



UNIVERSIDADE DA CORUÑA

Facultade de Ciencias

## Grao en Química

### Memoria do Traballo de Fin de Grao

#### **Synthesis of terphenyl derivatives for the iterative preparation of graphene nanoribbons in solution**

Síntesis de derivados de terfenilo para la preparación iterativa de nanocintas de grafeno en disolución

Síntese de derivados de terfenilo para a preparación iterativa de nanocintas de grafeno en disolución

**Rubén Villamor Ferro**

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*Directores:* Alejandro Criado Fernández  
Elena Pazos Chantero



## Abbreviations

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<b>AcO</b>	acetate
<b>Ar</b>	aryl
<b>δ</b>	chemical shift
<b>Bpin</b>	bis(pinacol)
<b>d</b>	doublet
<b>dba</b>	dibenzalacetone
<b>DMF</b>	dimethylformamide
<b>DMSO</b>	dimethyl sulfoxide
<b>dppf</b>	1,1'-bis(diphenylphosphino)ferrocene
<b>FET</b>	field-effect transistors
<b>GC</b>	gas chromatography
<b>GNR</b>	graphene nanoribbon
<b>GQD</b>	graphene quantum dots
<b><sup>1</sup>H NMR</b>	proton nuclear magnetic resonance
<b>J</b>	coupling constant
<b>m</b>	multiplet
<b>m/z</b>	mass/charge ratio
<b>MIDA (DAN)</b>	1,8-diaminonaphthalene
<b>MS</b>	mass spectrometry
<b>MW</b>	microwaves
<b>OTf</b>	triflate

<b>PAH</b>	polycyclic aromatic hydrocarbon
<b>pin</b>	pinacol
<b>s</b>	singlet
<b>S<sub>E</sub>Ar</b>	electrophilic aromatic substitution
<b>S<sub>N</sub>Ar</b>	nucleophilic aromatic substitution
<b>T</b>	temperature
<b>t</b>	triplet
<b>THF</b>	tetrahydrofuran
<b>TLC</b>	thin layer chromatography
<b>UV</b>	ultraviolet

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## Abstract

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Graphene is an allotrope of carbon with exceptional properties that make it a very interesting compound because of its potential applications. One of those properties is the absence of a band gap in its electronic structure which gives graphene high charge-carrier mobilities. For some applications, this property became a problem and they were studied different alternatives to try to open a band gap. This possibility was developed when graphene was divided into segments that were structurally defined and showed non-zero band gap. In that moment, graphene nanoribbons were discovered.

Graphene nanoribbons (GNRs) are one-dimensional extensions of graphene with a width shorter than 10 nm. It was observed that their properties were highly dependent on the structural factors like the edge structure, the width and the length. This fact gives importance to the way these compounds are synthesized. Bottom-up synthesis was observed to be the best method to control with atomic precision the structure of the GNRs. It consists of forming a GNR by a polymerization process with molecules that acted as monomers or building blocks.

In this work, we will study the synthesis of p-terphenyl derivatives as GNR precursors for an iterative bottom-up synthesis in solution. This synthetic methodology will be based on a controlled polymer elongation method through Suzuki-Miyaura cross-coupling reactions. Additionally, we will explore the synthesis of more complex p-terphenyl derivatives as precursors for the synthesis of functionalized GNRs through the above-mentioned methodology. NMR spectroscopy will be the principal technique used for the characterization of the obtained molecules.

**Keywords:** graphene, graphene nanoribbon, iterative synthesis, bottom-up synthesis, p-terphenyl derivative, Suzuki-Miyaura cross-coupling reaction.

## Resumen

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El grafeno es un alótropo del carbono con unas propiedades excepcionales que lo convierten en un compuesto muy interesante debido a sus potenciales aplicaciones. Una de esas propiedades es la ausencia de un “band gap” en su estructura electrónica, la cual le da al grafeno altas movilidades como transportador de carga. Para algunas aplicaciones, esta propiedad se volvió un problema y se estudiaron diferentes alternativas para intentar abrir un “band gap”. Esta posibilidad se desarrolló cuando el grafeno fue dividido en segmentos estructuralmente definidos que presentaban un “band gap” distinto de cero. En ese momento, se descubrieron las nanocintas de grafeno.

Las nanocintas de grafeno (GNRs) son extensiones unidimensionales de grafeno con una anchura inferior a 10 nm. Se observó que sus propiedades eran muy dependientes de los factores estructurales como la estructura del borde, la anchura o la longitud. Este hecho le da importancia a la forma en la que son sintetizados estos compuestos. Se observó que la síntesis ascendente era el mejor método para controlar con precisión atómica la estructura de los GNRs. Consiste en formar una GNR mediante un proceso de polimerización con moléculas que actuaban como monómeros o bloques de construcción.

En este trabajo estudiaremos la síntesis de derivados de p-terfenilo como precursores de GNR para una síntesis iterativa ascendente en disolución. Esta metodología sintética se basará en un método de elongación controlada de polímeros a través de reacciones de acoplamiento cruzado de Suzuki–Miyaura. Además, exploraremos la síntesis de derivados de p-terfenilo más complejos como precursores para la síntesis de GNR funcionalizados a través de la metodología mencionada anteriormente. La espectroscopía RMN será la principal técnica utilizada en la caracterización de las moléculas obtenidas.

**Palabras clave:** grafeno, nanocinta de grafeno, síntesis iterativa, síntesis ascendente, derivados de p-terfenilo, acoplamiento cruzado de Suzuki–Miyaura.



## Resumo

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O grafeno é un alótropo do carbono cunhas propiedades excepcionais que o converten nun composto moi interesante debido ás súas potenciais aplicacións. Unha desas propiedades é a ausencia dun “band gap” na súa estrutura electrónica, a cal lle dá ao grafeno altas mobilidades como transportador de carga. Para algunhas aplicacións, esta propiedade volveuse un problema e estudiáronse diferentes alternativas para intentar abrir un “band gap”. Esta posibilidade desenvolveuse cando o grafeno foi dividido en segmentos estruturalmente definidos e que presentaban un “band gap” distinto de cero. Nese momento, descubríronse as nanocintas de grafeno.

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Neste traballo estudaremos a síntese de derivados de p-terfenilo como precursores de GNR para unha síntese iterativa ascendente en disolución. Esta metodoloxía sintética basearase nun método de elongación controlada de polímeros a través de reaccións de acoplamento cruzado de Suzuki–Miyaura. Ademais, exploraremos a síntese de derivados de p-terfenilo máis complexos como precursores para a síntese de GNR funcionalizados a través da metodoloxía mencionada anteriormente. A espectroscopía RMN será a principal técnica utilizada na caracterización das moléculas obtidas.

**Palabras chave:** grafeno, nanocinta de grafeno, síntese iterativa, síntese ascendente, derivados de p-terfenilo, acoplamento cruzado de Suzuki–Miyaura.

# 1. Introduction

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## 1.1. Graphene

Graphene, an allotrope of carbon, is a two-dimensional compound made of carbon atoms with  $sp^2$  hybridization, which are forming a honeycomb lattice or hexagonal network.<sup>1,2</sup> In 2004, at the Centre for Mesoscopic and Nanotechnology of the University of Manchester, United Kingdom, Geim and Novoselov were the first scientists to report graphene.<sup>3</sup> They obtained the first isolated single-layer graphene in a very curious way: they took a tape and they applied mechanical exfoliation to graphite crystals.<sup>4</sup> Since its discovery, a wide variety of research groups have investigated this compound. Even nowadays it keeps being a very attractive compound for the scientists.

Such investigations have shown that graphene has exceptional electronic, thermal and mechanical properties, which are the reason why it keeps being so interesting.<sup>1</sup> If one of them can be highlighted, that would be its exceptionally high charge-carrier mobilities, which makes it a very good candidate for future nanoelectronics.<sup>5</sup> There is a problem with this property because, due to lack of band gap in its electronic structure, it is not possible to develop graphene-based electronic devices like field-effect transistors (FETs) as switch.<sup>2</sup> Other properties that graphene has shown during the investigations are outstanding transparency, mechanical strength and thermal and electrical conductivity.<sup>4</sup> Due to all of them, it has become a very good candidate for practical applications in a wide variety of fields such as electronics, catalysis, energy storage and much more.<sup>1</sup>

Graphene receives different names depending on its scale (Figure 1). Nanographene is how a graphene fragment is named when its diameter is lower than 100 nm.<sup>1</sup> In this work, it is going to be explained in detail the structures of less than 10 nm, named nanographene and graphene nanoribbons (GNRs).

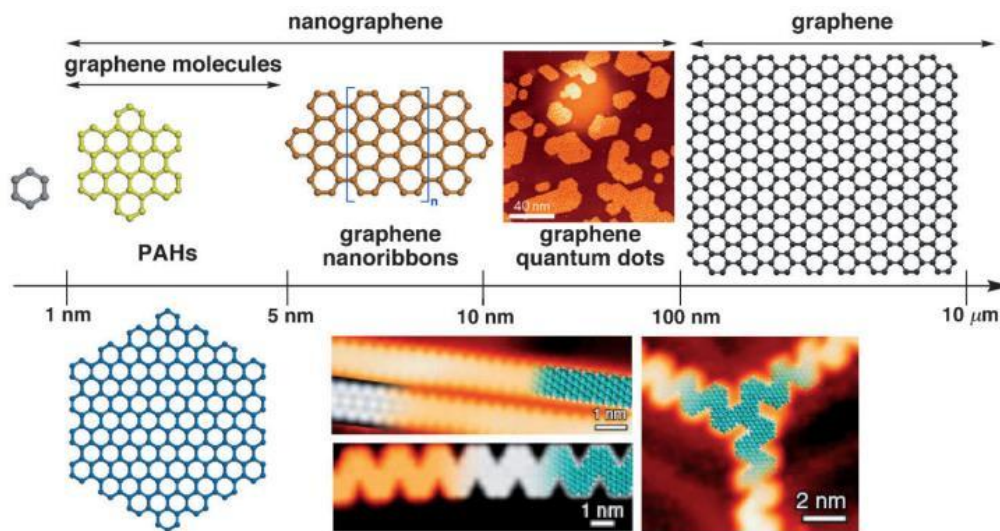


Figure 1. Graphene and its terminology based on its size scale.<sup>1</sup>

## 1.2. Graphene nanoribbons (GNRs)

In the previous section, it was mentioned that graphene had not a band gap in its electronic structure and that property was observed to be an inconvenient in some applications. To solve that problem, scientists started investigating how a band gap in graphene could be opened.<sup>4</sup> During this research, it was observed that, when graphene was divided into nanoscale graphene segments which were structurally confined, it appeared a non-zero band gap. These segments were called graphene quantum dots (GQDs) and their band gap values were observed to be dependant of their size and edge configurations.<sup>5</sup>

A wide variety of GQDs were developed, but one of them got more interest. They were GNRs, GQDs that were developed by cutting a graphene sheet into narrow strips. GNRs are one-dimensional extensions of graphene with a width shorter than 10 nm.<sup>1,5</sup> It was highlighted due to the exceptional properties that it shows: band gap, conductivity, carrier mobility, thermal conductivity, spin polarization and on-off behaviour. The most interesting part of GNRs is that the properties have a big dependence on the structural factors like edge structure, width (always shorter than 10 nm) and length.<sup>4</sup> This fact has made its synthesis really important and it will be discussed why in the following section.

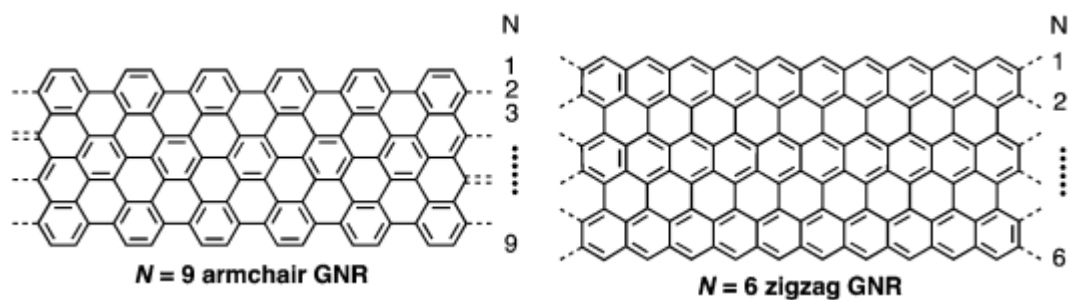


Figure 2. Classification of GNRs due to its edge structure.<sup>5</sup>

Actually, two types of GNRs which differ in their edge structure were more investigated than others: nanoribbons with armchair and zigzag configurations. Their widths are defined by a number  $N$  as it is shown in Figure 2. As expected, different edge structures and widths will change the properties of the GNRs. It was observed that nanoribbons with zigzag configuration showed localized edge states which could be spin-polarized, making this type of GNRs good candidates for spintronic devices as spin valve. In the other side, nanoribbons with armchair configuration have shown non-magnetic metallic to semiconducting behaviour with band gaps that increase as the width decreases. Theoretically, it was also observed that this last type of GNRs possessed high charge-carrier mobilities, which make them very useful in nanoelectronics.<sup>5</sup>

### 1.3. Synthesis of GNRs

Nowadays, GNRs are being studied by a wide variety of researching groups due to its unique properties. The fact that properties of nanoribbons are highly dependent of their edge structure, width and length gives relevance to the synthesis of these compounds. Since then, it was crucial in the synthesis of GNRs to control the structural factors with atomic precision to be able to obtain the desired properties. The question is clear: how should be the synthetic procedure to obtain GNRs? As an answer to this question, two different synthetic approaches that are going to be explained in the following section were developed (Figure 3).

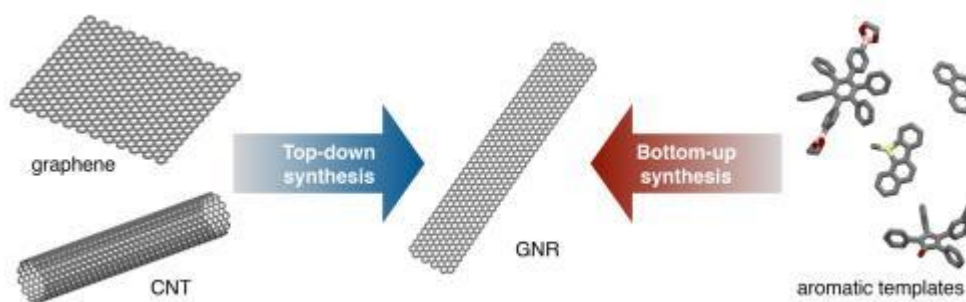


Figure 3. Scheme of the two approaches used in the synthesis of GNRs.<sup>4</sup>

### 1.3.1. Top-down synthetic approach

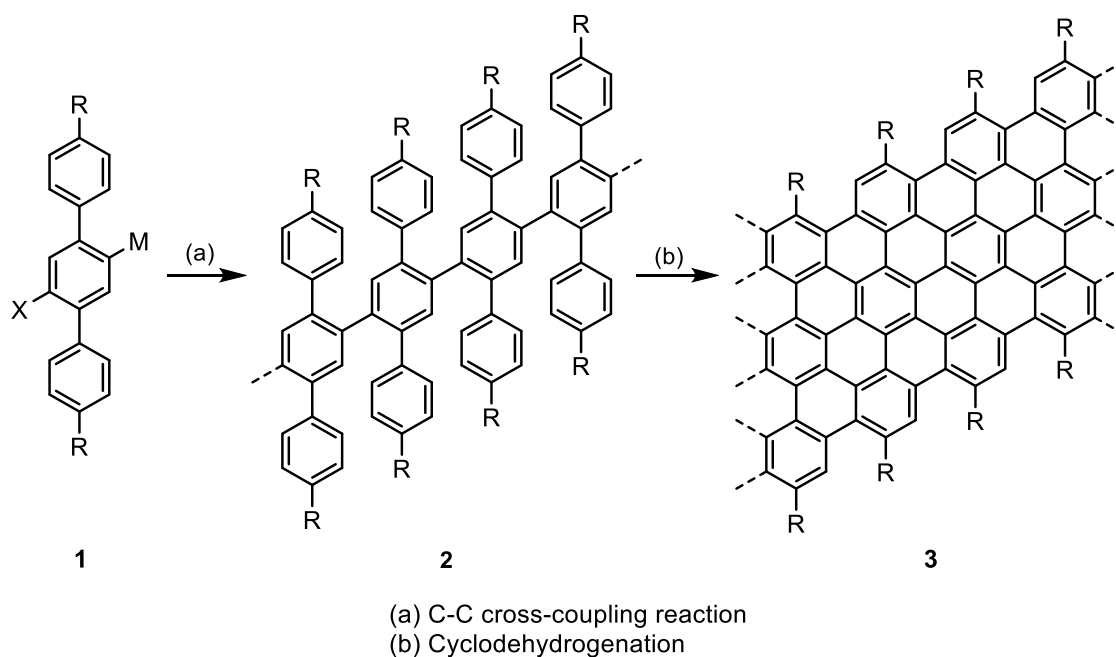
Knowing that GNRs came from cutting a graphene sheet into narrow strips or remembering how graphene was developed, it does not seem strange that top-down synthetic approach was the one used first, because it was more intuitive.

