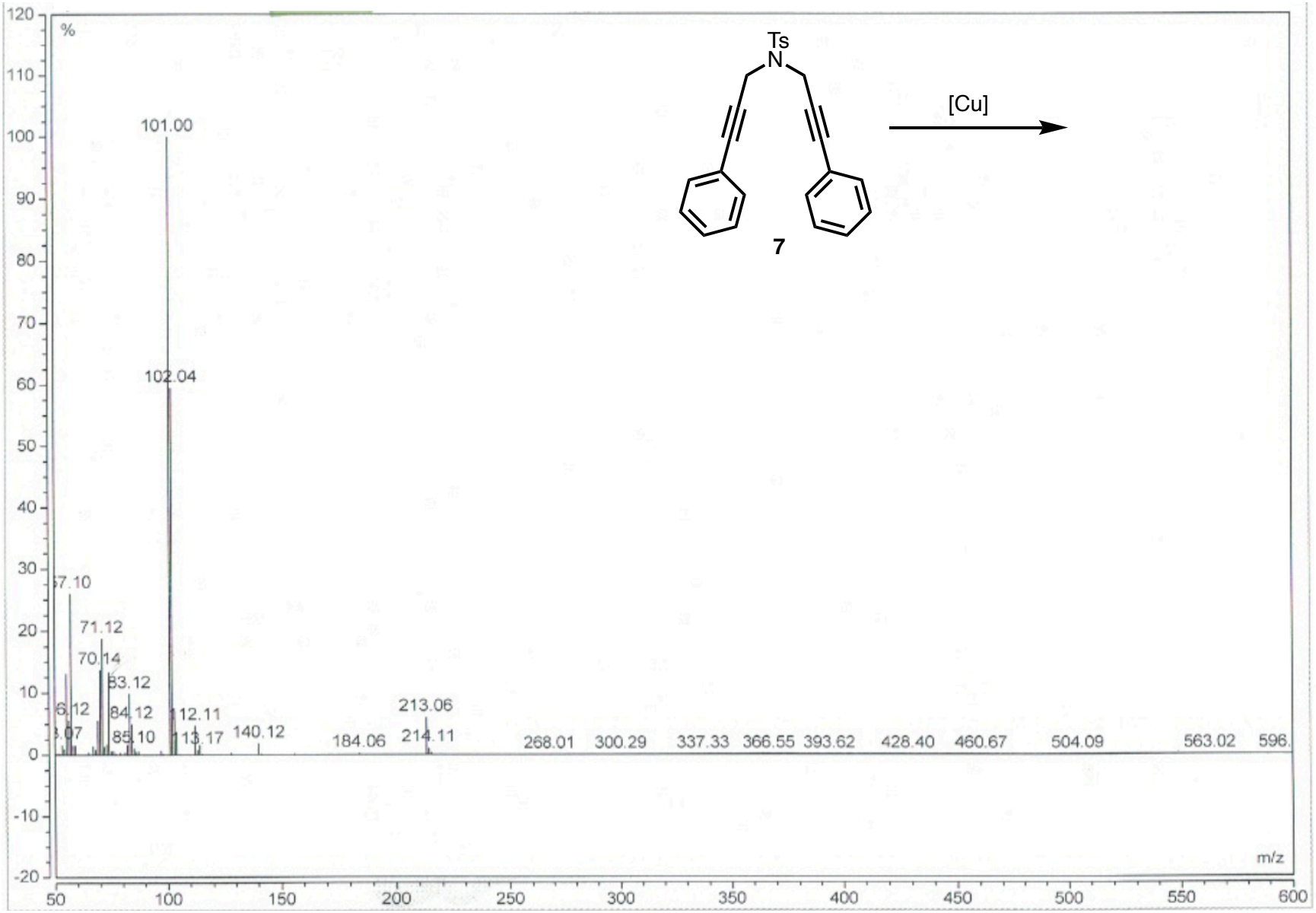

7.75
7.73
7.61
7.42
7.41
7.40
7.39
7.38
7.36
7.35
7.32
7.26 CDCl3
6.87
6.85
6.85
6.83
4.76
4.35
2.41
Ts
N
F
F
F
F
F
F
8
[Cu]
product 1 of 1
1.85
0.90
3.09
1.70
1.76
1.77
3.00
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)


7.50
7.47
7.45
7.39
7.37
7.36
7.34
7.26 CDCl3
7.21
7.14
7.12
7.10
7.10
7.03
7.01
6.96
6.91
3.97
3.81
3.70
3.67
3.54
3.37
3.35
3.33
2.23
2.04
1.38
1.28
1.26
1.26
1.24
0.88
0.86
0.83
O
O
H3CO
OCH3
[Pd]
product 1 of 1
6
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

