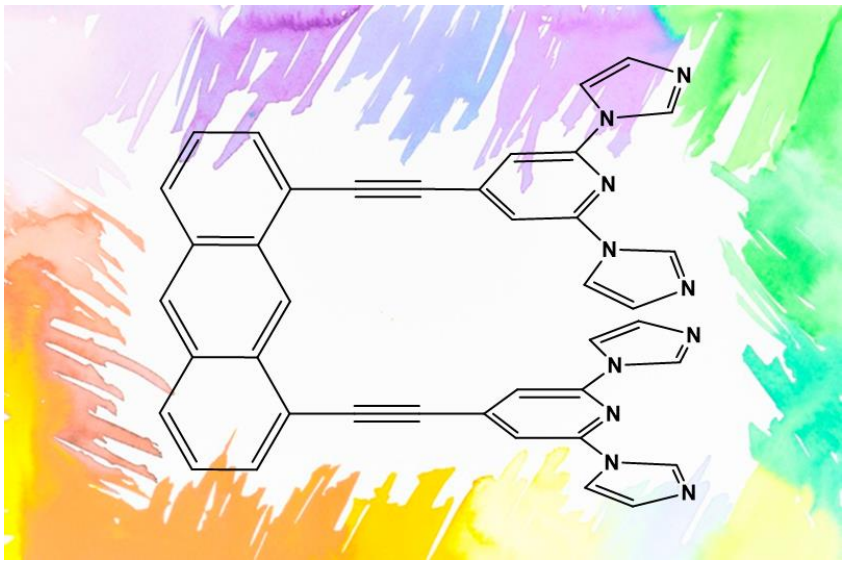
UNIVERSITAT JAUME I

Departament de Química Inorgànica I Orgànica

Àrea de Quimica Inorgànica

Synthetic route to a *pincer-tweezer* precursor



Degree Final Project

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Castelló de la Plana, June 2020

ACKNOWLEDGEMENTS

En primer lugar, me gustaría dar las gracias a mi tutora Macarena Poyatos, por toda la ayuda que me ha proporcionado, por sus ganas de trabajar y de querer que todo salga perfecto, por las cosas que he podido aprender con ella y de ella. Gracias por la paciencia corrigiendo mi trabajo y gracias por tener esa capacidad de motivar a la gente y de buscar una solución para todo, eres una gran profesora.

Por otro lado, me gustaría dar las gracias a los compañeros del laboratorio por hacer sentirme como uno más en mi breve estancia. A mis amigos de la universidad con los que he vivido estos años donde no me llevo amigos ya que los considero parte de mi familia.

Y finalmente, dar las gracias a las personas más importantes para mí, mis padres y mi hermano. Sin ellos no estaría donde estoy ahora mismo, ya que han trabajado mucho para poder estar donde estoy.

Por todo esto, GRACIAS.

List of abbreviations

Δ		refluxing temperature
NHC		N-heterocyclic carbene
$CDCl_3$		deuterated chloroform
CuI		copper(I) iodide
DMSO-d_6		deuterated dimethylsulfoxide
NaH		sodium hydride
DIPA		diisopropylamine
NMR		Nuclear Magnetic Resonance
	δ	chemical shift
	d	doublet
	dd	double doublet
	dt	double triplet
	m	multiplet
	ppm	parts per million
	s	singlet
	t	triplet
	MHz	megahertz
ESI-MS		Electrospray Ionization Mass Spectrometry
	m/z	mass to charge
EtOAc		ethyl acetate
THF		tetrahydrofuran
t		time
T		temperature

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1. INTRODUCTION

1.1 Molecular tweezers

The concept of molecular tweezer became popular due to their application in host-guest chemistry in the early 90s by Whitlock and co-workers.[1] A molecular tweezer may be defined as a molecular receptor containing two polyaromatic interaction sites (**IS**) extended from a more or less rigid connector or spacer (**S**).[2]

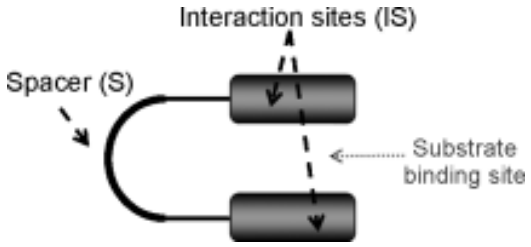


Figure 1.1 Schematic representation of a molecular tweezer

Tweezers are molecules with open cavities capable of binding guest molecules, thus acting as hosts. Their cavity may bind guests using non-covalent bonding interactions, which includes hydrogen bonding, metal coordination, hydrophobic forces, van der Waals forces, π-π interactions or electrostatics effects. In the particular case of π-π interactions, tweezers must possess an inner void of *ca.* 7 Å in order to facilitate the complexation of aromatic substrates *via* π-stacking interactions, as aromatic groups stack at an average interplanar distance of *ca*. 3.5 Å. Some of these guests can be polycyclic aromatic hydrocarbons (PAHs) such as anthracene, pyrene, triphenylene, perylene or coronene (**1**, **2**, **3**, **4** and **5**, respectively in Figure 1.2). PAHs are hazardous materials that have gathered significant environmental concern.

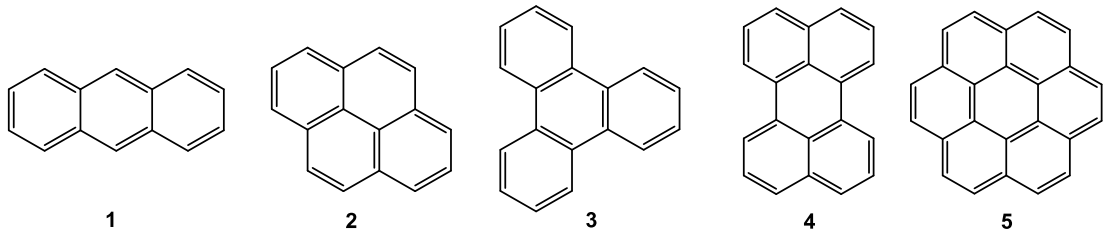


Figure 1.2. Some examples of polycyclic aromatic hydrocarbons (PAHs)

Taken to the molecular level, the concept of tweezers opens a rich and fascinating field at the convergence of molecular recognition, biomimetic chemistry and nanomachines. Operating through an "induced-fit" recognition mechanism, flexible molecular tweezers select the most appropriate conformation(s) for substrate binding. Their adaptability allows them to be used in a variety of binding modes and they have found applications in chirality signaling. Rigid spacers,

on the contrary, display a limited number of binding states, which lead to selective and strong substrate binding following a “lock and key” model.

Many of the first examples of molecular tweezers were based on organic moieties. During the last decade, some research groups integrated metal centers, preparing metallo-tweezers and introducing a new dimension in their properties and applications. Figure 1.3 depicts three of the most noteworthy examples. The bis-corannulene-based Pt(II) complex **A** was successfully employed for the recognition of fullerenes,[3] the phosphorescent double-decker tweezer **B** establishes strong host-guest interactions with square-planar platinum(II) guest complexes[4] and the bis-alkynylplatinum(II) terpyridine tweezer **C** exhibits enhanced complexation abilities toward napthol-derived guests due to the intermolecular hydrogen bonding to the nitrogen of the central pyridine ring of the spacer ligand.[5]

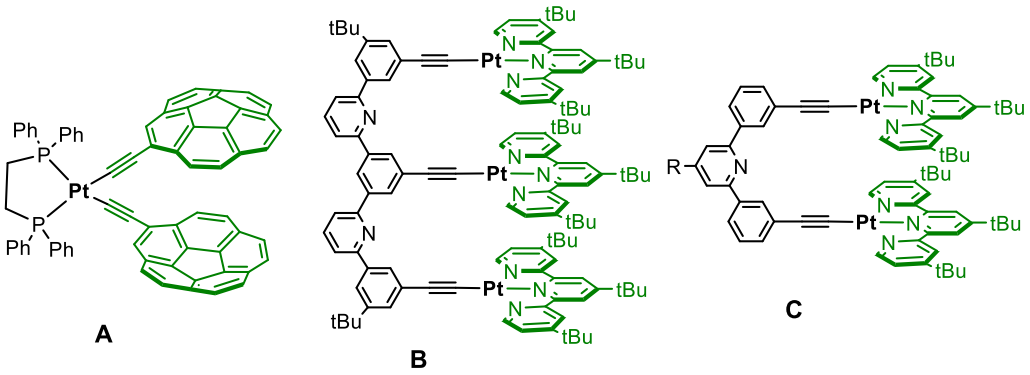


Figure 1.3. Some examples of metallo-tweezers

1.2 N-heterocyclic carbene (NHC) ligands

N-heterocyclic carbene (NHC) ligands are defined as heterocyclic species containing a carbene carbon and at least one nitrogen atom within the ring structure. NHC ligands are an important class of Fischer carbenes. Carbenes have Fischer character in complexes containing late transition metals with low oxidation states. The stability of NHCs as ligands for transition metals can be explained by their σ-donor ability with a sp^2-hybridized lone pair available for donation into a σ-accepting orbital of the transition metal (Figure 1.4, top). The π-back-donation into the carbene *p*-orbital (Figure 1.4, bottom) is also an important component of the metal-ligand binding.

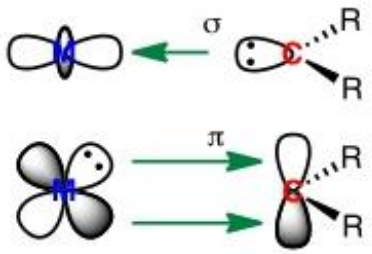


Figure 1.4. The two contributions of the M-L binding for NHCs

NHC ligands combine several properties that make them especially suitable for the design of complexes with interesting chemical and electro-optical properties:

- They afford strong M-C bonds, providing highly stable organometallic complexes
- Their precursors, normally imidazolium salts, are relatively easy to prepare and functionalize, allowing the access to a wide variety of organometallic topologies
- Their steric and electronic properties can be tuned in a reliable and predictable way

Among NHCs, poly(N-heterocyclic carbene)s have also attracted great attention because they allow the preparation of compounds with a wide variety of geometries. Figure depicts some of the known NHC frameworks including mono-, bis- and tris-NHC ligands (**6-8**, **9-10** and **11**, respectively). Bis- and tris-NHCs can act as bis-chelating, tridentate-*mer* (so-called *pincer*) or tridentate-*fac* (so-called *tripodal*) or bridging ligands.