It consists of the obtention of GNR structures using techniques that reduce the size of the graphene slide. Different techniques have been employed, for example lithographical cutting of graphene or unzipping of carbon nanotubes with electron-beam or chemical oxidants. This approach was very useful in the synthesis of a wide variety of GNRs, which had also shown the semiconducting behaviour of some of them.<sup>2,4</sup>

Even though some progresses were obtained using the top-down approach, this had some important disadvantages. Techniques used presented low yields and they did not have any structural control in the preparation of GNRs. This makes difficult to control their properties because they are structural dependent.<sup>2</sup>

### 1.3.2. Bottom-up synthetic approach

Therefore, synthetic strategies with structural precision are crucial. Thus, the bottom-up approach becomes very relevant. It consists of producing graphene structures from small molecules as carbon precursors through different chemical reactions, in which well controlled structures with atomic precision can be done. This is mainly possible through the design of defined templates. However, the current methods present some disadvantages, such as the difficulty of accessing to heterostructures or having a length controlled GNR because it depends on the polymer elongation method, among others.<sup>2,4</sup>



**SCHEME 1**

There are two main methods in this approach: on-surface polymerizations and solution-phase polymerizations.<sup>4</sup> On surface polymerization is a technique where one- and two-dimensional molecular networks can be synthesized on a substrate using molecular building blocks with pre-defined connection sites to polymerize.<sup>7</sup> Solution-phase polymerization is similar but, instead of using a surface where the reaction takes place, it occurs in a non-reactive solvent where the monomer can be dissolved previously and a catalyst is usually needed. In both cases, it is performed a subsequently cyclodehydrogenation step is performed, which implies the graphitization and planarization of tailor-made 3D polyphenylene precursors (Scheme 1). These precursors (1), whose structure can be tailored, can be previously synthesized by performing well-known reactions with small molecules.

In Table 1 it is summarized the advantages and disadvantages of both synthetic approaches for the synthesis of GNRs.

Table 1. Comparison between top-down and bottom-up approaches.

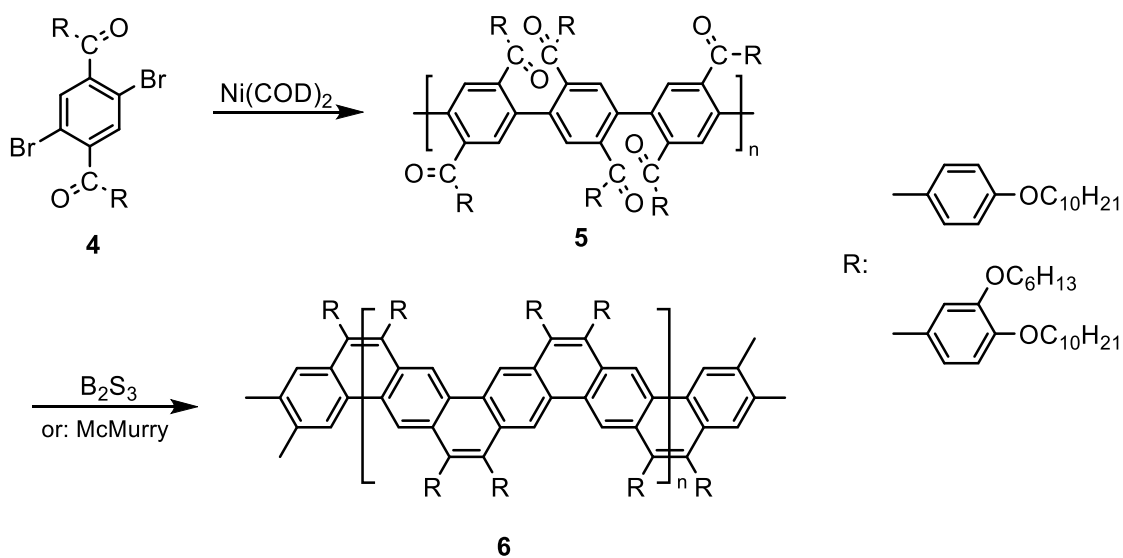
	TOP-DOWN APPROACH	BOTTOM-UP APPROACH	
		On-surface	Solution-phase
<b>PROS</b>	Simple method	Structural control	Structural control High Solubility
<b>CONS</b>	No structural control No length control Insoluble	Low solubility No length control No access to heterostructure	Intramolecular reactions Low stability No length control No access to heterostructure

### 1.3.2.1 Solution-phase bottom-up synthesis

As mentioned above, the GNRs properties depend on structural factors; therefore, the control on these properties becomes essential. To this end, on surface and solution phase bottom-up approaches are the most promising. We will now focus on solution phase bottom-up synthesis as it is the main topic of this work.

In 1970, Stille *et al.* reported the first attempt of synthesizing a fully conjugated polymer made of pentagonal and hexagonal aromatic rings using the bottom-up approach, but the obtained product was not recognized as a proper GNRs as it also presented some problems when characterizing it.<sup>8</sup>

In 1993, Scherf *et al.* reported what was named “angular polyacene”, a fully conjugated ladder-type polymer made only of six-membered rings. This can be considered as one of the narrowest possible GNRs with a define structure.<sup>9,10</sup> The synthesis was performed by carbonyl olefination of functionalized poly(para-phenylene) with B<sub>2</sub>S<sub>3</sub> or performing a McMurry coupling (Scheme 2).<sup>11</sup>

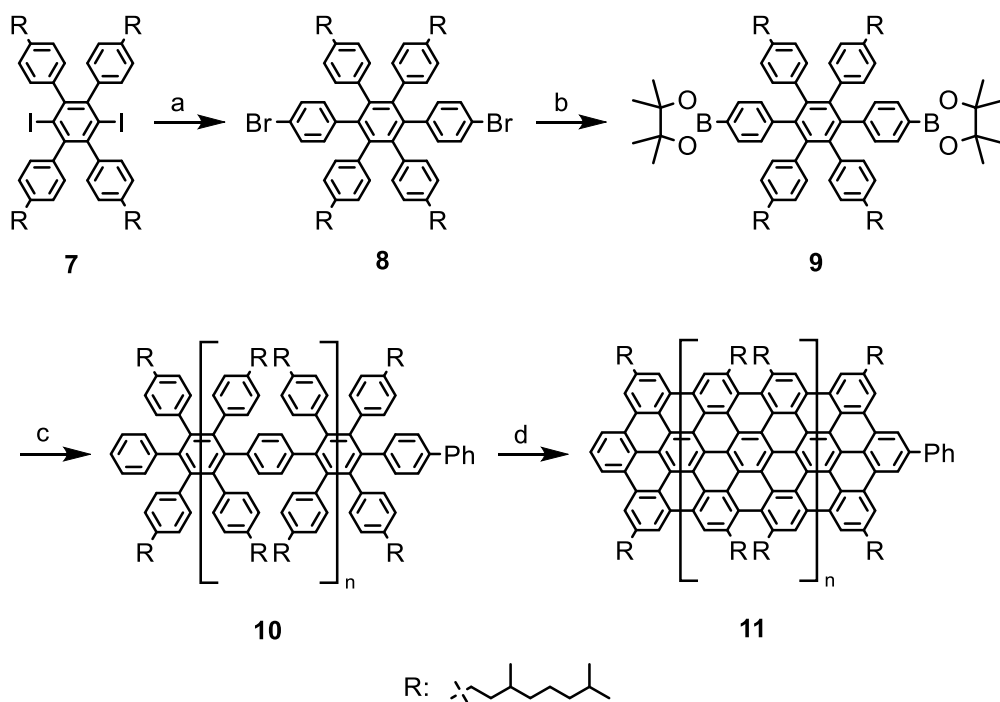


**SCHEME 2**

By the time, intentions were done in preparing GNRs by applying oxidative cyclodehydrogenation to polymeric systems using as precursors longitudinally elongated polyphenylenes.<sup>2</sup> In 2001, it was attempted the synthesis of structurally defined GNRs using  $A_2B_2$ -type Diels–Alder polymerization, but it was discarded because obtained structural isomers were obtained during the polymerization step which generated a mixture of different GNRs.<sup>12,13</sup>

The next attempt was to synthesize GNRs through  $A_2B_2$ -type Suzuki polymerization. In 2008, the first time that GNRs were obtained using this method (Scheme 3).<sup>14</sup> Since then, this method keeps being studied with a wide variety of different building blocks, trying in most of the cases to improve yields, conditions, etc.

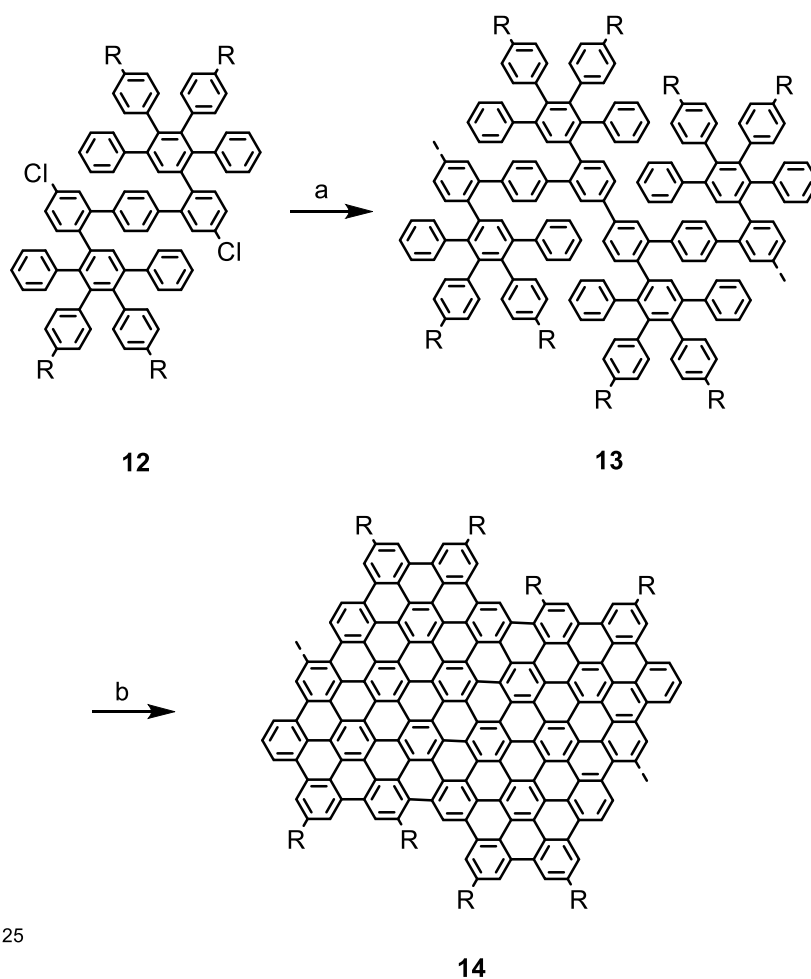




- (a) 4-bromophenylboronic acid, Pd(PPh<sub>3</sub>)<sub>4</sub>, aliquat 336, K<sub>2</sub>CO<sub>3</sub>, toluene, 80 °C, 24 h, 93%.  
 (b) (i) n-BuLi, THF, -78 °C, 1 h; (ii) 2-isopropoxy-4,4,5,5-tetramethyl[1,3,2]dioxaborolane, rt, 2 h, 82%.  
 (c) compound 1, Pd(PPh<sub>3</sub>)<sub>4</sub>, aliquat 336, K<sub>2</sub>CO<sub>3</sub>, toluene/H<sub>2</sub>O, reflux, 72 h, 75%.  
 (d) FeCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>NO<sub>2</sub>, 25 °C, 48 h, 65%.

### SCHEME 3

Even though A<sub>2</sub>B<sub>2</sub>-type Suzuki polymerization was very useful to prepare a variety of GNRs, their longitudinal extensions were limited due to the inefficiency of that polymerization and/or stoichiometric problems of using two different monomers. These issues were solved using AA-type Yamamoto polymerization (Scheme 4), which was shown to be very efficient in sterically hindered systems.<sup>15,16</sup> Thus, the synthesis of sterically congested GNR precursors was achieved.



(a) bis(cycloocta-(1,5)-diene)nickel(0) cycloocta-(1,5)-diene, 2,2'-bipyridine, toluene/DMF, 80 °C, 81%  
 (b) FeCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>/CH<sub>3</sub>NO<sub>2</sub>, rt, 92%.

#### SCHEME 4

### 1.4. Carbon–Carbon cross–coupling reactions

As previously mentioned, the bottom–up approach is the best option to synthesize structural controlled GNRs, tailoring its structure by the polymerization of small molecules. This work will be focused on a solution–phase method to synthesize GNRs, in which C–C cross–coupling reactions will be employed to perform an iterative process. In these reactions, a new carbon–carbon bond is formed by reacting an organometallic reagent with an organic halide or triflate in the presence of a transition metal catalyst. The type of bond that is formed is one of the most difficult to synthesize in organic chemistry, that is why C–C cross–coupling have been so attractive for chemists.<sup>17</sup>

C–C cross–coupling reactions get its importance in the fact that they are able to couple two different components that can be differentiated by what they are bonded to: a metal

(M) or a halide or triflate (X). These components are aryl, vinyl or alkyl halides or equivalents (e.g. triflates); and organometallic compounds as nucleophiles. The mechanism will be explained later with a concrete C–C cross-coupling reaction. It is important for the reaction to proceed properly the selection of the halide and the metal partners, which have different possibilities (X: I, Br, Cl, OTf or OPO(OR)<sub>2</sub>; M: Mg, Zn, Cu, Sn, Si, Zr, Al, In or B).<sup>17</sup>

The C–C cross-coupling reactions that are catalysed by Pd have become really important in organic synthesis due to the advantages that they present: there is no presence of any homo-coupled product when the cross-coupled molecule is synthesized and its mechanism has three common steps in organic chemistry. This catalysed reactions have been classified (Table 2) depending on the organometallic nucleophile used and they are known with the name of the scientist that has discovered the reaction.

Table 2. Classification of Pd-catalysed C–C cross-coupling reactions.

<b>Cross-coupling reaction</b>	<b>Nucleophile</b>	<b>Halide</b>
Suzuki	ArB(OH) <sub>2</sub>	Aryl or vinyl
Stille	ArSnR <sub>3</sub>	Aryl or vinyl
Heck	Alkene	Aryl or vinyl
Hiyama	R <sub>3</sub> Si–R'	Aryl, vinyl or alkyl
Kumada	RMgX	Aryl, vinyl or alkyl
Negishi	RZnX	Aryl, vinyl or alkyl

This work will be focused on Suzuki–Miyaura coupling (or Suzuki coupling) because it is going to be used during the experimental work.

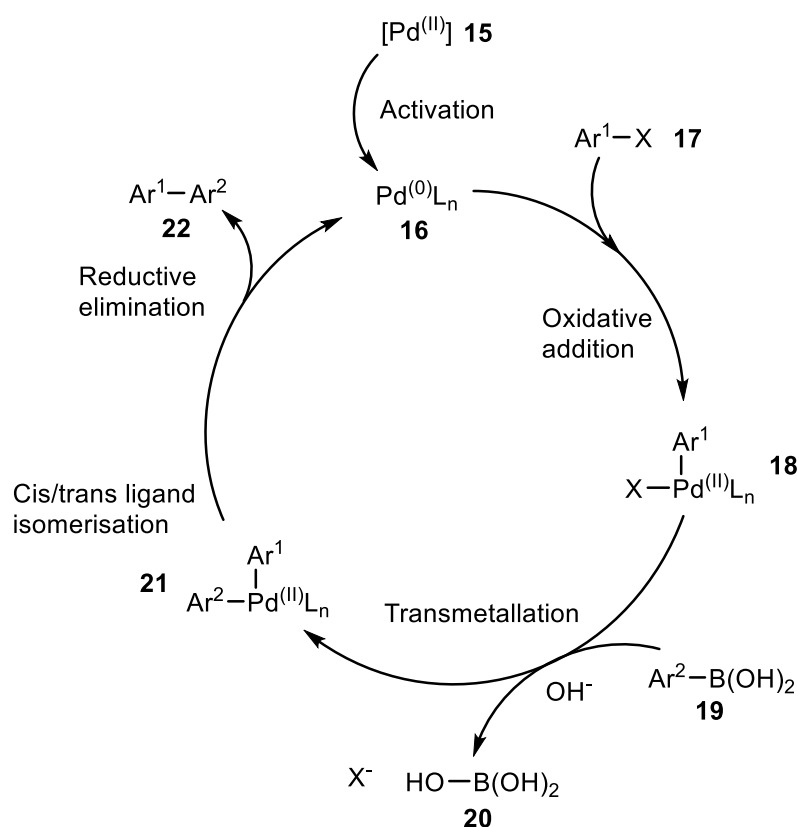
#### 1.4.1. Suzuki–Miyaura cross-coupling reaction

Nowadays, Suzuki–Miyaura cross-coupling reaction is one of the most relevant transition metal catalysed carbon–carbon bond forming.<sup>18</sup> It consists of coupling a boronic acid or ester with a vinyl or aryl halide (or triflate) in the presence of Pd acting as catalyst.<sup>17</sup> As in every cross-coupling, there must be the presence of an halide partner (or equivalent) and a metalorganic partner, that can be defined for this concrete reaction:

- Halide partner (X<sup>δ-</sup>–C<sup>δ+</sup>): the halide will give to the carbon next to it a partially positive charge that represents the electrophilic nature needed in Suzuki cross-coupling reaction. This halide can be bromine (Br), iodine (I), triflate (OTf) or others.<sup>17</sup>

- Organometallic partner ( $M^{\delta+}-C^{\delta-}$ ): the metal will give to the carbon next to it a partially negative charge that represents the nucleophilic nature needed in Suzuki cross-coupling reaction. The organometallic must be a boronic acid or ester ( $B(OR)_2$ ).<sup>17</sup>

The reaction consists of coupling chemically different fragment that will participate in an electronically divergent process with the Pd catalyst. In Scheme 5 the mechanism is shown, which is explained below.<sup>18</sup>



The first step is the activation of the  $Pd^{(II)}$  catalyst (**15**) into the active catalytic  $Pd^{(0)}$  (**16**). Then, the haloarene **17** is added to the catalyst by oxidative addition, forming the organometallic complex **18**. After that, **19** is treated with a base. The activation of the boron atom enhances the polarisation of the organic ligand and facilitates transmetalation, which occurs by adding the metal partner (**19**) to the catalyst while the halide leaves the complex. Finally, the aryl groups that are attached to the Pd catalyst suffer cis/trans ligand isomerisation in order to be one aryl next to the other (**21**). Subsequently, they will undergo reductive elimination that will result in the coupled

product **22** and it will be recovered **16**, ending with a cycle mechanism of the transition metal catalyst.