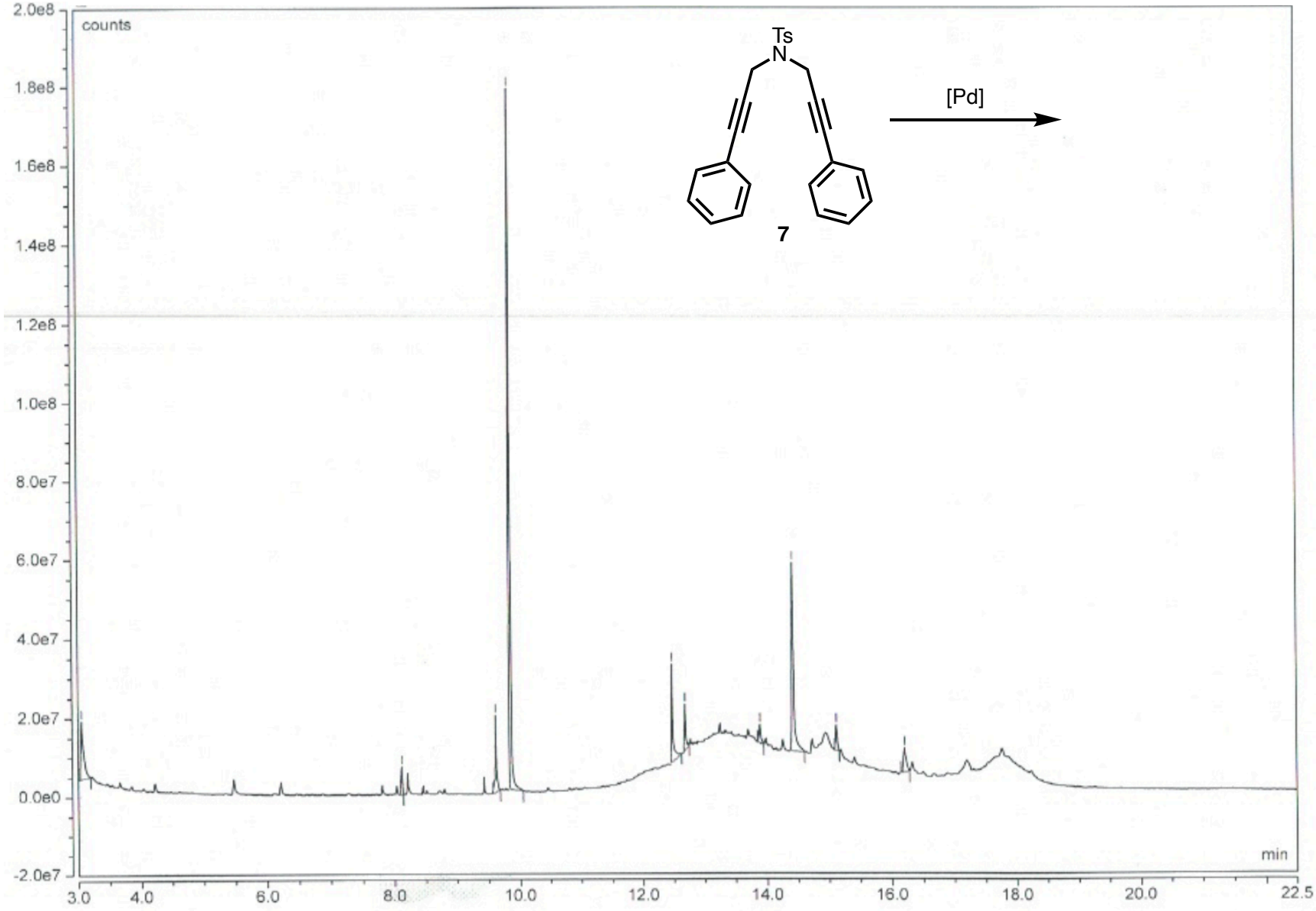

7.67
7.64
7.47
7.44
7.34
7.33
7.31
7.30
7.26 CDCl3
7.26
7.16
7.13
7.12
7.11
7.11
7.06
7.05
7.04
6.91
6.89
6.88
6.86
6.70
6.68
4.40
4.23
3.15
2.43
2.13
Ts
N
[Pd]
product 1 of 1
7
1.97
3.32
4.21
8.22
4.19
3.99
1.93
3.80
1.97
1.89
3.15
3.00
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