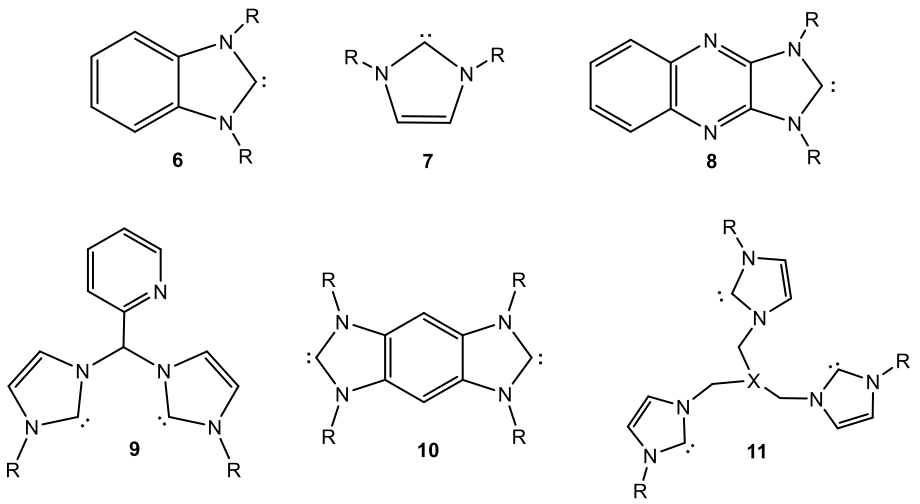


Figure 1.5. Some examples of NHC frameworks

QOMCAT group achieved the combination of metallo-tweezers with NHCs, describing Au(I)-based metallo-tweezer **D** that dimerizes in the presence of M^+ (M = Cu, Ag, Tl) ions, as a consequence of the combination of π-stacking and metallophilic interactions.[6] The presence of a H-bonding group in the linker enables the Au(I)-based tweezer **E** to show significant enhanced

binding abilities towards polycyclic aromatic hydrocarbons (PAHs) functionalized with H-bonding groups, through combined π-π-stacking and H-bonding.[7] Noteworthy, in all cases, the carbazole-bis-alkynyl linker possesses some flexibility that can be used for trapping aromatic guests between the two polyaromatic hands.

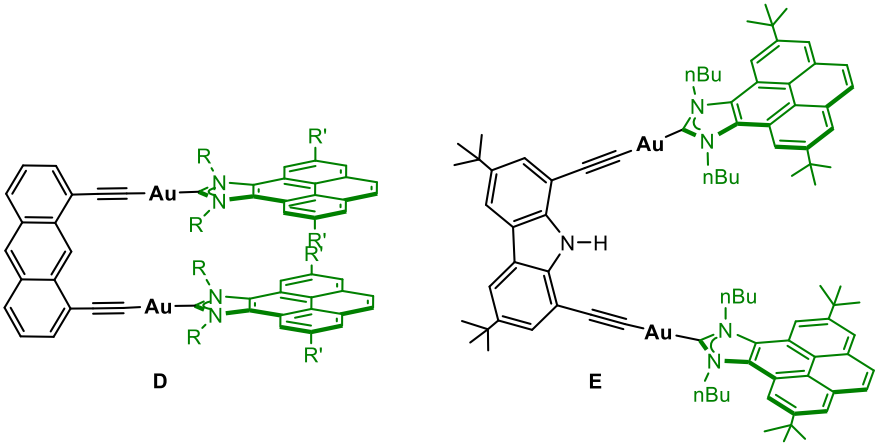


Figure 1.6. Examples of metallo-tweezers described by QOMCAT group

1.3 Tridentate-*mer* (*pincer*) NHC ligands

In the last decades, tridentate-*mer* ligands (so-called *pincer* ligands) have risen to prominence for their versatility and ease of use. The first organometallic complexes containing tridentate ligands adopting meridional geometry were described in the late 1970s.[8] The term *pincer* was coined in 1989 by Prof. Van Koten, to initially refer to tridentate ligands with a central anionic carbon and two flaking binding units that enforce a meridional coordination about the metal center.[9]

In a *pincer* complex, depicted in Figure 1.7, we have a central 2,6-substituted aromatic ring. The variation of the nature of the flaking arms (Y) can produce a profound modification in the steric crowding about the metal. Bulky R groups have a direct impact on the steric hindrance about the metal, while the size of the linker arms (Y) determine the size of the ring and therefore influences the bite angle, a factor that also affects the reactivity of the complex. The modification of the electronic properties of the ligand may be modulated by fine control of the nature of the group labeled as Z, substituent on the central aromatic ring, which exerts minimum influence on the sterics of the ligand. The nature of the central donor atom X (typically C or N) may also have an important electronic impact, particularly through the variation of the trans influence.[10] In addition to these factors, *pincer* ligands may introduce chirality in the complex, normally by employing chiral LRn groups.[11]

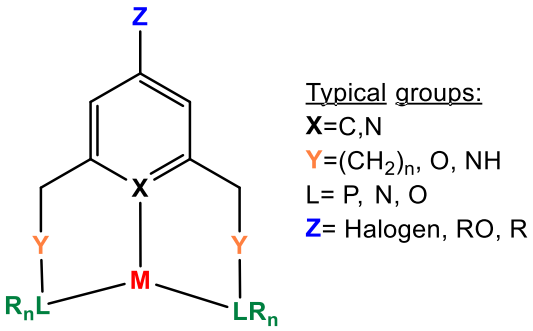


Figure 1.7. Schematic representation of *pincer*-type coordination

The robustness of the *pincer* coordination of the ligand may be used for the stabilization of complexes with unusual oxidation states and has special interest for the design of catalysts that need to be stable enough to stand harsh reaction conditions required for activating inert bonds. Figure 1.8 shows some tridentate ligands capable to coordinate in a *pincer* coordination form. In particular, ligand **14** allowed the preparation of the first complex with an NHC ligand coordinated in a *pincer* coordination form in 2001.[12] The importance of these *pincer* coordination arises from the combination of the stability of the M-$C_{carbene}$ bond established with the entropic stability due to the chelate effect.

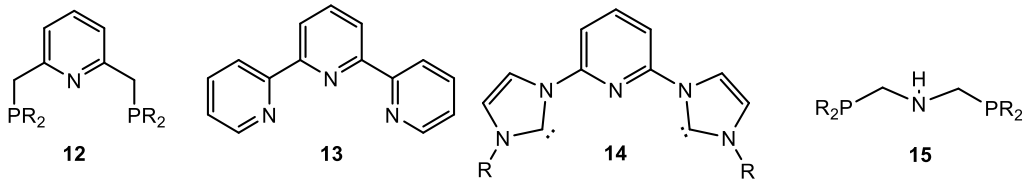


Figure 1.8. Examples of tridentate ligands capable of coordinating in *pincer* form

The *pincer* ligand motif has gained the status of a privileged platform in organometallic and coordination chemistry, mainly due to its many successful applications in homogeneous transition metal catalysis.

Figure 1.9 shows some NHC-based complexes with *pincer* coordination with applications in homogeneous catalysis. The Pd(II) complex **F** showed high activity in the Heck carbon-carbon bond cross-coupling reaction with excellent stability, even in air.[12] The Ru(II) complex **G** was found active in the in the catalytic hydrogen transfer from alcohols to ketones and in the oxidation of olefins.[13]

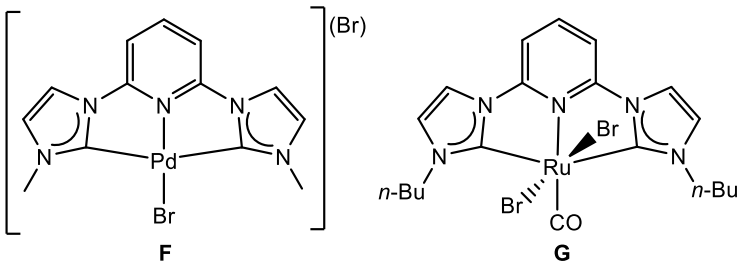


Figure 1.9. Examples of *pincer*-NHC complexes

1.4 *Pincer*-tweezers

The combination of the structural features of tweezers with the privileged ligand platforms provided by *pincer* ligands will give access to a new family of *pincer*-tweezer ligands with unprecedented chemical properties. The coordination of such ligands to metals will provide examples of new catalysts merging a polymetallic nature, with the benefits provided by *pincers* (robustness, fixity and tunability) and those arising from the use of tweezers (U-shape, proximity of metal centers and recognition abilities arising from the presence of a cavity and stereo-directing groups). Figure 1.10 depicts two specific examples of the proposed *pincer*-tweezers, containing bis-alkynyl linkers based on anthracene and carbazole, in which a *pincer* pyridine-bis-imidazolylidene ligand is coordinated to the metal center. The anthracene-based Pt(II) complex may possess interesting photophysical attributes, given that cyclometallated *pincer*-type platinum complexes benefit from extraordinary photophysical properties.[14] The carbazole-based complexes introduce additional reactive centers as new variables in our system, widening their potential applications.