The importance of this reaction lies in its excellent mild and functional group tolerant reaction conditions, the good advantages of organoboron reagents (stability and favourable with the environment) and the fast transmetallation with Pd<sup>(II)</sup> complexes.<sup>18</sup>

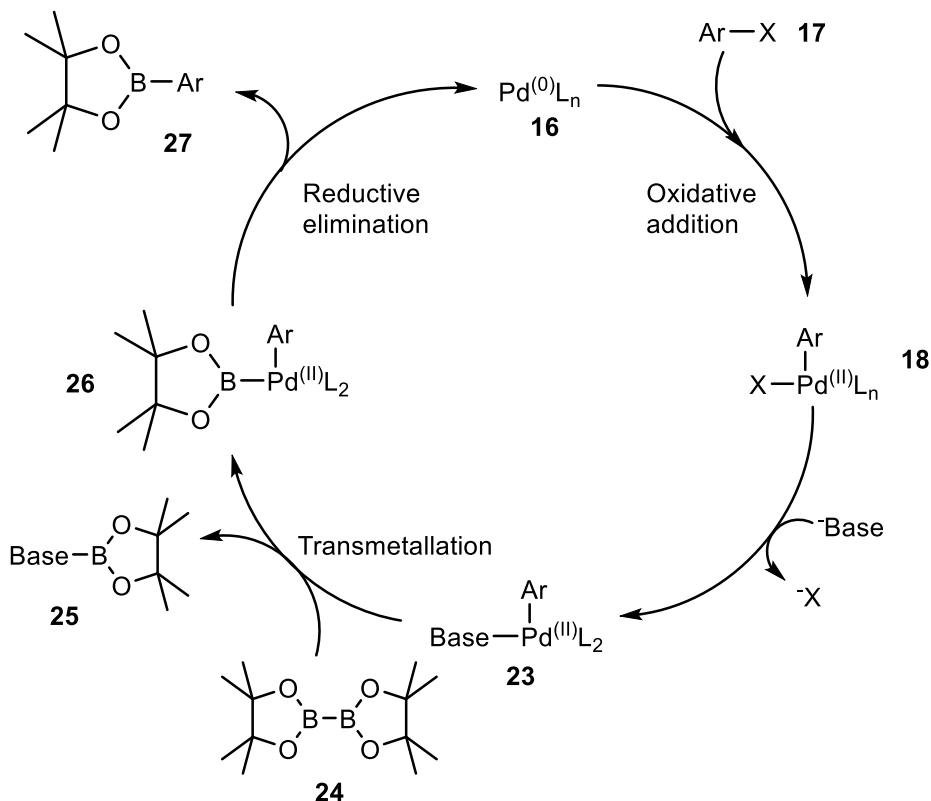
#### **1.4.2. Boronic esters by Miyaura borylation reaction**

One of the characteristics that makes Suzuki–Miyaura cross–coupling such an important reaction is the use of organoboranes because of the advantages that they present: 1) they are relatively stable, 2) they can be easily synthesized, 3) they are not toxic, and they allow the use of mild and functional group tolerant conditions.<sup>18</sup> Therefore, its synthesis is highly important.

In this reaction, boronic esters are synthesized, compounds that are extensively used in Suzuki–Miyaura cross–coupling reactions. In particular, boronic acids present some problems in the cross–coupling reaction: as they are waxy solids, their purification is difficult, and they can affect the stoichiometry of the reaction due to the formation of a trimeric specie (boroxine) in solution. However, the use of boronic esters instead solves these problems even though they are more difficult to obtain.<sup>19</sup> In particular, the protecting character of the esters over the boron is also relevant for iterative synthesis as will be explained below. Pinacol, neopentyl and catechol boronic esters are the most employed ones in the coupling reaction.<sup>18</sup> They have good reactivity and stability, they are easy to prepare compared with other boronic esters and not expensive.<sup>18</sup>

How can these boronic esters be synthesized? There are different ways to get these compounds, such as hydroborations, by electrophilic arene borylation, by radical pathways, using organometallics, etc.<sup>18</sup> This work will be focused on the preparation of boronic esters by Miyaura borylation.<sup>20</sup>

Miyaura borylation is a reaction catalysed by Pd in which an aryl or alkenyl halide is converted into the corresponding boronic ester.<sup>18,20</sup> The mechanism followed (Scheme 6) is very similar to the Suzuki–Miyaura cross–coupling because it proceeds through the same Pd catalyst cycle.<sup>18</sup>



**SCHEME 6**

The haloarene **17** is added to **16** by an oxidative addition. As the mechanisms are very similar, to avoid the competition with Suzuki–Miyaura coupling, a base is carefully selected to avoid that pathway, being KOAc the base with the greatest selectivity. Once the base has joined the catalytic complex (**23**), it reacts with 4,4,4',4',5,5,5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (**24**) in order to give the intermediate complex **26** that will suffer a reductive elimination to yield the aryl boronate **27**.<sup>20</sup>

It is worth mentioning that the importance of Miyaura borylation in the synthesis of boronic is due to the use of available starting materials its tolerance with different functional groups.<sup>18</sup> For example, its mild reaction conditions allow the synthesis of boronates which are not accessible *via* lithium or Grignard intermediates followed by borylation.

## 2. Objective

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The main objective of this project is the synthesis of GNR precursors compatible with iterative processes for solution–phase bottom-up approach. The current solution–phase synthesis of GNRs shows high polydispersibility and it is limited to the preparation of homogeneous structures. On the contrary, iterative synthesis applied to the polymer elongation may overcome these disadvantages. The general objective of this Chemistry Degree Final Project will be achieved through the following specific steps:

- The synthesis of p–terphenyl derivatives as precursors for non–functionalized GNRs (*i.e.* no edge–substitution). In particular, these aromatic molecules will be compatible to iterative Suzuki–Miyaura cross–coupling reactions.
- Then, the synthesis of more complex p–terphenyl derivatives as precursors for the synthesis of functionalized GNRs (*i.e.* edge–substitution) will be tackled.

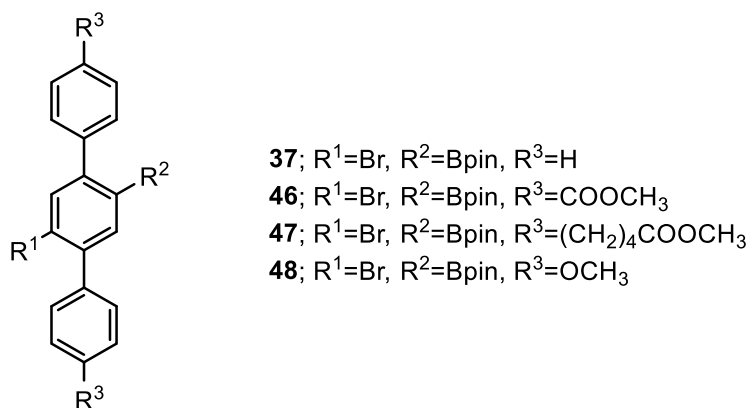


Figure 4. Objectives of this Chemistry Degree Final Project.

### 3. Results and discussion

The target molecules of this work are p-terphenyl derivatives which can act as precursors in the iterative preparation of GNRs. In previous sections, the bottom-up synthetic approach was mentioned as one of the main options for synthesizing GNRs, but it presented some problems: 1) as it is related to polymerization strategies, it is difficult to have complete length control, which gives polydisperse GNRs; and 2) the introduction of different monomers is hindered. In order to solve these issues, an iterative synthesis using Suzuki-Miyaura cross-coupling reactions is proposed. Iterative synthesis is an organic methodology where reaction sequences are automated in order to synthesize molecules at nano-scale.<sup>21</sup> The iterative synthesis is based on the employment of protecting group chemistry to regulate reactivity. Thus, specific boronic ester groups allow using Suzuki-Miyaura cross-coupling in this kind of synthesis (Figure 5).

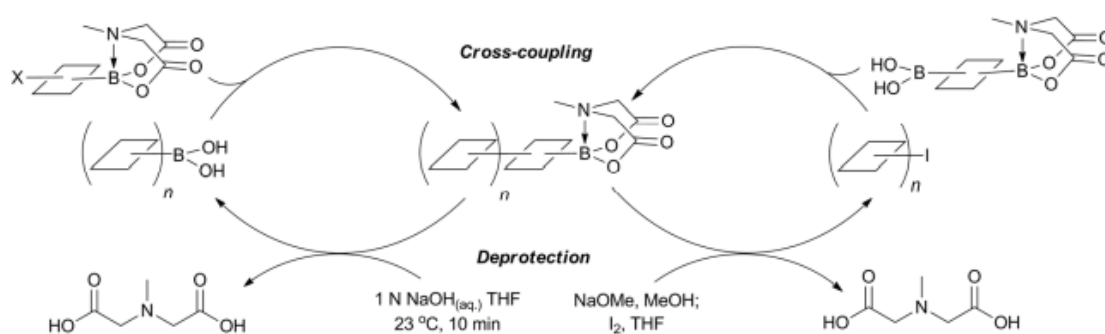
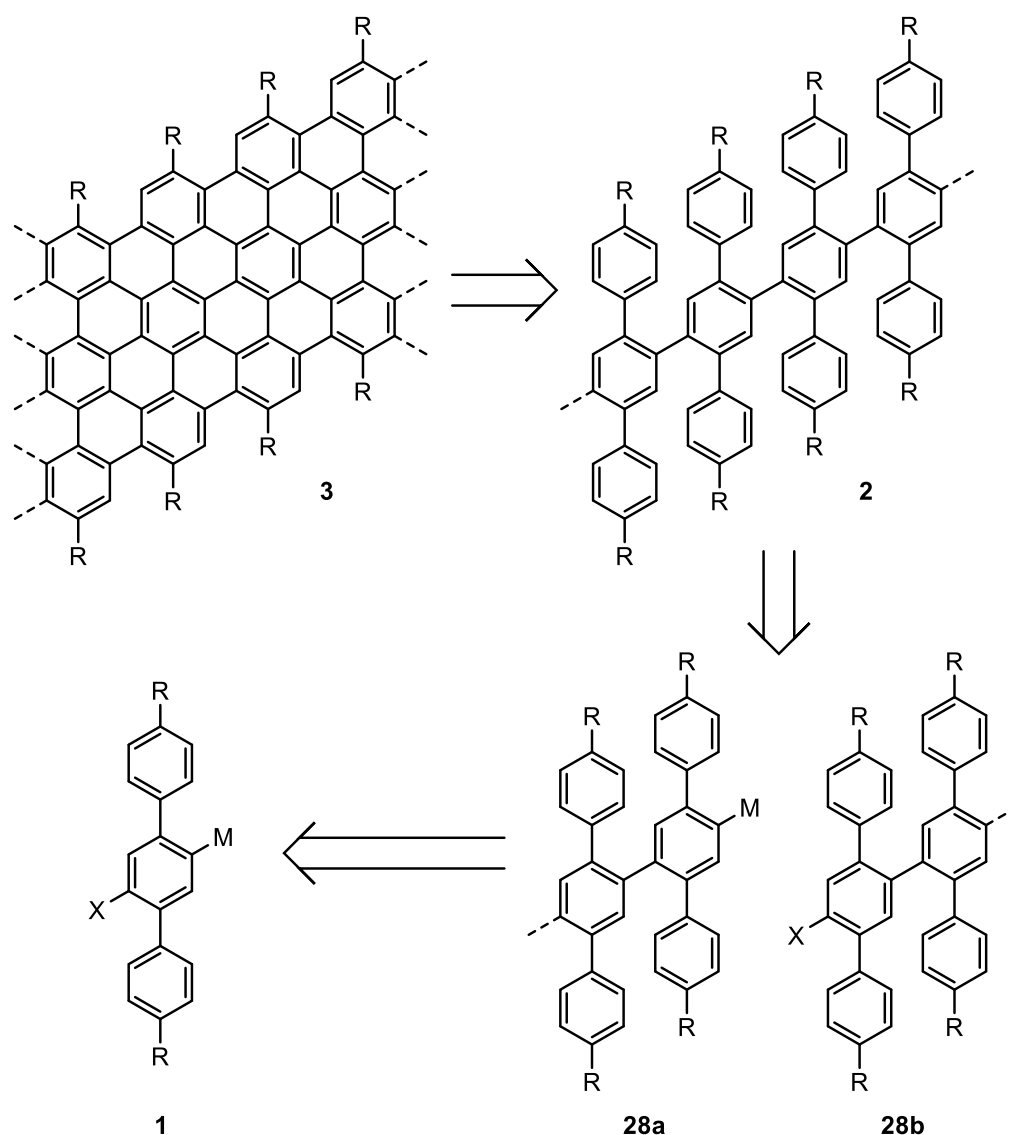


Figure 5. Two different routes for iterative cross-coupling based on MIDA boronates.<sup>18</sup>

In this work, the synthesis of GNR precursors with structure **1** are proposed (Scheme 7), which are synthetically accessible. There are several synthetic procedures described for the synthesis of these precursors, for example the use of carbon-carbon cross-coupling reactions like Stille cross-coupling or Suzuki cross-coupling. In fact, this work will be based on the Suzuki cross-coupling reaction, which will determine the structure of the **1**.





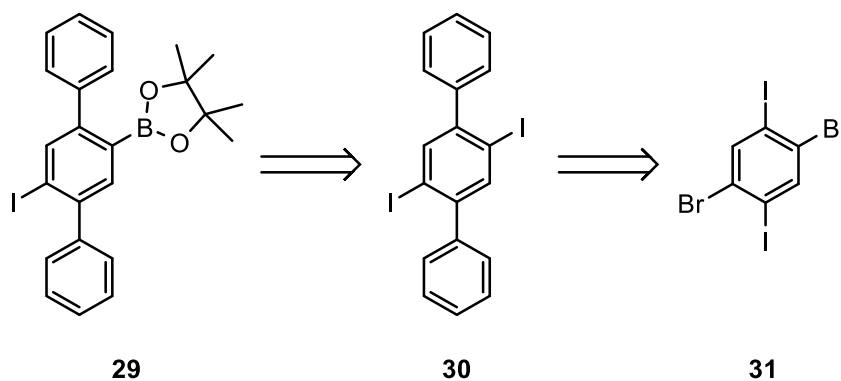
**SCHEME 7**

The preparation of the armchair GNR **3** by an iterative synthesis will be based on Suzuki coupling reactions using the p-terphenyl derivative **1** as starting precursor. As shown Scheme 7, the precursor **1** has on its structure a halide partner ( $X^{\delta-}-C^{\delta+}$ ), and a metal partner ( $M^{\delta+}-C^{\delta-}$ ) which must be a boronic acid or ester ( $B(OR)_2$ ). In addition, the boronic ester must be previously protected (e.g. MIDA boronate) to successfully perform the iterative cross coupling and it must be compatible with the reaction conditions (Figure 5).

In particular, the preparation of p-terphenyl derivatives has been tackled with different substituents to modulate the solubility and functionalities of the final GNR for future applications.