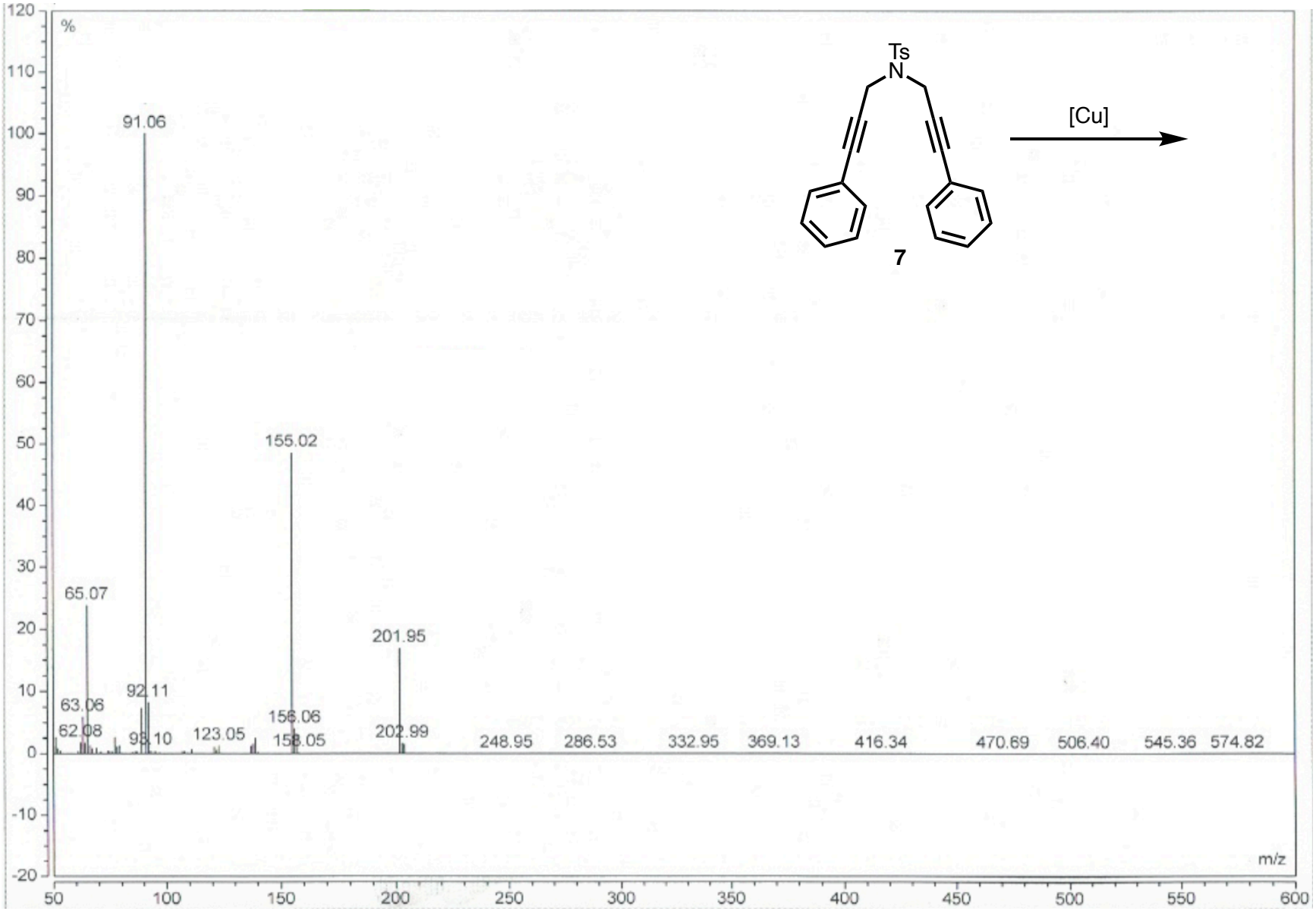
TIC


counts
4.0e8
3.5e8
3.0e8
2.5e8
2.0e8
1.5e8
1.0e8
5.0e7
0.0e0
-5.0e7
min
3.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0
20.0
22.5
Ts
N
[Cu]
7


%
Ts
N
[Cu]
7
101.00
102.04
67.10
71.12
70.14
83.12
84.12
85.10
112.11
113.17
140.12
184.06
213.06
214.11
268.01
300.29
337.33
366.55
393.62
428.40
460.67
504.09
563.02
m/z

TIC


counts
2.0e8
1.8e8
1.6e8
1.4e8
1.2e8
1.0e8
8.0e7
6.0e7
4.0e7
2.0e7
0.0e0
-2.0e7
min
3.0
4.0
6.0
8.0
10.0
12.0
14.0
16.0
18.0
20.0
22.5
Ts
N
[Pd]
7


%
Ts
N
[Cu]
7
91.06
155.02
65.07
201.95
92.11
63.06
62.08
95.10
123.05
156.06
158.05
202.99
248.95
286.53
332.95
369.13
416.34
470.69
506.40
545.36
574.82
m/z

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