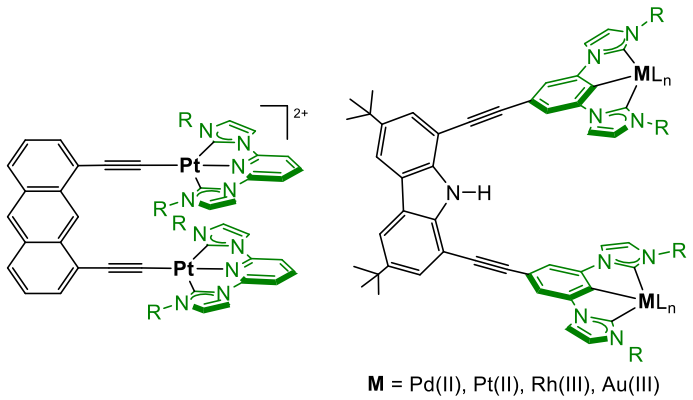


Figure 1.10. Some specific examples of *pincer*-tweezers

2. OBJECTIVES

The generic objective of this Final Degree project is to design the synthetic route to a precursor of a *pincer-tweezer* N-heterocyclic carbene-based ligand. This general objective can be divided in the following more specific steps:

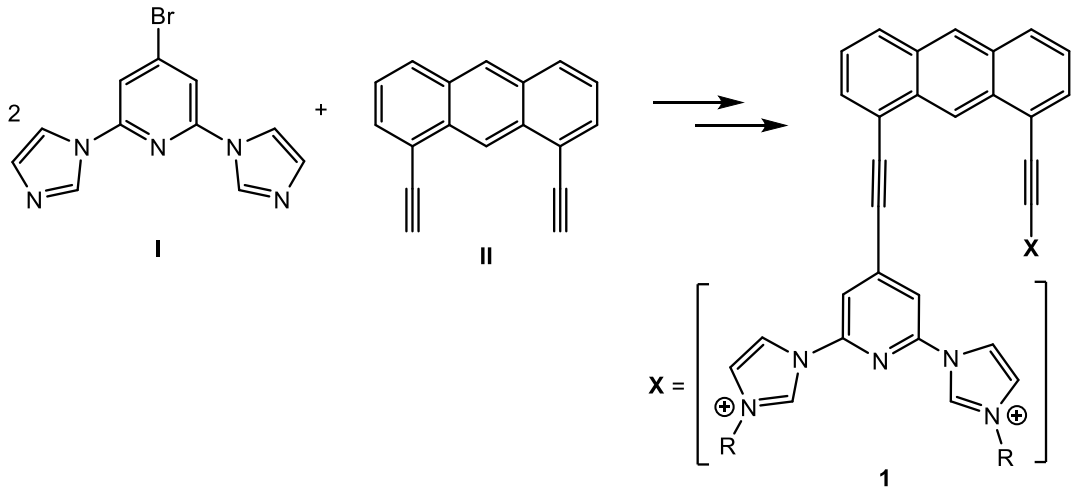
- Synthesis of a pyridine-linked bis-imidazole compound (**I**) following a synthetic route designed in the group, starting from commercially available 2,4,6-trifluoropyridine.
- Synthesis of a bis-alkynyl compound (**II**) connected by an anthracene linker following the procedure reported in the literature.
- Combination of compounds **I** and **II**, in order to prepare the precursor of the pursued ligand.

3. RESULTS AND DISCUSSION

In this section, the results from the Final Degree project will be presented and discussed. First, we will show the synthetic protocol designed to prepare the pursued tetra-imidazolium salt. Secondly, the steps in which we can divide the synthetic route will be explained in detail. The characterization of the intermediate compounds will also be presented. All the details can be found in the Experimental Section.

3.1 Designed route to tetra-imidazolium salt 1

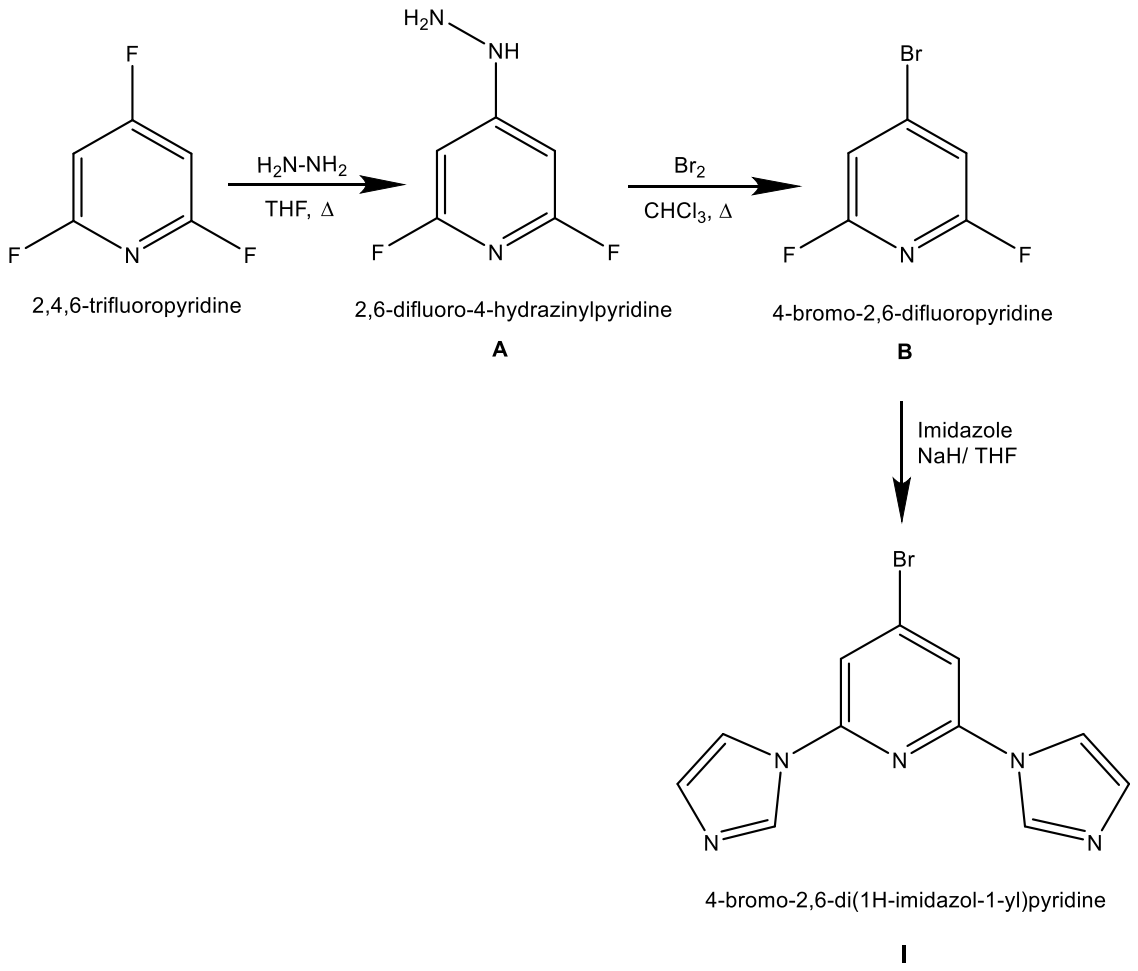
With the aim of obtaining the tetra-imidazolium salt labelled as **1**, we designed the synthetic route depicted in Scheme 3.1. The reaction of two equivalents of bis-imidazole compound **I** with one equivalent of 1,8-diethynylanthracene **II** under Sonogashira C-C coupling conditions, and subsequent N-quaternization of the four nitrogen atoms of the imidazole rings, would allow us to prepare tetra-imidazolium salt **1**. Compound **1** is the precursor of an N-heterocyclic carbene (NHC) ligand that combines the structural features of a tweezer with the privileged platforms provided by *pincer* ligands.



Scheme 3.1 Synthetic route to tetra-imidazolium salt **1**

3.2 Synthesis and characterization of compound I

As depicted in Scheme 3.2, 4-bromo-2,6-di(1H-imidazol-1-yl)pyridine (**I**) was prepared following a three-steps synthetic protocol, starting from 2,4,6-triflouropyridine which is commercially available. The first step involves a nucleophilic aromatic substitution of the fluorine atom at the 4-position of 2,4,6-triflouropyridine by reacting it with hydrazine monohydrate.



Scheme 3.2 Synthesis of 4-bromo-2,6-di(1H-imidazol-1-yl)pyridine (**I**)

A mixture of 2,4,6-trifluoropyridine and hydrazine monohydrate was reacted in THF under N_2 atmosphere. The mixture was heated at 50°C for 2h and then allowed to reach room temperature. A white solid was isolated upon removal of the volatiles, which was subsequently crystallized from hot EtOAc, yielding compound **A** as a white crystalline solid. A second crystallization from hot EtOAc, allowed us to recover an extra amount of **A** (50% overall yield) and separate it from another compound. The characterization of these two compounds by means of NMR and mass spectroscopy, confirmed the concomitant formation of an isomer of **A** in this reaction, as will be discussed in detail bellow.

The second step involves the replacement of the hydrazine group by a bromine using elemental bromine for the dehydrogenation of the hydrazinopyridine **A**, as reported by Schlosser and co-workers.[15] As explained in the literature, it is crucial to carry out this reaction starting with a large amount of compound **A** since it would not work otherwise. Bromine was added dropwise with the help of an addition funnel, to a solution of 13.24g of **A** in chloroform stabilized with amylenes. The reaction mixture was refluxed at 60°C for 6h, under N_2 atmosphere. We use

chloroform stabilized with amylenes since regular chloroform is stabilized with ethanol, and this can quench bromine avoiding its reaction with **A**. The mixture was washed by liquid-liquid extraction yielding an orange oil. Compound **B** was further purified by vacuum distillation. We have to be careful during the distillation because the compound is volatile.

The last step of the synthesis involves a nucleophilic aromatic substitution of the fluorine atoms by an imidazole fragment. This reaction involved the use of two different Schlenk tubes, both under N_2 atmosphere. In the first Schlenk tube, imidazole was suspended in dry THF and deprotonated with sodium hydride. In the second Schlenk tube, compound **B** was dissolved in dry THF. The latter solution was cannulated over the Schlenk tube containing sodium imidazoline. The resulting mixture was stirred overnight at room temperature. After this time, the volatiles were removed under vacuum and a purple solid was obtained. Since the isolated solid is partially soluble in dichloromethane, it was re-precipitated in dichloromethane/diethylether. Compound **I** was isolated by filtration as a purple solid in a 67% yield.

The already known compounds, namely **A** and **B,** were identified according to previously spectroscopic data. Compound **I** was characterized by NMR spectroscopy.

Figure 3.1 shows the ^{1}H NMR spectrum of the crude solid coming from the reaction of 2,4,6-trifluoropyridine and hydrazine monohydrate. As can be seen in the spectrum, there is a second compound along with compound **A**. Figures 3.2 and 3.3 show the ^{1}H NMR spectra of compound **A** and its isomer, respectively, after their separation by recrystallization from hot EtOAc.