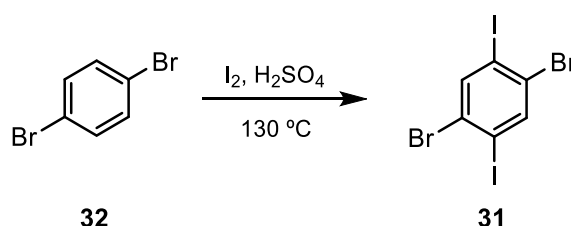
### 3.1. Synthesis of p-terphenyl **37** as non-functionalized GNR precursor

In order to prepare a simple and synthetically accessible GNR precursor, we decided to synthesize **29** from **31** (Scheme 8).



**SCHEME 8**

Thus, the first step was the preparation of 1,4-dibromo-2,5-diiodobenzene (**31**, Scheme 9) following a very similar methodology as Martínez *et al.* reported.<sup>22</sup> The iodination of 1,4-dibromobenzene (**32**) is an electrophilic aromatic substitution ( $S_{E}Ar$ ) with iodine. This reactant is oxidized at the electrophile Iodonium ion by  $H_2SO_4$ , which is then attacked by **32**. Thus, **31** was obtained in a 55% yield. It is worth noting that the preparation of **31** was performed at gram scale (2.84 g) since it is essential to synthesize all the proposed p-terphenyl structures.

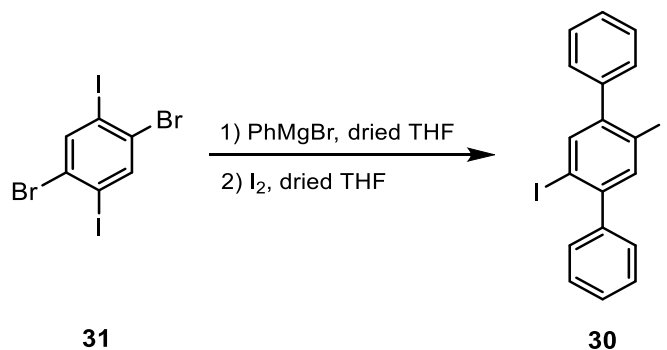


**SCHEME 9**

The spectroscopic data obtained are in agreement with the structure of **31**. The  $^1H$  NMR spectrum shows a singlet at 8.05 ppm, which corresponds to aromatic hydrogens.

The next step was to obtain a p-terphenyl structure from **31**. The presence of two different halogen atoms (Br and I) in **31** allows diverse substitutions to be made on the phenyl ring due to their different susceptibility to react ( $C-I > C-Br$ ).

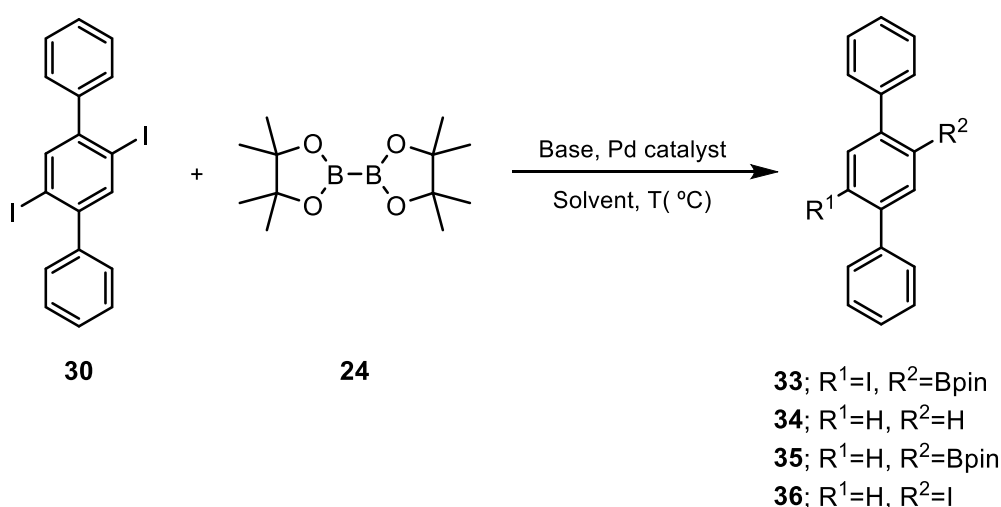
Thus 2',5'-diiodo-1,1':4',1''-terphenyl (**30**) was obtained through a two-step synthesis from **31** (Scheme 10) following the methodology that Hart *et al* proposed.<sup>23</sup> The reagent **31** reacted with phenylmagnesium bromide by a nucleophilic aromatic substitution (S<sub>N</sub>Ar). The nucleophilic carbon of the Grignard reagent attacks the most labile bond of **31**, the C-I bond, substituting iodide by a phenyl group. The resulting molecule, 2',5'-dibromo-1,1':4',1''-terphenyl (**38**), then reacted with iodine to exchange the halogen atom, leading to **30** in a 36% yield.



**SCHEME 10**

The p-terphenyl **30** was characterized by <sup>1</sup>H NMR spectroscopy. The presence of a multiplet at 7.49–7.35 ppm which integrates to 10 aromatic hydrogens and a singlet at 7.87 ppm which integrates to 2 aromatic hydrogens is in agreement with the presence of **30**.

Once **30** was obtained, a boronic ester group is introduced to end up with the target p-terphenyl derivative **33**. To do that, it was performed a Miyaura borylation reaction controlling the equivalents of the dioxaborolane **24** (Scheme 11).



**SCHEME 11**

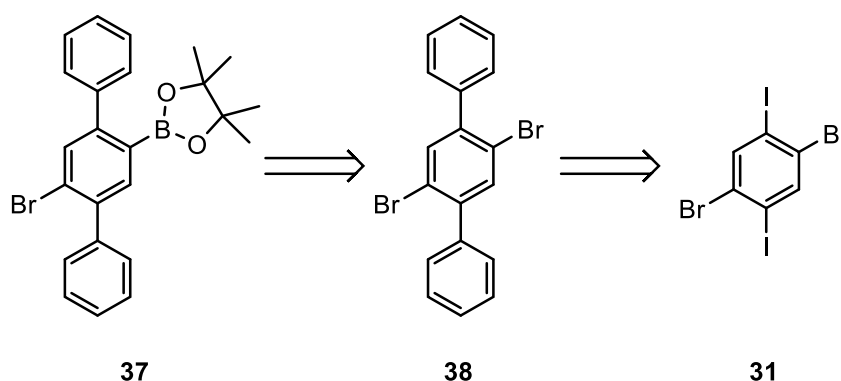
To perform this borylation, different reaction conditions were studied (Table 3). In particular, Pd(dppf)Cl<sub>2</sub> and KOAc were used as Pd catalyst and base, respectively; while two different solvents as DMF and DMSO were employed (Entry 1 and 2, respectively) in order to reach high reaction temperatures.

Table 3. Experimental conditions for the synthesis of **33**.

Entry	Base	Pd catalyst	Solvent	T (°C)	Yield (%)
1	KOAc	Pd(dppf)Cl <sub>2</sub>	DMF	150	-
2	KOAc	Pd(dppf)Cl <sub>2</sub>	DMSO	85	-

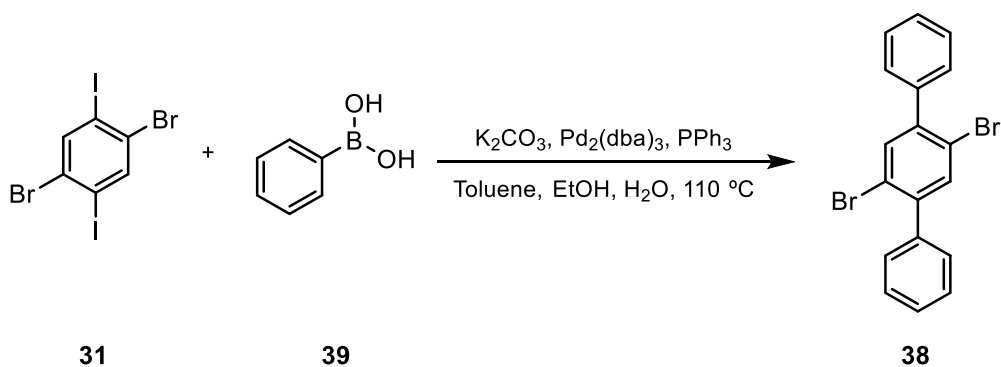
The reactions were monitored by GC–MS. A complex reaction mixture was obtained in any of the reaction conditions, in which the compound **33** was not present. Instead of the expected molecule, a variety of other molecules were detected. For Entry 1, the mass detected by GC–MS *m/z* 230.1 and 356.2 suggested the presence of **34** and **35**, respectively. For Entry 2, apart from the starting material **30**, the side products probably obtained were **34–36** with the mass *m/z* 230.1, 356.2 and 356.2, respectively, associated to three different peaks in the chromatogram. The present of these side compounds suggests that a protodeborylation is occurring.<sup>24</sup>

In view of the above results, it was decided to study then the synthesis of the GNR precursor **37** from **31** based on cross-coupling reactions catalyzed by Pd (Scheme 12). The presence of bromide atom in **37** should hinder the deborylation by decreasing the electron density of the aromatic structure by inductive effect compared to **29**. In addition, the higher stability of C–Br bond compared C–I could facilitate the monoborylation of intermediate **38** by Miyaura reaction.



SCHEME 12

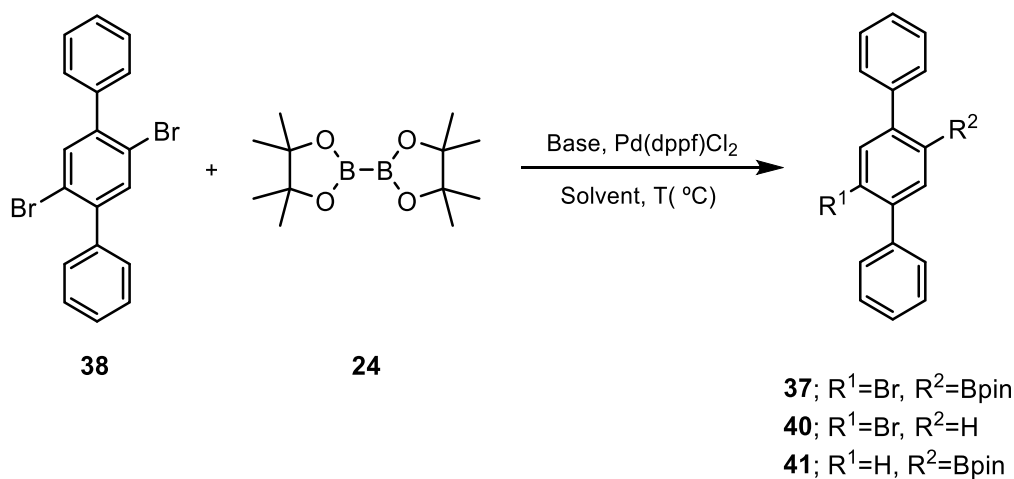
Thus, a new synthetic route was designed to prepare the dibromo-*p*-terphenyl derivative **38**. As a first synthetic step, a double Suzuki cross-coupling reaction of **31** with **39**, lead to **38** in 96 % yield (Scheme 13), following a similar methodology to the one proposed by Wehrmann *et al.*<sup>25</sup>



**SCHEME 13**

The compound **38** was characterized by  $^1H$  NMR spectroscopy. The presence of a doublet at 7.44 ppm which integrates to 10 aromatic hydrogens and a singlet at 7.65 ppm which integrates to 2 aromatic hydrogens is in agreement with the presence of **38**.

Once **38** was synthesized, its monoborylation was address by Miyaura borylation reaction (Scheme 14). A competitive Suzuki–Miyaura reaction coupling can appear at the later stage of the reaction, when the proportion of ester is high. To prevent this, the election of the base is crucial. To this end, different reaction conditions were studied. In particular, diverse bases, solvents and temperatures were analysed. Table 4 summarizes the most relevant conditions for this reaction. It is worth mentioning that special attention was paid to work under dried conditions.



**SCHEME 14**

Table 4. Experimental conditions for the synthesis of **37**.

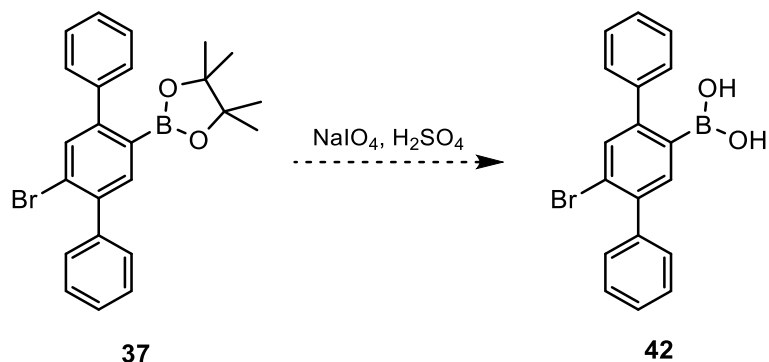
Entry	Base	Solvent	T (°C)	[Pd] (equiv.)	Heating	<b>37</b> (%)
1	K <sub>2</sub> CO <sub>3</sub>	DMSO	80	0.3	Classical	-
2	KOAc	DMSO	80	0.3	Classical	-
3	KOAc	DMF	150	0.3	Classical	35
4	KOAc	DMF	150	0.3	MW	21
5	KOAc	DMF	150	0.1	MW	-

All the reactions were monitored by GC–MS. The p–terphenyl **37** was not obtained when Pd(dppf)Cl<sub>2</sub> as catalyst, K<sub>2</sub>CO<sub>3</sub> as base and DMSO as solvent at 80 °C were employed (Entry 1). Instead, these conditions resulted in a complex reaction mixture. The employment of the hard–Lewis base KOAc, which was found to be able to suppress Suzuki–Miyaura coupling and which shows a great selectiveness for Miyaura borylation, also did not lead to obtaining **37** (Entry 2) recovering **38**. However, by changing using DMF as solvent to reach 150 °C (Entry 3), **37** was synthesized in 35 % yield. Then the optimization of this reaction was tackled under microwave irradiation. Microwave–assisted Suzuki reactions is currently considered an efficient synthetic methodology because is able to reduce side reactions, reaction time (from hours to minutes) and increase yields.<sup>26</sup> Similar conditions to the defined in Entry 3 were performed using microwave heating and **37** was synthesized in 21 % yield (Entry 4). Lower equivalents of palladium catalyst were also tested (Entry 5) but the starting material **38** was detected together with the side products **40** and **41**. Unfortunately, microwave irradiation has not improved the preparation of **37**. At this point, we considered the conditions defined in Entry 3 acceptable for the synthesis of the GNR precursor **37**; however, further optimization studies will be necessary.

In order to confirm the structure of **37**, it was characterized <sup>1</sup>H NMR. The spectrum shows two doublets, one at 7.68 ppm which corresponds to 2 aromatic hydrogens and another one at 7.42 ppm which corresponds to 10 aromatic hydrogens more, that in addition to the singlet at 1.19 ppm which integrates to 12 alkyl hydrogens confirms the presence of **37**.

Finally, a first attempt at hydrolysis of the boronic ester group was performed for **37**. It should be noted that this hydrolysis is very important for the exchange of boronic acid esters with one that is compatible with an iterative preparation of GNRs, as for example MIDA or DAN boronates (Figure 5). Therefore, **37** was hydrolysed by NaIO<sub>4</sub> and H<sub>2</sub>SO<sub>4</sub> treatment (Scheme 15). However, a highly complex mixture was obtained hindering the

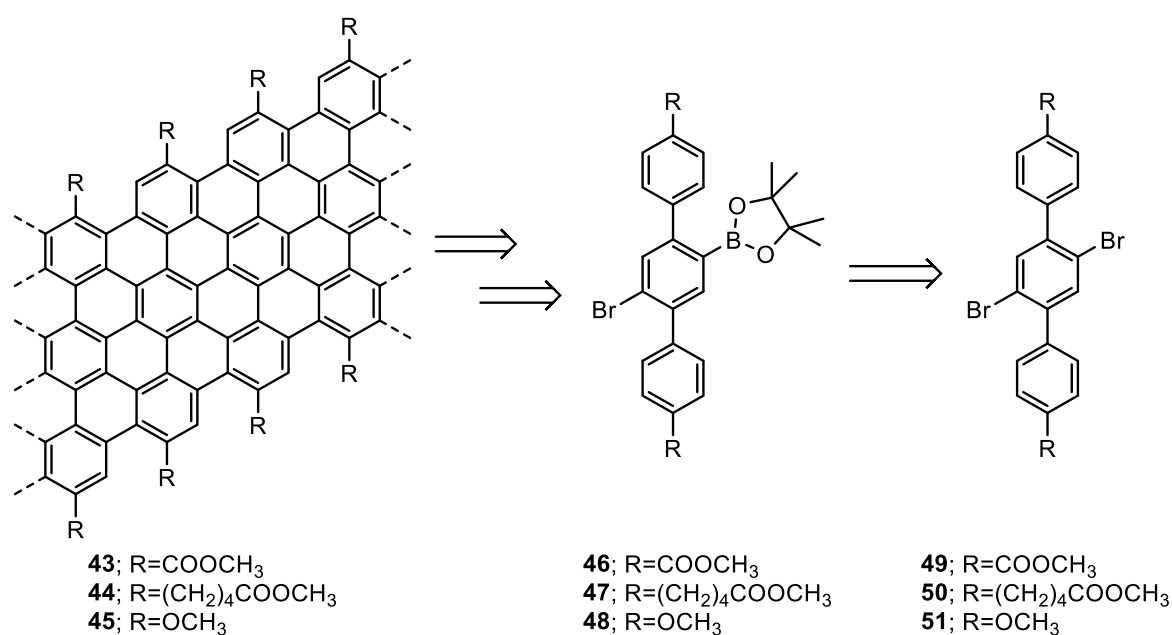
isolation of any compound. In a future, other methodologies of hydrolysis should be considered.