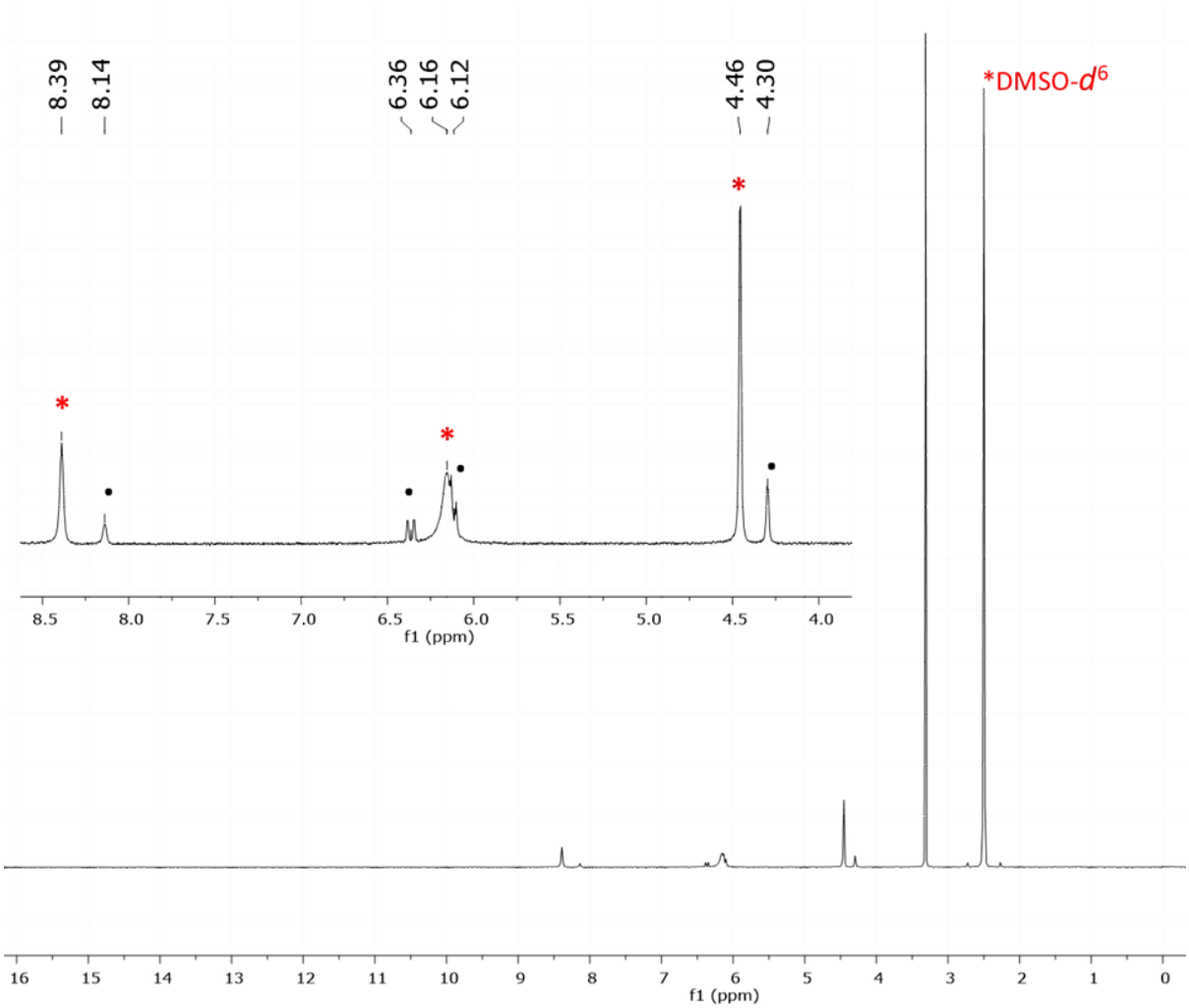


Figure 3.1 ^{1}H NMR spectrum in $CDCl_3$ (300 MHz) of the mixture of compound **A** (*) and its isomer (•)

*^{1}H NMR spectrum of **A** in DMSO-d^{6}*

Figure 3.2 shows the ^{1}H NMR spectrum of compound **A**. The number of signals and their integration are consistent with the two-fold symmetry of the compound. The signal attributed to the aromatic protons of pyridine core (b) is observed as a singlet at 6.16 ppm. The signals due to the hydrazine group protons (a, c) appear as singlets at 8.39 and 4.46 ppm, respectively.

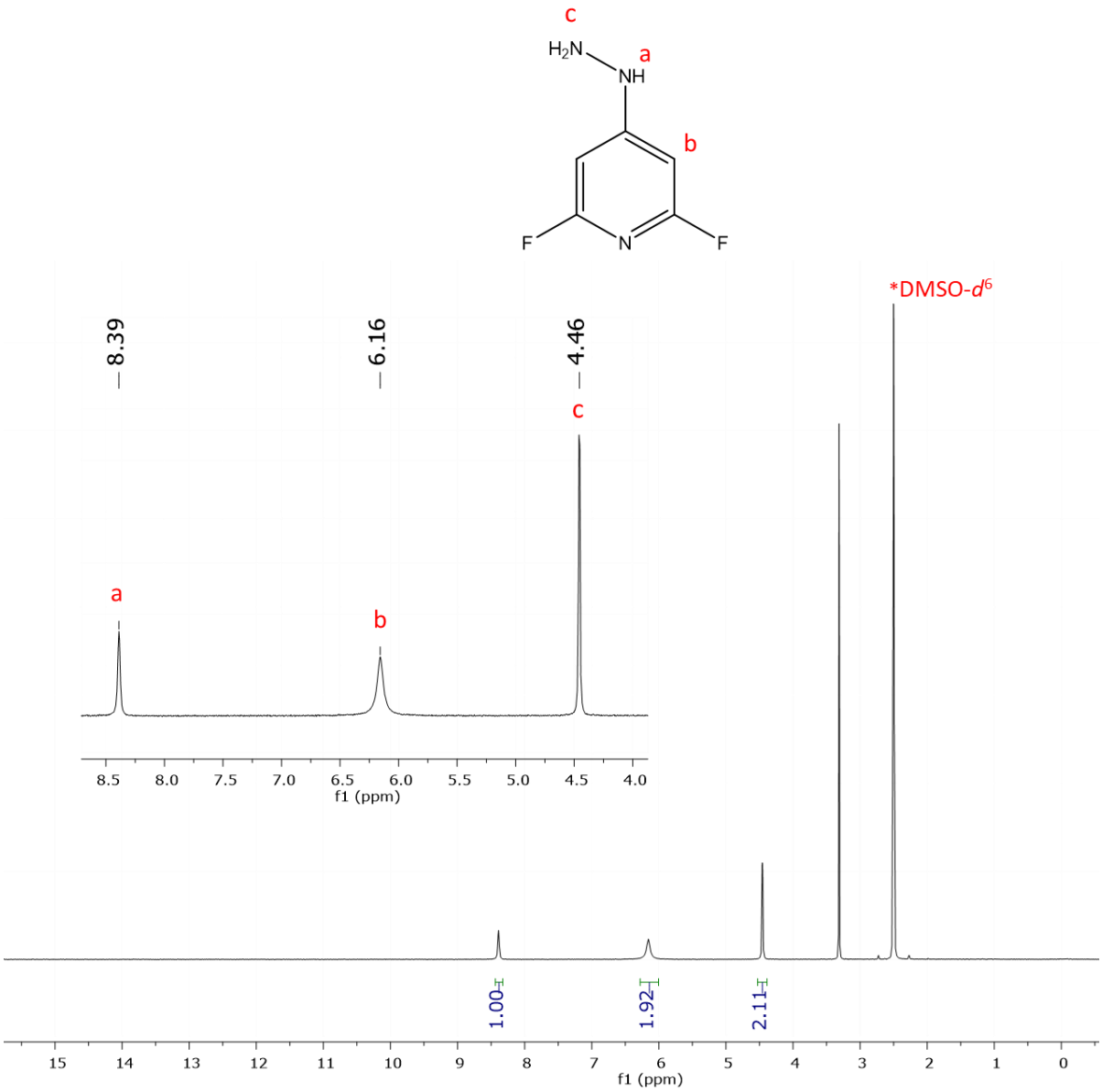


Figure 3.2 ^{1}H NMR spectrum of compound **A** in DMSO-d^6 (300 MHz)

*^{1}H NMR spectrum of the isomer of **A** in DMSO-d^6*

Figure 3.3 shows the ^{1}H NMR spectrum of the isomer of **A**. The signal of the proton corresponding to the NH group appears as singlet at 8.14 ppm (a). The signals of the protons of the pyridine core (b, c) appear as a double doublet and a double triplet at 6.37 and 6.12, respectively. The signal due to proton atoms of the NH_2 group appears as a doublet at 4.30 ppm (d).

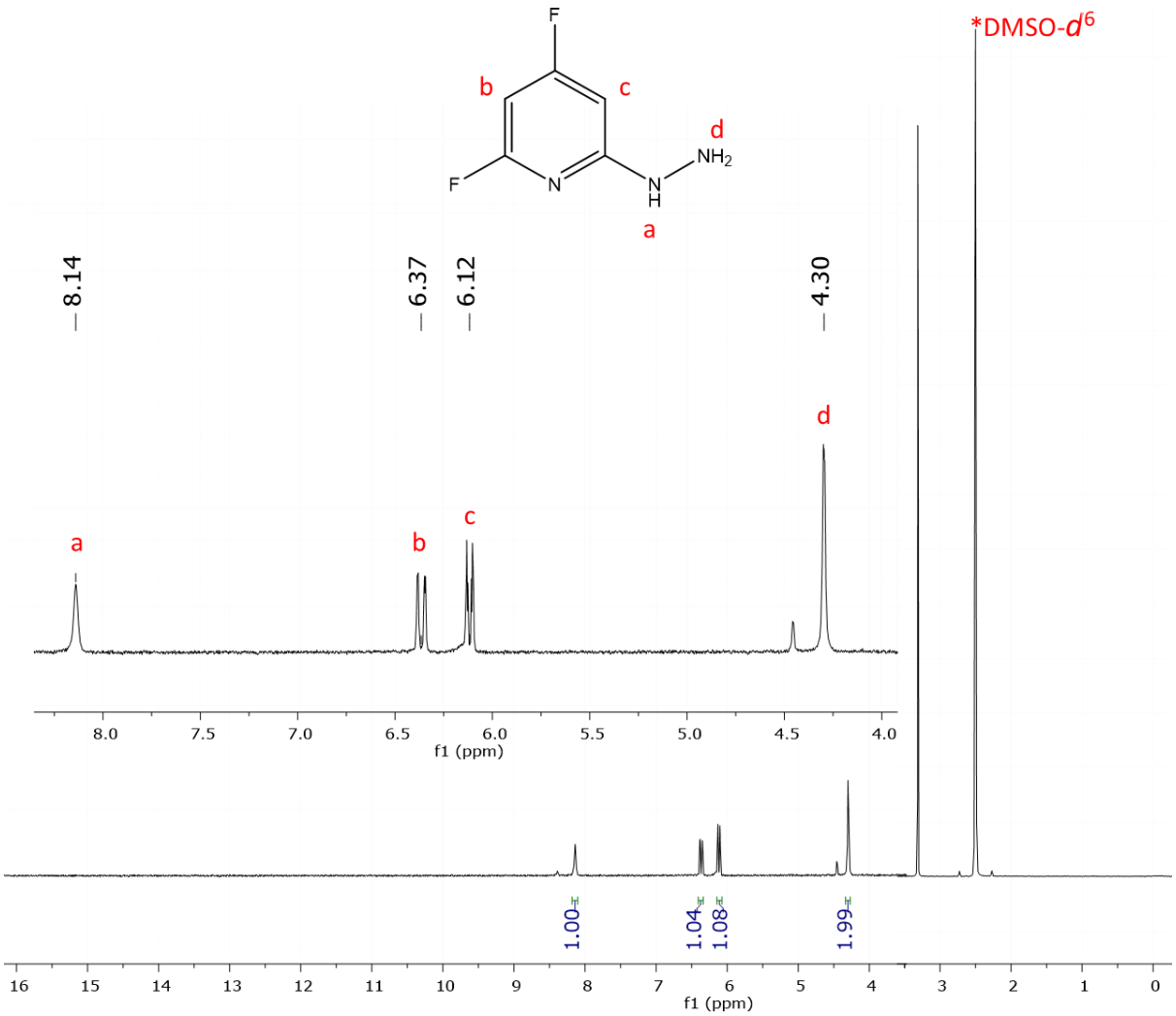


Figure 3.3 ^{1}H NMR spectrum of the isomer of **A** in DMSO-d^{6} (300 MHz)

Figure 3.4 shows the mass spectrum of **A**, in which the more intense signal is the molecular peak with a molecular mass 146 m/z. Figure 3.5 shows the mass spectrum of the other product isolated in the reaction, which also shows the molecular peak at 146 m/z, thus probing that the two compounds are isomers.

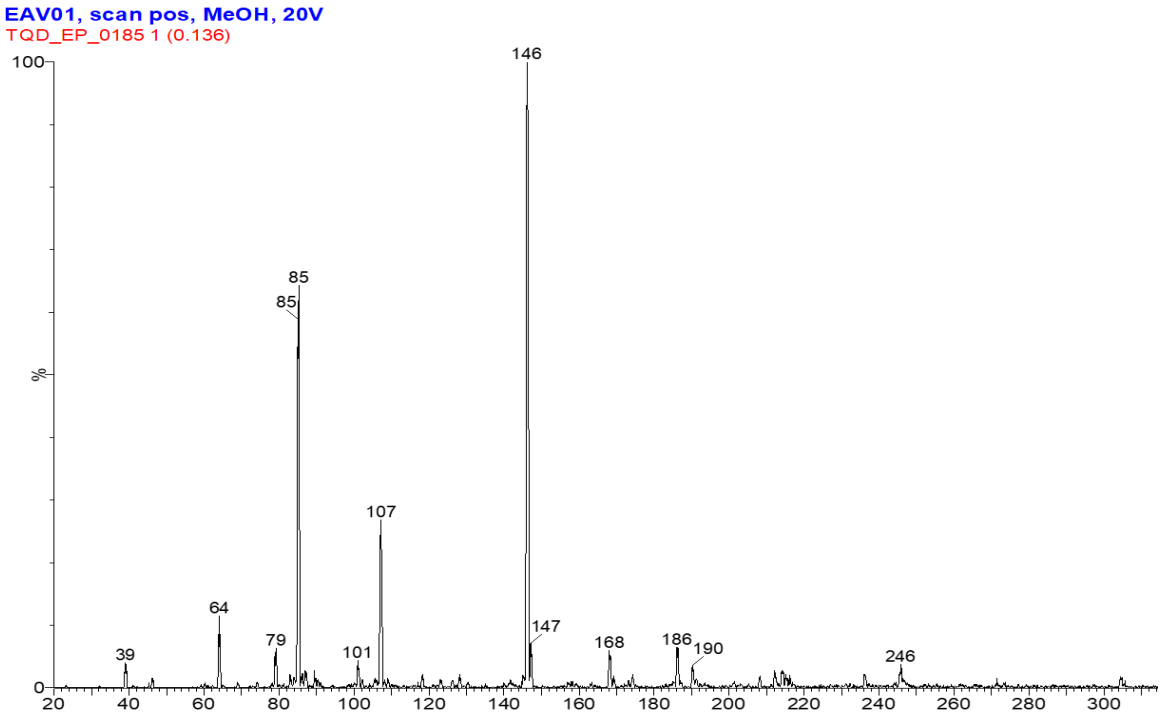


Figure 3.4 Mass spectrum of compound **A**

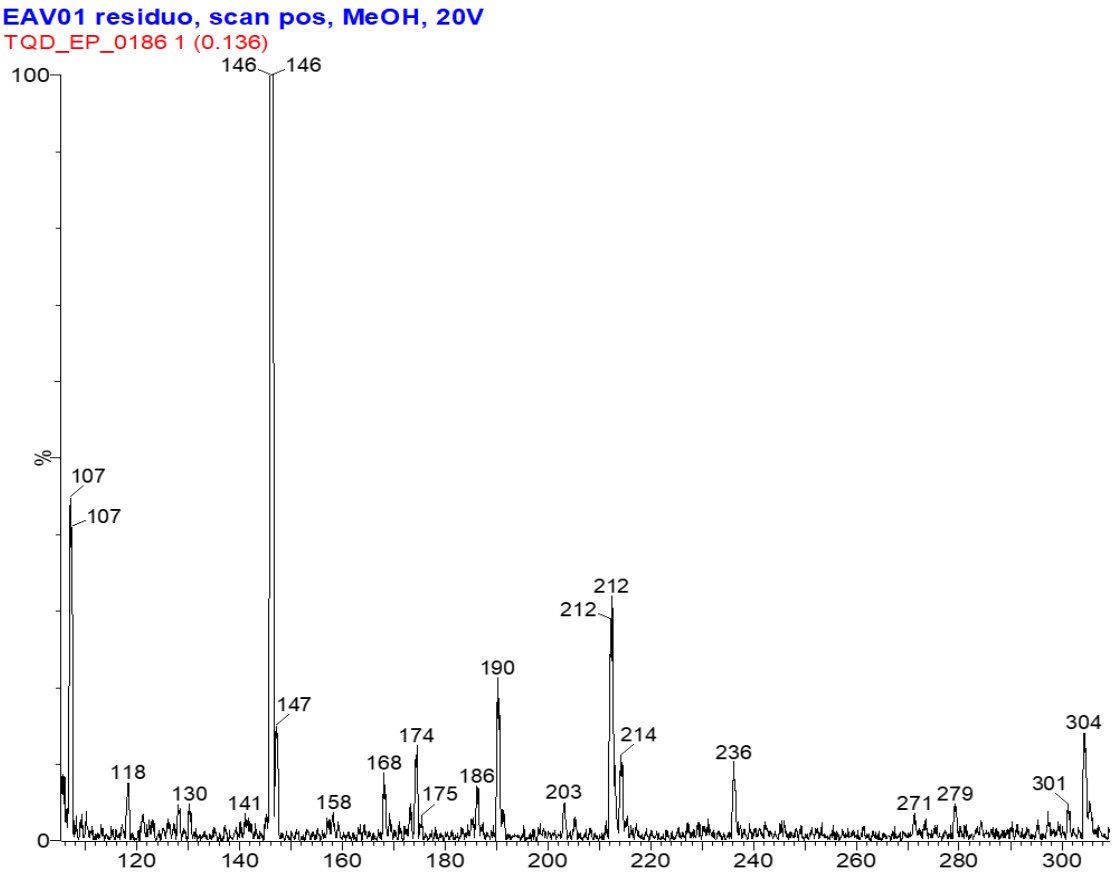


Figure 3.5 Mass spectrum of the isomer of compound **A**

*^{1}H NMR spectrum of **B** in $CDCl_3$*

Figure 3.6 shows the ^{1}H NMR spectrum of 4-bromo-2,6-difluoropyridine (**B**). The number of signals and their integration are consistent with the two-fold symmetry of the compound. The only signal is observed as a triplet at 7.03 ppm, which can be attributed to the aromatic proton of the pyridine (a).