**SCHEME 15**

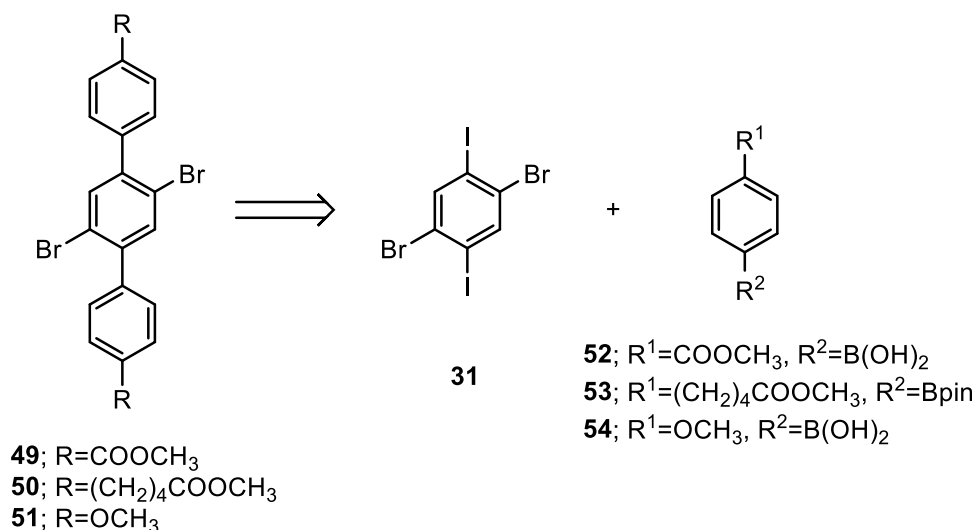
### 3.2. Synthesis of p-terphenyl derivatives 46, 47 and 48 as functionalized GNR precursors

GNRs are composed only of  $sp^2$  carbon atoms, so they have low solubility in aqueous media. This property hinders their synthesis and/or growth by bottom-up approach in solution. In addition, functionalized GNRs showed promising applications for neurophysiological recovery,<sup>27</sup> batteries,<sup>28</sup> etc. Therefore, the synthesis of functionalized GNRs with different entities are highly interest. In this work, we have also explored the preparation of the p-terphenyl **46–48** as precursors of functionalized GNRs (Scheme 16).



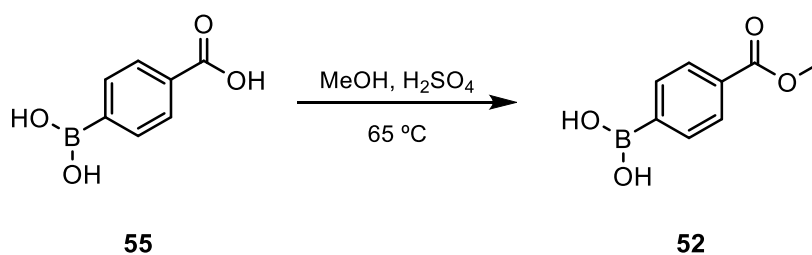
**SCHEME 16**

Taking into account the previous results in obtaining **37**, the synthesis of **49–51** was firstly addressed. To this end, Suzuki cross coupling reactions of **31** and the corresponding boronic acids **52–54** were studied (Scheme 17).



**SCHEME 17**

Firstly, the boronic acids **52** and **53** were synthesized, while **54** was commercially available. The (4-(methoxycarbonyl)phenyl)boronic acid (**52**) was prepared by esterification of **55** with MeOH in acid media (Scheme 18) following the methodology proposed by Alezi *et al.*<sup>29</sup> Thus, **52** was obtained in 95 % yield.

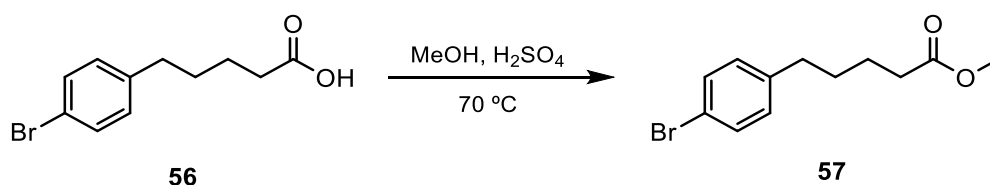


**SCHEME 18**

The structure of **52** was studied by <sup>1</sup>H NMR spectroscopy. Apart from the 4 aromatic hydrogens that the multiplets at 8.53–8.28 and 8.19–8.14 ppm, the characteristic singlet at 3.98 ppm which integrates to 3 alkyl hydrogens confirms the presence of **52**.

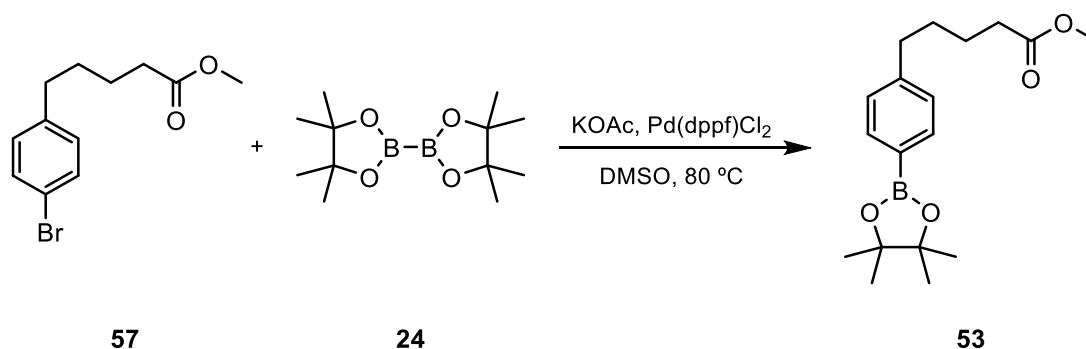
The boronic acid **57** was prepared in two synthetic steps. First, 5-(4-bromophenyl)pentanoic acid (**56**) was esterified with MeOH in acid media to give **57** in 99 % yield (Scheme 19) following the methodology proposed by Betori *et al.*<sup>30</sup>





**SCHEME 19**

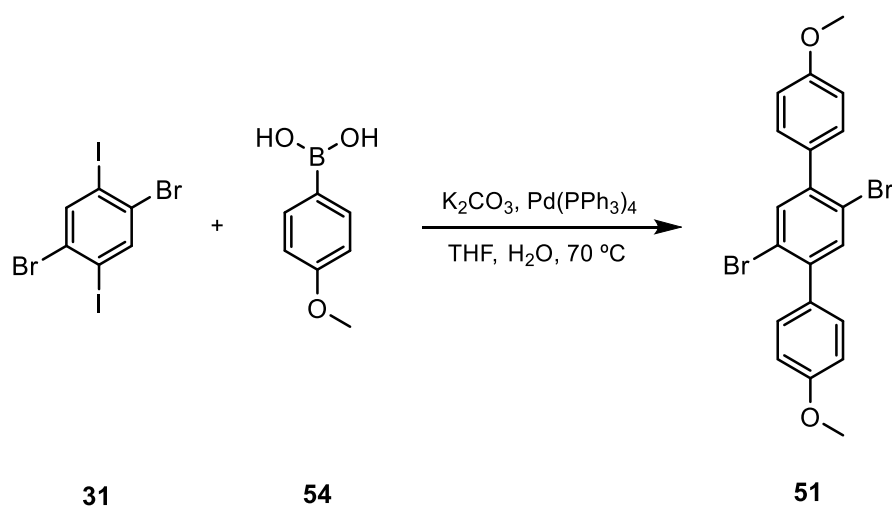
Then, methyl 5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl)pentanoate (**53**) was synthesized performing a Miyaura borylation reaction to obtain **53** in 77 % yield (Scheme 20) following the methodology that Cheng *et al.* proposed.<sup>31</sup>



**SCHEME 20**

<sup>1</sup>H NMR spectroscopy was used to study the presence of **53**. In the spectrum it can be seen two multiplets at 7.77–7.70 and 7.20–7.15 ppm which integrate for 2 aromatic hydrogens each, three multiplets at 2.68–2.60, 2.34–2.28 and 1.68–1.62 ppm, which integrates for a total of 8 alkyl hydrogens, a singlet at 3.64 ppm which corresponds to 3 methoxy hydrogens and a characteristic singlet at 1.33 ppm which corresponds to 12 alkyl hydrogens. All of them are in agreement with **53**.

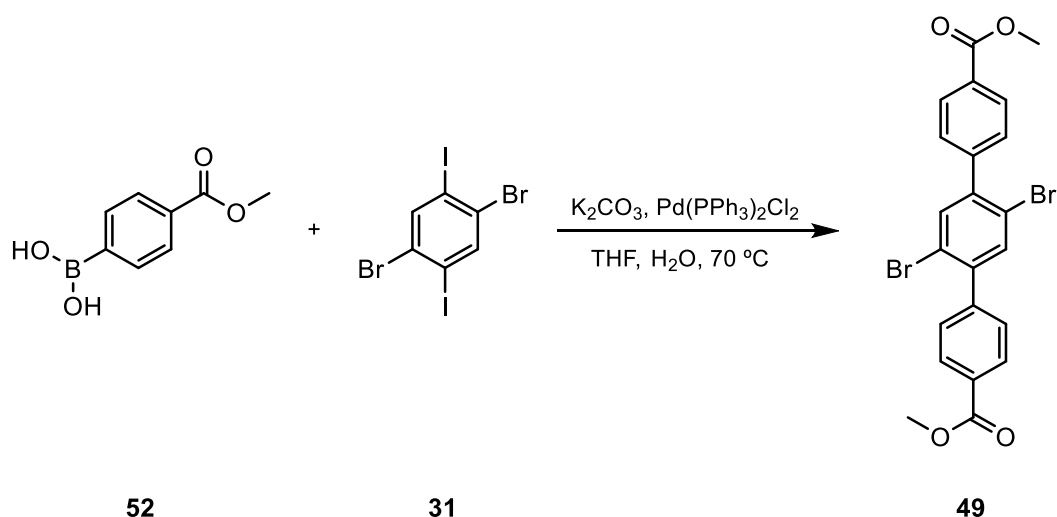
With the boronic acid derivatives **52–54** in hands, the *p*-terphenyls **49–51** were synthesized by a double Suzuki cross-coupling reaction. In particular, **51** was prepared from **31** and **54** using K<sub>2</sub>CO<sub>3</sub> as base and Pd(PPh)<sub>3</sub> as catalyst in THF/H<sub>2</sub>O mixture at 70 °C (Scheme 21). The dibromo-*p*-terphenyl **51** was obtained in 40 % yield.



**SCHEME 21**

The presence of **51** was verified using  $^1\text{H}$  NMR spectroscopy. The following signals are in agreement to all the aromatic hydrogens of **51**: a singlet at 7.61 ppm which corresponds to 2 hydrogens, a multiplet at 7.42–7.35 which corresponds to 4 hydrogens and another multiplet at 7.02–6.95 ppm which corresponds also to 4 hydrogens. The last signal, a singlet at 3.87 ppm which integrates to 6 methoxy hydrogens, clearly shows the presence of **51**.

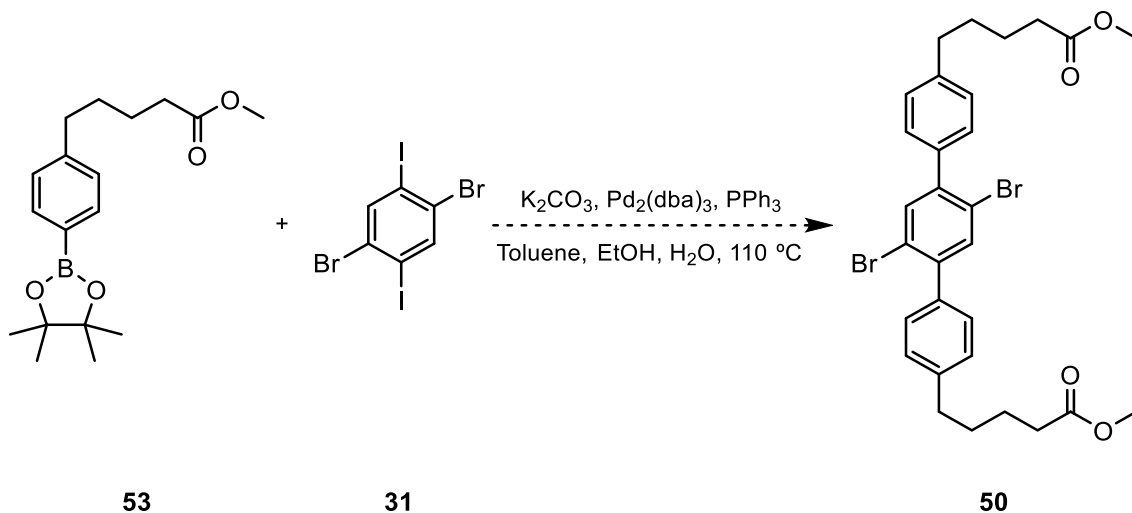
The aromatic compound **49** was synthesized similarly to **51** (Scheme 22). In this case, the dibromo-terphenyl **49** was obtained in 27 % yield.



**SCHEME 22**

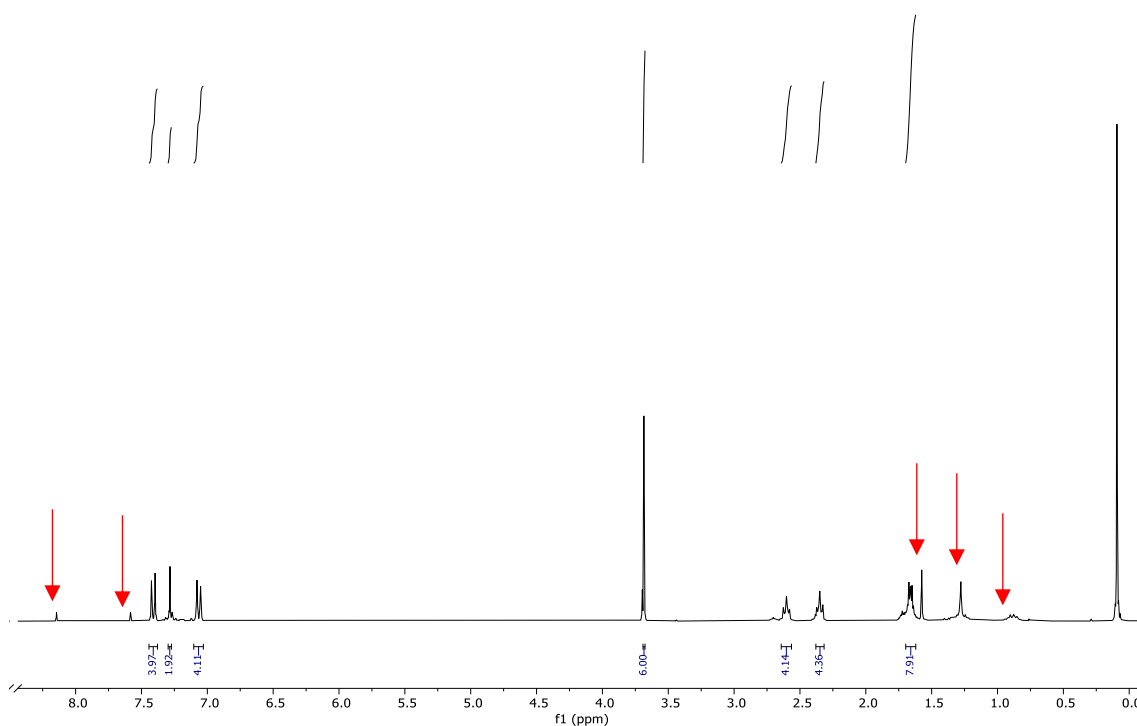
Again,  $^1\text{H}$  NMR was used to study the presence of **49**. The presence of a multiplet at 8.16–8.11 ppm which integrates to 4 aromatic hydrogens, a singlet at 7.65 ppm which

integrates to 2 aromatic hydrogens, another multiplet at 7.55–7.50 ppm which integrates to 4 aromatic hydrogens and a singlet at 3.96 ppm which integrates to 6 methoxy hydrogens is in agreement with the structure of **49**.