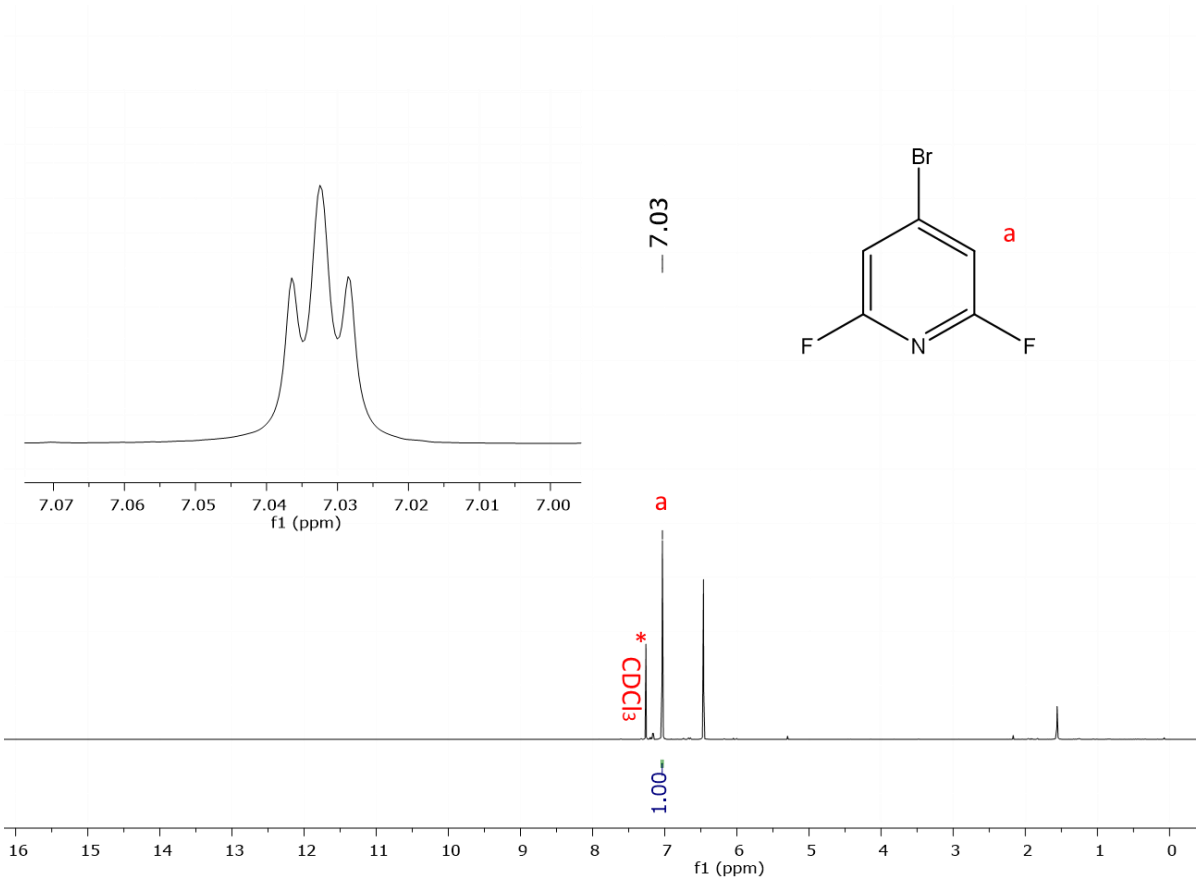


Figure 3.6 ^{1}H NMR spectrum of **B** in $CDCl_3$ (300 MHz)

*^{1}H NMR spectrum of **I** in DMSO-d^6*

Figure 3.7 shows the ^{1}H NMR spectrum of 4-bromo-2,6-di(1H-imidazol-1-yl)pyridine (**I**). Again, the number of signals and their integration is in agreement with the two-fold symmetry of the compound. The signals due to the protons of the imidazole groups appear as singlets at 8.79, 8.17 and 8.12 ppm (a, b and c, respectively in Fig. 3.7). The signal of the protons of the pyridine core (d) appears as a singlet at 7.15 ppm.

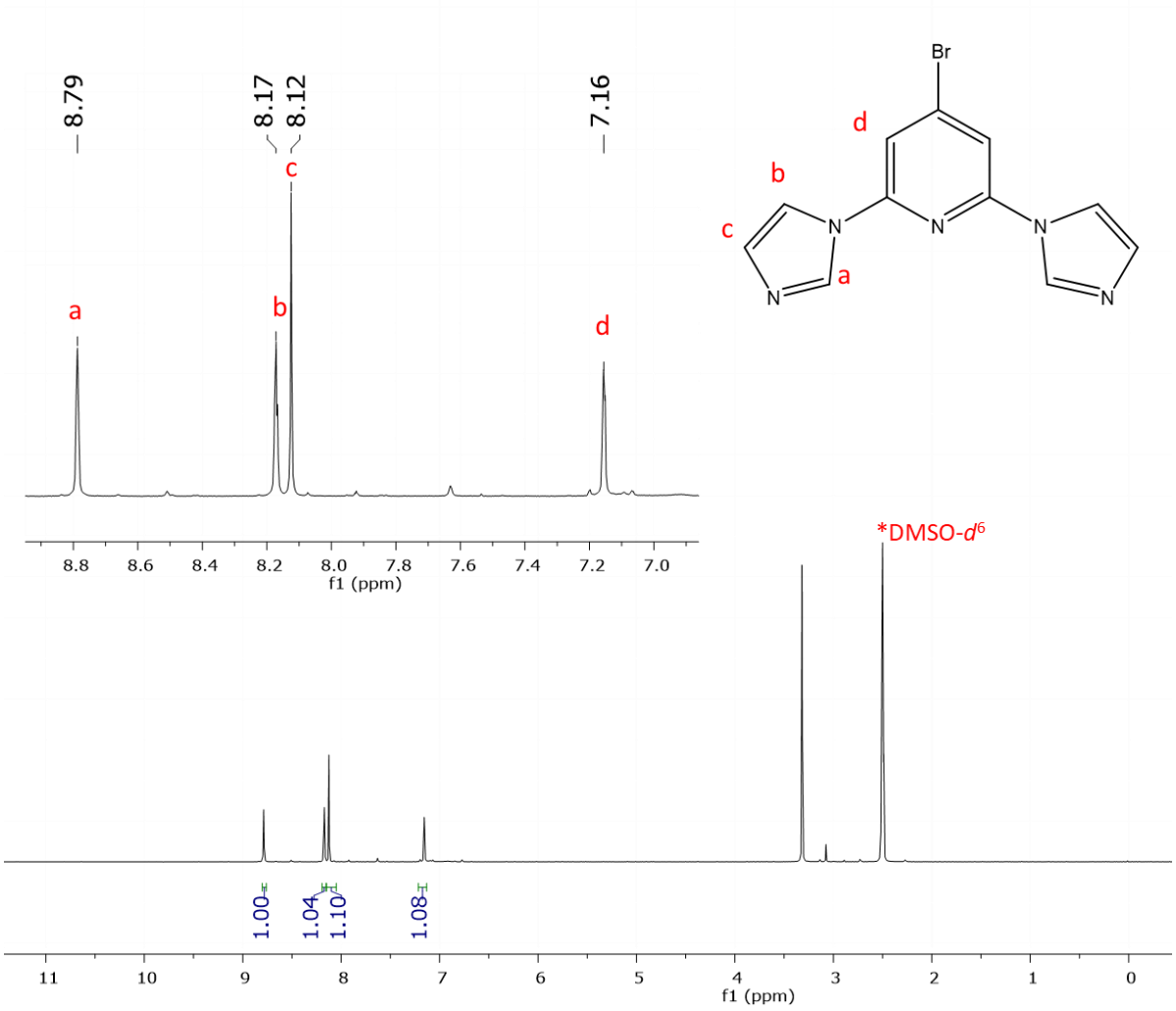


Figure 3.7 ^{1}H NMR spectrum of **I** in DMSO-d^{6} (300 MHz)

*$^{13}C\{^{1}H\}$ NMR spectrum of compound **I** in DMSO*

Figure 3.8 shows the $^{13}C\{^{1}H\}$ NMR spectrum of compound **I**. Again, the number of signals and their integration are consistent with the two-fold symmetry of the compound. The quaternary carbon atoms of the pyridine fragment **1** and **2** appear at 148.25 and 136.93 ppm, respectively. The resonances attributed to the carbon atoms of the imidazole rings appear at 135.86, 130.45 and 116.93 ppm (**3**, **4** and **5**). Finally, the tertiary carbon atom of the pyridine fragment 3 appears at 112.73 ppm.

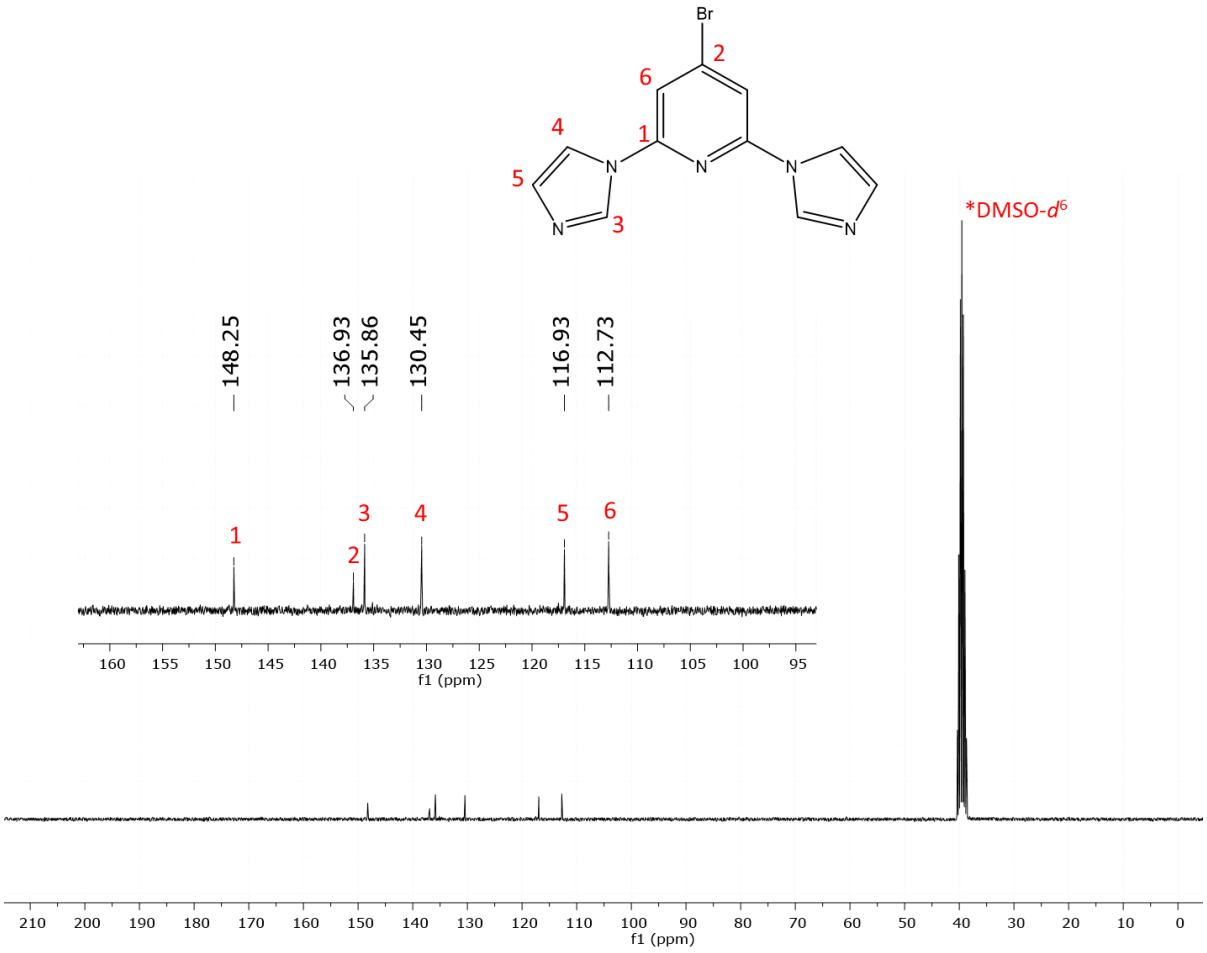
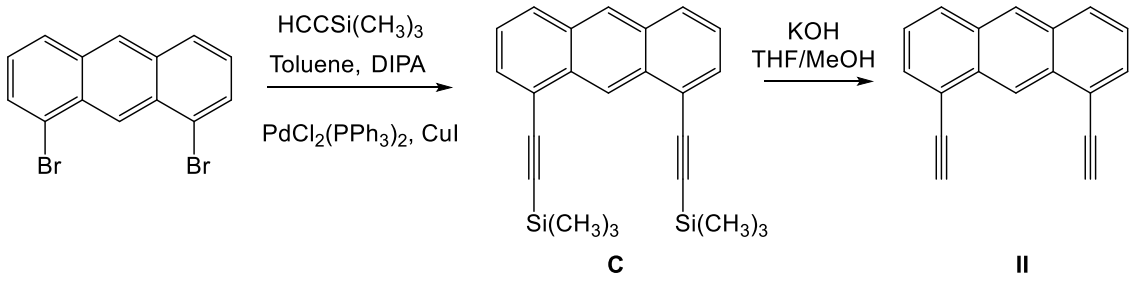


Figure 3.8. $^{13}C\{^{1}H\}$ NMR spectrum of **I** in DMSO-d^6 (300 MHz)

3.3 Synthesis and characterization of compound II

As depicted in Scheme 3.2, 1,8-bis((trimethylsilyl)ethynyl)anthracene (**C**) was prepared in one step starting from commercially available 1,8-dibromoanthracene through a Sonogashira C-C cross-coupling reaction, following the procedure described in the literature.[16]



Scheme 3.3 Synthesis of 1,8-diethynylanthracene (**II**)

In a typical Sonogashira reaction, we react a terminal alkyne with an organohalide in the presence of a base, using a palladium catalyst and a copper catalyst, to give the coupled product. The base is employed to neutralize the hydrogen halide produced as the byproduct. Under N_2

atmosphere, 1,8-dibromoanthracene, $PdCl_2(PPh_3)_2$ and CuI were dissolved in a small amount of dry toluene and diisopropylamine (DIPA). Ethynyltrimethylsilane was then added dropwise to the solution and the mixture was stirred at 60°C overnight. After this time, the mixture was filtered through Celite to remove insoluble salts. After that, the volatiles were removed under vacuum. Thin-layer chromatography (TLC) using hexane indicated the presence of other two by-products that were not isolated. Compound **C** was purified by column chromatography eluting with hexane. The desired product was isolated as a green solid, in 46% yield. The removal of the trimethylsilane groups in **C** under basic conditions, would lead to compound **II** (Scheme 3.2).[16] Unfortunately, given the time constraints, we were not able to prepare compound **II** and further react it with compound **I**.

*^{1}H NMR spectrum of **C** in $CDCl_3$*

Figure 3.9 shows the ^{1}H NMR spectrum of 1,8-bis((trimethylsilyl)ethynyl)anthracene (**C**). The number of signals and their integration are consistent with the two-fold symmetry of the compound. The resonances attributed to the aromatic protons of the anthracene core are displayed as singlets (a, b), doublets (c, d) and a doublet of doublets (e) at 9.32, 8.42, 7.98, 7.78 and 7.42 ppm, respectively. Finally, the signal due to the protons of the trimethylsilane groups appears as a singlet at 0.38 ppm (f).

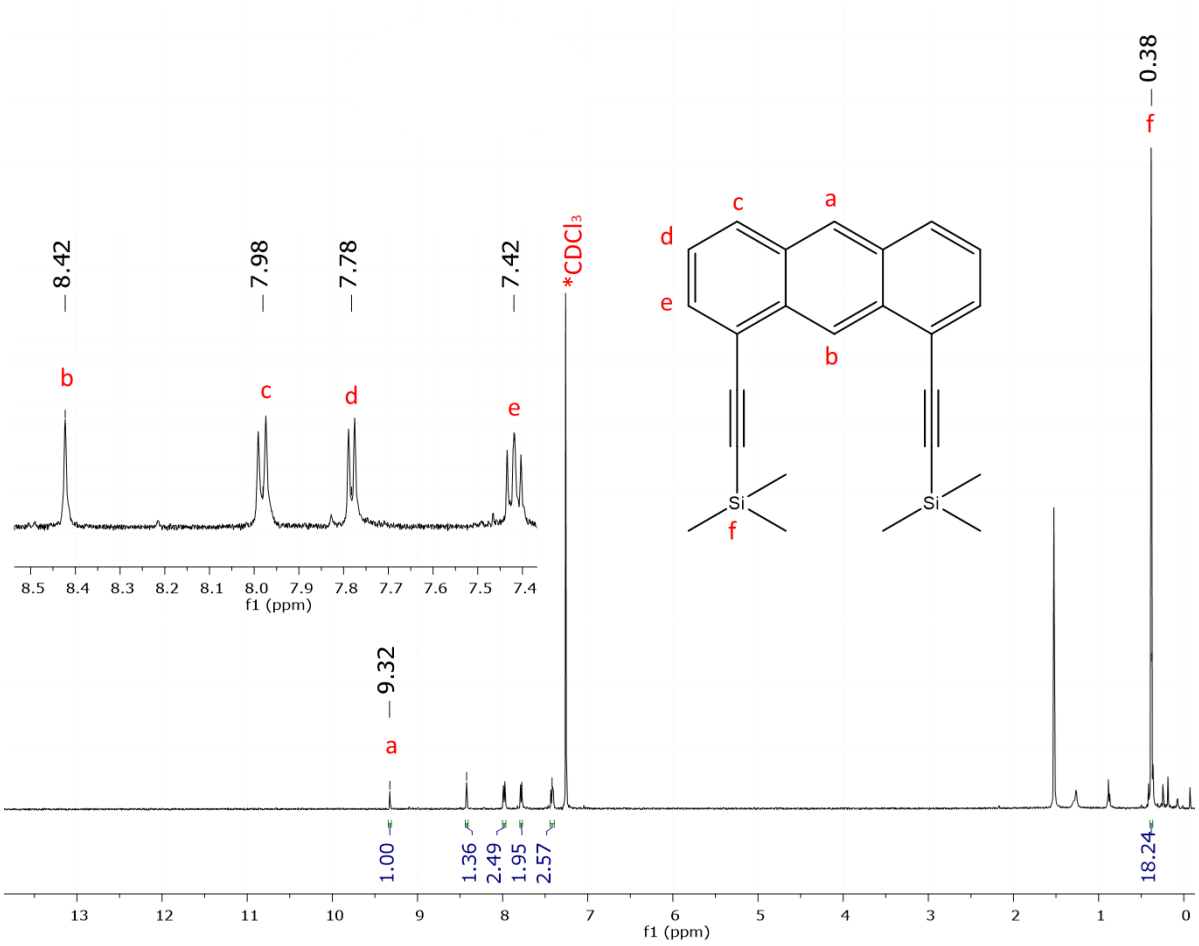
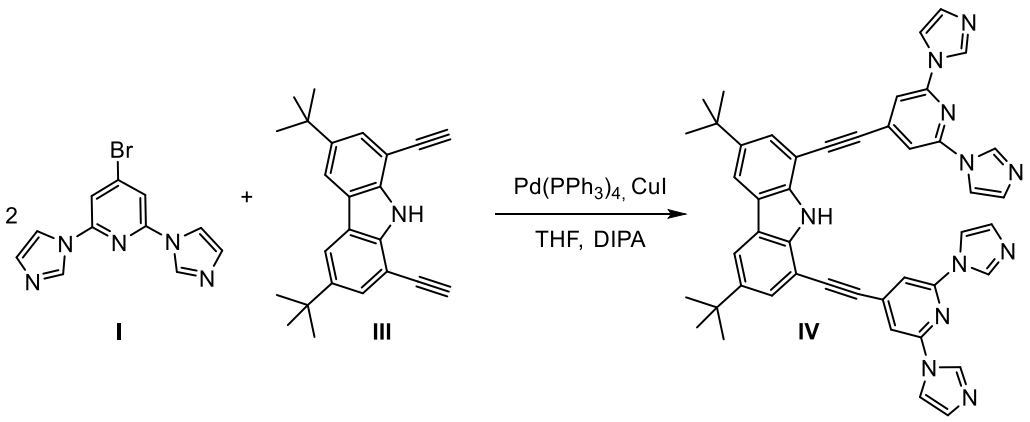


Figure 3.9 ^{1}H NMR spectrum of **C** in $CDCl_3$ (300 MHz)

3.4 Synthesis of the tetra-imidazole compound

As stated earlier, given the time constrains, we were not able to prepare compound **II**. For this reason, we carried out the coupling reaction of compound **I** with a bis-alkynyl compound already prepared in the group connected by carbazole, namely 3,6-di(tert-butyl)-1,8-diethynyl-9H-carbazole (**III** in Scheme 3.4).