**SCHEME 23**

Finally, double Suzuki cross-coupling reaction was carried out using **53** and **31**. Unfortunately, the p-terphenyl was not purely isolated by flash column chromatography as shown the  $^1H$  NMR (Figure 6). Due to lack of time, the purification of **50** could not be optimized.



**Figure 6.**  $^1H$  NMR spectrum of impure **50**.

In conclusion, the dibromo-*p*-terpehnyl **49** and **51** were successfully synthesized. However, the preparation of the precursors **46** and **48** was not explored due to the limited time of this Chemistry Degree Final Project.

## 4. Experimental Part

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### 4.1. Reagents, solvents and materials

It was not done any treatment to the glass material before performing any reaction. At the end of every reaction, all the glass material used was washed with soap, rinsed with water and finally rinsed with acetone. They were air dried or dried in the oven depending on the material.

Solvents were provided by Fisher Chemical and they did not have any additional purification or drying. At the end of every reaction, solvents were recovered.

Commercial reagents were provided by BLDpharm and they were used without doing any previous purification. Pd catalysts were used carefully, and they were saved in special conditions for its conservation.  $\text{Pd}_2(\text{dba})_3$ ,  $\text{Pd}(\text{dppf})\text{Cl}_2$  and  $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$  were saved in amber glass bottles under anhydrous conditions in a desiccator.  $\text{Pd}(\text{PPh}_3)_4$  needed even more sophisticated conditions: it was saved in an amber glass bottle also, but this bottle was inside an special bag that do not allow the pass of light, it was under an inert atmosphere and everything was saved inside a fridge. Reagents that were synthesized in the laboratory were purified before its use in other reactions by washing them with methanol or ethanol or by performing a column chromatography.

For those reactions where an inert atmosphere was necessary due of the presence of a Pd catalyst which could be destroyed by the presence of oxygen, a flow of an inert gas ( $\text{N}_2$ ) was used.

### 4.2. Instrumentation

To perform thin layer chromatography (TLC), it was used aluminium plates with silica gel as stationary phase. Hexane or mixtures with different compositions of hexane and DCM were used as mobile phases. The composition of the mobile phase was chosen depending on the polarity of the molecules that were going to be separated. The spots were visualized with UV light at 254 nm in all cases.

For the flash column chromatography, the stationary phase used was silica gel. Hexane or solutions with different composition of hexane and DCM were used as mobile phases. The composition of the solution was previously chosen performing TLCs with different

mixtures. The mobile phase went through the stationary phase by pressure, using a flow of N<sub>2</sub>. The composition of the fractions that were recovered were studied doing TLCs.

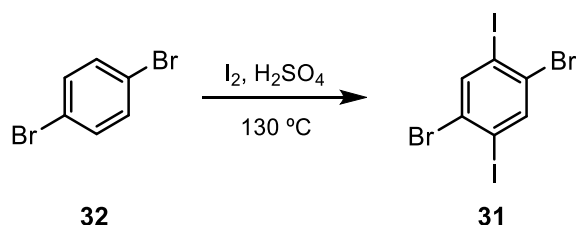
For the obtention of <sup>1</sup>H NMR spectra it was use a Nuclear Magnetic Resonance Spectrometer (NMR) – advance 300 MHz – Bruker – Advance 300. The solvent used in the samples that were going to be analysed was, in all cases, deuterated chloroform (CDCl<sub>3</sub>).

To perform the gas chromatography–mass spectrometry (GC–MS), it was used a Quadrupole Gas Chromatography System with Mass Detector – Thermo Scientific – ISQ-QD.

During the microwave–assisted reactions, the microwave used was Anton Paar Monowave 300 microwave.

### 4.3. Synthetic procedures

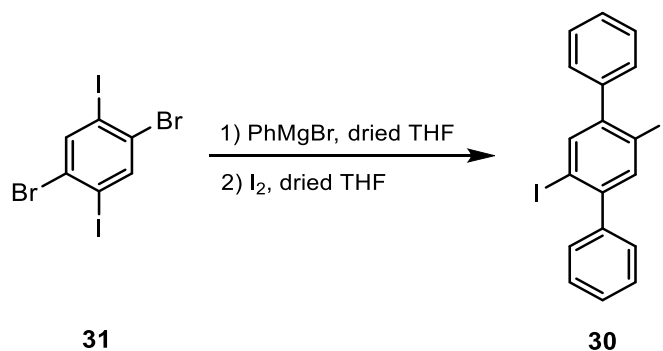
#### 4.3.1. Synthesis of 1,4–dibromo–2,5–diiodobenzene



In a 100 mL round bottom flask, it was added **32** (2.50 g, 10.6 mmol), I<sub>2</sub> (10.2 g, 40.3 mmol) and H<sub>2</sub>SO<sub>4</sub> (40 mL). This mixture was stirred and heated at 130 °C for 24 h. Ice/water was added, and it was filtrated under vacuum. The precipitate was extracted with DCM/Na<sub>2</sub>SO<sub>3</sub>. The total organic phase was dried under vacuum and washed with methanol. It was obtained the compound **31** (2.84 g, 55 %) as a white powder.<sup>22</sup>

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>), δ: 8.05 (s, 2H) ppm.

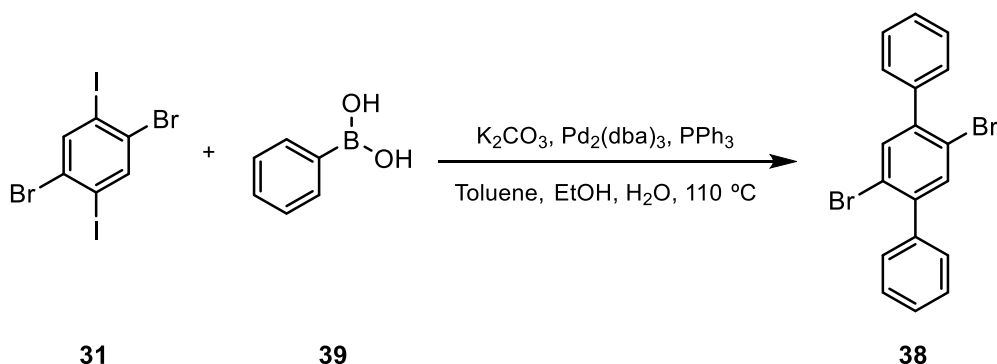
#### 4.3.2. Synthesis of 2',5'-diiodo-1,1':4',1''-terphenyl



In a 25 mL round bottom flask, **31** (0.500 g, 1.03 mmol) was added and it was dissolved with dried THF (4 mL). Phenylmagnesium bromide (5.10 mL, 5.13 mmol) was added dropwise to the round bottom flask. The mixture was stirred for 4 hours. I<sub>2</sub> (1.04 g, 4.10 mmol) was dissolved with dried THF (3.30 mL) and the solution was added dropwise to the reaction mixture, which was stirred for 24 h at room temperature. A solution of Na<sub>2</sub>SO<sub>3</sub> was added to the reaction mixture. The aqueous phase was extracted with DCM. The organic phase was dried under vacuum and washed with ethanol. The diiodo **30** (0.178 g, 36 %) was obtained as white powder.<sup>23</sup>

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>), δ: 7.87 (s, 2H), 7.49–7.35 (m, 10H) ppm.

#### 4.3.3. Synthesis of 2',5'-dibromo-1,1':4',1''-terphenyl

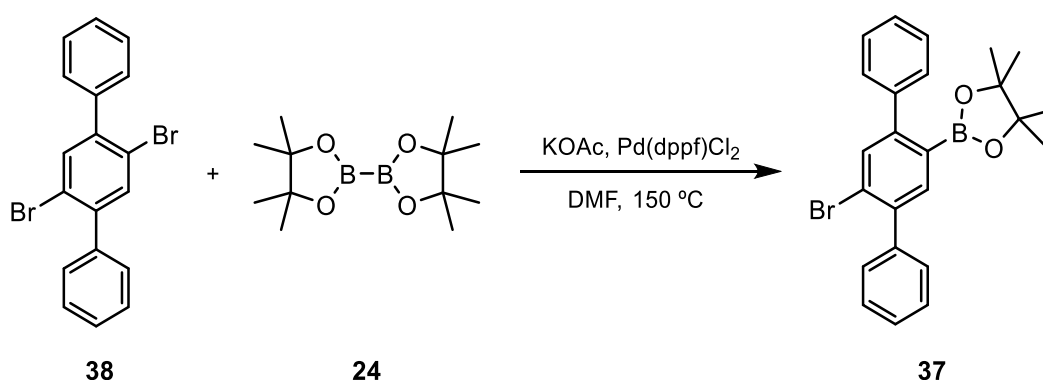


In a 25 mL round bottom flask, **31** (70.0 mg, 0.144 mmol), **39** (102 mg, 0.832 mmol) and K<sub>2</sub>CO<sub>3</sub> (59.5 mg, 0.431 mmol) were added and they were dissolved with toluene (5 mL), ethanol (1 mL) and water (1 mL). Pd<sub>2</sub>(dba)<sub>3</sub> (6.57 mg, 0.007 mmol) and PPh<sub>3</sub> (7.53 mg, 0.029 mmol) were added to the reaction mixture, which was heated for 24 h at 110 °C.

The reaction mixture was extracted with DCM and dried with MgSO<sub>4</sub>. The mixture was filtered under gravity and the solvent was evaporated under vacuum. The product obtained was purified washing it with ethanol. The final product **38** (53.5 mg, 96 %) was obtained as a white powder.<sup>25</sup>

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>), δ: 7.65 (s, 2H), 7.44 (d, J = 2.8 Hz, 10H) ppm.

#### 4.3.4. Synthesis of 2-(5'-bromo-[1,1':4',1''-terphenyl]-2'-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

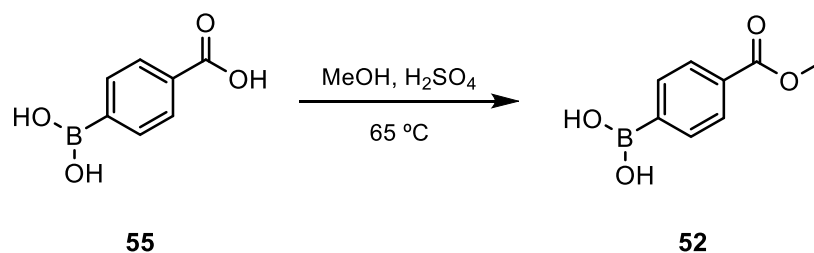


In a 10 mL round bottom flask, **38** (25.0 mg, 0.064 mmol), **24** (18.0 mg, 0.071 mmol) and KOAc (19.0 mg, 0.193 mmol) were added and they were dissolved with DMF (3.50 mL). Pd(dppf)Cl<sub>2</sub> (14.1 mg, 0.019 mmol) was added to the reaction mixture, which was heated for 24 h at 150°C. The mixture was extracted with DCM and dried with MgSO<sub>4</sub>. The solid obtained was purified by chromatographic column (SiO<sub>2</sub>, Hexane, CH<sub>2</sub>Cl<sub>2</sub>, 3:1). The final product **37** (9.81 mg, 35 %) obtained was a greenish yellow powder.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>), δ: 7.68 (d, J = 13.8 Hz, 2H), 7.42 (d, J = 16.0 Hz, 10H), 1.19 (s, 12H) ppm.



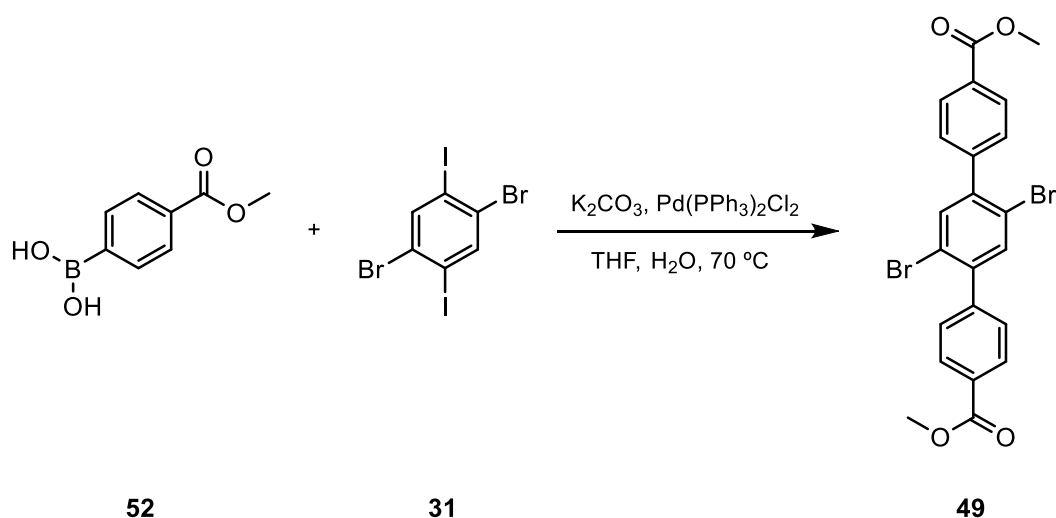
#### 4.3.5. Synthesis of (4-(methoxycarbonyl)phenyl)boronic acid



In a 25 mL round bottom flask, **55** (0.500 g, 3.01 mmol) was added and it was dissolved with methanol (4 mL) and H<sub>2</sub>SO<sub>4</sub> (0.1 mL, 1.81 mmol). The mixture was refluxed for 30 h. The solvent was evaporated under vacuum, obtaining **52** (0.515 g, 95 %) as a white powder.<sup>29</sup>

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>), δ: 8.33–8.28 (m, 2H), 8.19–8.14 (m, 2H), 3.98 (s, 3H) ppm.

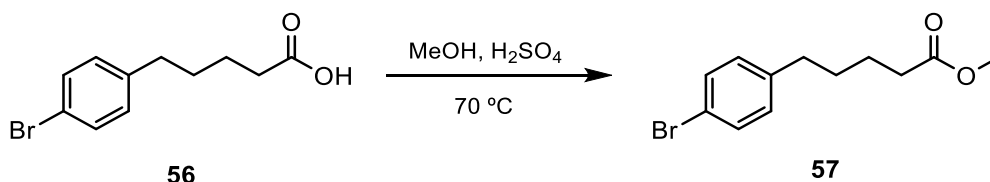
#### 4.3.6. Synthesis of dimethyl 2',5'-dibromo-[1,1':4',1''-terphenyl]-4,4''-dicarboxylate



In a 25 mL und bottom flask, **52** (81.2 mg, 0.451 mmol), **31** (100 mg, 0.205 mmol) and K<sub>2</sub>CO<sub>3</sub> (227 mg, 1.64 mmol) were added and they were dissolved with THF (5 mL) and water (1.5 mL). Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (7.20 mg, 0.010 mmol) was added to the reaction mixture, which was refluxed for 24 h. The mixture was extracted with DCM. The total organic phase was dried with MgSO<sub>4</sub>. The residue obtained was purified by chromatographic column (SiO<sub>2</sub>, Hexane, CH<sub>2</sub>Cl<sub>2</sub>, 1:1), obtaining the dibromo compound **49** (27.9 mg, 27 %) as a yellow powder.

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ),  $\delta$ : 8.16–8.11 (m, 4H), 7.65 (s, 2H), 7.55–7.50 (m, 4H), 3.96 (s, 6H) ppm.

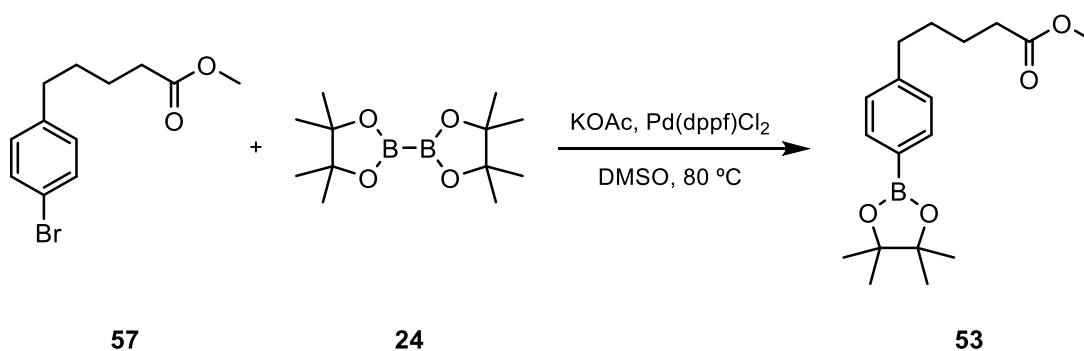
#### 4.3.7. Synthesis of methyl 5-(4-bromophenyl)pentanoate



In a 25 mL round bottom flask, **56** (0.500 g, 1.945 mmol) was added and it was dissolved with methanol (12,5 mL) and  $\text{H}_2\text{SO}_4$  (0.1 mL, 0.097 mmol). The mixture was refluxed for 2 h. Solvent was dried under vacuum, obtaining the ester **57** (0.521 g, 99 %) as a yellow liquid.<sup>30</sup>

$^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ),  $\delta$ : 7.39–7.33 (m, 2H), 7.05–6.99 (m, 2H), 3.64 (s, 3H), 2.56 (t,  $J = 6.9\text{ Hz}$ , 2H), 2.31 (t,  $J = 6.8\text{ Hz}$ , 2H), 1.70–1.54 (m, 4H) ppm

#### 4.3.8. Synthesis of methyl 5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)phenyl)pentanoate

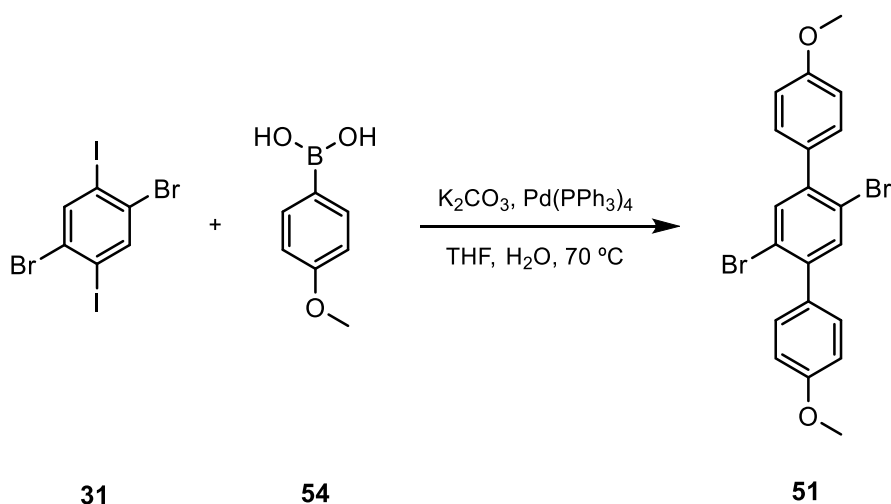


In a 50 mL round bottom flask, **57** (0.521 g, 1.92 mmol), **24** (0.537 g, 2.11 mmol) and KOAc (0.566 g, 5.76 mmol) were added, and they were dissolved with DMSO (12 mL).  $\text{Pd}(\text{dppf})_2\text{Cl}_2$  (0.422 g, 0.576 mmol) was added to the reaction mixture, which was heated for 27 h at  $80\text{ }^\circ\text{C}$ . The aqueous phase was extracted with DCM. The total organic phase

was dried with  $\text{MgSO}_4$ . The residue was purified by chromatographic column ( $\text{SiO}_2$ ,  $\text{CH}_2\text{Cl}_2$ ), obtaining the product **53** (0.471 g, 77 %) as a yellow oil.<sup>31</sup>

**$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ ),  $\delta$ : 7.77–7.70 (m, 2H), 7.20–7.15 (m, 2H), 3.64 (s, 3H), 2.68–2.60 (m, 2H), 2.34–2.28 (m, 2H), 1.68–1.62 (m, 4H), 1.33 (s, 12H) ppm.

#### 4.3.9. Synthesis of 2',5'-dibromo-4,4''-dimethoxy-1,1':4',1''-terphenyl



In a 25 mL round bottom flask, **31** (0.500 g, 1.03 mmol), **54** (0.342 g, 2.26 mmol) and  $\text{K}_2\text{CO}_3$  (0.567 g, 4.10 mmol) were added and they were dissolved with THF (8.3 ml) and water (1.7 mL).  $\text{Pd}(\text{PPh}_3)_4$  (0.118 g, 0.103 mmol) were added to the reaction mixture, which was refluxed for 24 h. The aqueous phase was extracted with  $\text{CHCl}_3/\text{H}_2\text{O}$ . The total organic phase was dried with  $\text{MgSO}_4$ . The residue was precipitated with MeOH and the final product **51** (0.206 g, 40 %) was obtained as a light yellow solid.

**$^1\text{H NMR}$**  (300 MHz,  $\text{CDCl}_3$ ),  $\delta$ : 7.61 (s, 2H), 7.42–7.35 (m, 4H), 7.02–6.95 (m, 4H), 3.87 (s, 6H) ppm.

## Conclusions

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Considering results obtained and the specific objectives proposed, the following conclusions may be drawn:

- The non-functionalized GNR precursor **37** was synthesized in a 33 % yield. In addition, **37** was characterized by NMR spectroscopy. It is worth noting that during this synthesis, deborylation of p-terphenyl boronic ester was solved by using a starting material analogue.
- The functionalized GNR precursors **46–48** was explored obtaining the dibromo-p-terphenyls **49** and **51** in 26 and 41 % yield, respectively.

## Conclusiones

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Teniendo en cuenta los resultados obtenidos y los objetivos específicos propuestos, se pueden extraer las siguientes conclusiones:

- El precursor de GNR no funcionalizado **37** se sintetizó con un rendimiento del 33 %. Además, **37** se caracterizó por espectroscopia de RMN. Vale la pena señalar que, durante esta síntesis, la desborilación del éster p-terfenil borónico se resolvió utilizando un material de partida análogo.
- Se exploraron los precursores de GNR funcionalizados **46–48** obteniendo los dibromo-p-terfenilos **49** y **51** con un 26 y 41 % de rendimiento respectivamente.

## Conclusións

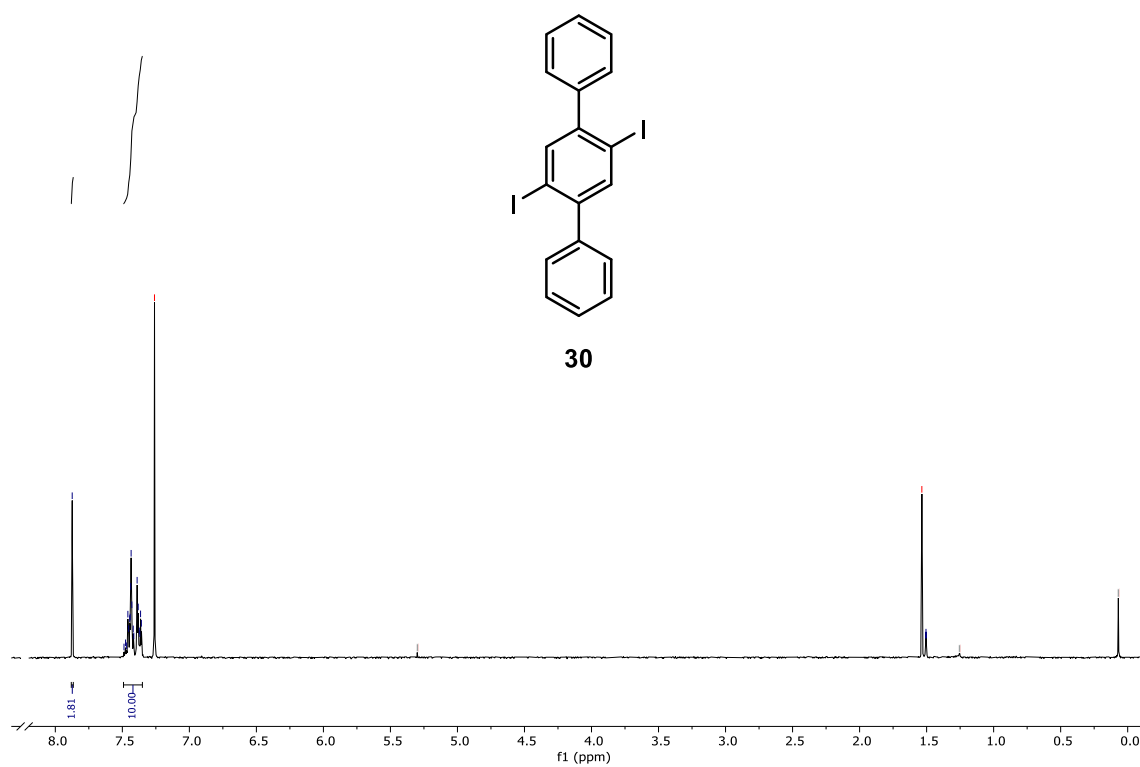
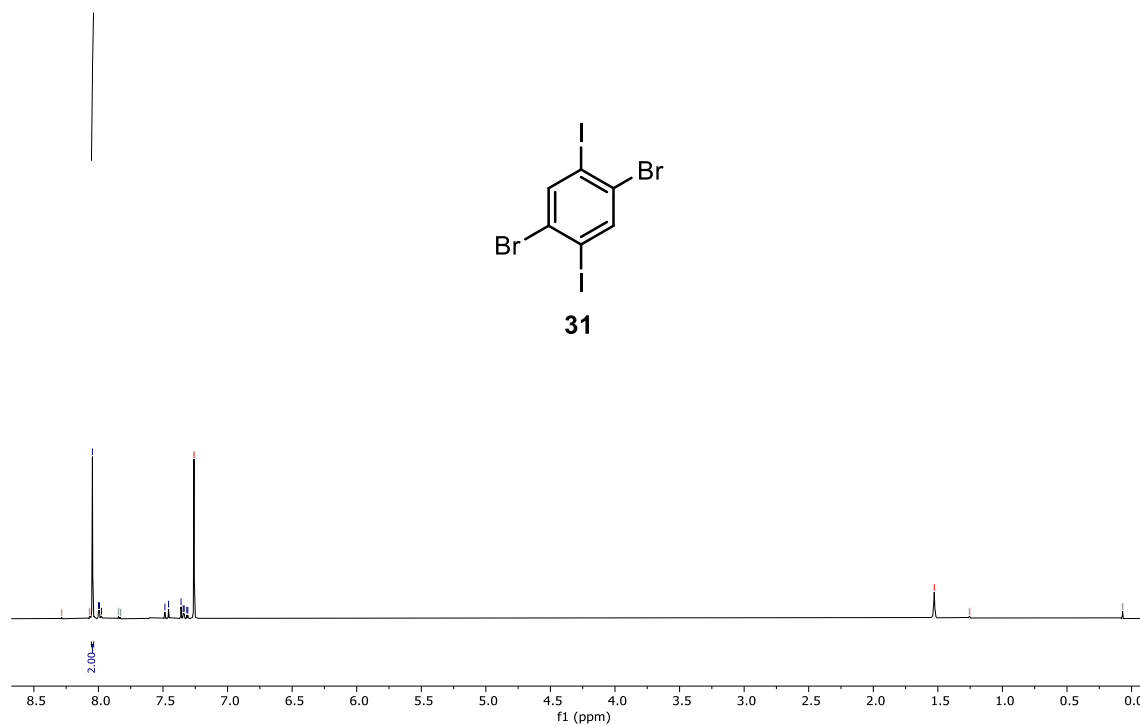
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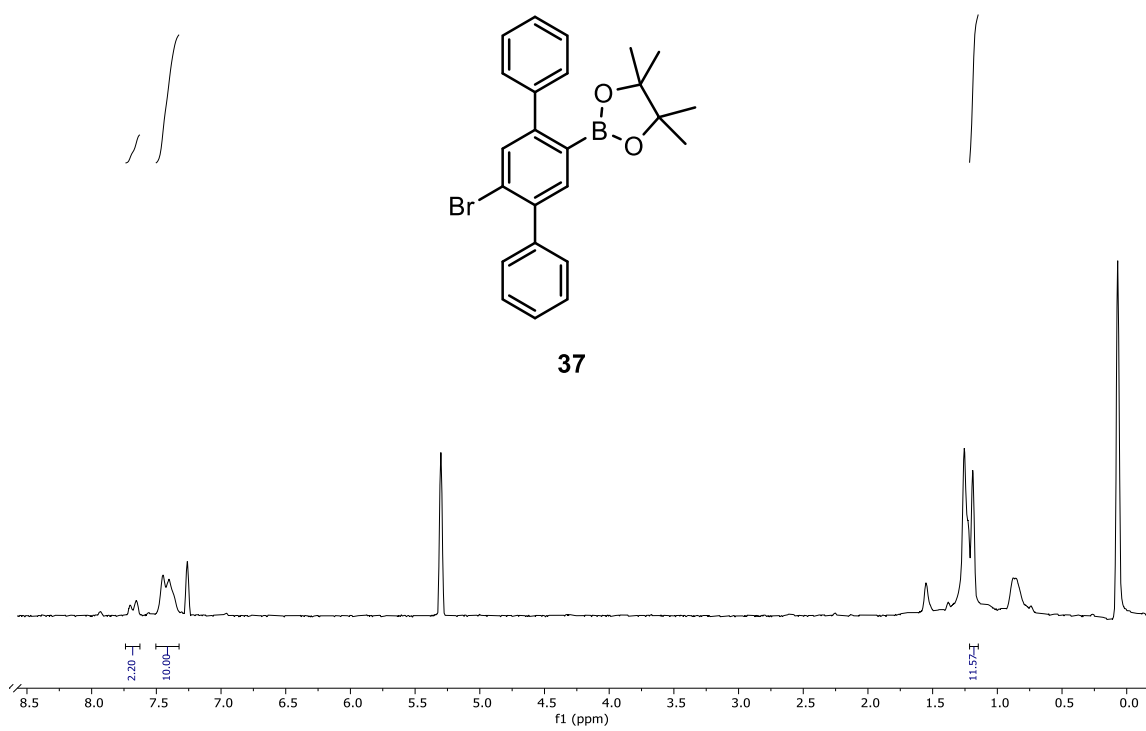
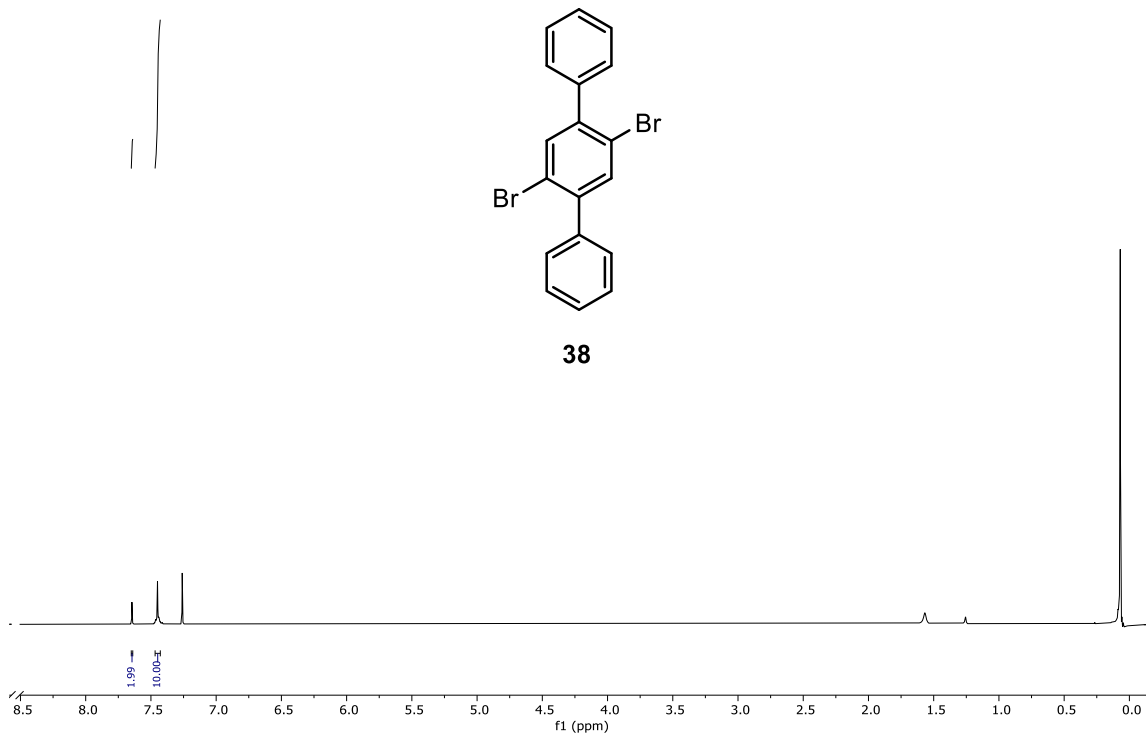
Tendo en conta os resultados obtidos e os obxectivos específicos propostos, pódense extraer as seguintes conclusións:

- O precursor de GNR non funcionalizado **37** sintetizouse cun rendemento do 33 %. Ademais, **37** caracterizouse por espectroscopia de RMN. Vale a pena sinalar que, durante esta síntese, a desborilación do éster p-terfenil borónico resolveuse utilizando un material de partida análogo.
- Exploráronse os precursores de GNR funcionalizados **46-48** obtendo os dibromo-p-terfenilos **49** y **51** cun 26 y 41 % de rendemento respectivamente.