Scheme 3.4 Synthesis of tetra imidazole compound **IV**

The reaction mixture was carried out under N_2 atmosphere. Compounds **I** and **III**, $Pd(PPh_3)_4$ and CuI were dissolved in small amount of dry THF and DIPA. The resulting mixture was stirred at 60°C overnight. After this time, the volatiles were removed under vacuum and a brown solid was isolated. The solid was dissolved in dichloromethane and then filtered through Celite. Upon removal of the volatiles, the product was isolated as a brown solid.

The solid was characterized by NMR spectroscopy and mass spectrometry. According to these experiments, we think that the isolated compound is the mono-substituted product. For this reason, we envisaged that longer reaction times are required.

4. CONCLUSIONS AND FUTURE PERSPECTIVES

In this work, we designed the route to a precursor of a *pincer*-tweezer N-heterocyclic carbene-based ligand. Our approach involves the synthesis of this compound by combining two fragments, namely 4-bromo-2,6-di(1H-imidazol-1-yl)pyridine (**I**) and 1,8-diethynylanthracene (**II**).

In one hand, we prepared compound **I** starting from 2,4,6-trifluoropyridine following a three-steps protocol. The first one involves a nucleophilic substitution of the fluorine atom in the 4-position by the hydrazine group to yield compound **A**. The next step involves the bromination at the same position to prepare compound **B** by a modified Sandmeyer-type reaction. The last step of the synthesis involves a nucleophilic aromatic substitution of the fluorine atoms by an imidazole fragment allowing to obtain compound **I**.

Additionally, we synthetized the alkynyl anthracene fragment **C** through a Sonogashira cross-coupling reaction. The removal of the TMS groups of compound **C** under basic conditions, would have led to compound **II**. However, given the time constrains, we carried out the final coupling reaction employing carbazole-linked bis-alkynyl compound **III** (Scheme 3.4). Although, we were not able to obtain the desired tetra-imidazole compound, we observed that the mono-substituted compound was present in the reaction mixture.

FUTURE PERSPECTIVES

In future experiments, we will try to prepare the pursued tetra-imidazole compound by coupling compounds **I** and **II**. Subsequently, we would perform the N-quaternization of the nitrogen groups of the imidazole rings to obtain the tetra-imidazolium salt **1** (Scheme 3.1). If successful, we will use **1** as precursor of a *pincer*-tweezer tetra-NHC ligand.

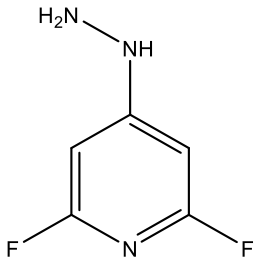
5. EXPERIMENTAL SECTION

5.1 General methods

Unless otherwise stated, all the reactions were carried out by using standard Schlenk tube techniques under nitrogen atmosphere. Compounds **A**, **B**[17] and **C**[16] were prepared according to literature methods and 4-bromo-2,6-di(1H-imidazol-1-yl)pyridine (**I**) was prepared following a procedure described in the literature for related compounds. Solvents were dried using a solvent purification system (SPS M RAUN). All other reagents were used as received from commercial suppliers. Column chromatography was performed in silica gel Merck, using the mixture of solvents indicated. NMR spectra were recorded on a Bruker 300-400 MHz, using DMSO-d^6 or $CDCl_3$ as solvents. Electrospray mass spectra (ESI-MS) were recorded on a Micro mass Quatro LC instrument; nitrogen was employed as drying and nebulizing gas.

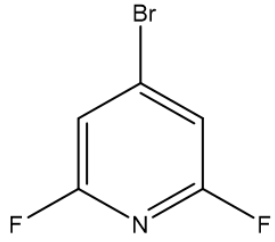
5.2 Synthesis and characterization

5.2.1 Synthesis and characterization of 2,6-difluoro-4-hydrazinylpyridine (A)



Under aerobic conditions, 2,4,6-trifluoropyridine (9 mL, 12.13 g, 91.2 mmol, 1equiv.) and hydrazine monohydrate (5.64 mL, 181.3 mmol, 2 equiv.) were dissolved in 90 mL of dry THF. The mixture was stirred at room temperature. The mixture was heated at 50°C for 2h, and then allowed to reach room temperature. The crude was triturated with water (2 x 20 mL) and hexane (2 x 20 mL), and then dried under vacuum overnight. The solid obtained was recrystallized from hot EtOAc to yield 2,6-difluoro-4-hydrazinylpyridine as a white crystalline solid. Yield: 6.7 g, 55%. ^{1}H NMR (300MHz, DMSO-d^6): δ 8.39 (s, 1H, NH), 6.16 (s, 2H, CH-pyridine), 4.46 (s, 2H, NH_2). Electrospray MS (20 V, *m/z*): 146 $[M+H]^+$.

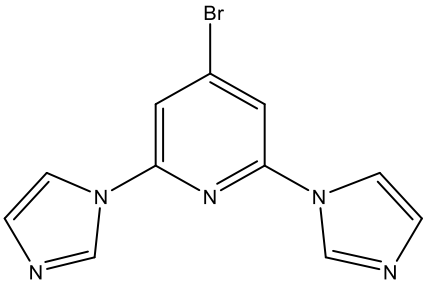
5.2.2 Synthesis and characterization of 4-bromo-2,6-difluoropyridine (B)



In a three-neck round bottom flask, 13.24 g of 2,6-difluoro-4-hydrazinylpyridine (91.31 mmol, 1 equiv.) were dissolved in chloroform stabilized with amylenes (97 mL, 0.78 M). The mixture was stirred under nitrogen atmosphere. Bromine (9.4 mL, 182.62 mmol, 2 equiv.) was added dropwise (via addition funnel). The mixture was heated at reflux at 60°C for 6h and then allowed to reach room temperature. The mixture was then filtered through Celite and washed with dichloromethane. The filtrate was subsequently washed, with a saturated aqueous solution of Na_2CO_3 (25mL) and brine (25mL) and dried over anhydrous magnesium

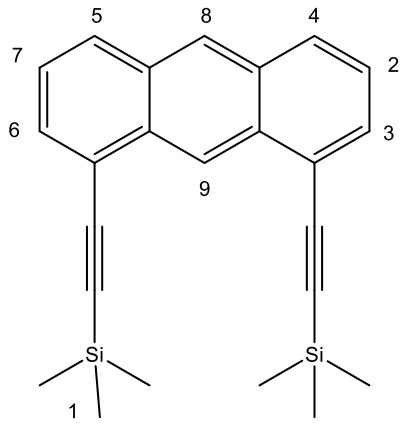
sulfate. The organic phase was filtered and concentrated. Distillation provided an orange oil. Yield: 8 g, 60%. ^{1}H NMR (300MHz, $CDCl_3$): δ 7.03 ppm (t, 2H, CH-pyridine).

5.2.3 Synthesis and characterization of the 4-bromo-2,6-di(1H-imidazol-1-yl)pyridine (I)



NaH (3.89 g, 99.6 mmol, 2.4 equiv.) was placed in a Schlenk tube. The tube was evacuated and filled with N_2 three times. The solid was suspended in 40 mL of dry THF and the tube subsequently introduced in a water/ice bath with vigorous stirring for 10 min. After this time, imidazole (6.21 g, 91.28 mmol, 2.2 equiv.) was added portion wise to minimize the effervescence. In a second Schlenk tube, compound **B** (8 g, 41.49 mmol, 1 equiv.) was dissolved in 40 mL of dry THF. The content of this second tube was cannulated over the first one through an oven-dried cannula. The resulting mixture was stirred overnight at room temperature. During this time, the initially yellow-solution turned purple. The crude reaction was filtered and subsequently washed with dichloromethane and diethyl ether. The desired product was isolated by filtration as a purple solid. Other conditions to prepare compound **I** were explored, but no improvement of the yield of the reaction was achieved. Yield: 5.33 g, 66 %. ^{1}H NMR (300MHz, DMSO-d^6): δ 8.79 (s, 2H, CH-imidazole), 8.17 (s, 2H, CH-imidazole), 8.12 (s, 2H, CH-imidazole), 7.15 (s, 2H, CH-pyridine). ^{13}C NMR (300 MHz, DMSO-d^6): δ = 148.25 (C_q pyridine), 136.93 (Br-C_q pyridine), 135.86 (CH-imidazole), 130.45 (CH-imidazole), 116.93 (CH-imidazole), 112.73 (CH-Pyridine).

5.2.4 Synthesis and characterization of 1,8-bis((trimethylsilyl)ethynyl)anthracene (C)



Under N_2 atmosphere, 1,8-dibromoanthracene (500 mg, 1.50 mmol, 1 equiv.), $PdCl_2(PPh_3)_2$ (8 mg, 0.019 mmol, 0.08 equiv.) and CuI (3 mg, 0.01636 mmol, 0.011 equiv.) were suspended in dry toluene (15 mL). Diisopropylamine (2 mL) was added to the resulting suspension. The mixture was stirred at room temperature for 10 minutes and then ethynyltrimethylsilane (0.8 mL, 4.46 mmol, 3 equiv.) was added. The resulting mixture was heated at 60°C overnight. During this time, the initially yellow solution turned dark green. Once at room temperature, the mixture was filtered through a pad of Celite and a dark green solution was collected. The solvent was removed under vacuum. The resulting

green solid was purified by column chromatography. Elution with hexane, afforded the separation of a green band that contained compound **C**. The desired compound was isolated as a green solid. Yield: 330 mg, 67%. ^{1}H NMR (300, $CDCl_3$): δ 9.32 (s, 1H, H9), 8.42 (s, 1H, H8), 7.98 (d, 2H, H4/H5), 7.78 (d, 2H, H3/H6), 7.42 (dd, 2H, H2/H7), 0.38 (s, 18H, $Si(CH_3)_3$).

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