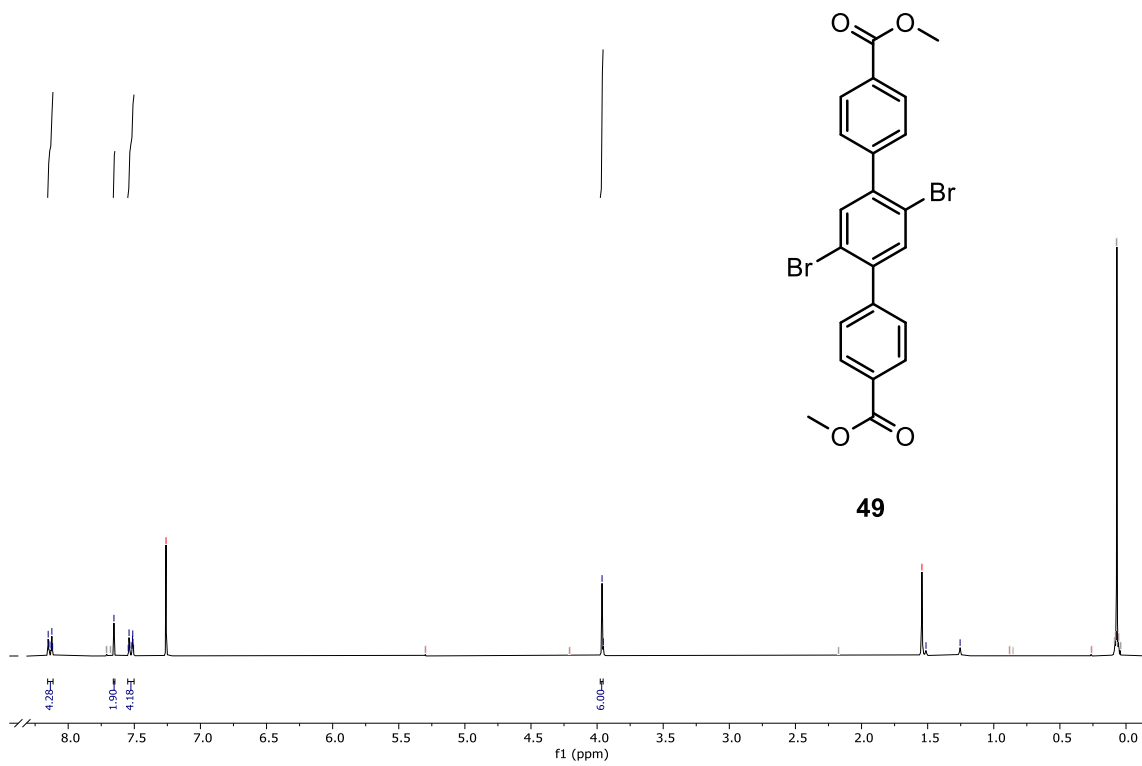
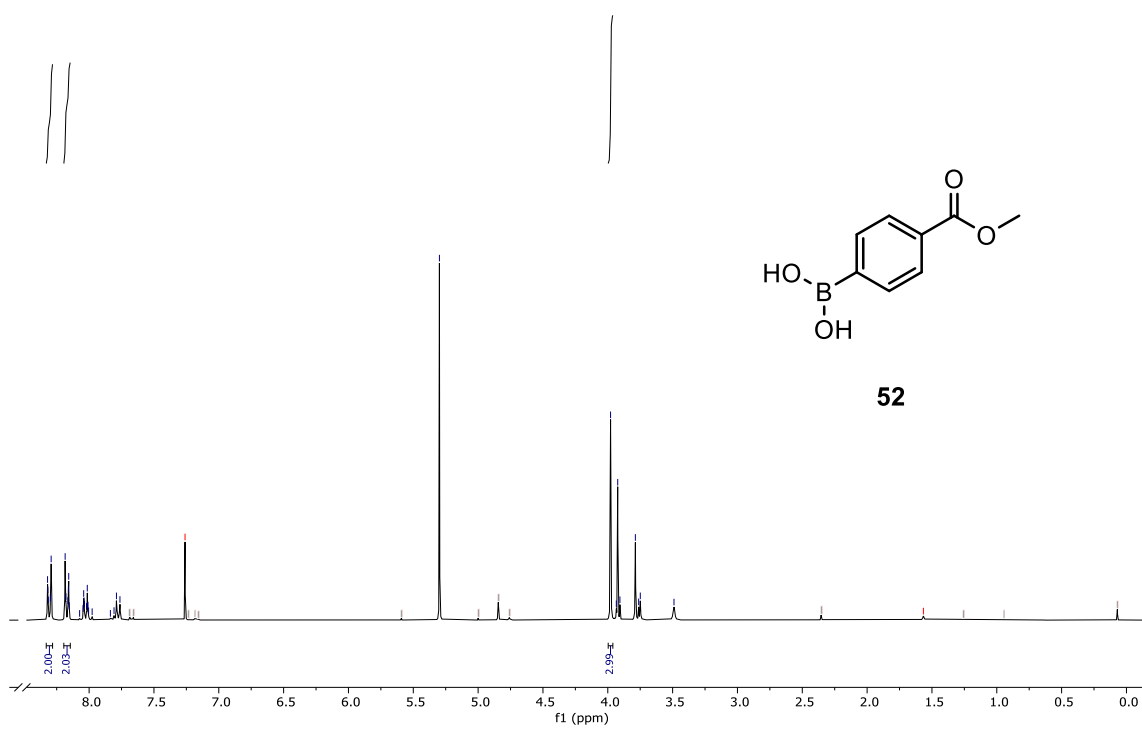
# Appendix

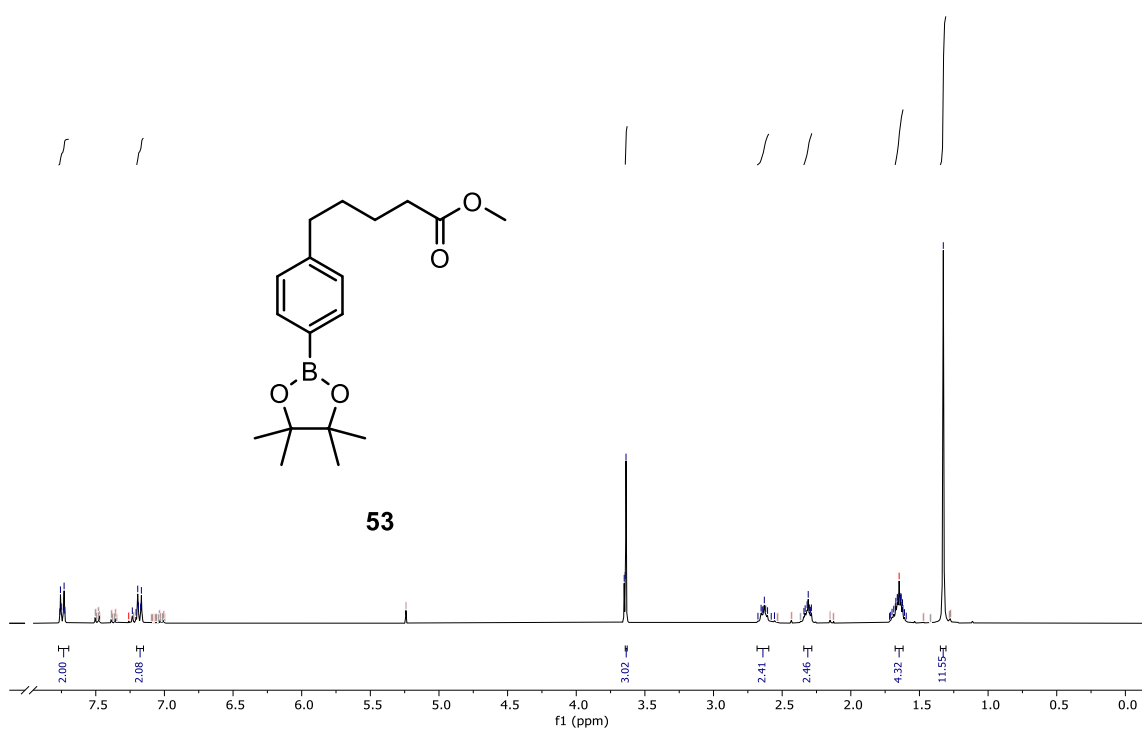
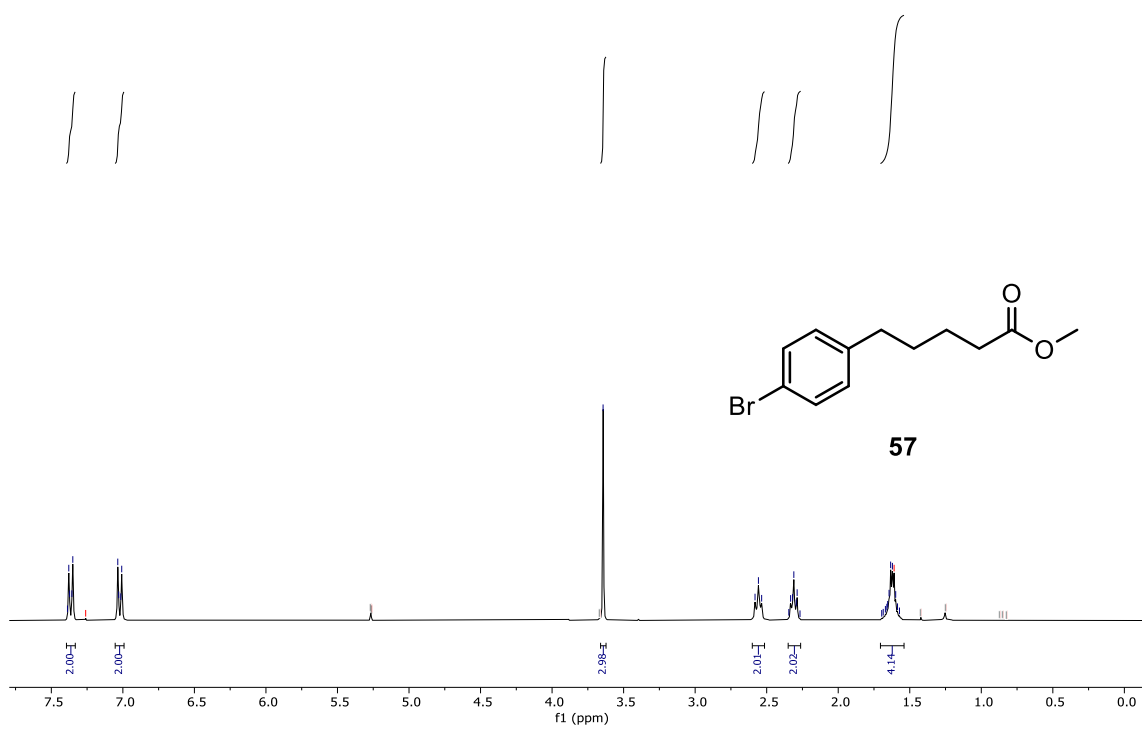
## <sup>1</sup>H NMR Spectra

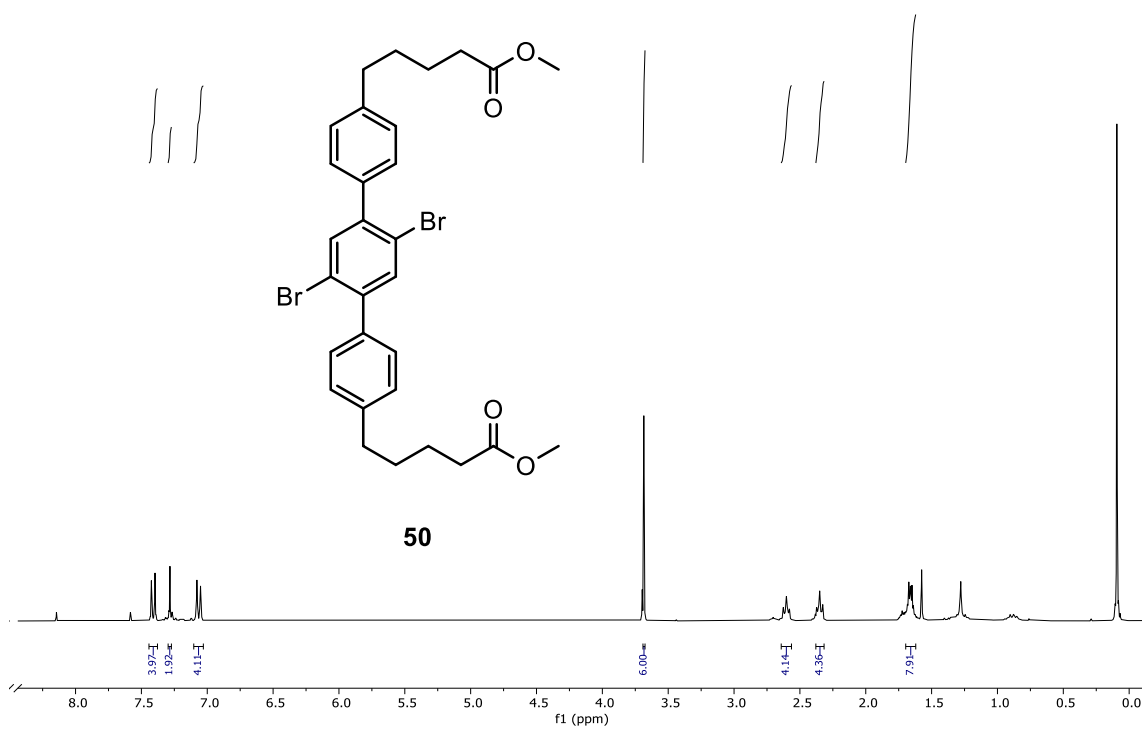
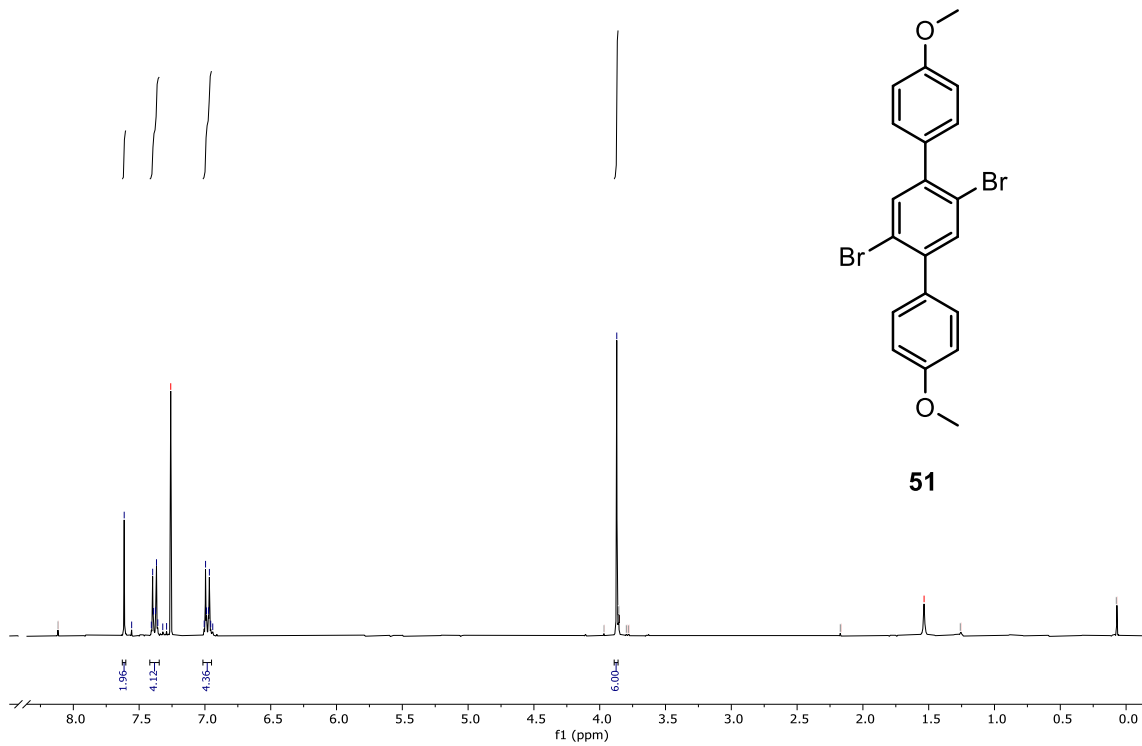












# Timeline

## YEAR 2022

February						
L	M	X	J	V	S	D
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28						

March						
L	M	X	J	V	S	D
	1	2	3	4	5	6
7	8	9	10	11	12	13
14	15	16	17	18	19	20
21	22	23	24	25	26	27
28	29	30	31			

April						
L	M	X	J	V	S	D
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

May						
L	M	X	J	V	S	D
2	3	4	5	6	7	1/8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					

June						
L	M	X	J	V	S	D
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30			

July						
L	M	X	J	V	S	D
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	31

	Experimental procedures
	Experimental procedures + Analysis of the obtained results
	Bibliographic research
	Writing

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